Complexity

Applications of Delay Differential Equations in Biological Systems

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Editorial Board

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Editorial

Applications of Delay Differential Equations in Biological Systems

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Mathematical modeling with delay differential equations (DDEs) is widely used for analysis and predictions in various areas of life sciences, for example, population dynamics, epidemiology, immunology, physiology, and neural networks [1–5]. The time delays or time lags, in these models, can be related to the duration of certain hidden processes like the stages of the life cycle, the time between infection of a cell and the production of new viruses, the duration of the infectious period, the immune period, and so on [6]. In ordinary differential equations (ODEs), the unknown state and its derivatives are evaluated at the same time instant. In a DDE, however, the evolution of the system at a certain time instant depends on the past history/memory. Introduction of time delays in a differential model significantly increases the complexity of the model. Therefore, studying qualitative behaviors of such models, using stability or bifurcation analysis, is necessary [7].

There is no doubt that some of the recent developments in the theory of DDEs have enhanced our understanding of the qualitative behavior of their solutions and have many applications in mathematical biology and other related fields. Both theory and applications of DDEs require a bit more mathematical maturity than their ODEs counterparts. The mathematical description of delay dynamical systems will naturally involve the delay parameter in some specified way. Nonlinearity and sensitivity analysis of DDEs have been studied intensely in recent years in diverse areas of science and technology, particularly in the context of chaotic dynamics [8, 9].

This special issue aims at creating a multidisciplinary forum of discussion on recent advances in differential equations with memory such as DDEs or fractional-order differential equations (FODEs) in biological systems as well as new applications to economics, engineering, physics, and medicine. It provides an opportunity to study the new trends and analytical insights of the delay differential equations, existence and uniqueness of the solutions, boundedness and persistence, oscillatory behavior of the solutions, stability and bifurcation analysis, parameter estimations and sensitivity analysis, and numerical investigations of solutions.

In the paper "Oscillation Criteria for Delay and Advanced Differential Equations With Nonmonotone Arguments" by G. E. Chatzarakis and T. Li, the authors study the oscillatory behavior of differential equations with nonmonotone deviating arguments and nonnegative coefficients. New oscillation criteria, involving lim sup and lim inf, are obtained based on an iterative method. Some numerical examples are given to illustrate the applicability and strength of the obtained conditions over known ones.

In the paper "Bifurcations and Dynamics of the Rb-E2F Pathway Involving miR449" by L. Li and J. Shen, the authors focus on the gene regulative network involving Rb-E2F pathway and microRNAs (miR449) and studied the influence of time delay on the dynamical behaviors of Rb-E2F pathway by using Hopf bifurcation theory. It is shown that under certain assumptions the steady state of the delay model is asymptotically stable for all delay values; there is a critical value under another set of conditions; the steady state is stable when the time delay is less than the critical value, while the steady state is changed to be unstable when the time delay is greater than the critical value. Hopf bifurcation appears at the steady state when the delay passes through the critical value. Numerical simulations are presented to illustrate the theoretical results.

In the paper "Maximum Likelihood Inference for Univariate Delay Differential Equation Models with Multiple Delays" by A. A. Mahmoud et al., the authors study statistical inference methodology based on maximum likelihoods for DDE models in the univariate setting. Maximum likelihood inference is obtained for single and multiple unknown delay parameters as well as other parameters of interest that govern the trajectories of the DDE models. The maximum likelihood estimator is obtained based on adaptive grid and Newton-Raphson algorithms. The methodology estimates correctly the delay parameters as well as other unknown parameters (such as the initial starting values) of the dynamical system based on simulation data. They also develop methodology to compute the information matrix and confidence intervals for all unknown parameters based on the likelihood inferential framework. The authors present three illustrative examples related to biological systems.

In the paper "Impact of Time Delay in Perceptual Decision-Making: Neuronal Population Modeling Approach" by U. Foryś et al., the authors study the basis of novel time-delayed neuronal population model, if the delay in self-inhibition terms can explain those impairments. Analysis of proposed system reveals that there can be up to three positive steady states, with the one having the lowest neuronal activity being always locally stable in nondelayed case. They show, however, that this steady state becomes unstable above a critical delay value for which, in certain parameter ranges, a subcritical Hopf bifurcation occurs. They apply psychometric function to translate model-predicted ring rates into probabilities that a decision is being made. Using numerical simulations, they demonstrate that for small synaptic delays the decision-making process depends directly on the strength of supplied stimulus and the system correctly identifies to which population the stimulus was applied. For delays above the Hopf bifurcation threshold they observe complex impairments in the decision-making process; that is, increasing the strength of the stimulus may lead to the change in the neuronal decision into a wrong one. Furthermore, above critical delay threshold, the system exhibits ambiguity in the decision-making.

In the paper "On Coupled p-Laplacian Fractional Differential Equations with Nonlinear Boundary Conditions" by A. Khan et al., the authors investigate the existence and uniqueness of solutions to a coupled system of fractional differential equations (FDEs) with nonlinear p-Laplacian operator by using fractional integral boundary conditions with nonlinear term and also to checking the Hyers-Ulam stability for the proposed problem. The functions involved in the proposed coupled system are continuous and satisfy certain growth conditions. By using topological degree theory some conditions are established which ensure the existence and uniqueness of solution to the proposed problem. Further, certain conditions are developed corresponding to Hyers-Ulam type stability for the positive solution of the considered coupled system of FDEs. Also, from applications point of view, an example is given.

In the paper "Analytical Solution of the Fractional Fredholm Integrodifferential Equation Using the Fractional Residual Power Series Method" by M. I. Syam, the author provides a numerical method to find the solution of fractional Fredholm integrodifferential equation. A modified version of the fractional power series method (RPS) is presented to extract an approximate solution of the model. The RPS method is a combination of the generalized fractional Taylor series and the residual functions. Numerical results are also presented.

In the paper "Hybrid Adaptive Pinning Control for Function Projective Synchronization of Delayed Neural Networks with Mixed Uncertain Couplings" by T. Botmart et al., the authors study the function projective synchronization problem of neural networks with mixed time-varying delays and uncertainties asymmetric coupling. The function projective synchronization of this model via hybrid adaptive pinning controls and hybrid adaptive controls, composed of nonlinear and adaptive linear feedback control, is investigated. Based on Lyapunov stability theory combined with the method of the adaptive control and pinning control, some novel and simple sufficient conditions are derived for the function projective synchronization problem of neural networks with mixed time-varying delays and uncertainties asymmetric coupling, and the derived results are less conservative. Particularly, the control method focuses on how to determine a set of pinned nodes with xed coupling matrices and strength values and randomly select pinning nodes. Based on adaptive control technique, the parameter update law, and the technique of dealing with some integral terms, the control may be used to manipulate the scaling functions such that the drive system and response systems could be synchronized up to the desired scaling function. Some numerical examples are given to illustrate the effectiveness of the proposed theoretical results.

In paper "Numerical Study for Time Delay Multistrain Tuberculosis Model of Fractional Order" by N. H. Sweilam et al., the authors provide a novel mathematical fractional model of multistrain tuberculosis with time delay memory. The proposed model is governed by a system of fractional-order DDEs, where the fractional derivative is defined in the sense of the Grünwald–Letinkov definition. Modified parameters are introduced to account for the fractional order. The stability of the equilibrium points is investigated for any time delay. Nonstandard finite deference method is proposed to solve the resulting system of fractional-order DDEs. The numerical simulations show that nonstandard finite difference method can be applied to solve such fractional-order DDEs simply and effectively.

In paper "Extinction and Persistence in Mean of a Novel Delay Impulsive Stochastic Infected Predator-Prey System with Jumps" by G. Liu et al., the authors explore an impulsive stochastic infected predator-prey system with Levy jumps and delays. The main aim of this paper is to investigate the effects of time delays and impulse stochastic interference on dynamics of the predator-prey model. They prove some properties of the subsystem of the system. Second, in view of comparison theorem and limit superior theory, the authors obtain some sufficient conditions for the extinction of this system. Furthermore, persistence in mean of the system is investigated by using the theory of impulsive stochastic differential equations and DDEs. The authors carry out some simulations to verify our main results and explain the biological implications.

In the paper “A Novel Approach to Numerical Modeling of Metabolic System: Investigation of Chaotic Behavior in Diabetes Mellitus” by P. S. Shabestari et al., the authors consider that some mathematical models have been presented for glucose and insulin interaction. The dynamical behavior of a regulatory system of glucose insulin incorporating time delay is studied and a new property of the presented model is revealed. This property can describe the diabetes disease better and therefore may help one in deeper understanding of the diabetes, interactions between glucose and insulin, and possible cures for the widespread disease.

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Research Article

A Novel Approach to Numerical Modeling of Metabolic System: Investigation of Chaotic Behavior in Diabetes Mellitus

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Although many mathematical models have been presented for glucose and insulin interaction, none of these models can describe diabetes disease completely. In this work, the dynamical behavior of a regulatory system of glucose-insulin incorporating time delay is studied and a new property of the presented model is revealed. This property can describe the diabetes disease better and therefore may help us in deeper understanding of diabetes, interactions between glucose and insulin, and possible cures for this widespread disease.

1. Introduction

Diabetes, technically called diabetes mellitus, is referred to types of disorders in the metabolic processes of the human body in which the controlling mechanism of sugar level in blood is disrupted. In these cases, insulin, the mainstay controlling element, is either not secreted or its presence is ignored by body cells [1]. There are three types of diabetes: type 1, type 2, and gestational diabetes. Type 1 diabetes is all about insulin. In this type of diabetes, the body's immune system intercepts insulin-releasing cells and destroys them. This type of diabetes accounts for 5 to 10 out of 100 diabetic people. In type 2 diabetes, the body is not able to use insulin in the right way. This type of diabetes is the most common in the world, and around 90 to 95 percent of diabetics have type 2. A third type of diabetes, gestational diabetes, is a temporary condition that occurs during pregnancy. It affects approximately two to four percent of all pregnancies [2–5].

The function of insulin alters for each organ in the human body, so the effects of environmental factors like stress and nourishing habits may cause blood glucose shift. As observed in various countries, diabetes is discernibly widespread and there is an increasing number of people suffering from this. Hence, the potentially lethal symptoms of the illness necessitate more meticulous treatments and precautionary activities. The essence for such cure procedures is even more accentuated in contemporary hectic life in which people have an increasing penchant to be nourished by artificially cultivated foods and do less exercise. The number of people suffering from this disease was approximately 415 million in 2015 with equal shares of both genders, which accounted for 8.3% of the overall adult population of the world. And nearly 1.5 to 5 million people have died because of diabetes every year between years 2012 and 2015 worldwide [1].

Speaking of the reasons triggering this illness, many elements can cause this irregularity behavior in the body, such as genetic factors inherited through generations that fertilize the body for other factors of the disease to easily disrupt the metabolic system, obesity due to malnutrition and urbanization as consequent of modern lifestyle, side effects of taking specific drugs like glucocorticoids and thyroid hormone, progression of other illnesses, and many other factors which cannot be wholly included [1]. Knowing about the causes of disease enables scientists to develop meditative procedures.

Besides the paramount and distinctive importance of experimental researches for developing effective treatment protocols, studying and developing mathematical models of glucose-insulin bilateral interplay have had an essential role in accelerating the research processes and making breakthroughs in this field by saving both money and time. Conventionally, it was believed that a linear relationship defines the mechanism of glucose-insulin negative feedback system. A linear model for diabetes assumes that the relationship between glucose and insulin concentration could be studied in isolation from other components [6]. In contrast, nonlinear models proposed in previous studies assume that the relationship between components is not always linear [7] and it could depend on initial blood glucose level [8]; moreover, they revealed the fact that statistical properties of the profile in some patients could alter substantially [6, 9, 10]. In glucose-insulin system, interactions between components are responsible for the overall behavior of the system, which makes this system a complex one. The basic structure of insulin secretion system is a negative feedback controller operating between two elements, namely, the pancreatic β-cells and plasma glucose concentration of the blood contacting these cells. A high level of glucose concentration is acquired, for example, when having a snack which provokes the production and release of insulin leading to a decrease in glucose levels by increasing the consumption rate of the extra sugar or initiation of storage process. On the contrary, if plasma blood is experiencing low levels of glucose concentration, insulin secretion is halted, preventing further declination of blood sugar. In this case, the metabolic system shifts condition from absorptive to postabsorptive [11, 12].

As delineated in the preceding paragraph, various mathematical models have been proposed in attempts to simulate the relation between plasma glucose concentration and plasma insulin concentration more accurately, so that scientists will be able to have an elaborate perspective of this metabolic interaction [13–17]. It is wondering that the recently submitted models show some kind of chaotic behavior in the mechanism of malfunctioning metabolic system which is revealed in the current study.

The investigation of chaotic dynamics has attracted the foci of many scientists, and a great deal of effort is put in this field as it has provided a successful method for studying biological systems [18–23]. Moreover, this novel vantage point of studying biological phenomena has made revolutionary effects on developing biological system models [24–27].

Because of the complexity of the system, the model that has been studied in this paper is a nonlinear model. The nonlinear model that we study reflects the relationship between injected insulin and blood glucose response. The studies about variation in the blood glucose indicate a chaotic component.

In the second section, the dynamical properties of the last presented model for glucose and insulin concentration are investigated. Eventually, conclusion remarks are given in Section 4.

2. Mathematical Model

In 1964, Ackerman et al. [16] proposed a linear model for glucose tolerance test consisting of two ordinary differentials (1), as demonstrated below.

$$\begin{aligned} \frac{dx}{dt} &= a_1 y(t) - a_2 x(t) + C_1, \\ \frac{dy}{dt} &= -a_3 y(t) - a_4 x(t) + C_2 + I(t), \end{aligned} \tag{1}$$

where $x(t)$ is the insulin concentration and $y(t)$ is the blood glucose concentration. $a_1 y(t)$ is the rate of increase in insulin concentration due to increase in glucose concentration, $a_2 x(t)$ represents the rate of insulin reduction, $a_3 y(t)$ represents the rate of glucose reduction independent to insulin, and $a_4 x(t)$ represents the rate of glucose removal due to insulin secretion. C_1 and C_2 are positive constants, and $I(t)$ is the rate of increase in blood glucose concentration due to absorption in the gastrointestinal system.

In 1987, Bajaj et al. [15] proposed a nonlinear mathematical model for glucose-insulin feedback system which incorporated β-cell kinetics. The mathematical relationships for the model are formulated as shown in

$$\begin{aligned} \frac{dx}{dt} &= R_1 y - R_2 x + C_1, \\ \frac{dy}{dt} &= \frac{R_3 N}{z} - R_4 x + C_2, \\ \frac{dz}{dt} &= R_5 y(T - z) + R_6 z(T - z) - R_7 z, \end{aligned} \tag{2}$$

where $x(t)$ and $y(t)$ represent the insulin and glucose concentrations, respectively, and $z(t)$ represents the number of β-cells. It has been discovered that β-cells have an essential role in regulating glucose and insulin concentration. Recent studies indicate two delays in glucose-insulin feedback control system [28–32]. Two important time lags can be noticed in the system, the lag in insulin secretion in response to an increase in blood glucose concentration, τ_g, and hepatic glucose response lag, τ_i.

In the current research, we study a nonlinear mathematical model for glucose-insulin feedback control system by incorporating the enhanced delay differential equations embracing β-cells proposed by the model presented by Sarika et al. [28]. The modified model is the compound of the model proposed by Bajaj et al. [15] and the one suggested by Sarika et al. [28]. The resulted model is the one presented by

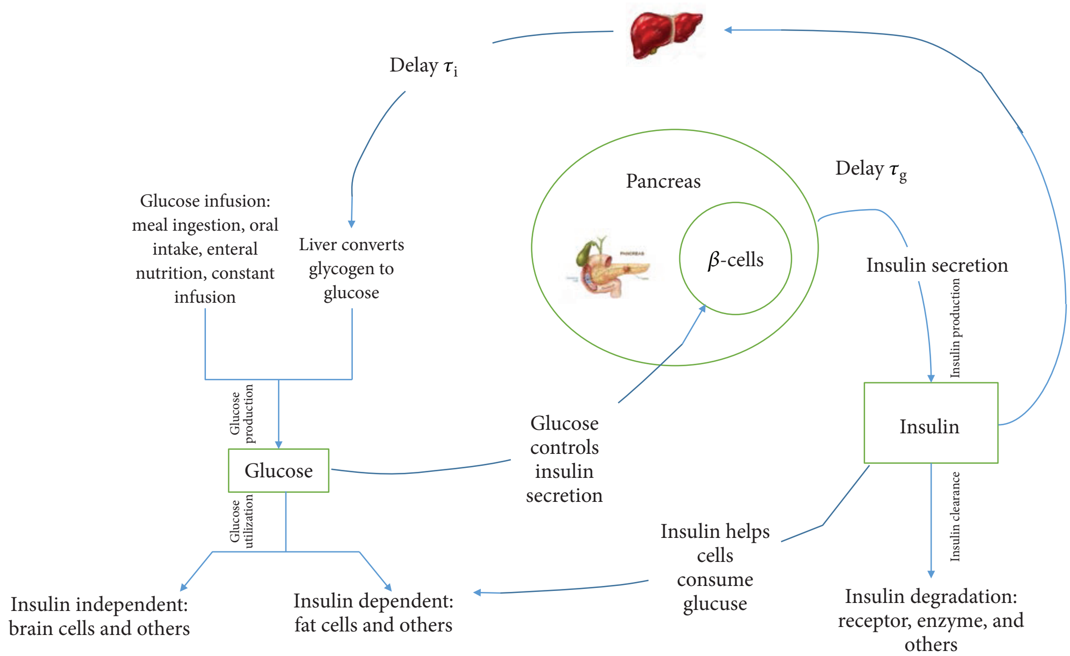


Figure 1: Two time delays in glucose-insulin system [11].

Chuedoung et al. [11] (Figure 1), which can be presented in delay differential equations as follows:

$$\begin{aligned}
\frac{dx}{dt} &= r_1 y(t-\tau_g) z(t-\tau_g) - r_2 x + c_1 z(t-\tau_g),\\
\frac{dy}{dt} &= \frac{R_3 N}{z} - R_4 x(t-\tau_i) + C_2,\\
\frac{dz}{dt} &= R_5(y-\widehat{y})(T-z) + R_6 z(T-z) - R_7 z,
\end{aligned} \tag{3}$$

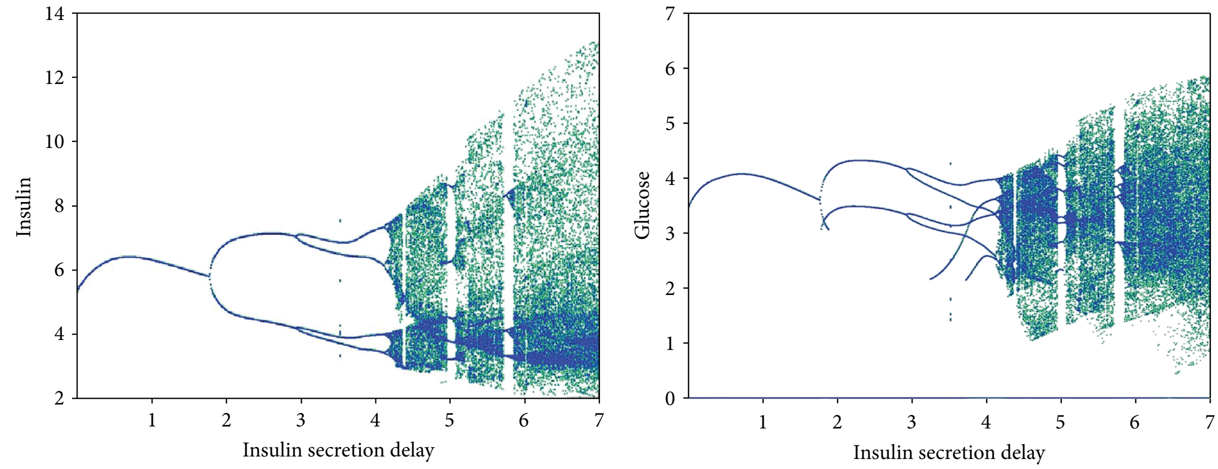
where $x(t)$ is the insulin concentration, $y(t)$ is the glucose concentration, $z(t)$ is the number of β-cells, and $\widehat{y}$ is the difference between glucose fasting level and its basal level. τ_g is the delay in insulin secretion in response to blood glucose level increase based on clinical evidence reported by Palumbo et al. [33], and τ_i is the delay in glucose drop due to increased insulin level based on clinical evidence reported by Prager et al. [34]. $r_1 y(t-\tau_g)z(t-\tau_g)$ shows the increase in insulin concentration in response to blood glucose increase with the time delay τ_g. $r_2 x$ is the rate of insulin decrease independent of glucose, and $c_1 z(t-\tau_g)$ is the increase of insulin level secreted by β-cells and is independent from other components. System (3) considers two time lags in insulin-glucose regulatory system; therefore, it is more realistic and is capable of showing the behavior of insulin-glucose regulatory system in different time delays. Previous models cannot display the behavior of aforementioned biological system with respect to time delays.

According to the model presented by Molnar et al. [17], if insulin secretion decreases to $1/N$ of the number of β-cells, designated by N, due to a reduction, then the blood glucose increases until insulin levels are restored to nearly normal standards. So the blood glucose level is a function of the β-cells' capacity N/n. N is the normal number of β-cells. $R_4 x(t-\tau_i)$ is the rate of glucose reduction in response to insulin secretion with the time delay τ_i. T is the total density of β-cells, and the term $R_5(y-\widehat{y})(T-z)$ represents the increase in dividing β-cells caused by the interaction between blood glucose above the fasting level and the nondividing β-cells. The term $R_6 z(T-z)$ represents the increase in z due to interaction between dividing and nondividing β-cells, and the term $R_7 z$ represents the reduction in z due to its current level.

3. Results and Discussion

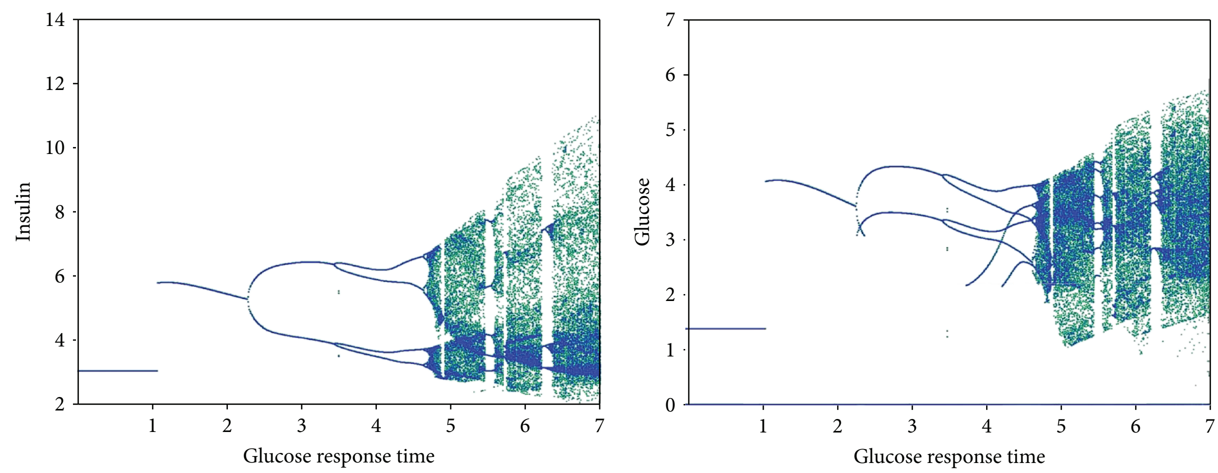
Based on the study by Chuedoung et al. [11], the mentioned model shows the different behaviors for different parameters. The proposed model comprises a number of parameters that their values are essential in changing the behavior of the system.

In current research, the new capability of the mentioned model is revealed. By increasing the insulin secretion delay by β-cells (τ_g), the system behaves in a chaotic way (Figure 2). Figure 2 is the bifurcation diagram of the system for the different values of τ_g. Figure 2 shows that if there is more delay on insulin secretion, insulin cannot track glucose and the concentration of blood glucose rises which results in diabetes disorder. Technically speaking, the time lag of insulin response in glucose-insulin negative feedback controlling mechanism is shown to be the main reason for this disease. Computer simulation of Figure 2 is done by the following parameters $r_1 = 0.472$, $r_2 = 0.25$, $R_3 = 0.82$, $R_4 = 0.6$, $R_5 = 0.3$, $R_6 = 0.3$, $R_7 = 0.2$, $c_1 = 0.1$, $C_2 = 0.8$, $\widehat{y} = 1.42$,



(a) (b)

Figure 2: The model bifurcation diagrams based on different values of parameter τ_g.



(a) (b)

Figure 3: The model bifurcation diagrams based on different values of parameter τ_i.

$T = 1.5$, $N = 1.27$, and $\tau_i = 0.05$. The values of the parameters are the same as the values presented by Chuedoung et al. [11].

With the increase in glucose response time caused by insulin secretion (τ_i), the system behaves chaotically (Figure 3). Figure 3 is the bifurcation diagram of the system for different values of τ_i. It shows that if there is more delay on response of glucose to insulin secretion, the system behaves in a chaotic manner. Note that the goal of this study is not to investigate the parameters quantitatively, but rather to show that a minute change in the quantities of parameters of the model can bring about changes in the behavior of the system. Computer simulation of Figure 3 is done by the following parameters $r_1 = 0.472$, $r_2 = 0.25$, $R_3 = 0.82$, $R_4 = 0.6$, $R_5 = 0.3$, $R_6 = 0.3$, $R_7 = 0.2$, $c_1 = 0.1$, $C_2 = 0.8$, $\hat{y} = 1.42$, $T = 1.5$, $N = 1.27$, and $\tau_g = 0.56$. The values of the parameters are the same as the values presented by Chuedoung et al. [11].

In the present study, we used the insulin-glucose model involving β-cells presented by Chuedoung et al. [11] and the effect of delays on insulin-glucose model have been investigated. The system is stable for small delays, and when the delays increase, the system exhibits chaotic behavior. According to the claim made by Bertram and Pernarowski [35], 1-2 min lag, representative of insulin secretion, is a common incident after bath application of glucose in islet electrical activity when investigating islet porosity and the permeability of a surrounding layer of acinar cells on the time required for glucose to diffuse through an isolated pancreatic islet of Langerhans and reach an equilibrium. And, based on a report by Forrest et al. [36], instantaneous insulin reflection was recorded in 14 out of the 20 monitored Jamaican children rehabilitated from malnutrition. The response time was about 1 minute for them; whereas, this delay ranged from 5 to 10 minutes for the other children. Hence, these observations support our claim about the range of τ_g and τ_i.

4. Adaptive Sliding Mode Control

A new sliding mode control scheme for a class of uncertain time-delay chaotic systems is proposed in [37]. It is shown that a linear time-invariant system with the desired system dynamics is used as a reference model for the output of a time-delay chaotic system to track. Chaos control for scalar-delayed chaotic systems using sliding mode control strategy is achieved in [38]. Sliding surface design is based on delayed feedback controller, and it is shown that the proposed controller can achieve stability for an arbitrary unstable fixed point (UPF) or unstable periodic orbit (UPO) with an arbitrary period.

In this section, we design the adaptive sliding mode controllers to suppress the chaotic oscillations in the model presented in (3). For the uncertainties, we assume that the parameters r_1, r_2, c_1, and c_2 are unknown. The entire control algorithm is designed with the delay elements as described in (3), and hence the sliding surface initialization is accounted with the respective time delays. Let us redefine the model in (3) with the controllers u_i, where $i = x, y, z$ as given in

$$\begin{aligned} \dot{x} &= r_1 y(t-\tau_g) z(t-\tau_g) - r_2 x + c_1 z(t-\tau_g) + u_x, \\ \dot{y} &= \frac{R_3 N}{z} - R_4 x(t-\tau_i) + c_2 + u_y, \\ \dot{z} &= R_5 \left(y - \widehat{y}\right)(T - z) + R_6 z(T - z) - R_7 z + u_z. \end{aligned} \tag{4}$$

We define the integral sliding mode surface as

$$\begin{aligned} s_x &= x + k_x \int_0^t x(\tau) d\tau, \\ s_y &= y + k_y \int_0^t y(\tau) d\tau, \\ s_z &= z + k_z \int_0^t z(\tau) d\tau. \end{aligned} \tag{5}$$

The sliding surface dynamics can be derived as

$$\begin{aligned} \dot{s}_x &= \dot{x} + k_x x, \\ \dot{s}_y &= \dot{y} + k_y y, \\ \dot{s}_z &= \dot{z} + k_z z. \end{aligned} \tag{6}$$

The parameter estimation errors are defined as

$$\begin{aligned} e_{r_1} &= \widehat{r}_1 - r_1, \\ e_{r_2} &= \widehat{r}_2 - r_2, \\ e_{c_1} &= \widehat{c}_1 - c_1, \\ e_{c_2} &= \widehat{c}_2 - c_2. \end{aligned} \tag{7}$$

The first derivatives of the estimation errors are

$$\begin{aligned} \dot{e}_{r_1} &= \dot{\widehat{r}}_1, \\ \dot{e}_{r_2} &= \dot{\widehat{r}}_2, \\ \dot{e}_{c_1} &= \dot{\widehat{c}}_1, \\ \dot{e}_{c_2} &= \dot{\widehat{c}}_2. \end{aligned} \tag{8}$$

Consider the following Lyapunov function:

$$V = \frac{1}{2}\left[s_x^2 + s_y^2 + s_z^2 + e_{r_1}^2 + e_{r_2}^2 + e_{c_1}^2 + e_{c_2}^2\right]. \tag{9}$$

The first derivative of the Lyapunov candidate function is

$$\dot{V} = s_1 \dot{s}_1 + s_2 \dot{s}_2 + s_3 \dot{s}_3 + e_{r_1} \dot{e}_{r_1} + e_{r_2} \dot{e}_{r_2} + e_{c_1} \dot{e}_{c_1} + e_{c_2} \dot{e}_{c_2}. \tag{10}$$

Applying (4), (6), and (8) in (10), we have

$$\begin{aligned} \dot{V} = {} & s_x \left[r_1 y(t-\tau_g) z(t-\tau_g) - r_2 x + c_1 z(t-\tau_g) + u_x + k_x x\right] \\ & + s_y \left[\frac{R_3 N}{z} - R_4 x(t-\tau_i) + c_2 + u_y + k_y y\right] \\ & + s_z \left[R_5 \left(y - \widehat{y}\right)(T - z) + R_6 z(T - z) - R_7 z + u_z + k_z z\right] \\ & + e_{r_1} \dot{\widehat{r}}_1 + e_{r_2} \dot{\widehat{r}}_2 + e_{c_1} \dot{\widehat{c}}_1 + e_{c_2} \dot{\widehat{c}}_2. \end{aligned} \tag{11}$$

By introducing uncertainties without changing the definition in (11),

$$\begin{aligned} \dot{V} = {} & s_x \begin{bmatrix} r_1 y(t-\tau_g) z(t-\tau_g) + \widehat{r}_1 y(t-\tau_g) z(t-\tau_g) - \widehat{r}_1 y(t-\tau_g) z(t-\tau_g) \\ -r_2 x + \widehat{r}_2 x - \widehat{r}_2 x + c_1 z(t-\tau_g) + \widehat{c}_1 z(t-\tau_g) - \widehat{c}_1 z(t-\tau_g) + u_x + k_x x \end{bmatrix} \\ & + s_y \left[\frac{R_3 N}{z} - R_4 x(t-\tau_i) + c_2 + \widehat{c}_2 - \widehat{c}_2 + u_y + k_y y\right] \\ & + s_z \left[R_5 \left(y - \widehat{y}\right)(T - z) + R_6 z(T - z) - R_7 z + u_z + k_z z\right] + e_{r_1} \dot{\widehat{r}}_1 + e_{r_2} \dot{\widehat{r}}_2 + e_{c_1} \dot{\widehat{c}}_1 + e_{c_2} \dot{\widehat{c}}_2. \end{aligned} \tag{12}$$

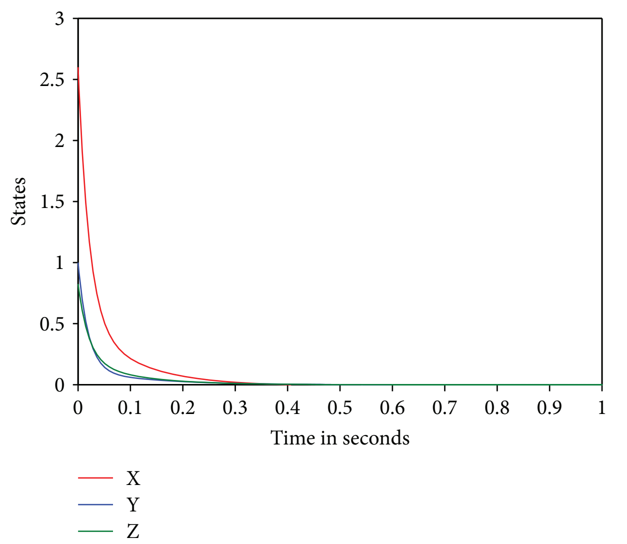


FIGURE 4: Time history of the states with control in action at $t = 0$ s.

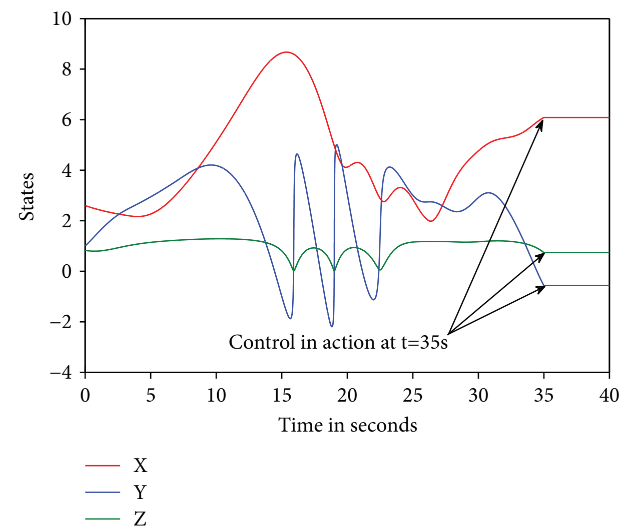


FIGURE 5: Time history of the states with control in action at $t = 35$ s.

After some mathematical simplifications, let us define the adaptive sliding mode controllers as

$$
\begin{aligned}
u_x &= -\widehat{r}_1 y(t-\tau_g) z(t-\tau_g) + \widehat{r}_2 x - \widehat{c}_1 z(t-\tau_g) \\
&\quad - k_x x - \eta_x \operatorname{sgn}(s_x) - \rho_x s_x, \\
u_y &= -\frac{R_3 N}{z} + R_4 x(t-\tau_i) - \widehat{c}_2 - k_y y - \eta_y \operatorname{sgn}(s_y) - \rho_y s_y, \\
u_z &= -R_5 \left(y - \widehat{y}\right)(T-z) - R_6 z(T-z) + R_7 z - k_z z \\
&\quad - \eta_z \operatorname{sgn}(s_z) - \rho_z s_z.
\end{aligned} \tag{13}
$$

The parameter estimate laws can be defined as

$$
\begin{aligned}
\dot{\widehat{r}}_1 &= s_x y(t-\tau_g) z(t-\tau_g), \\
\dot{\widehat{r}}_2 &= -s_x x, \\
\dot{\widehat{c}}_1 &= s_x z(t-\tau_g), \\
\dot{\widehat{c}}_2 &= s_y.
\end{aligned} \tag{14}
$$

Using (13) and (14) in (12), we simplify the Lyapunov candidate function dynamics to

$$
\dot{V} \le -\eta_x |s_x| - \eta_y |s_y| - \eta_z |s_z| - \rho_x s_x^2 - \rho_y s_y^2 - \rho_z s_z^2. \tag{15}
$$

As ρ_i and η_i are positive for $i = x, y, z$, the Lyapunov first derivative (15) is a negative definite function which infers that the controller is stable as per the theorem discussed in [39, 40] and is valid for any bounded initial conditions. For numerical simulations, the initial conditions are taken as 2.6, 1, and 0.825 and the sliding surface initial conditions are defined as −2.6, −1, and −0.825 with the time delays $\tau_g = 3.56$ and $\tau_i = 3.35$. The initial conditions of the parameter estimates are defined as $\widehat{r}_1 = 1$, $\widehat{r}_2 = 3$, $\widehat{c}_1 = 6$, and $\widehat{c}_2 = 7$. Figures 4 and 5 show the time history of states controlled with adaptive sliding mode controllers in action at $t = 0$ s and $t = 35$ s, respectively. Figure 6 shows the estimated parameters with parameter update laws and controllers in action at $t = 0$ s.

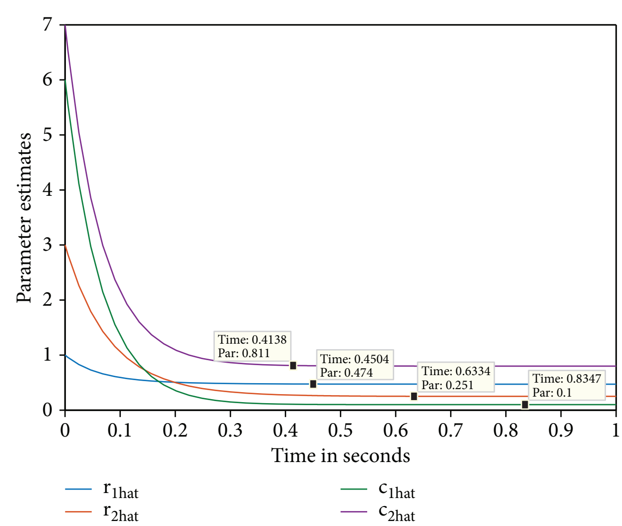


FIGURE 6: Time history of parameter estimates.

5. FPGA Implementation

Implementation of chaotic and hyperchaotic systems using Field Programmable Gate Arrays (FPGA) has been widely investigated [41–43]. Chaotic random number generators have been implemented in FPGA for applications in image cryptography [44]. FPGA-implemented Duffing oscillator-based signal detectors have been proposed by Rashtchi et al. [45]. Digital implementations of chaotic multiscroll

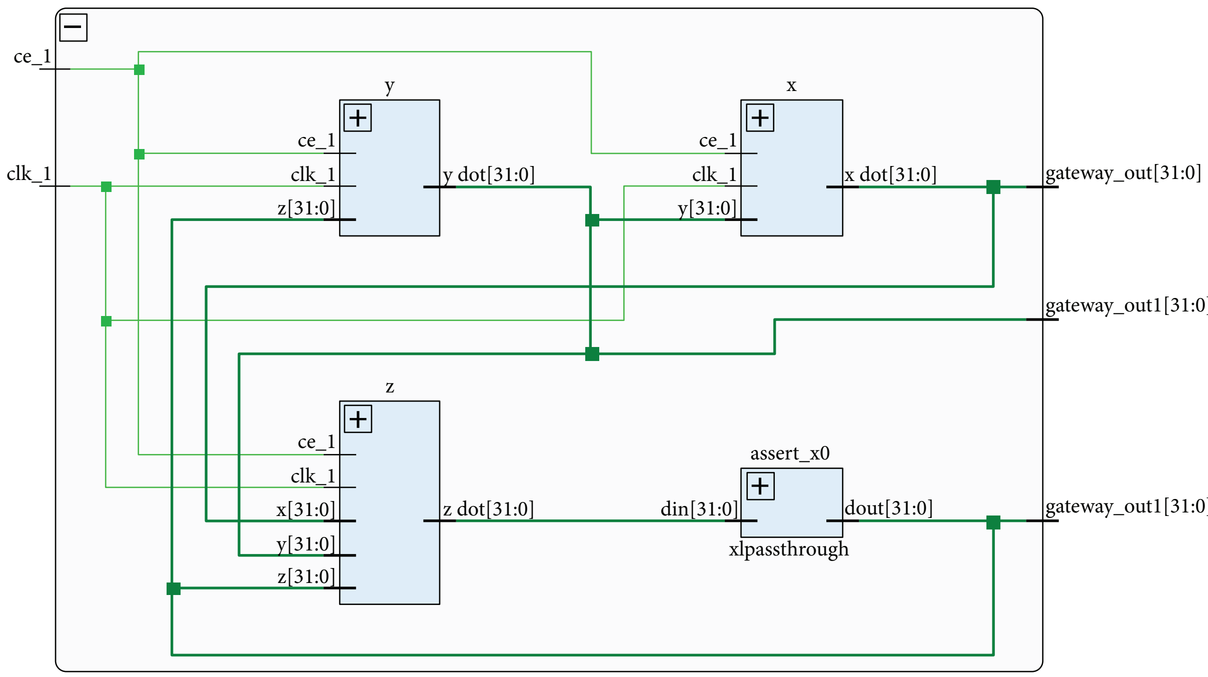


Figure 7: Overall RTL schematics of (3).

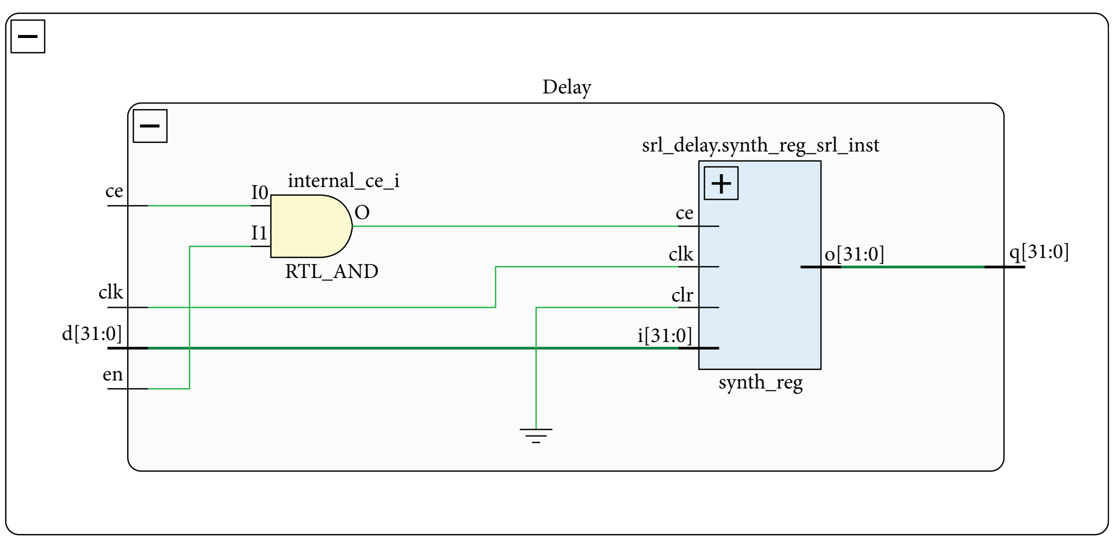


Figure 8: RTL schematics of the implemented delay (3).

attractors have been extensively investigated [41, 46]. Memristor-based chaotic system and its FPGA circuits have been proposed by Ya-Ming et al. [47]. A FPGA implementation of fractional order chaotic system using approximation method has been investigated by Rajagopal et al. [48–50].

In this section, we implement a circuit for the model (3) by FPGA. To the best of our knowledge, only a few literatures [51, 52] have implemented delay chaotic systems. However, those works discuss about indirect realizations which will increase the time slack factor as the programs run sequentially on the processor. But we use a direct realization, and hence the power utilization and the time slack delays are reduced. For the design of delay chaotic model (3), first, we configure the available built-in blocks of the System generator toolbox. The Add/Sub blocks are configured with zero latency and 32/16 bit fixed point settings. The delays are introduced by an additional delay block introduced with the defined time delays as in (3). The output of the block is configured to rounded quantization in order to reduce the bit latency. Then, we design the integer order integrator which is not a readily available block in the System Generator. Hence, we implement the integrators using the mathematical relation $(dx_i/dt) = \lim_{h\to 0}([x_i(n+1) - x_i(n)]/h)$ and the value of h is taken as 0.001.

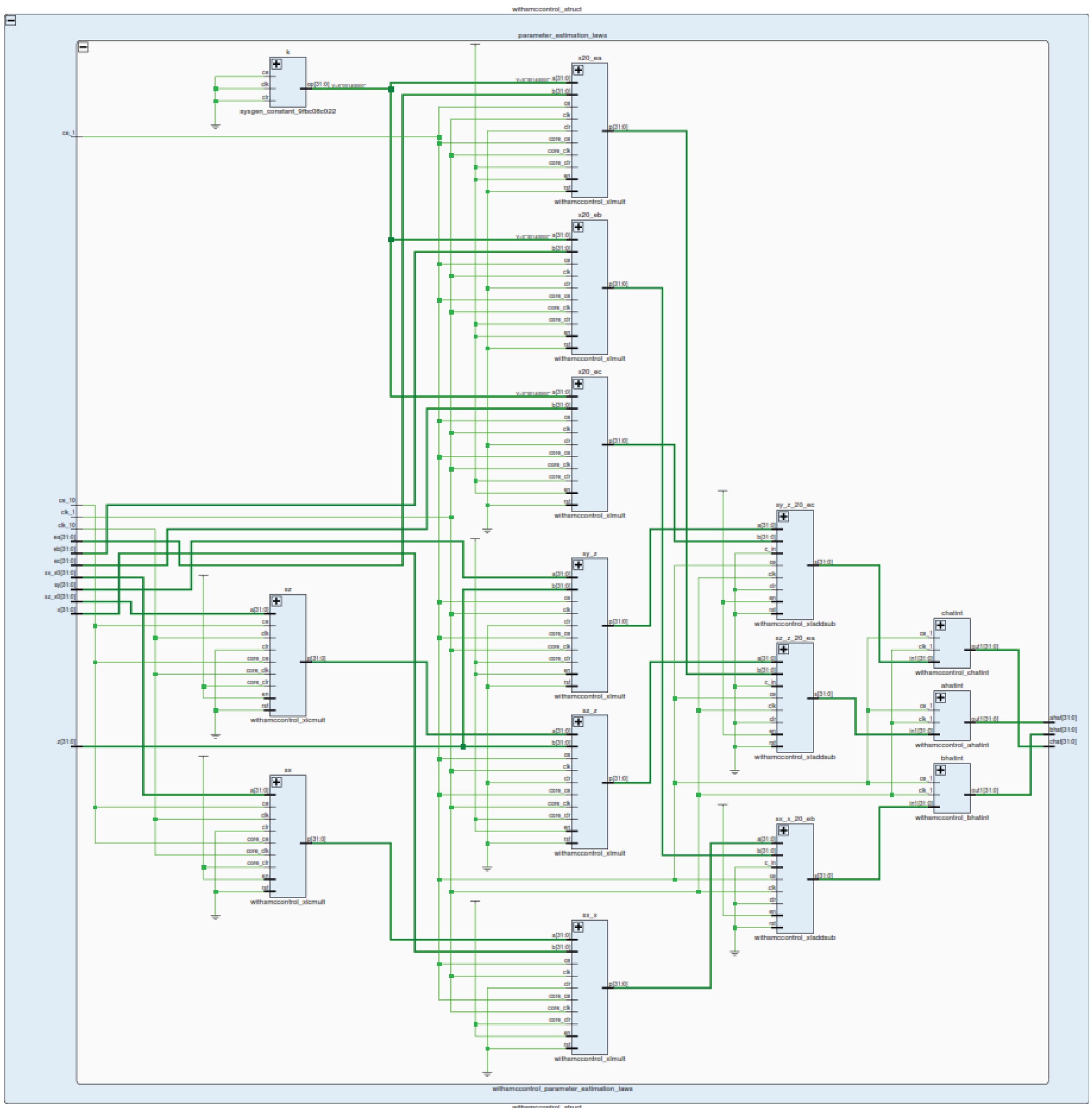


Figure 9: Xilinx RTL schematics of the controllers with sliding surfaces and parameter estimate laws.

The initial conditions are fed into the forward register. Figure 7 shows the overall RTL schematics of the system with time delays. Figure 8 shows the RTL schematics of the implemented delay (3). Figure 9 shows the Xilinx RTL schematics of the controllers with sliding surfaces and parameter estimate laws. Figures 10 and 11 show the controlled states of the delay systems and estimated parameters with the control in action at $t = 0.5$ s, respectively.

6. Discussion and Conclusion

By studying presented mathematical models for glucose-insulin interaction, according to the value of parameters, a chaotic model for describing the glucose-insulin regulatory system was found. In the present study, it is expected to observe periodic behavior in the proposed system under normal metabolic conditions and chaotic behavior under abnormal metabolic conditions. It is noteworthy to say that the chaotic behavior of a system is a sign of a faulty condition in the biological systems [18–23].

The effect of two time delays on glucose-insulin regulatory system was investigated. Two main results of this study are listed as below.

(i) If the time lag of insulin response to glucose increases, system exits from periodic region and enters to chaotic region, and if there is more delay on response of glucose to insulin secretion, the system displays chaotic manner, which was in line with previous studies [35, 36]

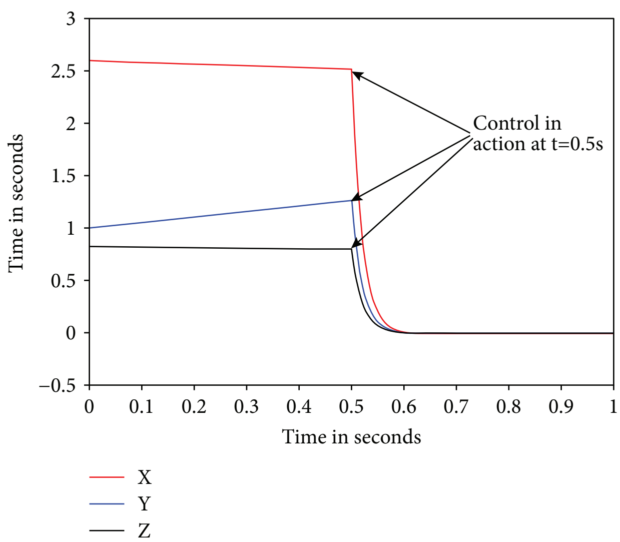


FIGURE 10: Time history of the delay (3) with controllers in action at $t = 0.5$ s using Xilinx system generator toolbox.

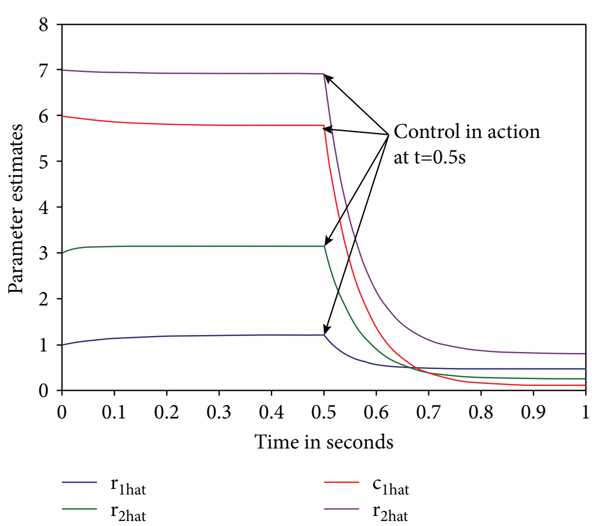


FIGURE 11: Time history of the parameter estimates with controllers in action at $t = 0.5$ s using Xilinx system generator toolbox.

(ii) If there is more delay on the response of glucose to insulin secretion, the behavior of system alters from periodic to chaotic

The proposed system can explain the interaction between glucose and insulin concentration in both normal and abnormal (diabetes disease) situations. Also, a control method was investigated with the hope of possible clinical applications.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Research Article

Oscillation Criteria for Delay and Advanced Differential Equations with Nonmonotone Arguments

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We study the oscillatory behavior of differential equations with nonmonotone deviating arguments and nonnegative coefficients. New oscillation criteria, involving lim sup and lim inf, are obtained based on an iterative method. Examples, numerically solved in MATLAB, are given to illustrate the applicability and strength of the obtained conditions over known ones.

1. Introduction

In mathematics, delay differential equations (DDEs) are that type of differential equations where the derivative of the unknown function, at a certain time, is given in terms of the values of the function, at previous times. DDEs are also referred in the literature as time-delay systems, systems with aftereffect or dead-time, hereditary systems, or equations with delay arguments.

Mathematical modelling involving DDEs is widely used for analysis and predictions in various areas of the life sciences, for example, population dynamics, epidemiology, immunology, physiology, neural networks. See, for example, [1–10] and the references cited therein. The time delays add to these models memory effects, taking into account the dependence of the model's present state on its past history [9]. The delay can be related to the duration of certain hidden processes, like the stages of the life cycle, the time between infection of a cell and the production of new viruses, the duration of the infectious period, the immune period, and so on.

In analogy, advanced differential equations (ADEs) are used in many applied problems where the evolution rate depends not only on the present, but also on the future. While delays in DDEs represent the retrospective memory of the past, advances in ADEs represent the prospective memory of the future, accounting for the influence on the system of potential future actions, which are available, at the present time. For instance, population dynamics, economics problems, or mechanical control engineering are typical fields where such phenomena are thought to occur (see [11, 12] for details).

The earliest delay model in mathematical biology is Hutchinson's equation, in 1948 [6]. Hutchinson modified the classical logistic equation, with a delay term to incorporate hatching and maturation periods into the model and account for oscillations, in the population of Daphnia,

$$y'(t) = ry(t)\left(1 - \frac{y(t-\tau)}{K}\right), \tag{1}$$

where $y(t)$ denotes the size of the population, in the present time t, $y'(t)$ describes the change of this size, at time t, $y(t-\tau)$ is the size, in some past time $t-\tau$, $\tau > 0$ is the delay, representing the time for new eggs to hatch, and r is the reproduction rate of the population, while K is the carrying capacity, for the population.

Many physiological processes, including the concentration of red blood cells, the concentration of CO_2 in the blood, causing the observed periodic oscillations in the breathing frequency, and the production of new blood cells, in the bone marrow, exhibit oscillations and several DDE models have been proposed to model these processes.

Below, we present two applications indicating the relevance of the DDEs we study in this paper to real world problems. The two examples are taken from the areas of physiology and population dynamics.

Application 1 (blood cells production [9]). The production of red and white blood cells, in the bone marrow, is regulated by the level of oxygen, in the blood. A reduction in the number of cells in the blood, as a result of the loss of cells, causes the level of oxygen in the blood to decrease. When the level of oxygen in the blood decreases, a substance is released that in turn leads to the release of blood elements, from the bone marrow. Thus, the concentration $c(t)$ of cells in the blood stream, at any time t, changes according to the loss of cells and the release of new cells, from the bone marrow. But the bone marrow responds to a reduction in the number of blood cells and the decrease in the level of oxygen, with a delay that is in the order of 6 days. That means the release of new cells, into the blood stream, at time t, depends on the cell concentration, at an earlier time, namely, $t-\tau$, where τ is the delay with which the bone marrow responds to a reduced level of oxygen in the blood. The simplest model of the concentration of the cells in the blood stream can be described by the DDE

$$c'(t) = \lambda c(t-\tau) - \gamma c(t), \tag{2}$$

where λ represents the flux of cells into the blood stream, γ is the death rate, and τ is the delay. All of them are positive constants. The solutions of the above equation exhibit similar oscillations to the actual oscillatory pattern observed in the concentration of cells in the blood stream.

Application 2. Imagine a biological population composed of adult and juvenile individuals. Let $N(t)$ denote the density of adults at time t. Assume that the length of the juvenile period is exactly h units of time for each individual. Assume that adults produce offspring at a per capita rate α and that their probability per unit of time of dying is μ. Assume that a newborn survives the juvenile period with probability ρ and put $t = \alpha\rho$. Then the dynamics of N can be described by the differential equation

$$N'(t) = -\mu N(t) + rN(t-h) \tag{3}$$

which involves a nonlocal term, $rN(t-h)$ meaning that newborns become adults with some delay. So the time variation of the population density N involves the current as well as the past values of N.

The use of DDEs, from the initial application, in population dynamics, has spread to every area of the life sciences: immunology, physiology, epidemiology, and cell growth. The original delay logistic equation has led to several new DDE forms, like Volterra's integrodifferential equations and neutral DDEs [9], and several new models, from the delayed Hopfield model, in neural networks to the SIR model, in epidemiology [7]. More recently, the idea of state dependent delays has been introduced, involving "a delay that itself is governed by a differential equation that represents adaptation to the system's state" [9].

From the above review of DDEs, in the biological sciences, it is apparent that if DDEs are so extensively used in this area, this is because the dynamics of those equations, namely, the stability and oscillatory properties of the solutions of those equations, replicate the stability and oscillatory patterns, we actually observe in processes, in those areas. Thus, the study of the stability and oscillatory behavior of the solutions of DDEs has become the principal subject of the research on those equations. For more advanced treatises on oscillation theory, the reader is referred to [13–33].

In the paper, we consider a differential equation with delay argument of the form

$$x'(t) + p(t)\,x(\tau(t)) = 0, \quad t \ge t_0, \tag{E}$$

where p is a function of nonnegative real numbers and τ is a function of positive real numbers such that

$$\begin{gathered} \tau(t) < t, \quad t \ge t_0, \\ \lim_{t\to\infty} \tau(t) = \infty. \end{gathered} \tag{4}$$

By a *solution* of (E) we understand a continuously differentiable function defined on $[\tau(T_0), \infty)$ for some $T_0 \ge t_0$ and such that (E) is satisfied for $t \ge T_0$. Such a solution is called *oscillatory* if it has arbitrarily large zeros, and otherwise it is called *nonoscillatory*. An equation is *oscillatory* if all its solutions oscillate.

A parallel problem to that of establishing oscillation criteria for the solutions of equation (E) is the one concerning the solutions of the advanced differential equation (ADE)

$$x'(t) - q(t)\,x(\sigma(t)) = 0, \quad t \ge t_0, \tag{E$'$}$$

where q is a function of nonnegative real numbers and σ is a function of positive real numbers such that

$$\sigma(t) > t, \quad t \ge t_0. \tag{5}$$

The objective of this paper is to consider the oscillatory dynamics of both delay and advanced differential equations, from the perspective of the qualitative analysis of those equations. In that framework, (i) we formulate new iterative oscillation conditions, for testing whether all solutions of a DDE of the form of (E) or an ADE of the form of (E$'$) are oscillatory, (ii) we show that these tests significantly improve on all the previous, iterative, and noniterative oscillation criteria which, briefly, are reviewed in the Historical and Chronological Review, in Section 2, requiring fewer iterations to determine whether an equation of the considered form is oscillatory, and (iii) these criteria apply to a more general class of equations, having nonmonotone arguments $\tau(t)$ or $\sigma(t)$, in contrast to the large majority of the other studies where the criteria apply to equations with nondecreasing arguments.

From this point onward, we will use the notation

$$\alpha := \liminf_{t\to\infty} \int_{\tau(t)}^{t} p(s)\,ds,$$
$$\beta := \liminf_{t\to\infty} \int_{t}^{\sigma(t)} q(s)\,ds,$$
$$D(\omega) := \begin{cases} 0, & \text{if } \omega > \dfrac{1}{e}, \\ \dfrac{1-\omega-\sqrt{1-2\omega-\omega^2}}{2}, & \text{if } \omega \in \left[0, \dfrac{1}{e}\right], \end{cases} \tag{6}$$
$$\mathrm{LD} := \limsup_{t\to\infty} \int_{\tau(t)}^{t} p(s)\,ds, \quad \text{where } \tau(t) \text{ is nondecreasing},$$
$$\mathrm{LA} := \limsup_{t\to\infty} \int_{t}^{\sigma(t)} q(s)\,ds, \quad \text{where } \sigma(t) \text{ is nondecreasing}.$$

2. Historical and Chronological Review

2.1. DDEs. The first systematic study for the oscillation of all solutions of equation (E) was made by Myškis in 1950 [31], when he proved that every solution of (E) oscillates, if

$$\limsup_{t\to\infty} [t-\tau(t)] < \infty,$$
$$\liminf_{t\to\infty} [t-\tau(t)] \liminf_{t\to\infty} p(t) > \frac{1}{e}. \tag{7}$$

In 1972, Ladas et al. [27] proved that if

$$\mathrm{LD} > 1, \tag{8}$$

then all solutions of (E) are oscillatory.

In 1982, Koplatadze and Chanturiya [24] improved (7) to

$$\alpha > \frac{1}{e}. \tag{9}$$

Regarding the constant $1/e$ in (9), it should be remarked that if the inequality

$$\int_{\tau(t)}^{t} p(s)\,ds \le \frac{1}{e} \tag{10}$$

holds eventually, then, according to [24], (E) has a nonoscillatory solution.

It is apparent that there is a gap between conditions (8) and (9), when

$$\lim_{t\to\infty} \int_{\tau(t)}^{t} p(s)\,ds \tag{11}$$

does not exist. How to fill this gap is an interesting problem which has been investigated by several authors. For example, in 2000, Jaroš and Stavroulakis [23] proved that if λ_0 is the smaller root of the equation $\lambda = e^{\alpha\lambda}$ and

$$\mathrm{LD} > \frac{1+\ln\lambda_0}{\lambda_0} - D(\alpha), \tag{12}$$

then all solutions of (E) oscillate.

Now we come to the general case where the argument $\tau(t)$ is nonmonotone. Set

$$h(t) := \sup_{s\le t} \tau(s), \quad t \ge t_0. \tag{13}$$

Clearly, the function $h(t)$ is nondecreasing and $\tau(t) \le h(t) < t$, for all $t \ge t_0$.

In 1994, Koplatadze and Kvinikadze [25] proved that if

$$\limsup_{t\to\infty} \int_{h(t)}^{t} p(s) \exp\left(\int_{h(s)}^{h(t)} p(u)\psi_j(u)\,du\right) ds > 1 - D(\alpha), \tag{14}$$

where

$$\psi_1(t) = 0,$$
$$\psi_j(t) = \exp\left(\int_{\tau(t)}^{t} p(u)\psi_{j-1}(u)\,du\right), \quad j \ge 2, \tag{15}$$

then all solutions of (E) oscillate.

In 2011, Braverman and Karpuz [14] proved that if

$$\limsup_{t\to\infty} \int_{h(t)}^{t} p(s) \exp\left(\int_{\tau(s)}^{h(t)} p(u)\,du\right) ds > 1, \tag{16}$$

then all solutions of (E) oscillate, while in 2014, Stavroulakis [32] improved (16) to

$$\limsup_{t\to\infty} \int_{h(t)}^{t} p(s) \exp\left(\int_{\tau(s)}^{h(t)} p(u)\,du\right) ds > 1 - D(\alpha). \tag{17}$$

In 2016, El-Morshedy and Attia [30] proved that if

$$\limsup_{t\to\infty} \left[\int_{g(t)}^{t} p_n(s)\,ds + D(\alpha)\exp\left(\int_{g(t)}^{t} \sum_{j=0}^{n-1} p_j(s)\,ds\right)\right] > 1, \tag{18}$$

where $p_0(t) = p(t)$ and

$$p_n(t) = p_{n-1}(t) \int_{g(t)}^{t} p_{n-1}(s) \exp\left(\int_{g(s)}^{t} p_{n-1}(u)\,du\right) ds, \quad n \ge 1, \tag{19}$$

then all solutions of (E) are oscillatory. Here, $g(t)$ is a nondecreasing continuous function such that $\tau(t) \leq g(t) \leq t$, $t \geq t_1$, for some $t_1 \geq t_0$. Clearly, $g(t)$ is more general than $h(t)$ defined by (13).

Recently, Chatzarakis [15, 16] proved that if, for some $j \in \mathbb{N}$,

$$\limsup_{t\to\infty} \int_{h(t)}^{t} p(s) \exp\left(\int_{\tau(s)}^{h(t)} p_j(u)\,du\right) ds > 1 \tag{20}$$

or

$$\limsup_{t\to\infty} \int_{h(t)}^{t} p(s) \exp\left(\int_{\tau(s)}^{h(t)} p_j(u)\,du\right) ds > 1 - D(\alpha), \tag{21}$$

where

$$p_j(t) = p(t)\left[1 + \int_{\tau(t)}^{t} p(s) \exp\left(\int_{\tau(s)}^{h(t)} p_{j-1}(u)\,du\right) ds\right], \tag{22}$$

with $p_0(t) = p(t)$, then all solutions of (E) are oscillatory.

Lately, Chatzarakis [17] studied a more general form of (E); namely,

$$x'(t) + \sum_{i=1}^{m} p_i(t)\, x(\tau_i(t)) = 0, \quad t \geq t_0, \tag{23}$$

and established sufficient oscillation conditions. Those conditions can lead to (20) and (21) when $m = 1$.

2.2. ADEs. By Theorem 2.4.3 [29], if

$$\mathrm{LA} > 1, \tag{24}$$

then all solutions of (E$'$) are oscillatory.

In 1984, Fukagai and Kusano [21] proved that if

$$\beta > \frac{1}{e}, \tag{25}$$

then all solutions of (E$'$) are oscillatory, while if

$$\int_{t}^{\sigma(t)} q(s)\,ds \leq \frac{1}{e} \quad \text{for all sufficiently large } t, \tag{26}$$

then (E$'$) has a nonoscillatory solution.

Assume that the argument $\sigma(t)$ is not necessarily monotone. Set

$$\rho(t) = \inf_{s\geq t} \sigma(s), \quad t \geq t_0. \tag{27}$$

Clearly, the function $\rho(t)$ is nondecreasing and $\sigma(t) \geq \rho(t) > t$, for all $t \geq t_0$.

In 2015, Chatzarakis and Öcalan [18] proved that if

$$\limsup_{t\to\infty} \int_{t}^{\rho(t)} q(s) \exp\left(\int_{\rho(t)}^{\sigma(s)} q(u)\,du\right) ds > 1, \tag{28}$$

or

$$\liminf_{t\to\infty} \int_{t}^{\rho(t)} q(s) \exp\left(\int_{\rho(t)}^{\sigma(s)} q(u)\,du\right) ds > \frac{1}{e}, \tag{29}$$

then all solutions of (E$'$) are oscillatory.

Recently, Chatzarakis [15, 16] proved that if, for some $j \in \mathbb{N}$,

$$\limsup_{t\to\infty} \int_{t}^{\rho(t)} q(s) \exp\left(\int_{\rho(t)}^{\sigma(s)} q_j(u)\,du\right) ds > 1, \tag{30}$$

or

$$\limsup_{t\to\infty} \int_{t}^{\rho(t)} q(s) \exp\left(\int_{\rho(t)}^{\sigma(s)} q_j(u)\,du\right) ds > 1 - D(\beta), \tag{31}$$

where

$$q_j(t) = q(t)\left[1 + \int_{t}^{\sigma(t)} q(s) \exp\left(\int_{\rho(t)}^{\sigma(s)} q_{j-1}(u)\,du\right) ds\right], \quad j \geq 1 \tag{32}$$

with $q_0(t) = q(t)$, then all solutions of (E$'$) oscillate.

Lately, Chatzarakis [17] studied a more general form of (E$'$), namely,

$$x'(t) - \sum_{i=1}^{m} q_i(t)\, x(\sigma_i(t)) = 0, \quad t \geq t_0, \tag{33}$$

and established sufficient oscillation conditions. Those conditions can lead to (30) and (31) when $m = 1$.

3. Main Results

3.1. DDEs. In our main results, we state theorems, establishing new sufficient oscillation conditions. For the proofs of those theorems, we use the following lemmas.

Lemma 3 (see [19, Lemma 2.1.1]). *Assume that $h(t)$ is defined by (13). Then*

$$\alpha := \liminf_{t\to\infty} \int_{\tau(t)}^{t} p(s)\,ds = \liminf_{t\to\infty} \int_{h(t)}^{t} p(s)\,ds. \tag{34}$$

Lemma 4 (see [19, Lemma 2.1.3]). *Assume that $h(t)$ is defined by (13), $\alpha \in (0, 1/e]$, and $x(t)$ is an eventually positive solution of (E). Then*

$$\liminf_{t\to\infty} \frac{x(t)}{x(h(t))} \geq D(\alpha). \tag{35}$$

Lemma 5 (see [26]). *Assume that $h(t)$ is defined by (13), $\alpha \in (0, 1/e]$, and $x(t)$ is an eventually positive solution of (E). Then*

$$\liminf_{t\to\infty} \frac{x(h(t))}{x(t)} \geq \lambda_0, \tag{36}$$

where λ_0 is the smaller root of the equation $\lambda = e^{\alpha\lambda}$.

Theorem 6. *Let $h(t)$ be defined by (13) and for some $j \in \mathbb{N}$*

$$\limsup_{t\to\infty} \int_{h(t)}^{t} p(s) \cdot \exp\left(\int_{\tau(s)}^{h(t)} p(u) \exp\left(\int_{\tau(u)}^{u} P_j(\xi)\, d\xi\right) du\right) ds > 1, \tag{37}$$

where

$$P_j(t) = p(t)\left[1 + \int_{\tau(t)}^{t} p(s) \cdot \exp\left(\int_{\tau(s)}^{t} p(u) \exp\left(\int_{\tau(u)}^{u} P_{j-1}(\xi)\, d\xi\right) du\right) ds\right] \tag{38}$$

with $P_0(t) = \lambda_0 p(t)$, and let λ_0 be the smaller root of the equation $\lambda = e^{\alpha\lambda}$. Then all solutions of (E) oscillate.

Proof. Assume, for the sake of contradiction, that there exists a nonoscillatory solution $x(t)$ of (E). Since $-x(t)$ is also a solution of (E), we can confine our discussion only to the case where the solution $x(t)$ is eventually positive. Then there exists a real number $t_1 > t_0$ such that $x(t), x(\tau(t)) > 0$ for all $t \ge t_1$. Thus, from (E) we have

$$x'(t) = -p(t)\, x(\tau(t)) \le 0 \quad \forall t \ge t_1, \tag{39}$$

which means that $x(t)$ is an eventually nonincreasing function of positive numbers. Taking into account the fact that $\tau(t) \le h(t)$, (E) implies that

$$x'(t) + p(t)\, x(h(t)) \le 0, \quad t \ge t_1. \tag{40}$$

Observe that (36) implies that, for each $\epsilon > 0$, there exists a real number t_ϵ such that

$$\frac{x(h(t))}{x(t)} > \lambda_0 - \epsilon \quad \forall t \ge t_\epsilon \ge t_1. \tag{41}$$

Combining inequalities (40) and (41), we obtain

$$x'(t) + p(t)(\lambda_0 - \epsilon)\, x(t) \le 0, \quad t \ge t_\epsilon, \tag{42}$$

or

$$x'(t) + P_0(t,\epsilon)\, x(t) \le 0, \quad t \ge t_\epsilon, \tag{43}$$

where

$$P_0(t,\epsilon) = p(t)(\lambda_0 - \epsilon). \tag{44}$$

Applying the Grönwall inequality in (43), we conclude that

$$x(s) \ge x(t) \exp\left(\int_s^t P_0(\xi,\epsilon)\, d\xi\right), \quad t \ge s \ge t_\epsilon. \tag{45}$$

Now we divide (E) by $x(t) > 0$ and integrate on $[s,t]$, so

$$-\int_s^t \frac{x'(u)}{x(u)} du = \int_s^t p(u) \frac{x(\tau(u))}{x(u)} du, \tag{46}$$

or

$$\ln\frac{x(s)}{x(t)} = \int_s^t p(u) \frac{x(\tau(u))}{x(u)} du, \quad t \ge s \ge t_\epsilon. \tag{47}$$

Since $\tau(u) < u$, equality (47) gives

$$\begin{aligned} \ln\frac{x(s)}{x(t)} &= \int_s^t p(u) \frac{x(\tau(u))}{x(u)} du \\ &\ge \int_s^t p(u) \frac{x(u)}{x(u)} \exp\left(\int_{\tau(u)}^{u} P_0(\xi,\epsilon)\, d\xi\right) du \\ &= \int_s^t p(u) \exp\left(\int_{\tau(u)}^{u} P_0(\xi,\epsilon)\, d\xi\right) du, \end{aligned} \tag{48}$$

or

$$x(s) \ge x(t) \exp\left(\int_s^t p(u) \exp\left(\int_{\tau(u)}^{u} P_0(\xi,\epsilon)\, d\xi\right) du\right). \tag{49}$$

Substituting $\tau(s)$ for s in (49), we get

$$x(\tau(s)) \ge x(t) \exp\left(\int_{\tau(s)}^t p(u) \exp\left(\int_{\tau(u)}^{u} P_0(\xi,\epsilon)\, d\xi\right) du\right). \tag{50}$$

Integrating (E) from $\tau(t)$ to t, we have

$$x(t) - x(\tau(t)) + \int_{\tau(t)}^{t} p(s)\, x(\tau(s))\, ds = 0. \tag{51}$$

Combining (50) and (51), we obtain

$$x(t) - x(\tau(t)) + x(t) \int_{\tau(t)}^{t} p(s) \cdot \exp\left(\int_{\tau(s)}^{t} p(u) \exp\left(\int_{\tau(u)}^{u} P_0(\xi,\epsilon)\, d\xi\right) du\right) ds \le 0. \tag{52}$$

Multiplying inequality (52) by $p(t)$, we find

$$p(t)x(t) - p(t)x(\tau(t)) + p(t)x(t) \int_{\tau(t)}^{t} p(s) \cdot \exp\left(\int_{\tau(s)}^{t} p(u) \exp\left(\int_{\tau(u)}^{u} P_0(\xi,\epsilon)\, d\xi\right) du\right) ds \le 0, \tag{53}$$

which, in view of (E), becomes

$$x'(t) + p(t)x(t) + p(t)x(t) \int_{\tau(t)}^{t} p(s) \cdot \exp\left(\int_{\tau(s)}^{t} p(u) \exp\left(\int_{\tau(u)}^{u} P_0(\xi,\epsilon)\, d\xi\right) du\right) ds \le 0. \tag{54}$$

Hence, for sufficiently large t,

$$x'(t)+p(t)\left[1+\int_{\tau(t)}^{t}p(s)\cdot\exp\left(\int_{\tau(s)}^{t}p(u)\exp\left(\int_{\tau(u)}^{u}P_0(\xi,\epsilon)\,d\xi\right)du\right)ds\right]\cdot x(t)\le 0, \tag{55}$$

or

$$x'(t)+P_1(t,\epsilon)\,x(t)\le 0, \tag{56}$$

where

$$P_1(t,\epsilon)=p(t)\left[1+\int_{\tau(t)}^{t}p(s)\cdot\exp\left(\int_{\tau(s)}^{t}p(u)\exp\left(\int_{\tau(u)}^{u}P_0(\xi,\epsilon)\,d\xi\right)du\right)ds\right]. \tag{57}$$

Clearly (56) resembles (43), if we replace P_0 by P_1. Thus, integrating (56) on $[s,t]$ yields

$$x(s)\ge x(t)\exp\left(\int_{s}^{t}P_1(\xi,\epsilon)\,d\xi\right). \tag{58}$$

Repeating steps (45) through (50), we can see that x satisfies the inequality

$$x(\tau(s))\ge x(t)\exp\left(\int_{\tau(s)}^{t}p(u)\exp\left(\int_{\tau(u)}^{u}P_1(\xi,\epsilon)\,d\xi\right)du\right). \tag{59}$$

Combining now (51) and (59), we obtain

$$x(t)-x(\tau(t))+x(t)\int_{\tau(t)}^{t}p(s)\cdot\exp\left(\int_{\tau(s)}^{t}p(u)\exp\left(\int_{\tau(u)}^{u}P_1(\xi,\epsilon)\,d\xi\right)du\right)ds\le 0. \tag{60}$$

Multiplying inequality (60) by $p(t)$, as before, we find

$$x'(t)+p(t)\left[1+\int_{\tau(t)}^{t}p(s)\cdot\exp\left(\int_{\tau(s)}^{t}p(u)\exp\left(\int_{\tau(u)}^{u}P_1(\xi,\epsilon)\,d\xi\right)du\right)ds\right]\cdot x(t)\le 0. \tag{61}$$

Therefore, for sufficiently large t, we have

$$x'(t)+P_2(t,\epsilon)\,x(t)\le 0, \tag{62}$$

where

$$P_2(t,\epsilon)=p(t)\left[1+\int_{\tau(t)}^{t}p(s)\cdot\exp\left(\int_{\tau(s)}^{t}p(u)\exp\left(\int_{\tau(u)}^{u}P_1(\xi,\epsilon)\,d\xi\right)du\right)ds\right]. \tag{63}$$

It becomes apparent, now, that, by repeating the above steps, we can build inequalities on $x'(t)$ with progressively higher indices $P_j(t,\epsilon)$, $j\in\mathbb{N}$. In general, for sufficiently large t, the positive solution $x(t)$ satisfies the inequality

$$x'(t)+P_j(t,\epsilon)\,x(t)\le 0,\quad j\in\mathbb{N}, \tag{64}$$

where

$$P_j(t,\epsilon)=p(t)\left[1+\int_{\tau(t)}^{t}p(s)\cdot\exp\left(\int_{\tau(s)}^{t}p(u)\exp\left(\int_{\tau(u)}^{u}P_{j-1}(\xi,\epsilon)\,d\xi\right)du\right)ds\right]. \tag{65}$$

Proceeding to final step, we recall that $h(t)$, defined by (13), is a nondecreasing function. Since $\tau(s)\le h(s)\le h(t)$, we have

$$x(\tau(s))\ge x(h(t))\cdot\exp\left(\int_{\tau(s)}^{h(t)}p(u)\exp\left(\int_{\tau(u)}^{u}P_j(\xi,\epsilon)\,d\xi\right)du\right). \tag{66}$$

Hence

$$x(t)-x(h(t))+x(h(t))\int_{h(t)}^{t}p(s)\cdot\exp\left(\int_{\tau(s)}^{h(t)}p(u)\exp\left(\int_{\tau(u)}^{u}P_j(\xi,\epsilon)\,d\xi\right)du\right)ds\le 0, \tag{67}$$

or

$$x(h(t))\left[\int_{h(t)}^{t}p(s)\cdot\exp\left(\int_{\tau(s)}^{h(t)}p(u)\exp\left(\int_{\tau(u)}^{u}P_j(\xi,\epsilon)\,d\xi\right)du\right)ds-1\right]<0. \tag{68}$$

Thus

$$\int_{h(t)}^{t}p(s)\cdot\exp\left(\int_{\tau(s)}^{h(t)}p(u)\exp\left(\int_{\tau(u)}^{u}P_j(\xi,\epsilon)\,d\xi\right)du\right)ds-1<0. \tag{69}$$

Taking the limit as $t\to\infty$, we have

$$\limsup_{t\to\infty}\int_{h(t)}^{t}p(s)\cdot\exp\left(\int_{\tau(s)}^{h(t)}p(u)\exp\left(\int_{\tau(u)}^{u}P_j(\xi,\epsilon)\,d\xi\right)du\right)ds\le 1. \tag{70}$$

Since ϵ may be taken arbitrarily small, this inequality contradicts (37).

This completes the proof of the theorem. □

Theorem 7. *Let $h(t)$ be defined by (13) and $\alpha \in (0, 1/e]$. If for some $j \in \mathbb{N}$*

$$\limsup_{t\to\infty} \int_{h(t)}^{t} p(s) \cdot \exp\left(\int_{\tau(s)}^{h(t)} p(u) \exp\left(\int_{\tau(u)}^{u} P_j(\xi)\, d\xi\right) du\right) ds > 1 - D(\alpha), \tag{71}$$

where P_j is defined by (38), then all solutions of (E) oscillate.

Proof. Assume x is an eventually positive solution of (E). Clearly, (67) is satisfied for sufficiently large t. Thus,

$$\int_{h(t)}^{t} p(s) \cdot \exp\left(\int_{\tau(s)}^{h(t)} p(u) \exp\left(\int_{\tau(u)}^{u} P_j(\xi,\epsilon)\, d\xi\right) du\right) ds \le 1 - \frac{x(t)}{x(h(t))}, \tag{72}$$

which implies that

$$\limsup_{t\to\infty} \int_{h(t)}^{t} p(s) \cdot \exp\left(\int_{\tau(s)}^{h(t)} p(u) \exp\left(\int_{\tau(u)}^{u} P_j(\xi,\epsilon)\, d\xi\right) du\right) ds \le 1 - \liminf_{t\to\infty} \frac{x(t)}{x(h(t))}. \tag{73}$$

Using Lemmas 3 and 4, it is evident that inequality (35) is satisfied. Thus, (73) leads to

$$\limsup_{t\to\infty} \int_{h(t)}^{t} p(s) \cdot \exp\left(\int_{\tau(s)}^{h(t)} p(u) \exp\left(\int_{\tau(u)}^{u} P_j(\xi,\epsilon)\, d\xi\right) du\right) ds \le 1 - D(\alpha). \tag{74}$$

Since ϵ may be taken arbitrarily small, this inequality contradicts (71).

This completes the proof of the theorem. □

Theorem 8. *Let $h(t)$ be defined by (13) and $\alpha \in (0, 1/e]$. If for some $j \in \mathbb{N}$*

$$\limsup_{t\to\infty} \int_{h(t)}^{t} p(s) \cdot \exp\left(\int_{\tau(s)}^{t} p(u) \exp\left(\int_{\tau(u)}^{u} P_j(\xi)\, d\xi\right) du\right) ds > \frac{1}{D(\alpha)}, \tag{75}$$

where P_j is defined by (38), then all solutions of (E) oscillate.

Proof. Assume x is an eventually positive solution of (E). Then, as in the proof of Theorem 6, for sufficiently large t, we conclude that

$$x(\tau(s)) \ge x(t) \exp\left(\int_{\tau(s)}^{t} p(u) \exp\left(\int_{\tau(u)}^{u} P_j(\xi,\epsilon)\, d\xi\right) du\right). \tag{76}$$

Integrating (E) from $h(t)$ to t and using (76), we obtain

$$x(t) - x(h(t)) + \int_{h(t)}^{t} p(s)\, x(t) \cdot \exp\left(\int_{\tau(s)}^{t} p(u) \exp\left(\int_{\tau(u)}^{u} P_j(\xi,\epsilon)\, d\xi\right) du\right) ds \le 0, \tag{77}$$

or

$$-x(h(t)) + \int_{h(t)}^{t} p(s)\, x(t) \cdot \exp\left(\int_{\tau(s)}^{t} p(u) \exp\left(\int_{\tau(u)}^{u} P_j(\xi,\epsilon)\, d\xi\right) du\right) ds < 0. \tag{78}$$

Hence

$$x(h(t)) \left[\frac{x(t)}{x(h(t))} \int_{h(t)}^{t} p(s) \cdot \exp\left(\int_{\tau(s)}^{t} p(u) \exp\left(\int_{\tau(u)}^{u} P_j(\xi,\epsilon)\, d\xi\right) du\right) ds - 1\right] < 0, \tag{79}$$

which yields, for all sufficiently large t,

$$\int_{h(t)}^{t} p(s) \cdot \exp\left(\int_{\tau(s)}^{t} p(u) \exp\left(\int_{\tau(u)}^{u} P_j(\xi,\epsilon)\, d\xi\right) du\right) ds < \frac{x(h(t))}{x(t)} \tag{80}$$

and consequently

$$\limsup_{t\to\infty}\int_{h(t)}^{t} p(s) \cdot \exp\left(\int_{\tau(s)}^{t} p(u)\exp\left(\int_{\tau(u)}^{u} P_j(\xi,\epsilon)\,d\xi\right)du\right)ds \le \limsup_{t\to\infty}\frac{x(h(t))}{x(t)}. \quad (81)$$

Taking into account the fact that (35) is satisfied, inequality (81) leads to

$$\limsup_{t\to\infty}\int_{h(t)}^{t} p(s) \cdot \exp\left(\int_{\tau(s)}^{t} p(u)\exp\left(\int_{\tau(u)}^{u} P_j(\xi,\epsilon)\,d\xi\right)du\right)ds \le \frac{1}{D(\alpha)}, \quad (82)$$

which contradicts (75), when $\epsilon \to 0$.

This completes the proof of the theorem. □

Theorem 9. *Let $h(t)$ be defined by (13) and $\alpha \in (0, 1/e]$. If for some $j \in \mathbb{N}$*

$$\limsup_{t\to\infty}\int_{h(t)}^{t} p(s) \cdot \exp\left(\int_{\tau(s)}^{h(s)} p(u)\exp\left(\int_{\tau(u)}^{u} P_j(\xi)\,d\xi\right)du\right)ds > \frac{1+\ln\lambda_0}{\lambda_0} - D(\alpha), \quad (83)$$

where P_j is defined by (38) and λ_0 is the smaller root of the equation $\lambda = e^{\alpha\lambda}$, then all solutions of (E) oscillate.

Proof. Let x be an eventually positive solution of (E). As in the proof of Theorem 8, we can show that (76) holds; namely,

$$x(\tau(s)) \ge x(t)\exp\left(\int_{\tau(s)}^{t} p(u)\exp\left(\int_{\tau(u)}^{u} P_j(\xi,\epsilon)\,d\xi\right)du\right). \quad (84)$$

Since $\tau(s) \le h(s)$, inequality (84) gives

$$x(\tau(s)) \ge x(h(s)) \cdot \exp\left(\int_{\tau(s)}^{h(s)} p(u)\exp\left(\int_{\tau(u)}^{u} P_j(\xi,\epsilon)\,d\xi\right)du\right). \quad (85)$$

By Lemma 5, for each $\epsilon > 0$, there exists a real number t_ϵ such that

$$\frac{x(h(t))}{x(t)} > \lambda_0 - \epsilon \quad \forall t \ge t_\epsilon \ge t_1. \quad (86)$$

Note that, by the nondecreasing nature of the function $x(h(t))/x(s)$ in s, it holds

$$1 = \frac{x(h(t))}{x(h(t))} \le \frac{x(h(t))}{x(s)} \le \frac{x(h(t))}{x(t)}, \qquad t_\epsilon \le h(t) \le s \le t. \quad (87)$$

In particular, for $\epsilon \in (0, \lambda_0 - 1)$, by continuity, we conclude that there exists a real number $t^* \in (h(t), t]$ satisfying

$$1 < \lambda_0 - \epsilon = \frac{x(h(t))}{x(t^*)}. \quad (88)$$

Integrating (E) from t^* to t and using (85), we obtain

$$x(t) - x(t^*) + x(h(t))\int_{t^*}^{t} p(s) \cdot \exp\left(\int_{\tau(s)}^{h(s)} p(u)\exp\left(\int_{\tau(u)}^{u} P_j(\xi,\epsilon)\,d\xi\right)du\right)ds \le 0, \quad (89)$$

or

$$\int_{t^*}^{t} p(s)\exp\left(\int_{\tau(s)}^{h(s)} p(u) \cdot \exp\left(\int_{\tau(u)}^{u} P_j(\xi,\epsilon)\,d\xi\right)du\right)ds \le \frac{x(t^*)}{x(h(t))} - \frac{x(t)}{x(h(t))}. \quad (90)$$

Using (88) and Lemma 4, we deduce that, for the ϵ considered, there exists a real number $t'_\epsilon \ge t_\epsilon$ such that

$$\int_{t^*}^{t} p(s) \cdot \exp\left(\int_{\tau(s)}^{h(s)} p(u)\exp\left(\int_{\tau(u)}^{u} P_j(\xi,\epsilon)\,d\xi\right)du\right)ds < \frac{1}{\lambda_0 - \epsilon} - D(\alpha) + \epsilon \quad (91)$$

for $t \ge t'_\epsilon$.

Dividing (E) by $x(t)$, integrating from $h(t)$ to t^*, and using (85), we deduce that

$$\int_{h(t)}^{t^*} p(s) \cdot \frac{x(h(s))}{x(s)}\exp\left(\int_{\tau(s)}^{h(s)} p(u)\exp\left(\int_{\tau(u)}^{u} P_j(\xi,\epsilon)\,d\xi\right)du\right)ds \le -\int_{h(t)}^{t^*}\frac{x'(s)}{x(s)}ds. \quad (92)$$

Clearly, by means of (36), $x(h(s))/x(s) > \lambda_0 - \epsilon$, for $s \geq h(t) \geq t'_\epsilon$. Hence, for all sufficiently large t, we conclude that

$$(\lambda_0 - \epsilon) \int_{h(t)}^{t^*} p(s) \cdot \exp\left(\int_{\tau(s)}^{h(s)} p(u) \exp\left(\int_{\tau(u)}^{u} P_j(\xi, \epsilon)\, d\xi\right) du\right) ds < -\int_{h(t)}^{t^*} \frac{x'(s)}{x(s)} ds \tag{93}$$

or

$$\int_{h(t)}^{t^*} p(s) \cdot \exp\left(\int_{\tau(s)}^{h(s)} p(u) \exp\left(\int_{\tau(u)}^{u} P_j(\xi, \epsilon)\, d\xi\right) du\right) ds < -\frac{1}{\lambda_0 - \epsilon} \int_{h(t)}^{t^*} \frac{x'(s)}{x(s)} ds = \frac{1}{\lambda_0 - \epsilon} \ln \frac{x(h(t))}{x(t^*)} = \frac{\ln(\lambda_0 - \epsilon)}{\lambda_0 - \epsilon}; \tag{94}$$

that is,

$$\int_{h(t)}^{t^*} p(s) \cdot \exp\left(\int_{\tau(s)}^{h(s)} p(u) \exp\left(\int_{\tau(u)}^{u} P_j(\xi, \epsilon)\, d\xi\right) du\right) ds < \frac{\ln(\lambda_0 - \epsilon)}{\lambda_0 - \epsilon}. \tag{95}$$

Using (91) along with (95), we get

$$\limsup_{t\to\infty} \int_{h(t)}^{t} p(s) \cdot \exp\left(\int_{\tau(s)}^{h(s)} p(u) \exp\left(\int_{\tau(u)}^{u} P_j(\xi, \epsilon)\, d\xi\right) du\right) ds \leq \frac{1 + \ln(\lambda_0 - \epsilon)}{\lambda_0 - \epsilon} - D(\alpha) + \epsilon, \tag{96}$$

which contradicts (83), when $\epsilon \to 0$.

This completes the proof of the theorem. □

Theorem 10. *Let $h(t)$ be defined by (13). If for some $j \in \mathbb{N}$*

$$\liminf_{t\to\infty} \int_{h(t)}^{t} p(s) \cdot \exp\left(\int_{\tau(s)}^{h(s)} p(u) \exp\left(\int_{\tau(u)}^{u} P_j(\xi)\, d\xi\right) du\right) ds > \frac{1}{e}, \tag{97}$$

where P_j is defined by (38), then all solutions of (E) oscillate.

Proof. For the sake of contradiction, let x be a nonincreasing eventually positive solution and $t_1 > t_0$ be such that $x(t) > 0$ and $x(\tau(t)) > 0$ for all $t \geq t_1$. We note that we may obtain (85) as in the proof of Theorem 9.

Dividing (E) by $x(t)$ and integrating from $h(t)$ to t, we have

$$\ln\left(\frac{x(h(t))}{x(t)}\right) = \int_{h(t)}^{t} p(s) \frac{x(\tau(s))}{x(s)} ds \quad \forall t \geq t_2 \geq t_1, \tag{98}$$

from which, in view of $\tau(s) \leq h(s)$ and (85), we get

$$\ln\left(\frac{x(h(t))}{x(t)}\right) \geq \int_{h(t)}^{t} p(s) \cdot \frac{x(h(s))}{x(s)} \exp\left(\int_{\tau(s)}^{h(s)} p(u) \exp\left(\int_{\tau(u)}^{u} P_j(\xi, \epsilon)\, d\xi\right) du\right) ds. \tag{99}$$

Since x is nonincreasing and $h(s) < s$, inequality (99) becomes

$$\ln\left(\frac{x(h(t))}{x(t)}\right) \geq \int_{h(t)}^{t} p(s) \cdot \exp\left(\int_{\tau(s)}^{h(s)} p(u) \exp\left(\int_{\tau(u)}^{u} P_j(\xi, \epsilon)\, d\xi\right) du\right) ds. \tag{100}$$

From (97), it is clear that there exists a constant $c > 0$ such that

$$\int_{h(t)}^{t} p(s) \cdot \exp\left(\int_{\tau(s)}^{h(s)} p(u) \exp\left(\int_{\tau(u)}^{u} P_j(\xi)\, d\xi\right) du\right) ds \geq c > \frac{1}{e}. \tag{101}$$

Choose c' such that $c > c' > 1/e$. For every $\epsilon > 0$, such that $c - \epsilon > c'$, we have

$$\int_{h(t)}^{t} p(s) \cdot \exp\left(\int_{\tau(s)}^{h(s)} p(u) \exp\left(\int_{\tau(u)}^{u} P_j(\xi, \epsilon)\, d\xi\right) du\right) ds > c - \epsilon > c' > \frac{1}{e}. \tag{102}$$

Combining inequalities (100) and (102), we obtain

$$\ln\left(\frac{x(h(t))}{x(t)}\right) > c', \tag{103}$$

or

$$\frac{x(h(t))}{x(t)} > e^{c'} > ec' > 1, \tag{104}$$

which yields

$$x(h(t)) > (ec')\, x(t). \tag{105}$$

Following the above steps, we can inductively show that, for any positive integer k,

$$\frac{x(h(t))}{x(t)} > (ec')^k \quad \text{for sufficiently large } t. \tag{106}$$

Since $ec' > 1$, there is a natural number $k \in \mathbb{N}$, satisfying $k > 2[\ln 2 - \ln c']/(1 + \ln c')$ such that for t sufficiently large

$$\frac{x(h(t))}{x(t)} > (ec')^k > \left(\frac{2}{c'}\right)^2. \tag{107}$$

Further (cf. [13, 24]), for sufficiently large t, there exists a real number $t_m \in (h(t), t)$, such that

$$\begin{gathered}\int_{h(t)}^{t_m} p(s) \\ \cdot \exp\left(\int_{\tau(s)}^{h(s)} p(u) \exp\left(\int_{\tau(u)}^{u} P_j(\xi, \epsilon)\, d\xi\right) du\right) ds \\ > \frac{c'}{2}, \\ \int_{t_m}^{t} p(s) \exp\left(\int_{\tau(s)}^{h(s)} p(u) \exp\left(\int_{\tau(u)}^{u} P_j(\xi, \epsilon)\, d\xi\right) du\right) ds \\ > \frac{c'}{2}.\end{gathered} \tag{108}$$

Integrating (E) from $h(t)$ to t_m, using (85) and the fact that $x(t) > 0$, we obtain

$$\begin{gathered}x(h(t)) > x(h(t_m)) \int_{h(t)}^{t_m} p(s) \\ \cdot \exp\left(\int_{\tau(s)}^{h(s)} p(u) \exp\left(\int_{\tau(u)}^{u} P_j(\xi, \epsilon)\, d\xi\right) du\right) ds,\end{gathered} \tag{109}$$

which, in view of the first inequality in (108), implies that

$$x(h(t)) > \frac{c'}{2} x(h(t_m)). \tag{110}$$

Similarly, integrating (E) from t_m to t, using (85) and the fact that $x(t) > 0$, we have

$$\begin{gathered}x(t_m) > x(h(t)) \int_{t_m}^{t} p(s) \\ \cdot \exp\left(\int_{\tau(s)}^{h(s)} p(u) \exp\left(\int_{\tau(u)}^{u} P_j(\xi, \epsilon)\, d\xi\right) du\right) ds,\end{gathered} \tag{111}$$

which, in view of the second inequality in (108), yields

$$x(t_m) > \frac{c'}{2} x(h(t)). \tag{112}$$

Combining inequalities (110) and (112), we deduce that

$$x(h(t_m)) < \frac{2}{c'} x(h(t)) < \left(\frac{2}{c'}\right)^2 x(t_m), \tag{113}$$

which contradicts (107).

The proof of the theorem is complete. □

3.2. ADEs. Analogous oscillation conditions to those obtained for the delay equation (E) can be derived for the (dual) advanced differential equation (E′) by following similar arguments with the ones employed for obtaining Theorems 6–10.

Theorem 11. *Let $\rho(t)$ be defined by (27) and for some $j \in \mathbb{N}$*

$$\begin{gathered}\limsup_{t\to\infty} \int_{t}^{\rho(t)} q(s) \\ \cdot \exp\left(\int_{\rho(t)}^{\sigma(s)} q(u) \exp\left(\int_{u}^{\sigma(u)} Q_j(\xi)\, d\xi\right) du\right) ds \\ > 1,\end{gathered} \tag{114}$$

where

$$\begin{gathered}Q_j(t) = q(t) \left[1 + \int_{t}^{\sigma(t)} q(s) \right. \\ \left. \cdot \exp\left(\int_{t}^{\sigma(s)} q(u) \exp\left(\int_{u}^{\sigma(u)} Q_{j-1}(\xi)\, d\xi\right) du\right) ds\right]\end{gathered} \tag{115}$$

with $Q_0(t) = \lambda_0 q(t)$, and let λ_0 be the smaller root of the equation $\lambda = e^{\beta\lambda}$. Then all solutions of (E′) oscillate.

Theorem 12. *Let $\rho(t)$ be defined by (27) and $\beta \in (0, 1/e]$. If for some $j \in \mathbb{N}$*

$$\begin{gathered}\limsup_{t\to\infty} \int_{t}^{\rho(t)} q(s) \\ \cdot \exp\left(\int_{\rho(t)}^{\sigma(s)} q(u) \exp\left(\int_{u}^{\sigma(u)} Q_j(\xi)\, d\xi\right) du\right) ds \\ > 1 - D(\beta),\end{gathered} \tag{116}$$

where Q_j is defined by (115), then all solutions of (E′) oscillate.

Theorem 13. *Let $\rho(t)$ be defined by (27) and $\beta \in (0, 1/e]$. If for some $j \in \mathbb{N}$*

$$\begin{gathered}\limsup_{t\to\infty} \int_{t}^{\rho(t)} q(s) \\ \cdot \exp\left(\int_{t}^{\sigma(s)} q(u) \exp\left(\int_{u}^{\sigma(u)} Q_j(\xi)\, d\xi\right) du\right) ds \\ > \frac{1}{D(\beta)},\end{gathered} \tag{117}$$

where Q_j is defined by (115), then all solutions of (E′) oscillate.

Theorem 14. *Let $\rho(t)$ be defined by (27) and $\beta \in (0, 1/e]$. If for some $j \in \mathbb{N}$*

$$\limsup_{t\to\infty} \int_t^{\rho(t)} q(s) \cdot \exp\left(\int_{\rho(s)}^{\sigma(s)} q(u) \exp\left(\int_u^{\sigma(u)} Q_j(\xi)\, d\xi\right) du\right) ds > \frac{1+\ln\lambda_0}{\lambda_0} - D(\beta), \tag{118}$$

where Q_j is defined by (115) and λ_0 is the smaller root of the equation $\lambda = e^{\beta\lambda}$, then all solutions of (E') oscillate.

Theorem 15. *Let $\rho(t)$ be defined by (27). If for some $j \in \mathbb{N}$*

$$\liminf_{t\to\infty} \int_t^{\rho(t)} q(s) \cdot \exp\left(\int_{\rho(s)}^{\sigma(s)} q(u) \exp\left(\int_u^{\sigma(u)} Q_j(\xi)\, d\xi\right) du\right) ds > \frac{1}{e}, \tag{119}$$

where Q_j is defined by (115), then all solutions of (E') oscillate.

3.3. Differential Inequalities. A slight modification in the proofs of Theorems 6–15 leads to the following results about differential inequalities.

Theorem 16. *Assume that all the conditions of Theorem 6 [11], 7 [12], 8 [13], 9 [14], or 10 [15] hold. Then*

(i) the delay [advanced] differential inequality

$$x'(t) + p(t)\, x(\tau(t)) \le 0 \quad \left[x'(t) - q(t)\, x(\sigma(t)) \ge 0\right], \quad t \ge t_0 \tag{120}$$

has no eventually positive solutions;

(ii) the delay [advanced] differential inequality

$$x'(t) + p(t)\, x(\tau(t)) \ge 0 \quad \left[x'(t) - q(t)\, x(\sigma(t)) \le 0\right], \quad t \ge t_0 \tag{121}$$

has no eventually negative solutions.

Remark 17. The oscillation criteria established in this paper all depend on λ_0 (see, e.g., (37) and (71)) in contrast to the conditions obtained in [15, 16] and in [17, for $m = 1$]. In fact, the left-hand side of conditions (37) and (71) depends on λ_0, which is not the case with the left-hand side of conditions (20) and (21). Since $\lambda_0 > 1$ when $\alpha \in (0, 1/e]$, it is obvious that

$$P_0(t) = \lambda_0 p(t) > p(t) = p_0(t). \tag{122}$$

Consequently, the left-hand side of conditions (37) and (71) is greater than the corresponding parts of (20) and (21), respectively. This is the reason why the conditions in this paper improve on all known conditions mentioned in Section 2.

4. Examples and Comments

The oscillation tests we have proposed and established, in the main results, involve an iterative procedure. We iteratively compute limsup and liminf on the terms $P_j(t)$ and $Q_j(t)$, $j \in \mathbb{N}$ of a recurrent relation defined on the coefficients and the deviating argument of an equation of the form (E) or (E$'$) to determine whether that equation is oscillatory. But this computation cannot be performed on paper, but by means of a program, numerically computing limsup and liminf. The examples below illustrate the significance of our results and indicate the high level of improvement in the oscillation criteria. The calculations were performed using MATLAB code.

Example 1. Consider the delay differential equation

$$x'(t) + \frac{3}{25} x(\tau(t)) = 0, \quad t \ge 0, \tag{123}$$

with (see Figure 1(a))

$$\tau(t) = \begin{cases} t-1, & \text{if } t \in [8k, 8k+2] \\ -4t+40k+9, & \text{if } t \in [8k+2, 8k+3] \\ 5t-32k-18, & \text{if } t \in [8k+3, 8k+4] \\ -4t+40k+18, & \text{if } t \in [8k+4, 8k+5] \\ 5t-32k-27, & \text{if } t \in [8k+5, 8k+6] \\ -2t+24k+15, & \text{if } t \in [8k+6, 8k+7] \\ 6t-40k-41, & \text{if } t \in [8k+7, 8k+8], \end{cases} \tag{124}$$

where $k \in \mathbb{N}_0$ and $\mathbb{N}_0$ is the set of nonnegative integers.

By (13), we see (Figure 1(b)) that

$$h(t) = \begin{cases} t-1, & \text{if } t \in [8k, 8k+2] \\ 8k+1, & \text{if } t \in \left[8k+2, 8k+\frac{19}{5}\right] \\ 5t-32k-18, & \text{if } t \in \left[8k+\frac{19}{5}, 8k+4\right] \\ 8k+2, & \text{if } t \in \left[8k+4, 8k+\frac{29}{5}\right] \\ 5t-32k-27, & \text{if } t \in \left[8k+\frac{29}{5}, 8k+6\right] \\ 8k+3, & \text{if } t \in \left[8k+6, 8k+\frac{44}{6}\right] \\ 6t-40k-41, & \text{if } t \in \left[8k+\frac{44}{6}, 8k+8\right]. \end{cases} \tag{125}$$

It is obvious that

$$\alpha = \liminf_{t\to\infty} \int_{\tau(t)}^t p(s)\, ds = \liminf_{t\to\infty} \int_{8k+1}^{8k+2} \frac{3}{25} ds = 0.12 \tag{126}$$

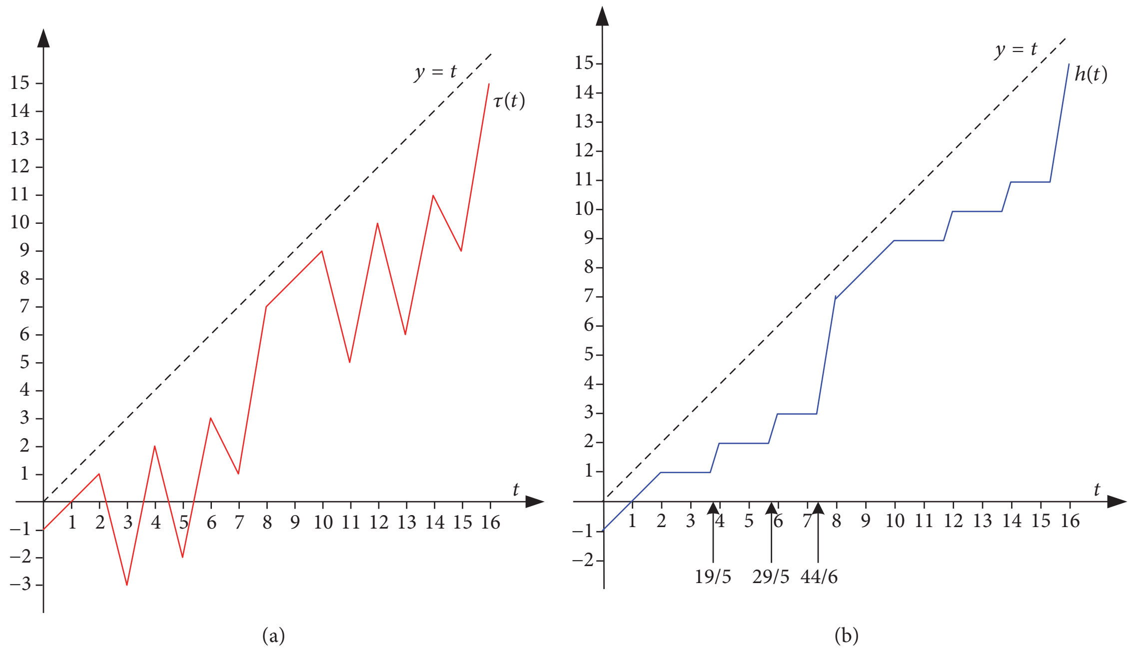

FIGURE 1: The graphs of $\tau(t)$ and $h(t)$.

and therefore, the smaller root of $e^{0.12\lambda} = \lambda$ is $\lambda_0 = 1.14765$.

Observe that the function $F_j : \mathbb{R}_0 \to \mathbb{R}_+$ defined as

$$F_j(t) = \int_{h(t)}^{t} p(s) \cdot \exp\left(\int_{\tau(s)}^{h(t)} p(u) \exp\left(\int_{\tau(u)}^{u} P_j(\xi)\, d\xi\right) du\right) ds \tag{127}$$

attains its maximum at $t = 8k + 44/6$, $k \in \mathbb{N}_0$, for every $j \in \mathbb{N}$. Specifically,

$$F_1\left(t = 8k + \frac{44}{6}\right) = \int_{8k+3}^{8k+44/6} p(s) \cdot \exp\left(\int_{\tau(s)}^{8k+3} p(u) \exp\left(\int_{\tau(u)}^{u} P_1(\xi)\, d\xi\right) du\right) ds \tag{128}$$

with

$$P_1(\xi) = p(\xi)\left[1 + \int_{\tau(\xi)}^{\xi} p(v) \cdot \exp\left(\int_{\tau(v)}^{\xi} p(w) \exp\left(\int_{\tau(w)}^{w} \lambda_0 p(z)\, dz\right) dw\right) dv\right]. \tag{129}$$

Using MATLAB, we obtain

$$F_1\left(t = 8k + \frac{44}{6}\right) \simeq 1.0417 \tag{130}$$

and therefore

$$\limsup_{t\to\infty} F_1(t) \simeq 1.0417 > 1. \tag{131}$$

Hence, condition (37) of Theorem 6 is satisfied, for $j = 1$. Consequently, all solutions of (123) are oscillatory.

Observe, however, that

$$\begin{aligned} \mathrm{LD} &= \limsup_{k\to\infty} \int_{8k+3}^{8k+44/6} \frac{3}{35} ds = 0.52 < 1, \\ \alpha &= 0.12 < \frac{1}{e}, \\ 0.52 &< \frac{1 + \ln \lambda_0}{\lambda_0} - D(\alpha) \simeq 0.9831. \end{aligned} \tag{132}$$

Note that the function Φ_j defined by

$$\Phi_j(t) = \int_{h(t)}^{t} p(s) \exp\left(\int_{h(s)}^{h(t)} p(u)\, \psi_j(u)\, du\right) ds, \quad j \geq 2, \tag{133}$$

attains its maximum at $t = 8k + 44/6$, $k \in \mathbb{N}_0$, for every $j \geq 2$. Specifically,

$$\begin{aligned} &\Phi_2\left(8k + \frac{44}{6}\right) \\ &= \int_{8k+3}^{8k+44/6} p(s) \exp\left(\int_{h(s)}^{8k+3} p(s)\, \psi_2(u)\, du\right) ds \\ &= \int_{8k+3}^{8k+44/6} \frac{3}{25} \exp\left(\int_{h(s)}^{8k+3} \frac{3}{25} \exp\left(\int_{\tau(u)}^{u} \frac{3}{25} \cdot 0\, dw\right) du\right) ds \\ &= \int_{8k+3}^{8k+44/6} \frac{3}{25} \exp\left(\int_{h(s)}^{8k+3} \frac{3}{25} \cdot 1\, du\right) ds \\ &= \frac{3}{25} \cdot \left[\int_{8k+3}^{8k+19/5} \exp\left(\frac{3}{25} \int_{8k+1}^{8k+3} du\right) ds\right. \end{aligned}$$

$$
\begin{aligned}
&+\int_{8k+19/5}^{8k+4}\exp\left(\frac{3}{25}\int_{5s-32k-18}^{8k+3}du\right)ds\\
&+\int_{8k+4}^{8k+29/5}\exp\left(\frac{3}{25}\int_{8k+2}^{8k+3}du\right)ds\\
&+\int_{8k+29/5}^{8k+6}\exp\left(\frac{3}{25}\int_{5s-32k-27}^{8k+3}du\right)ds\\
&+\left.\int_{8k+6}^{8k+44/6}\exp\left(\frac{3}{25}\int_{8k+3}^{8k+3}du\right)ds\right]\simeq 0.57983.
\end{aligned}
\tag{134}
$$

Thus

$$
\limsup_{t\to\infty}\Phi_2(t)\simeq 0.57983<1-D(\alpha)\simeq 0.99174. \tag{135}
$$

Also

$$
\begin{aligned}
&\limsup_{t\to\infty}\int_{h(t)}^{t}p(s)\exp\left(\int_{\tau(s)}^{h(t)}p(u)\,du\right)ds\\
&\quad=\limsup_{k\to\infty}\int_{8k+3}^{8k+44/6}\frac{3}{25}\exp\left(\int_{\tau(s)}^{8k+3}\frac{3}{25}du\right)ds\\
&\quad=\frac{3}{25}\cdot\limsup_{t\to\infty}\left[\int_{8k+3}^{8k+4}\exp\left(\frac{3}{25}\int_{5s-32k-18}^{8k+3}du\right)ds\right.\\
&\quad+\int_{8k+4}^{8k+5}\exp\left(\frac{3}{25}\int_{-4s+40k+18}^{8k+3}du\right)ds\\
&\quad+\int_{8k+5}^{8k+6}\exp\left(\frac{3}{25}\int_{5s-32k-27}^{8k+3}du\right)ds\\
&\quad+\int_{8k+6}^{8k+7}\exp\left(\frac{3}{25}\int_{-2s+24k+15}^{8k+3}du\right)ds\\
&\quad+\left.\int_{8k+7}^{8k+44/6}\exp\left(\frac{3}{25}\int_{6s-40k-41}^{8k+3}du\right)ds\right]\simeq 0.7043\\
&\quad<1,\\
&0.7043<1-D(\alpha)\simeq 0.99174.
\end{aligned}
\tag{136}
$$

In addition,

$$
\begin{aligned}
&\limsup_{t\to\infty}\int_{h(t)}^{t}p(s)\exp\left(\int_{\tau(s)}^{h(t)}p_1(u)\,du\right)ds\simeq 0.8052\\
&\quad<1,\\
&0.8052<1-D(\alpha)\simeq 0.99174.
\end{aligned}
\tag{137}
$$

That is, none of conditions (8), (9), (12), (14) (for $j=2$), (16), (17), (20) (for $j=1$), and (21) (for $j=1$) is satisfied.

Comment. The improvement of condition (37) over the corresponding condition (8) is significant, approximately 100.33%. We get this measure by comparing the values, in the left-hand side of those conditions. Also, the improvement over conditions (14), (16), and (20) is very satisfactory, around 79.66%, 47.9%, and 29.37%, respectively. In addition, condition (37) is satisfied from the first iteration, while conditions (14), (20), and (21) need more than one iteration.

Example 2 (taken and adapted from [17]). Consider the advanced differential equation

$$
x'(t)-\frac{333}{2500}x(\sigma(t))=0,\quad t\ge 0, \tag{138}
$$

with (see Figure 2(a))

$$
\sigma(t)=\begin{cases}5k+3, & \text{if } t\in[5k,5k+1]\\ 4t-15k-1, & \text{if } t\in[5k+1,5k+2]\\ -3t+20k+13, & \text{if } t\in[5k+2,5k+3]\\ 5t-20k-11, & \text{if } t\in[5k+3,5k+4]\\ -t+10k+13, & \text{if } t\in[5k+4,5k+5],\end{cases} \tag{139}
$$

where $k\in\mathbb{N}_0$ and $\mathbb{N}_0$ is the set of nonnegative integers.

By (27), we see (Figure 2(b)) that

$$
\rho(t)=\begin{cases}5k+3, & \text{if } t\in[5k,5k+1]\\ 4t-15k-1, & \text{if } t\in[5k+1,5k+1.25]\\ 5k+4, & \text{if } t\in[5k+1.25,5k+3]\\ 5t-20k-11, & \text{if } t\in[5k+3,5k+3.8]\\ 5k+8, & \text{if } t\in[5k+3.8,5k+5].\end{cases} \tag{140}
$$

It is obvious that

$$
\beta=\liminf_{t\to\infty}\int_{5k+3}^{5k+4}\frac{333}{2500}ds=0.1332 \tag{141}
$$

and therefore, the smaller root of $e^{0.1332\lambda}=\lambda$ is $\lambda_0=1.16839$.

Observe, that the function $G_j:\mathbb{R}_0\to\mathbb{R}_+$ defined as

$$
\begin{aligned}
G_j(t)&=\int_{t}^{\rho(t)}q(s)\\
&\cdot\exp\left(\int_{\rho(t)}^{\sigma(s)}q(u)\exp\left(\int_{u}^{\sigma(u)}Q_j(\xi)\,d\xi\right)du\right)ds
\end{aligned}
\tag{142}
$$

attains its maximum at $t=5k+3.8$, $k\in\mathbb{N}_0$, for every $j\in\mathbb{N}$. Specifically,

$$
\begin{aligned}
G_1(t=5k+3.8)&=\int_{5k+3.8}^{5k+8}q(s)\\
&\cdot\exp\left(\int_{5k+8}^{\sigma(s)}q(u)\exp\left(\int_{u}^{\sigma(u)}Q_1(\xi)\,d\xi\right)du\right)ds
\end{aligned}
\tag{143}
$$

with

$$
\begin{aligned}
Q_1(\xi)&=q(\xi)\left[1+\int_{\xi}^{\sigma(\xi)}q(v)\right.\\
&\cdot\left.\exp\left(\int_{\xi}^{\sigma(v)}q(w)\exp\left(\int_{w}^{\sigma(w)}\lambda_0 q(z)\,dz\right)dw\right)dv\right].
\end{aligned}
\tag{144}
$$

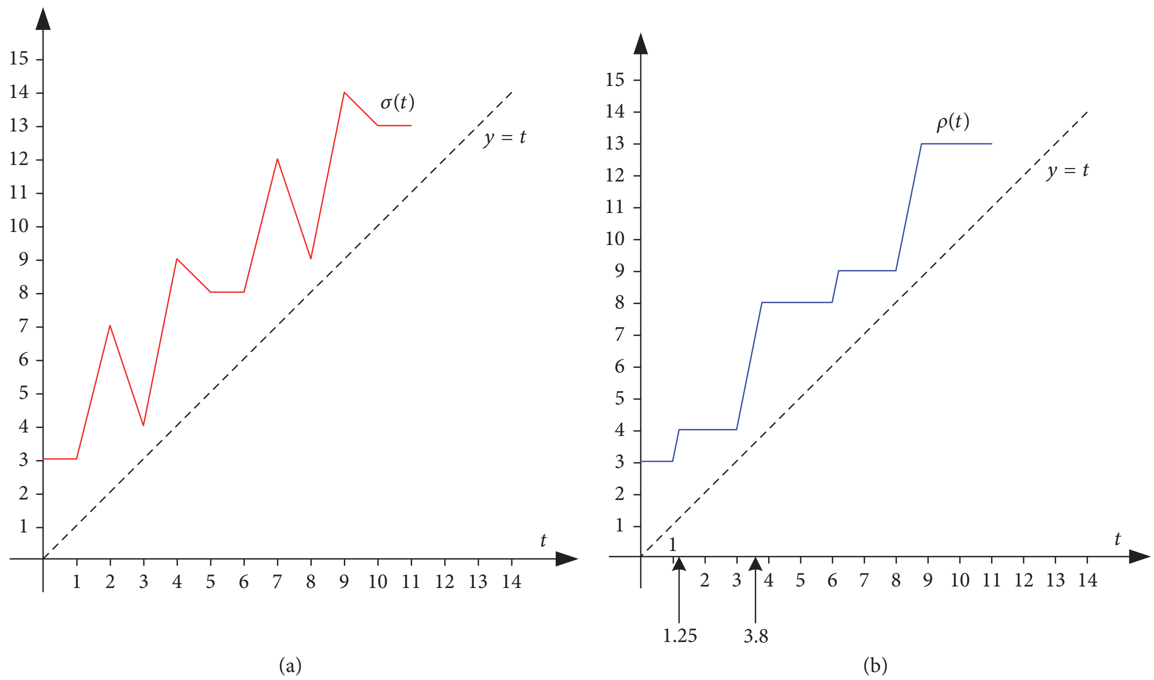

Figure 2: The graphs of $\sigma(t)$ and $\rho(t)$.

Using MATLAB, we obtain

$$G_1\left(t = 5k + 3.8\right) \simeq 0.9915. \tag{145}$$

Therefore

$$\limsup_{t\to\infty} G_1\left(t\right) \simeq 0.9915 > 1 - D\left(\beta\right) \simeq 0.9896. \tag{146}$$

Hence, condition (116) of Theorem 12 is satisfied, for $j = 1$. Consequently, all solutions of (138) oscillate.

Observe, however, that

$$\begin{aligned}
&LA = \limsup_{k\to\infty} \int_{5k+3.8}^{5k+8} \frac{333}{2500} ds = 0.55944 < 1, \\
&\beta = 0.1332 < \frac{1}{e}, \\
&\limsup_{t\to\infty} \int_{t}^{\rho(t)} q\left(s\right) \exp\left(\int_{\rho(t)}^{\sigma(s)} q\left(u\right) du\right) ds \\
&\quad = \limsup_{k\to\infty} \int_{5k+3.8}^{5k+8} q\left(s\right) \exp\left(\int_{5k+8}^{\sigma(s)} q\left(u\right) du\right) ds \\
&\quad = \limsup_{k\to\infty} \left[\int_{5k+3.8}^{5k+4} q\left(s\right)\right. \\
&\quad \cdot \exp\left(\int_{5k+8}^{5s-20k-11} q\left(u\right) du\right) ds + \int_{5k+4}^{5k+5} q\left(s\right) \\
&\quad \cdot \exp\left(\int_{5k+8}^{-s+10k+13} q\left(u\right) du\right) ds + \int_{5k+5}^{5k+6} q\left(s\right) \\
&\quad \cdot \exp\left(\int_{5k+8}^{5k+8} q\left(u\right) du\right) ds + \int_{5k+6}^{5k+7} q\left(s\right) \\
&\quad \cdot \exp\left(\int_{5k+8}^{4s-15k-16} q\left(u\right) du\right) ds + \int_{5k+7}^{5k+8} q\left(s\right) \\
&\quad \left.\cdot \exp\left(\int_{5k+8}^{-3s+20k+33} q\left(u\right) du\right) ds\right] \simeq 0.6672 < 1, \\
&\liminf_{t\to\infty} \int_{t}^{\rho(t)} q\left(s\right) \exp\left(\int_{\rho(t)}^{\sigma(s)} q\left(u\right) du\right) ds \\
&\quad = \liminf_{t\to\infty} \int_{5k+3}^{5k+4} q\left(s\right) \exp\left(\int_{5k+4}^{\sigma(s)} q\left(u\right) du\right) ds \\
&\quad \simeq 0.1893 < \frac{1}{e}, \\
&\limsup_{t\to\infty} \int_{t}^{\rho(t)} q\left(s\right) \exp\left(\int_{\rho(t)}^{\sigma(s)} q_1\left(u\right) du\right) ds \simeq 0.7196 \\
&\quad < 1, \\
&0.7196 < 1 - D\left(\beta\right) \simeq 0.9896.
\end{aligned} \tag{147}$$

That is, none of conditions (24), (25), (28), (29), (30) (for $j = 1$), and (31) (for $j = 1$) is satisfied.

Comment. The improvement of condition (116) over the corresponding condition (24) is significant, approximately 77.23%. We get this measure by comparing the values, in the left-hand side of those conditions. Also, the improvement over conditions (28) and (30) is very satisfactory, around 48.61% and 37.78%, respectively. In addition, condition (116) is satisfied from the first iteration, while conditions (30) and (31) need more than one iteration.

Remark 3. Similarly, one can provide examples, illustrating the other main results.

5. Concluding Remarks

In the present paper, we have considered the oscillatory dynamics of differential equations, having nonmonotone deviating arguments and nonnegative coefficients. New sufficient conditions have been established, for the oscillation of all solutions of (E) and (E′). These conditions include (37), (71), (75), (83), and (97) and (114), (116), (117), (118), and (119), for (E) and (E′), respectively. Applying these conditions involves a procedure that checks for oscillations by iteratively computing limsup and liminf, on terms recursively defined on the equation's coefficients and deviating argument.

The main advantage of these conditions is that they achieve a major improvement over all the related oscillation conditions for (E) [(E′)], in the literature. For example, condition (37) [(114)] improves upon the noniterative conditions that are reviewed in the introduction, namely, conditions (8) [(24)], (12), (16)≡(20) (for $j = 1$) [(28)≡(30) (for $j = 1$)], and (17)≡(21) (for $j = 1$) [(31) (for $j = 1$)]. That immediately becomes evident by inspecting the left-hand side of (37) [(114)] and the left-hand side of each of the above conditions.

The improvement of (37) [(114)] over the other iterative conditions, namely, (14) (for j > 2), (20) (for $j > 1$) [(30) (for $j > 1$)], and (21) (for $j > 1$) [(31) (for $j > 1$)], is that it requires far fewer iterations to establish oscillation than the other conditions.

This advantage, easily, can be verified computationally, by running the MATLAB programs (see Appendix), for computing limsup and liminf and comparing the number of iterations required by each condition to establish oscillation. Then we see that we achieve a significant improvement over all known oscillation criteria.

Another advantage and a significant departure from the large majority of the other studies is that the criteria in this paper apply to a more general class of equations, having nonmonotone arguments $\tau(t)$ or $\sigma(t)$, in contrast to most of the other oscillation criteria that apply to equations with nondecreasing arguments.

Appendix

In this appendix, for completeness, we give the algorithm on MATLAB software used in Example 1 for calculation of $\limsup_{t\to\infty} F_1(t) \simeq 1.0417$. For Example 2, the algorithm is omitted since it is similar to the one in Example 1.

Algorithm for Example 1

```
clear; clc;
c = .12;
n = 50;
λ0 = 1.14765;
a5 = 19;
b5 = 70/3;
h5 = (b5 − a5)/n;
for i5 = 1 : 1 : n + 1;
x5 = a5 + (i5 − 1) ∗ h5;
a4 = TFunction(x5);
b4 = 19;
h4 = (b4 − a4)/n;
for i4 = 1 : 1 : n + 1;
x4 = a4 + (i4 − 1) ∗ h4;
a3 = TFunction(x4);
b3 = x4;
h3 = (b3 − a3)/n;
for i3 = 1 : 1 : n + 1;
x3 = a3 + (i3 − 1) ∗ h3;
a2 = TFunction(x3);
b2 = x3;
h2 = (b2 − a2)/n;
for i2 = 1 : 1 : n + 1;
x2 = a2 + (i2 − 1) ∗ h2;
a1 = TFunction(x2);
b1 = x3;
h1 = (b1 − a1)/n;
for i1 = 1 : 1 : n + 1;
x1 = a1 + (i1 − 1) ∗ h1;
f1(i1) = c ∗ exp(λ0 ∗ c ∗ (x1 − TFunction(x1)));
end
I1 = f1(1) + f1(n + 1);
for i1 = 2 : 2 : n;
I1 = I1 + f1(i1) ∗ 4;
end
for i1 = 3 : 2 : n − 1;
I1 = I1 + f1(i1) ∗ 2;
end
I1 = I1 ∗ h1/3;
f2(i2) = c ∗ exp(I1);
end
I2 = f2(1) + f2(n + 1);
for i2 = 2 : 2 : n;
I2 = I2 + f2(i2) ∗ 4;
end
for i2 = 3 : 2 : n − 1;
I2 = I2 + f2(i2) ∗ 2;
end
I2 = I2 ∗ h2/3;
f3(i3) = c ∗ (1 + I2);
end
```

```
I3 = f3(1) + f3(n + 1);
for i3 = 2 : 2 : n;
I3 = I3 + f3(i3) * 4;
end
for i3 = 3 : 2 : n − 1;
I3 = I3 + f3(i3) * 2;
end
I3 = I3 * h3/3;
f4(i4) = c * exp(I3);
end
I4 = f4(1) + f4(n + 1);
for i4 = 2 : 2 : n;
I4 = I4 + f4(i4) * 4;
end
for i4 = 3 : 2 : n − 1;
I4 = I4 + f4(i4) * 2;
end
I4 = I4 * h4/3;
f5(i5) = c * exp(I4);
end
I5 = f5(1) + f5(n + 1);
for i5 = 2 : 2 : n;
I5 = I5 + f5(i5) * 4;
    end
    for i5 = 3 : 2 : n − 1;
    I5 = I5 + f5(i5) * 2;
    end
    I5 = I5 * h5/3
```

Algorithms for functions $\tau(t)$ and $h(t)$

```
function[a] = TFunction(x)
r = mod(x, 8);
k = floor(x/8);
if (r >= 0) && (r < 2)
a = x − 1;
end
if (r >= 2) && (r < 3)
a = −4 * x + 40 * k + 9;
end
if (r >= 3) && (r < 4)
a = 5 * x − 32 * k − 18;
end
if (r >= 4) && (r < 5)
a = −4 * x + 40 * k + 18;
end
if (r >= 5) && (r < 6)
a = 5 * x − 32 * k − 27;
end
if (r >= 6) && (r < 7)
a = −2 * x + 24 * k + 15;
end
if (r >= 7) && (r < 8)
a = 6 * x − 40 * k − 41;
end
end
function[a] = HFunction(x)
r = mod(x, 8);
k = floor(x/8);
if (r >= 0) && (r < 2)
a = x − 1;
end
if (r >= 2) && (r < 19/5)
a = 8 * k + 1;
end
if (r >= 19/5) && (r < 4)
a = 5 * x − 32 * k − 18;
end
if (r >= 4) && (r < 29/5)
a = 8 * k + 2;
end
if (r >= 29/5) && (r < 6)
a = 5 * x − 32 * k − 27;
end
if (r >= 6) && (r < 44/6)
a = 8 * k + 3;
end
if (r >= 44/6) && (r < 8)
a = 6 * x − 40 * k − 41;
end
end
```

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Research Article

Bifurcations and Dynamics of the Rb-E2F Pathway Involving miR449

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We focused on the gene regulative network involving Rb-E2F pathway and microRNAs (miR449) and studied the influence of time delay on the dynamical behaviors of Rb-E2F pathway by using Hopf bifurcation theory. It is shown that under certain assumptions the steady state of the delay model is asymptotically stable for all delay values; there is a critical value under another set of conditions; the steady state is stable when the time delay is less than the critical value, while the steady state is changed to be unstable when the time delay is greater than the critical value. Thus, Hopf bifurcation appears at the steady state when the delay passes through the critical value. Numerical simulations were presented to illustrate the theoretical results.

1. Introduction

In the last few years, an increasing number of noncoding RNA (or microRNA) have been discovered to play central regulatory roles in gene regulation processes of prokaryotes and eukaryotes [1]. It has become evident that miRNAs regulate a variety of biological processes, and their expression is often deregulated in human malignancy. On one hand, miRNAs play roles in tumorigenesis by modulating oncogenic and tumor suppressor pathways. On the other hand, the expressions of miRNAs can be regulated by several oncogenic or tumor suppressor transcription factors [2]. In this paper, we focus on miR449, which can induce cell senescence and apoptosis and act as a tumor suppressor through regulating Rb/E2F activity [2, 3]. In recent years, large numbers of researches have focused on the mechanisms controlling cellular proliferation associated with human cancer regulated by Rb-E2F pathway experimentally [4–7]. Rb and E2F proteins play important roles in the regulation of cell division, cell growth, and programmed cell death by controlling the expressions of genes involved in these processes, which are best known for their regulation of the cell cycle at the G1/S transition [8]. As the first identified tumor suppressor gene [9], Rb is recognized to play a fundamental role in a signaling pathway that controls cell proliferation [10]. Rb regulates the transcription of genes that are essential for DNA replication and cell cycle progression by binding and inhibiting E2F transcription factors [11]. In the Rb-E2F pathway including negative feedback loops involving miR449, miR449 provides a twofold safety mechanism to avoid excessive E2F-induced proliferation by cell cycle arrest and apoptosis [12]. Mathematical models have been established to explain the nonlinear dynamical behaviors of the Rb-E2F pathway [12–14], which mainly concentrate on the stability and bifurcation of the deterministic systems, but not taking into account the effects of time delay.

Time delay is one of the most important characteristics of gene regulation. In many cases, a gene regulates the expression of another gene by its products (RNAs or proteins). Since it takes time to generate those products and different processes need different amounts of time, time delayed regulation is ubiquitous in cellular processes [15]. Time-delay system is also called system with aftereffect or hereditary system [16, 17], and it is common in mathematical biology, such as population dynamics, the chemostat, neural network, blood cell maturation, transcriptional regulator dynamics, virus dynamics, and genetic network [18–23]. Recent papers have demonstrated that complex dynamical behaviors can arise

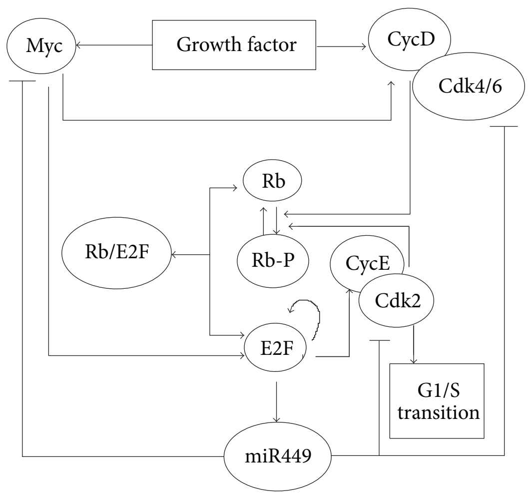

Figure 1: Rb-E2F pathway mediated by miR449.

as a consequence of time delays in biological systems. For example, in gene regulatory networks, time delays may lead to oscillations in protein levels and existing oscillations may become more robust [24, 25]. Oscillatory cellular dynamics, in particular periodic oscillation, plays an important role in maintaining homeostasis of living organisms. In addition, taking into account time delays in models of gene regulatory networks is often essential to capture the whole range of dynamic behaviors. For example, in experiments, a single self-repressed gene has been observed to display oscillatory behavior, but which cannot be deduced by models that ignore time delays. However, this oscillatory behavior is reproduced by a mathematical model including time delays. In addition, theoretical analysis that ignored time delays led to the erroneous conclusion that oscillations were not possible for this single gene [18, 26]. Many kinds of methods have been introduced to infer time delayed gene regulatory network [27–31]. Here, we mainly use the local linearization approach to analyze the nonlinear system.

In this paper, firstly, we will introduce Rb-E2F pathway network involving miR449 modeled by time delayed differential equations. Secondly, we will study the dynamical behaviors of the model and derive sufficient conditions of the oscillation by using Hopf bifurcation theory. Particularly, we will also prove that there are periodic solutions under certain conditions. Finally, numerical simulations will be showed to illustrate the theoretical results.

2. A Simple Gene Regulatory Network Mediated by miR449

2.1. A Simple Mathematical Model of Gene Regulation with a Delayed Negative Feedback Loop. A simplified model (Figure 1) of the Rb-E2F pathway begins with growth signals activating CycD. Initially, E2F is bound to and repressed by Rb, a tumor suppressor protein that is dysfunctional in several major cancers. CycD represses the repressor Rb and allows E2F to be turned on. Myc also induces E2F transcription. Subsequently, E2F activates the transcription of CycE, which forms a complex with Cdk2 to further remove Rb repression, establishing a positive feedback loop. E2F also activates its own transcription, constituting another positive feedback loop. An interesting addition to the regulatory mechanism of Rb-E2F network is the recent discovery that miR449 modulates E2F activity. It has been demonstrated that E2F strongly upregulates the expression of miR449. In turn, E2F is inhibited by miR449 through regulating different transcripts. On one hand, miR449 directly affects level of its target transcript Myc and therefore lowers E2F concentration. On the other hand, miR449 directly affects E2F inducer Cdk6 and CycE, thus forming negative feedback loops [12, 14]. Yao et al. [14] provided a mathematical model in the absence of miR449 and indicated that the Rb-E2F pathway acts as a bistable switch to convert signal inputs into all-or-none E2F responses. Yan et al. [12] gave another mathematical model and further investigated the stabilities and bifurcations of E2F, CycE, and miR449 in the participation of miR449. Our main work in this paper is considering the effects of time delays on the dynamic behaviors of the model including miR449. When time delays are taken into account, the time delayed differential equation model of the network including miR449 is described by the following system:

$$\begin{aligned}
\frac{dx_1}{dt} &= k_{11}\frac{x_3}{k_{12}+x_3}\frac{x_1}{k_{13}+x_1} + k_{14}\frac{x_3}{k_{15}+x_3} \\
&\quad + k_{16}x_4\frac{x_8}{k_{17}+x_8} + k_{18}x_5\frac{x_8}{k_{19}+x_8} - k_{110}x_1 \\
&\quad - k_{111}x_6x_1, \\
\frac{dx_2}{dt} &= k_{21}\frac{x_1}{k_{22}+x_1} - k_{23}x_2 - k_{24}x_2\frac{x_3}{k_{25}+x_3} \\
&\quad - k_{26}x_2\frac{x_4}{k_{27}+x_4} - k_{28}x_2\frac{x_5}{k_{29}+x_5}, \\
\frac{dx_3}{dt} &= k_{31}\frac{S}{k_{32}+S} - k_{33}x_3 - k_{34}x_2\left(t-\tau_1\right)\frac{x_3}{k_{35}+x_3}, \\
\frac{dx_4}{dt} &= k_{41}\frac{S}{k_{42}+S} + k_{43}\frac{x_3}{k_{44}+x_3} - k_{45}x_4 \\
&\quad - k_{46}x_2\left(t-\tau_2\right)\frac{x_4}{k_{47}+x_4}, \\
\frac{dx_5}{dt} &= k_{51}\frac{x_1}{k_{52}+x_1} - k_{53}x_5 - k_{54}x_2\left(t-\tau_3\right)\frac{x_5}{k_{55}+x_5}, \\
\frac{dx_6}{dt} &= k_{61} + k_{62}\frac{x_7}{k_{63}+x_7} - k_{64}x_6x_1 - k_{65}x_4\frac{x_8}{k_{78}+x_8} \\
&\quad - k_{67}x_5\frac{x_6}{k_{68}+x_6} - k_{69}x_6, \\
\frac{dx_7}{dt} &= k_{71}x_4\frac{x_6}{k_{72}+x_6} + k_{73}x_5\frac{x_6}{k_{74}+x_6} \\
&\quad + k_{75}x_4\frac{x_8}{k_{76}+x_8} + k_{77}x_5\frac{x_8}{k_{78}+x_8} \\
&\quad - k_{79}\frac{x_7}{k_{710}+x_7} - k_{711}x_7,
\end{aligned}$$

$$\frac{dx_8}{dt} = k_{81}x_6x_1 - k_{82}x_4\frac{x_8}{k_{83}+x_8} - k_{84}x_5\frac{x_8}{k_{85}+x_8} - k_{86}x_8. \tag{1}$$

$x_1, x_2, x_3, x_4, x_5, x_6, x_7, x_8$ represent the concentrations of E2F, miR449, Myc, CycD-Cdk4/6 complex, CycE-Cdk2 complex, Rb, phosphorylated Rb, and Rb/E2F complex, respectively. And S is intensity of growth factor. In the following simulations, all the values of parameters are shown in Table 1 unless specified elsewhere.

2.2. Oscillation Induced by Time Delay. In this subsection, we consider system (1) with $(x_1, x_2, x_3, x_4, x_5, x_6, x_7, x_8)$ as state variables. The linearized system of (1) at equilibrium point $(x_{10}, x_{20}, x_{30}, x_{40}, x_{50}, x_{60})$ is as follows:

$$\frac{dx}{dt} = A_0x + B_0x(t-\tau), \quad x = (x_1, x_2, x_3, x_4, x_5, x_6, x_7, x_8)^T. \tag{2}$$

$$A_0 = \begin{pmatrix} a_{11} & 0 & a_{13} & a_{14} & a_{15} & a_{16} & 0 & a_{18} \\ a_{21} & a_{22} & a_{23} & a_{24} & a_{25} & 0 & 0 & 0 \\ 0 & 0 & a_{33} & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & a_{43} & a_{44} & 0 & 0 & 0 & 0 \\ a_{51} & 0 & 0 & 0 & a_{55} & 0 & 0 & 0 \\ a_{61} & 0 & 0 & a_{64} & a_{65} & a_{66} & a_{67} & 0 \\ 0 & 0 & 0 & a_{74} & a_{75} & a_{76} & a_{77} & a_{78} \\ a_{81} & 0 & 0 & a_{84} & a_{85} & a_{86} & 0 & a_{88} \end{pmatrix},$$
$$B_0 = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & b_{32} & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & b_{42} & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & b_{52} & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}, \tag{3}$$

where

$$a_{11} = \frac{k_{11}x_{30}}{(k_{12}+x_{30})(k_{13}+x_{10})} - \frac{k_{11}x_{30}x_{10}}{(k_{12}+x_{30})(k_{13}+x_{10})^2} - k_{110} - k_{111}x_{60},$$

$$a_{13} = \frac{k_{11}x_{10}}{(k_{12}+x_{30})(k_{13}+x_{10})} - \frac{k_{11}x_{30}x_{10}}{(k_{13}+x_{10})(k_{12}+x_{30})^2}\frac{k_{14}}{k_{15}+x_{30}}$$

Table 1: Parameters for the model.

Rate constant	Value
k_{11}	0.4
k_{12}	0.15
k_{13}	0.15
k_{14}	0.003
k_{15}	0.15
k_{16}	18
k_{17}	0.92
k_{18}	18
k_{19}	0.92
k_{110}	0.25
k_{111}	180
k_{21}	1.4
k_{22}	0.15
k_{23}	0.02
k_{24}	0.6
k_{25}	0.15
k_{26}	1
k_{27}	0.92
k_{28}	0.7
k_{29}	0.92
k_{31}	1
k_{32}	0.5
k_{33}	0.7
k_{34}	0.6
k_{35}	0.15
k_{41}	0.45
k_{42}	0.5
k_{43}	0.03
k_{44}	0.15
k_{45}	1.5
k_{46}	1
k_{47}	0.92
k_{51}	0.35
k_{52}	0.15
k_{53}	1.5
k_{54}	0.7
k_{55}	0.92
k_{61}	0.18
k_{62}	3.6
k_{63}	0.01
k_{64}	180
k_{65}	18
k_{66}	0.92
k_{67}	18
k_{68}	0.92
k_{69}	0.06
k_{71}	18
k_{72}	0.92
k_{73}	18

Table 1: Continued.

Rate constant	Value
k_{74}	0.92
k_{75}	18
k_{76}	0.92
k_{77}	18
k_{78}	0.92
k_{79}	3.6
k_{710}	0.01
k_{711}	0.06
k_{81}	180
k_{82}	18
k_{83}	0.92
k_{84}	18
k_{85}	0.92
k_{86}	0.03

Note. The descriptions of the parameters in Table 1 are shown in [13, 15].

$$- \frac{k_{14}x_{30}}{(k_{15}+x_{30})^2},$$

$$a_{14} = \frac{k_{16}x_{80}}{k_{17}+x_{80}},$$

$$a_{15} = \frac{k_{18}x_{80}}{k_{19}+x_{80}},$$

$$a_{16} = -k_{111}x_{10},$$

$$a_{18} = \frac{k_{16}x_{40}}{k_{17}+x_{80}} - \frac{k_{16}x_{40}x_{80}}{(k_{17}+x_{80})^2} + \frac{k_{18}}{k_{50}}k_{19} + x_{80} - \frac{k_{18}x_{50}x_{80}}{(k_{19}+x_{80})^2},$$

$$a_{21} = \frac{k_{21}}{k_{22}+x_{10}} - \frac{k_{21}x_{10}}{(k_{22}+x_{10})^2},$$

$$a_{22} = -k_{23} - \frac{k_{24}x_{30}}{k_{25}+x_{30}} - \frac{k_{26}x_{40}}{k_{27}+x_{40}} - \frac{k_{28}x_{50}}{k_{29}+x_{50}},$$

$$a_{23} = -\frac{k_{24}x_{20}}{k_{25}+x_{30}} + \frac{k_{24}x_{20}x_{30}}{(k_{25}+x_{30})^2},$$

$$a_{24} = -\frac{k_{26}x_{20}}{k_{27}+x_{40}} + \frac{k_{26}x_{20}x_{40}}{(k_{27}+x_{40})^2},$$

$$a_{25} = -\frac{k_{28}x_{20}}{k_{29}+x_{50}} + \frac{k_{28}x_{20}x_{50}}{(k_{29}+x_{50})^2},$$

$$a_{33} = -k_{33} - \frac{k_{34}x_{20}}{k_{35}+x_{30}} + \frac{k_{34}x_{20}x_{30}}{(k_{35}+x_{30})^2},$$

$$a_{43} = \frac{k_{43}}{k_{44}+x_{30}} - \frac{k_{43}x_{30}}{(k_{44}+x_{30})^2},$$

$$a_{44} = -k_{45} - \frac{k_{46}x_{20}}{k_{47}+x_{40}} + \frac{k_{46}x_{20}x_{40}}{(k_{47}+x_{40})^2},$$

$$a_{51} = \frac{k_{51}}{k_{52}+x_{10}} - \frac{k_{51}x_{10}}{(k_{52}+x_{10})^2},$$

$$a_{53} = -k_{53} - \frac{k_{54}x_{20}}{k_{55}+x_{50}} + \frac{k_{54}x_{20}x_{50}}{(k_{55}+x_{50})^2},$$

$$a_{61} = -k_{64}x_{60},$$

$$a_{64} = -\frac{k_{65}x_{60}}{k_{66}+x_{60}},$$

$$a_{65} = -\frac{k_{67}x_{60}}{k_{68}+x_{60}},$$

$$a_{66} = -k_{64}x_{10} - \frac{k_{65}x_{40}}{k_{66}+x_{60}} + \frac{k_{65}x_{40}x_{60}}{(k_{66}+x_{60})^2} - \frac{k_{67}x_{50}}{k_{68}+x_{60}} + \frac{k_{67}x_{50}x_{60}}{(k_{68}+x_{60})^2} - k_{69},$$

$$a_{67} = \frac{k_{62}}{k_{63}+x_{70}} - \frac{k_{62}x_{70}}{(k_{63}+x_{70})^2},$$

$$a_{74} = \frac{k_{71}x_{60}}{k_{72}+x_{60}} + \frac{k_{75}x_{80}}{k_{76}+x_{80}},$$

$$a_{75} = \frac{k_{73}x_{60}}{k_{74}+x_{60}} + \frac{k_{77}x_{80}}{k_{78}+x_{80}},$$

$$a_{76} = \frac{k_{71}x_{40}}{k_{72}+x_{60}} - \frac{k_{71}x_{40}x_{60}}{(k_{72}+x_{60})^2} + \frac{k_{73}x_{50}}{k_{74}+x_{60}} - \frac{k_{73}x_{50}x_{60}}{(k_{74}+x_{60})^2},$$

$$a_{77} = -\frac{k_{79}}{k_{710}+x_{70}} + \frac{k_{79}x_{70}}{(k_{710}+x_{70})^2} - k_{711},$$

$$a_{78} = \frac{k_{75}x_{40}}{k_{76}+x_{80}} - \frac{k_{75}x_{40}x_{80}}{(k_{76}+x_{80})^2} + \frac{k_{77}x_{50}}{k_{78}+x_{80}} - \frac{k_{77}x_{50}x_{80}}{(k_{78}+x_{80})^2},$$

$$a_{81} = k_{81}x_{60},$$

$$a_{84} = -\frac{k_{82}x_{80}}{k_{83}+x_{80}},$$

$$a_{85} = -\frac{k_{84}x_{80}}{k_{85}+x_{80}},$$

$$a_{86} = k_{81}x_{10},$$

$$a_{88} = -\frac{k_{82}x_{40}}{k_{83}+x_{80}} + \frac{k_{82}x_{40}x_{80}}{(k_{83}+x_{80})^2} - \frac{k_{84}x_{50}}{k_{85}+x_{80}}$$

$$+\frac{k_{84}x_{50}x_{80}}{\left(k_{85}+x_{80}\right)^2}-k_{86},$$

$$b_{32}=-\frac{k_{34}x_{30}}{k_{35}+x_{30}},$$

$$b_{42}=-\frac{k_{46}x_{40}}{k_{47}+x_{40}},$$

$$b_{52}=-\frac{k_{54}x_{50}}{k_{55}+x_{50}}. \tag{4}$$

Then we can obtain the characteristic equation of (2) at the equilibrium $(x_{10}, x_{20}, x_{30}, x_{40}, x_{50}, x_{60}, x_{70}, x_{80})$ as follows:

$$\left|\lambda I - A_0 - B_0 e^{-\lambda\tau}\right| = 0, \tag{5}$$

where I is the $8 * 8$ identity matrix, and the characteristic equation (5) has the following form:

$$\begin{aligned}&\lambda^8+A_1\lambda^7+A_2\lambda^6+A_3\lambda^5+A_4\lambda^4+A_5\lambda^3+A_6\lambda^2\\&\quad+A_7\lambda+A_8+\left(B_1\lambda^6+B_2\lambda^5+B_3\lambda^4+B_4\lambda^3+B_5\lambda^2\right.\\&\quad\left.+B_6\lambda+B_7\right)e^{-\lambda\tau_1}+\left(C_1\lambda^6+C_2\lambda^5+C_3\lambda^4+C_4\lambda^3\right.\\&\quad\left.+C_5\lambda^2+C_6\lambda+C_7\right)e^{-\lambda\tau_2}+\left(E_1\lambda^6+E_2\lambda^5+E_3\lambda^4\right.\\&\quad\left.+E_4\lambda^3+E_5\lambda^2+E_6\lambda+E_7\right)e^{-\lambda\tau_3}=0,\end{aligned} \tag{6}$$

where the values of $A_{1-8}, B_{1-7}, C_{1-7}, E_{1-7}$ are showed in the Appendix.

If we assume that $\tau_1 = \tau_2 = \tau_3 = \tau$, we will have

$$\begin{aligned}&\lambda^8+A_1\lambda^7+A_2\lambda^6+A_3\lambda^5+A_4\lambda^4+A_5\lambda^3+A_6\lambda^2\\&\quad+A_7\lambda+A_8+\left(D_1\lambda^6+D_2\lambda^5+D_3\lambda^4+D_4\lambda^3\right.\\&\quad\left.+D_5\lambda^2+D_6\lambda+D_7\right)e^{-\lambda\tau}=0,\end{aligned} \tag{7}$$

where $D_j = B_j + C_j + E_j$, $j = 1, 2, 3, 4, 5, 6, 7$.

(1) If $\tau = 0$, (7) becomes

$$\begin{aligned}&\lambda^8+G_1\lambda^7+G_2\lambda^6+G_3\lambda^5+G_4\lambda^4+G_5\lambda^3+G_6\lambda^2\\&\quad+G_7\lambda+G_8=0,\end{aligned} \tag{8}$$

where

$$\begin{aligned}G_1&=A_1,\\G_2&=A_2+D_1,\\G_3&=A_3+D_2,\\G_4&=A_4+D_3,\\G_5&=A_5+D_4,\\G_6&=A_6+D_5,\\G_7&=A_7+D_6,\\G_8&=A_8+D_7.\end{aligned} \tag{9}$$

According to the Routh-Hurwitz criterion, all roots of (8) have negative real parts if and only if all the subdeterminants in the diagonal are positive; that is,

$$\begin{aligned}H_1&=G_1>0,\\H_2&=\begin{vmatrix}G_1&1\\G_3&G_2\end{vmatrix}>0,\\H_3&=\begin{vmatrix}G_1&1&0\\G_3&G_2&G_1\\G_5&G_4&G_3\end{vmatrix}>0,\\H_4&=\begin{vmatrix}G_1&1&0&0\\G_3&G_2&G_1&1\\G_5&G_4&G_3&G_2\\G_7&G_6&G_5&G_4\end{vmatrix}>0,\\H_5&=\begin{vmatrix}G_1&1&0&0&0\\G_3&G_2&G_1&1&0\\G_5&G_4&G_3&G_2&G_1\\G_7&G_6&G_5&G_4&G_3\\0&G_8&G_7&G_6&G_5\end{vmatrix}>0,\\H_6&=\begin{vmatrix}G_1&1&0&0&0&0\\G_3&G_2&G_1&1&0&0\\G_5&G_4&G_3&G_2&G_1&1\\G_7&G_6&G_5&G_4&G_3&G_2\\0&G_8&G_7&G_6&G_5&G_4\\0&0&0&G_8&G_7&G_6\end{vmatrix}>0,\\H_7&=\begin{vmatrix}G_1&1&0&0&0&0&0\\G_3&G_2&G_1&1&0&0&0\\G_5&G_4&G_3&G_2&G_1&1&0\\G_7&G_6&G_5&G_4&G_3&G_2&G_1\\0&G_8&G_7&G_6&G_5&G_4&G_3\\0&0&0&G_8&G_7&G_6&G_5\\0&0&0&0&0&G_8&G_7\end{vmatrix}>0,\\H_8&=G_8H_7>0.\end{aligned} \tag{10}$$

(2) If $\tau > 0$, considering the transcendental equation (7), clearly $i\omega$ $(\omega > 0)$ is a root of (7) if and only if

$$\begin{aligned}&-\omega^8+A_2\omega^6-A_4\omega^4+A_6\omega^2-A_8\\&\quad+i\left(A_1\omega^7-A_3\omega^5+A_5\omega^3-A_7\omega\right)\\&\quad=-D_1\omega^6+D_3\omega^4-D_5\omega^2+D_7\\&\qquad+i\left(D_2\omega^5-D_4\omega^3+D_6\omega\right)\left(\cos(\omega\tau)-i\sin(\omega\tau)\right).\end{aligned} \tag{11}$$

Separating the real and imaginary parts of (11), we have

$$\begin{aligned} &-\omega^8 + A_2\omega^6 - A_4\omega^4 + A_6\omega^2 - A_8 \\ &\quad = \left(-D_1\omega^6 + D_3\omega^4 - D_5\omega^2 + D_7\right)\cos(\omega\tau) \\ &\qquad + \left(D_2\omega^5 - D_4\omega^3 + D_6\omega\right)\sin(\omega\tau), \\ &A_1\omega^7 - A_3\omega^5 + A_5\omega^3 - A_7\omega \\ &\quad = \left(D_1\omega^6 - D_3\omega^4 + D_5\omega^2 - D_7\right)\sin(\omega\tau) \\ &\qquad + \left(D_2\omega^5 - D_4\omega^3 + D_6\omega\right)\cos(\omega\tau). \end{aligned} \tag{12}$$

Adding up the squares of both equations of (12), we have

$$\begin{aligned} &\omega^{16} + F_1\omega^{14} + F_2\omega^{12} + F_3\omega^{10} + F_4\omega^8 + F_5\omega^6 + F_6\omega^4 \\ &\quad + F_7\omega^2 + F_8 = 0, \end{aligned} \tag{13}$$

where

$$\begin{aligned} F_1 &= -2A_2 + A_1^2, \\ F_2 &= -D_1^2 - 2A_1A_3 + A_2^2 + 2A_4, \\ F_3 &= 2A_1A_5 - 2A_2A_4 - D_2^2 + A_3^2 - 2A_6 + 2D_1D_3, \\ F_4 &= -2A_3A_5 - 2A_1A_7 - D_3^2 + 2D_2D_4 + 2A_2A_6 \\ &\quad + 2A_8 + A_4^2 - 2D_1D_5, \\ F_5 &= -D_4^2 - 2A_4A_6 - 2A_2A_8 - 2D_2D_6 + 2D_3D_5 \\ &\quad + 2D_1D_7 + 2A_3A_7 + A_5^2, \\ F_6 &= -2D_3D_7 + 2D_4D_6 + 2A_4A_8 - 2A_5A_7 + A_6^2 \\ &\quad - D_5^2, \\ F_7 &= -D_6^2 - 2A_6A_8 + 2D_5D_7 + A_7^2, \\ F_8 &= -D_7^2 + A_8^2. \end{aligned} \tag{14}$$

Let $z = \omega^2$; (13) becomes

$$\begin{aligned} &z^8 + F_1z^7 + F_2z^6 + F_3z^5 + F_4z^4 + F_5z^3 + F_6z^2 + F_7z \\ &\quad + F_8 = 0. \end{aligned} \tag{15}$$

Denote

$$\begin{aligned} h(z) &= z^8 + F_1z^7 + F_2z^6 + F_3z^5 + F_4z^4 + F_5z^3 + F_6z^2 \\ &\quad + F_7z + F_8. \end{aligned} \tag{16}$$

Lemma 1. *If $F_8 < 0$, (15) has at least one positive root.*

Proof. Clearly, $h(0) = F_8 < 0$, and $\lim_{z\to\infty}h(z) = \infty$. Hence, there exists $z_0 \in (0,\infty)$, so that $h(z_0) = 0$. This completes the proof. □

Lemma 2. *If $F_8 > 0$, the sufficient condition for (15) has positive roots being $z'(7) > 0$ and $h(z'(7)) < 0$.*

Proof. From (16), we have $h'(z) = 8z^7 + 7F_1z^6 + 6F_2z^5 + 5F_4z + 4F_4z^3 + 3F_5z^2 + 2F_6z + F_7$; suppose the equation $h'(z) = 0$ has seven real roots and satisfies $z'(1) < z'(2) < z'(3) < z'(4) < z'(5) < z'(6) < z'(7)$, and $z'(7)$ is the local minimum value, if $z'(7) > 0$ and $h(z'(7)) < 0$; there exists $z \in (z'(7),\infty)$, so that $h(z) = 0$; this completes the proof. □

Lemma 3. *If $F_8 > 0$, according to the Routh-Hurwitz criterion, all the roots of (15) have negative real parts if and only if the subdeterminants in the diagonal are positive, that is, $\Delta j > 0$, $j = 1, 2, \ldots, 8$.*

Suppose that (15) has positive roots; without loss of generality, we assume that it has eight positive roots, denoted by $z_1, z_2, z_3, z_4, z_5, z_6, z_7, z_8$, respectively. Hence, (13) has eight positive roots, say $\omega_1 = \sqrt{z_1}$, $\omega_2 = \sqrt{z_2}$, $\omega_3 = \sqrt{z_3}$, $\omega_4 = \sqrt{z_4}$, $\omega_5 = \sqrt{z_5}$, $\omega_6 = \sqrt{z_6}$, $\omega_7 = \sqrt{z_7}$, $\omega_8 = \sqrt{z_8}$.

From (12), we can get

$$\tau_k^j = \arccos\left(\frac{R_1R_2 + R_3R_4}{R_2^2 + R_4^2}\right), \quad k = 1, 2, 3, \ldots, 8, \; j = 0, 1, 2, 3, \ldots, \tag{17}$$

where

$$\begin{aligned} R_1 &= -\omega_k^8 + A_2\omega_k^6 - A_4\omega_k^4 + A_6\omega_k^2 - A_8, \\ R_2 &= -D_1\omega_k^6 + D_3\omega_k^4 - D_5\omega_k^2 + D_7, \\ R_3 &= A_1\omega_k^7 - A_3\omega_k^5 + A_5\omega_k^3 - A_7\omega_k, \\ R_4 &= D_2\omega_k^5 - D_4\omega_k^3 + D_6\omega_k. \end{aligned} \tag{18}$$

Define

$$\tau_0 = \tau_{k_0}^{j_0} = \min_{\substack{1\le k\le 8 \\ j\ge 0}} \left\{\tau_k^j\right\}. \tag{19}$$

Let $\lambda(\tau) = \eta(\tau) + i\omega(\tau)$ be the root of (7) satisfying $\eta(\tau_0) = 0$, $\omega(\tau_0) = \omega_0$.

Lemma 4. *Consider the exponential polynomial $P(\lambda, e^{-\lambda\tau_1}, \ldots, e^{-\lambda\tau_m}) = p_1(\lambda) + p_2(\lambda)e^{-\lambda\tau_1} + \cdots + p_m(\lambda)e^{-\lambda\tau_m}$, where $\tau_i > 0$ $(i = 1, 2, \ldots, m)$ and $p_i(\lambda)$ is polynomial about λ. As $(\tau_1, \tau_2, \ldots, \tau_m)$ vary, the sum of the orders of the zeros of $P(\lambda, e^{-\lambda\tau_1}, \ldots, e^{-\lambda\tau_m})$ on the open right half plane can change only if a zero appears on or cross the imaginary axis.*

Then, we have the following theoretical results.

Theorem 5. *Suppose that conditions (10) are satisfied.*

(i) *If $\Delta j > 0$ $(j = 1, 2, \ldots, 8)$, then all roots of (7) have negative real parts for all $\tau \ge 0$; thus the steady state $(x_{10}, x_{20}, x_{30}, x_{40}, x_{50}, x_{60}, x_{70}, x_{80})$ of system (2) is absolutely stable.*

(ii) *If $F_8 < 0$ or $F_8 \ge 0, z'(7) > 0$, and $h(z'(7)) < 0$, then all the roots of (7) have negative real parts when $\tau \in [0, \tau_0)$; thus the steady state of system (2) is asymptotically stable.*

(iii) *If the condition of (ii) is satisfied,* $\tau = \tau_0$, *and* $h'(z_0) \neq 0, z_0 = \omega_0^2$, *then* $\pm i\omega_0$ *is a pair of simple purely imaginary roots of (15) and all other roots have negative real parts. Moreover,* $(d\,\mathrm{Re}\,\lambda(\tau_0)/d\tau)|_{\tau=\tau_0} > 0$. *Thus, system (2) exhibits the Hopf bifurcation at* $(x_{10}, x_{20}, x_{30}, x_{40}, x_{50}, x_{60}, x_{70}, x_{80})$.

3. Numerical Analysis

In this section, we demonstrate the above theoretical results by numerical method. When we take $S = 5$, $k_{21} = 1.4$, and the other parameters are shown in Table 1, system (1) becomes

$$\begin{aligned}
\frac{dx_1}{dt} &= \frac{0.4x_3x_1}{(0.15+x_3)(0.15+x_1)} + \frac{0.003x_3}{0.15+x_3} + \frac{18x_4x_8}{0.92+x_8} + \frac{18x_5x_8}{0.92+x_8} - 0.25x_1 - 180x_6x_1,\\
\frac{dx_2}{dt} &= \frac{1.4x_1}{0.15+x_1} - 0.02x_2 - \frac{0.6x_2x_3}{0.15+x_3} - \frac{x_2x_4}{0.92+x_4} - \frac{0.7x_2x_5}{0.92+x_5},\\
\frac{dx_3}{dt} &= 0.9090909090 - 0.7x_3 - \frac{0.6x_2(t-\tau_1)x_3}{0.15+x_3},\\
\frac{dx_4}{dt} &= 0.4090909090 + \frac{0.03x_3}{0.15+x_3} - 1.5x_4 - \frac{x_2(t-\tau_2)x_4}{0.92+x_4},\\
\frac{dx_5}{dt} &= \frac{0.35x_1}{0.15+x_1} - 1.5x_5 - \frac{0.7x_2(t-\tau_3)x_5}{0.92+x_5},\\
\frac{dx_6}{dt} &= 0.18 + \frac{3.6x_7}{0.01+x_7} - 180x_6x_1 - \frac{18x_4x_6}{0.92+x_6} - \frac{18x_5x_6}{0.92+x_6} - 0.06x_6,\\
\frac{dx_7}{dt} &= \frac{18x_4x_6}{0.92+x_6} + \frac{18x_5x_6}{0.92+x_6} + \frac{18x_4x_8}{0.92+x_8} + \frac{18x_5x_8}{0.92+x_8} - \frac{3.6x_7}{0.01+x_7} - 0.06x_7,\\
\frac{dx_8}{dt} &= 180x_6x_1 - \frac{18x_4x_8}{0.92+x_8} - \frac{18x_5x_8}{0.92+x_8} - 0.03x_8.
\end{aligned} \tag{20}$$

The system has a positive equilibrium point $Z = (0.4102, 1.6027, 0.3430, 0.1429, 0.0985, 0.0478, 1.2301, 3.4433)$. Using Theorem 5, there is a critical value of the time delay $\tau_0 = 0.122632125$. The equilibrium point is stable when $\tau < \tau_0$ (see Figures 2 and 3); the equilibrium point becomes unstable and a Hopf bifurcation occurs when τ passes through the critical value τ_0 (see Figure 4). The bifurcation diagrams of system (20) are shown in Figure 5, where the control parameter is the time delay τ.

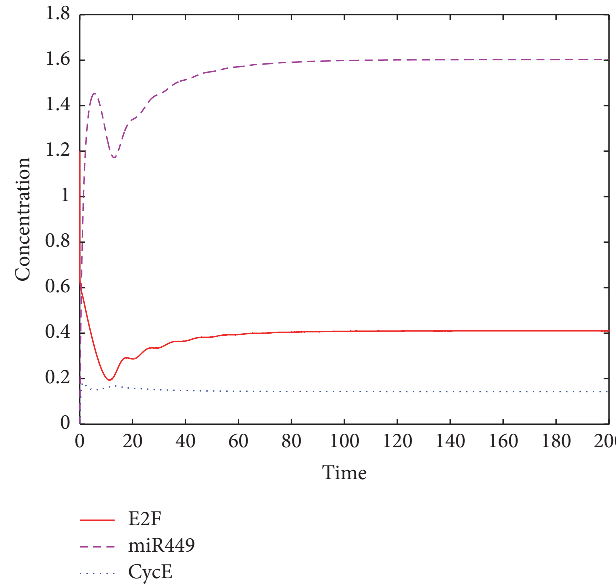

FIGURE 2: An asymptotically stable equilibrium for $\tau = \tau_1 = \tau_2 = \tau_3 = 0$. Assume initial conditions are $x_1 = 1.2$, $x_2 = 0$, $x_3 = 0$, $x_4 = 0$, $x_5 = 0$, $x_6 = 0.55$, $x_7 = 0$, $x_8 = 0$, and $S = 5$, $k_{21} = 1.4$.

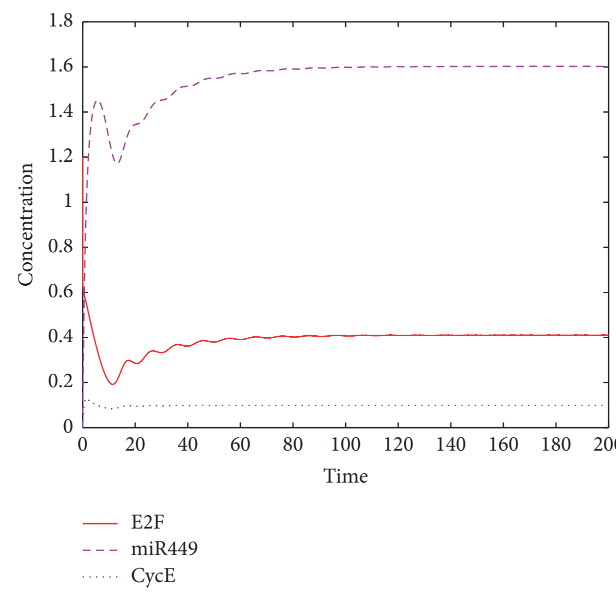

FIGURE 3: An asymptotically stable equilibrium for $\tau = \tau_1 = \tau_2 = \tau_3 < \tau_0$. Assume initial conditions are $x_1 = 1.2$, $x_2 = 0$, $x_3 = 0$, $x_4 = 0$, $x_5 = 0$, $x_6 = 0.55$, $x_7 = 0$, $x_8 = 0$, and $S = 5$, $k_{21} = 1.4$.

When we take $S = 3$, $k_{21} = 2.5$, and the other parameters are shown in Table 1, system (1) becomes

$$\frac{dx_1}{dt} = \frac{0.4x_3x_1}{(0.15+x_3)(0.15+x_1)} + \frac{0.003x_3}{0.15+x_3} + \frac{18x_4x_8}{0.92+x_8} + \frac{18x_5x_8}{0.92+x_8} - 0.25x_1$$

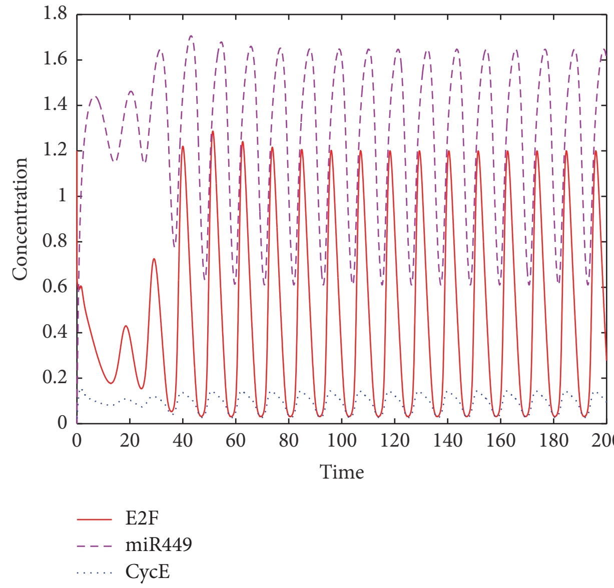

Figure 4: A periodic solution bifurcated from equilibrium for $\tau = \tau_1 = \tau_2 = \tau_3 > \tau_0$. Assume initial conditions are $x_1 = 1.2$, $x_2 = 0$, $x_3 = 0$, $x_4 = 0$, $x_5 = 0$, $x_6 = 0.55$, $x_7 = 0$, $x_8 = 0$, and $S = 5$, $k_{21} = 1.4$.

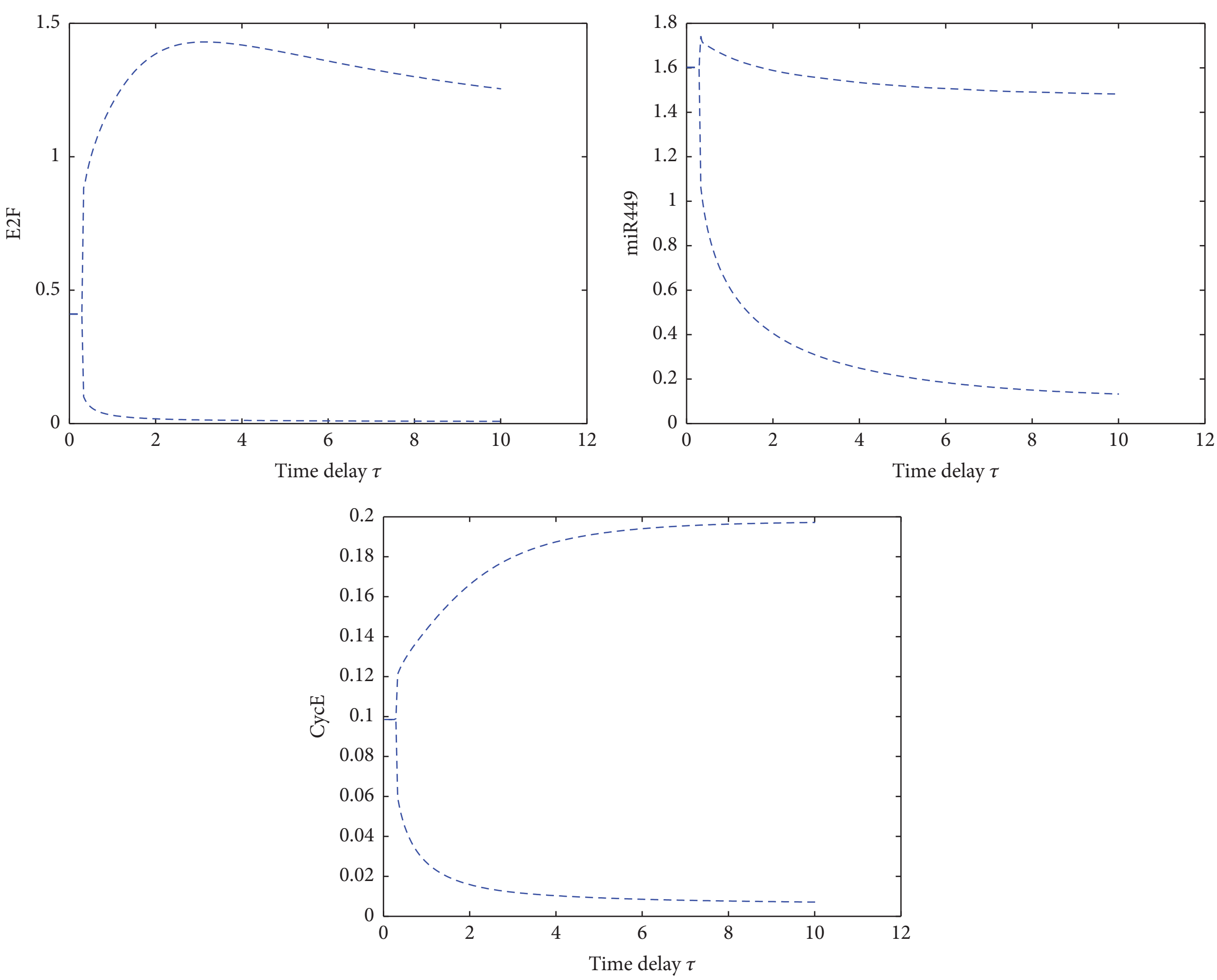

Figure 5: Bifurcation induced by time delay with $S = 5$, $k_{21} = 1.4$. Assume initial conditions are $x_1 = 1.2$, $x_2 = 0$, $x_3 = 0$, $x_4 = 0$, $x_5 = 0$, $x_6 = 0.55$, $x_7 = 0$, $x_8 = 0$, and $S = 5$, $k_{21} = 1.4$.

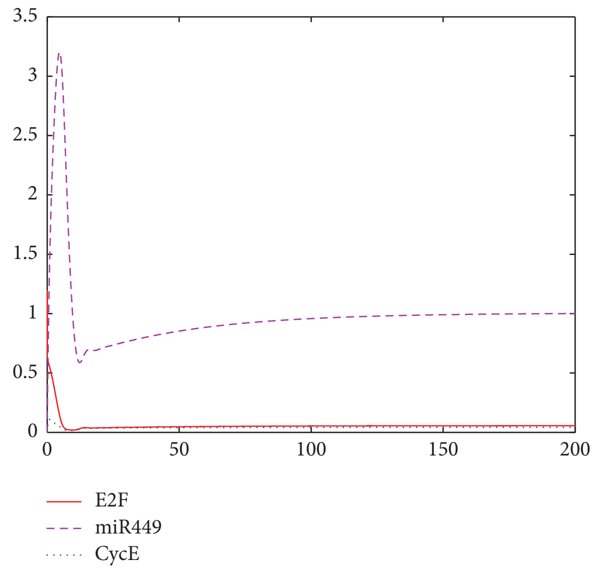

FIGURE 6: An asymptotically stable equilibrium for $\tau = \tau_1 = \tau_2 = \tau_3 = 0$. Assume initial conditions are $x_1 = 1.2,\ x_2 = 0,\ x_3 = 0,\ x_4 = 0,\ x_5 = 0,\ x_6 = 0.55,\ x_7 = 0,\ x_8 = 0$, and $S = 3,\ k_{21} = 2.5$.

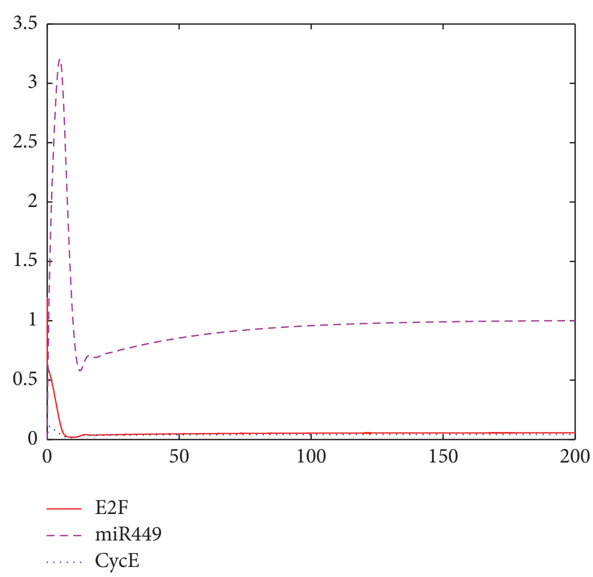

FIGURE 7: An asymptotically stable equilibrium for $\tau = \tau_1 = \tau_2 = \tau_3 < \tau_0$. Assume initial conditions are $x_1 = 1.2,\ x_2 = 0,\ x_3 = 0,\ x_4 = 0,\ x_5 = 0,\ x_6 = 0.55,\ x_7 = 0,\ x_8 = 0$, and $S = 3,\ k_{21} = 2.5$.

$$
\begin{aligned}
& - 180 x_6 x_1, \\
\frac{dx_2}{dt} &= \frac{1.4x_1}{0.15 + x_1} - 0.02x_2 - \frac{0.6x_2x_3}{0.15 + x_3} - \frac{x_2x_4}{0.92 + x_4} \\
&\quad - \frac{0.7x_2x_5}{0.92 + x_5}, \\
\frac{dx_3}{dt} &= 0.9090909090 - 0.7x_3 - \frac{0.6x_2\left(t - \tau_1\right)x_3}{0.15 + x_3},
\end{aligned}
$$

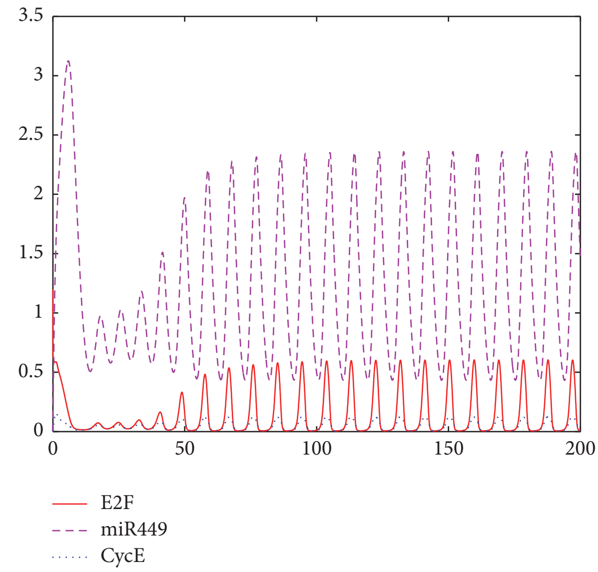

FIGURE 8: A periodic solution bifurcated from equilibrium for $\tau = \tau_1 = \tau_2 = \tau_3 > \tau_0$. Assume initial conditions are $x_1 = 1.2,\ x_2 = 0,\ x_3 = 0,\ x_4 = 0,\ x_5 = 0,\ x_6 = 0.55,\ x_7 = 0,\ x_8 = 0$, and $S = 3,\ k_{21} = 2.5$.

$$
\begin{aligned}
\frac{dx_4}{dt} &= 0.4090909090 + \frac{0.03x_3}{0.15 + x_3} - 1.5x_4 \\
&\quad - \frac{x_2\left(t - \tau_2\right)x_4}{0.92 + x_4}, \\
\frac{dx_5}{dt} &= \frac{0.35x_1}{0.15 + x_1} - 1.5x_5 - \frac{0.7x_2\left(t - \tau_3\right)x_5}{0.92 + x_5}, \\
\frac{dx_6}{dt} &= 0.18 + \frac{3.6x_7}{0.01 + x_7} - 180x_6x_1 - \frac{18x_4x_6}{0.92 + x_6} \\
&\quad - \frac{18x_5x_6}{0.92 + x_6} - 0.06x_6, \\
\frac{dx_7}{dt} &= \frac{18x_4x_6}{0.92 + x_6} + \frac{18x_5x_6}{0.92 + x_6} + \frac{18x_4x_8}{0.92 + x_8} \\
&\quad + \frac{18x_5x_8}{0.92 + x_8} - \frac{3.6x_7}{0.01 + x_7} - 0.06x_7, \\
\frac{dx_8}{dt} &= 180x_6x_1 - \frac{18x_4x_8}{0.92 + x_8} - \frac{18x_5x_8}{0.92 + x_8} - 0.03x_8.
\end{aligned}
\tag{21}
$$

The system has a positive equilibrium point $Z' = (0.0561, 1.0057, 0.5478, 0.1689, 0.0427, 0.2816, 1.4875, 2.4618)$. Using Theorem 5, there is a critical value of the time delay $\tau_0' = 0.1334173317$. The equilibrium point is stable when $\tau < \tau_0'$ (see Figures 6 and 7); the equilibrium point becomes unstable and a Hopf bifurcation occurs when τ passes through the critical value τ_0' (see Figure 8). The bifurcation diagrams of system (21) are shown in Figure 9, where the control parameter is the time delay τ.

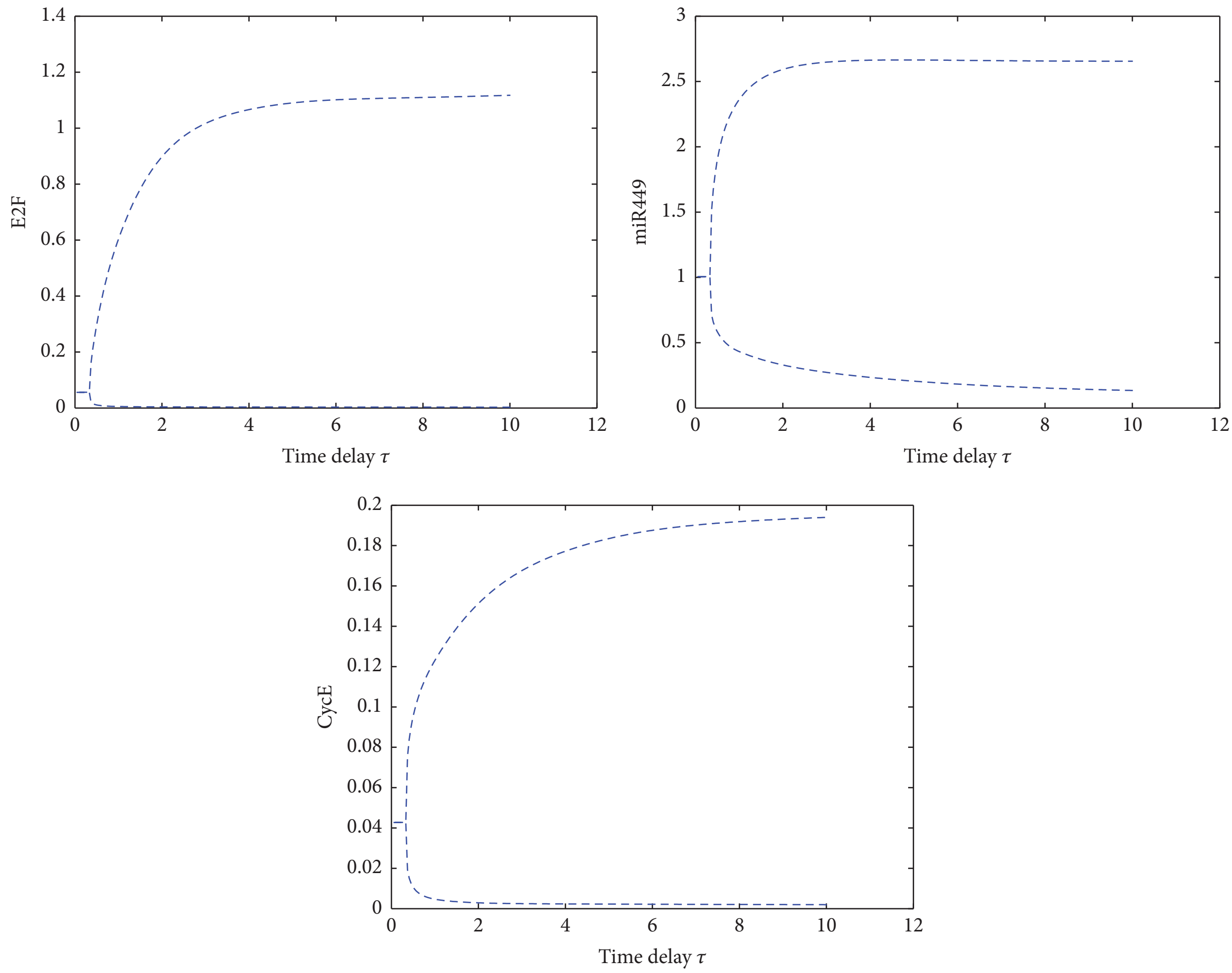

FIGURE 9: Bifurcation induced by time delay with $S = 3,\ k_{21} = 2.5$. Assume initial conditions are $x_1 = 1.2,\ x_2 = 0,\ x_3 = 0,\ x_4 = 0,\ x_5 = 0,\ x_6 = 0.55,\ x_7 = 0,\ x_8 = 0$, and $S = 3,\ k_{21} = 2.5$.

4. Discussion

In this paper, we studied the dynamical behaviors of the Rb-E2F pathway including negative feedback loops involving miR449 by using Hopf bifurcation theory. On one hand, we gave the detailed theoretical analysis of system (1) in which there are some dynamical behaviors, and it is shown that, under certain conditions, the equilibrium point is asymptotically stable for all the delay $\tau \geq 0$; however, if these conditions are not met, there is a critical delay τ_0; when $\tau < \tau_0$, the equilibrium point is asymptotically stable; when $\tau > \tau_0$, periodic oscillations occur. Thus, Hopf bifurcation appears at the steady state when the delay passes through the critical value τ_0. On the other hand, through numerical simulations, we calculated the critical value of τ_0, giving the time courses of E2F, CycE, and miR449 both $\tau < \tau_0$ and $\tau > \tau_0$, drawing the bifurcation diagrams of E2F, CycE, and miR449, respectively, and testifying the correctness of the theory.

Appendix

$$A_1 = -a_{66} - a_{22} - a_{11} - a_{55} - a_{33} - a_{44} - a_{88} - a_{77},$$

$$\begin{aligned}A_2 = {} & a_{33}a_{44} - a_{61}a_{16} - a_{81}a_{18} + a_{11}a_{22} + a_{11}a_{66} + a_{44}a_{66} + a_{66}a_{88} + a_{33}a_{88} + a_{22}a_{77} - a_{76}a_{67} + a_{11}a_{88} + a_{33}a_{66} + a_{55}a_{88} + a_{55}a_{77} \\ & + a_{22}a_{66} + a_{44}a_{88} + a_{33}a_{55} - a_{51}a_{15} + a_{55}a_{11} + a_{66}a_{77} + a_{55}a_{22} + a_{44}a_{55} + a_{33}a_{22} + a_{44}a_{77} + a_{33}a_{11} + a_{77}a_{88} + a_{44}a_{22} + a_{22}a_{88} \\ & + a_{55}a_{66} + a_{11}a_{77} + a_{44}a_{11} + a_{33}a_{77},\end{aligned}$$

$$\begin{aligned}A_3 = {} & -a_{33}a_{44}a_{55} - a_{33}a_{66}a_{88} - a_{33}a_{66}a_{77} - a_{33}a_{55}a_{22} - a_{44}a_{11}a_{88} - a_{44}a_{11}a_{22} - a_{44}a_{66}a_{77} + a_{55}a_{61}a_{16} + a_{33}a_{61}a_{16} - a_{44}a_{55}a_{77} \\ & + a_{44}a_{81}a_{18} - a_{44}a_{22}a_{66} - a_{33}a_{55}a_{11} - a_{33}a_{77}a_{88} - a_{44}a_{55}a_{22} - a_{44}a_{55}a_{88} - a_{33}a_{22}a_{77} + a_{44}a_{61}a_{16} - a_{33}a_{44}a_{77} - a_{11}a_{22}a_{66}\end{aligned}$$

$$
\begin{aligned}
&-a_{55}a_{66}a_{88}-a_{33}a_{55}a_{77}-a_{33}a_{22}a_{66}-a_{44}a_{22}a_{77}-a_{44}a_{55}a_{11}-a_{44}a_{11}a_{77}-a_{55}a_{66}a_{77}-a_{44}a_{22}a_{88}+a_{44}a_{76}a_{67}-a_{33}a_{44}a_{88}\\
&-a_{33}a_{11}a_{77}-a_{44}a_{66}a_{88}-a_{55}a_{11}a_{77}-a_{33}a_{55}a_{88}-a_{33}a_{22}a_{88}-a_{55}a_{11}a_{22}+a_{33}a_{81}a_{18}-a_{33}a_{11}a_{66}-a_{33}a_{11}a_{22}-a_{44}a_{11}a_{66}\\
&+a_{33}a_{76}a_{67}-a_{33}a_{11}a_{88}-a_{33}a_{44}a_{22}-a_{44}a_{77}a_{88}+a_{55}a_{81}a_{18}-a_{61}a_{86}a_{18}+a_{61}a_{22}a_{16}+a_{81}a_{22}a_{18}+a_{81}a_{18}a_{66}-a_{55}a_{22}a_{66}\\
&-a_{33}a_{44}a_{66}-a_{33}a_{44}a_{11}-a_{55}a_{77}a_{88}-a_{44}a_{55}a_{66}-a_{55}a_{11}a_{66}-a_{55}a_{22}a_{88}+a_{55}a_{76}a_{67}-a_{55}a_{11}a_{88}+a_{81}a_{18}a_{77}-a_{55}a_{22}a_{77}\\
&+a_{51}a_{15}a_{66}+a_{51}a_{33}a_{15}+a_{51}a_{15}a_{88}-a_{51}a_{65}a_{16}+a_{51}a_{15}a_{77}-a_{11}a_{77}a_{88}-a_{51}a_{85}a_{18}+a_{22}a_{76}a_{67}+a_{11}a_{76}a_{67}-a_{11}a_{66}a_{88}\\
&-a_{11}a_{66}a_{77}-a_{66}a_{77}a_{88}+a_{61}a_{16}a_{88}-a_{11}a_{22}a_{88}+a_{61}a_{16}a_{77}-a_{22}a_{66}a_{88}-a_{22}a_{77}a_{88}+a_{76}a_{67}a_{88}-a_{86}a_{67}a_{78}-a_{11}a_{22}a_{77}\\
&+a_{51}a_{22}a_{15}+a_{51}a_{44}a_{15}-a_{22}a_{66}a_{77}-a_{33}a_{55}a_{66},\\
A_4 = {}&a_{44}a_{11}a_{22}a_{77}+a_{44}a_{61}a_{86}a_{18}-a_{44}a_{61}a_{22}a_{16}-a_{44}a_{81}a_{18}a_{77}+a_{44}a_{55}a_{11}a_{66}-a_{44}a_{81}a_{18}a_{66}-a_{44}a_{81}a_{22}a_{18}+a_{44}a_{55}a_{22}a_{77}\\
&+a_{44}a_{55}a_{77}a_{88}+a_{44}a_{55}a_{22}a_{88}-a_{44}a_{55}a_{76}a_{67}+a_{44}a_{55}a_{66}a_{88}-a_{44}a_{55}a_{61}a_{16}+a_{44}a_{55}a_{11}a_{77}+a_{44}a_{55}a_{11}a_{22}-a_{44}a_{55}a_{81}a_{18}\\
&-a_{33}a_{22}a_{76}a_{67}+a_{33}a_{11}a_{77}a_{88}+a_{33}a_{11}a_{66}a_{88}+a_{33}a_{11}a_{66}a_{77}-a_{33}a_{11}a_{76}a_{67}+a_{33}a_{11}a_{22}a_{88}+a_{33}a_{11}a_{22}a_{66}-a_{33}a_{61}a_{16}a_{88}\\
&-a_{33}a_{61}a_{16}a_{77}+a_{33}a_{22}a_{66}a_{88}+a_{33}a_{66}a_{77}a_{88}+a_{33}a_{22}a_{66}a_{77}+a_{33}a_{86}a_{67}a_{78}+a_{33}a_{61}a_{86}a_{18}-a_{33}a_{76}a_{67}a_{88}+a_{33}a_{22}a_{77}a_{88}\\
&+a_{33}a_{11}a_{22}a_{77}+a_{51}a_{65}a_{16}a_{88}-a_{51}a_{15}a_{66}a_{77}+a_{51}a_{85}a_{18}a_{66}+a_{51}a_{85}a_{18}a_{77}-a_{51}a_{75}a_{16}a_{67}+a_{44}a_{55}a_{11}a_{88}+a_{44}a_{55}a_{22}a_{66}\\
&+a_{44}a_{55}a_{66}a_{77}-a_{51}a_{33}a_{15}a_{88}-a_{51}a_{15}a_{66}a_{88}-a_{51}a_{65}a_{86}a_{18}+a_{51}a_{22}a_{85}a_{18}-a_{51}a_{22}a_{15}a_{66}-a_{51}a_{22}a_{15}a_{88}-a_{51}a_{22}a_{15}a_{77}\\
&+a_{51}a_{22}a_{65}a_{16}+a_{51}a_{44}a_{85}a_{18}-a_{51}a_{44}a_{15}a_{66}-a_{51}a_{44}a_{15}a_{88}-a_{51}a_{44}a_{15}a_{77}+a_{51}a_{44}a_{65}a_{16}-a_{51}a_{44}a_{22}a_{15}+a_{51}a_{33}a_{85}a_{18}\\
&-a_{51}a_{33}a_{15}a_{66}-a_{51}a_{33}a_{15}a_{77}+a_{51}a_{33}a_{65}a_{16}-a_{51}a_{33}a_{22}a_{15}-a_{51}a_{33}a_{44}a_{15}-a_{81}a_{22}a_{18}a_{77}-a_{11}a_{76}a_{67}a_{88}+a_{11}a_{86}a_{67}a_{78}\\
&+a_{11}a_{22}a_{77}a_{88}+a_{11}a_{22}a_{66}a_{88}-a_{81}a_{16}a_{67}a_{78}-a_{81}a_{18}a_{66}a_{77}+a_{81}a_{76}a_{18}a_{67}-a_{61}a_{16}a_{77}a_{88}+a_{61}a_{86}a_{18}a_{77}-a_{61}a_{22}a_{16}a_{88}\\
&+a_{22}a_{66}a_{77}a_{88}-a_{22}a_{76}a_{67}a_{88}+a_{22}a_{86}a_{67}a_{78}+a_{11}a_{66}a_{77}a_{88}-a_{55}a_{22}a_{76}a_{67}+a_{55}a_{11}a_{77}a_{88}+a_{55}a_{11}a_{66}a_{88}+a_{55}a_{11}a_{66}a_{77}\\
&-a_{55}a_{11}a_{76}a_{67}+a_{55}a_{11}a_{22}a_{88}+a_{55}a_{11}a_{22}a_{66}-a_{55}a_{61}a_{16}a_{88}-a_{55}a_{61}a_{16}a_{77}+a_{55}a_{66}a_{77}a_{88}-a_{55}a_{76}a_{67}a_{88}+a_{55}a_{86}a_{67}a_{78}\\
&+a_{55}a_{22}a_{77}a_{88}+a_{55}a_{22}a_{66}a_{88}+a_{55}a_{22}a_{66}a_{77}+a_{55}a_{11}a_{22}a_{77}+a_{55}a_{61}a_{86}a_{18}-a_{55}a_{61}a_{22}a_{16}-a_{55}a_{81}a_{18}a_{77}-a_{55}a_{81}a_{18}a_{66}\\
&-a_{55}a_{81}a_{22}a_{18}-a_{44}a_{22}a_{76}a_{67}-a_{44}a_{11}a_{76}a_{67}+a_{44}a_{11}a_{77}a_{88}+a_{44}a_{11}a_{66}a_{88}+a_{44}a_{11}a_{66}a_{77}+a_{44}a_{11}a_{22}a_{88}+a_{44}a_{11}a_{22}a_{66}\\
&-a_{44}a_{61}a_{16}a_{88}-a_{44}a_{61}a_{16}a_{77}+a_{44}a_{66}a_{77}a_{88}-a_{44}a_{76}a_{67}a_{88}+a_{44}a_{86}a_{67}a_{78}+a_{44}a_{22}a_{77}a_{88}+a_{44}a_{22}a_{66}a_{88}+a_{44}a_{22}a_{66}a_{77}\\
&+a_{33}a_{44}a_{55}a_{11}-a_{33}a_{61}a_{22}a_{16}-a_{33}a_{81}a_{18}a_{77}+a_{33}a_{55}a_{22}a_{77}-a_{33}a_{81}a_{18}a_{66}-a_{33}a_{81}a_{22}a_{18}+a_{33}a_{55}a_{77}a_{88}+a_{33}a_{55}a_{11}a_{66}\\
&+a_{33}a_{55}a_{22}a_{88}-a_{33}a_{55}a_{76}a_{67}+a_{33}a_{55}a_{66}a_{88}+a_{33}a_{55}a_{11}a_{88}+a_{33}a_{55}a_{66}a_{77}-a_{33}a_{55}a_{61}a_{16}+a_{33}a_{55}a_{22}a_{66}+a_{33}a_{55}a_{11}a_{77}\\
&+a_{33}a_{55}a_{11}a_{22}-a_{33}a_{55}a_{81}a_{18}+a_{33}a_{44}a_{22}a_{77}+a_{33}a_{44}a_{11}a_{66}+a_{33}a_{44}a_{77}a_{88}+a_{33}a_{44}a_{11}a_{88}-a_{33}a_{44}a_{76}a_{67}+a_{33}a_{44}a_{22}a_{88}\\
&+a_{33}a_{44}a_{66}a_{77}+a_{33}a_{44}a_{66}a_{88}+a_{33}a_{44}a_{22}a_{66}-a_{33}a_{44}a_{61}a_{16}+a_{33}a_{44}a_{11}a_{77}+a_{33}a_{44}a_{11}a_{22}+a_{33}a_{44}a_{55}a_{88}-a_{33}a_{44}a_{81}a_{18}\\
&+a_{33}a_{44}a_{55}a_{77}+a_{33}a_{44}a_{55}a_{66}+a_{33}a_{44}a_{55}a_{22}+a_{51}a_{15}a_{76}a_{67}-a_{51}a_{15}a_{77}a_{88}-a_{61}a_{22}a_{16}a_{77}+a_{61}a_{22}a_{86}a_{18}+a_{11}a_{22}a_{66}a_{77}\\
&-a_{11}a_{22}a_{76}a_{67}-a_{81}a_{22}a_{18}a_{66}+a_{51}a_{65}a_{16}a_{77},\\
A_5 = {}&-a_{55}a_{22}a_{66}a_{77}a_{88}+a_{81}a_{22}a_{16}a_{67}a_{78}-a_{81}a_{22}a_{76}a_{18}a_{67}+a_{81}a_{22}a_{18}a_{66}a_{77}-a_{55}a_{22}a_{86}a_{67}a_{78}-a_{55}a_{11}a_{66}a_{77}a_{88}\\
&-a_{44}a_{55}a_{11}a_{66}a_{77}+a_{44}a_{55}a_{81}a_{22}a_{18}-a_{44}a_{22}a_{66}a_{77}a_{88}-a_{44}a_{11}a_{86}a_{67}a_{78}-a_{44}a_{11}a_{22}a_{66}a_{77}+a_{44}a_{11}a_{76}a_{67}a_{88}\\
&+a_{44}a_{22}a_{76}a_{67}a_{88}+a_{55}a_{22}a_{76}a_{67}a_{88}-a_{44}a_{11}a_{66}a_{77}a_{88}-a_{44}a_{11}a_{22}a_{66}a_{88}+a_{44}a_{61}a_{16}a_{77}a_{88}+a_{44}a_{81}a_{22}a_{18}a_{66}\\
&+a_{44}a_{61}a_{22}a_{16}a_{77}+a_{44}a_{11}a_{22}a_{76}a_{67}+a_{44}a_{81}a_{18}a_{66}a_{77}+a_{44}a_{55}a_{61}a_{16}a_{88}-a_{44}a_{55}a_{11}a_{22}a_{66}+a_{44}a_{81}a_{22}a_{18}a_{77}\\
&+a_{44}a_{55}a_{22}a_{76}a_{67}-a_{44}a_{61}a_{22}a_{86}a_{18}-a_{44}a_{55}a_{11}a_{77}a_{88}+a_{44}a_{81}a_{16}a_{67}a_{78}-a_{44}a_{11}a_{22}a_{77}a_{88}-a_{44}a_{55}a_{11}a_{22}a_{88}\\
&-a_{44}a_{61}a_{86}a_{18}a_{77}-a_{44}a_{81}a_{76}a_{18}a_{67}+a_{44}a_{55}a_{81}a_{18}a_{66}-a_{44}a_{22}a_{86}a_{67}a_{78}-a_{44}a_{55}a_{11}a_{66}a_{88}+a_{44}a_{55}a_{11}a_{76}a_{67}\\
&+a_{44}a_{61}a_{22}a_{16}a_{88}+a_{44}a_{55}a_{81}a_{18}a_{77}+a_{44}a_{55}a_{61}a_{22}a_{16}-a_{44}a_{55}a_{61}a_{86}a_{18}-a_{44}a_{55}a_{11}a_{22}a_{77}-a_{44}a_{55}a_{22}a_{66}a_{77}\\
&-a_{44}a_{55}a_{22}a_{66}a_{88}-a_{44}a_{55}a_{22}a_{77}a_{88}-a_{44}a_{55}a_{86}a_{67}a_{78}+a_{44}a_{55}a_{76}a_{67}a_{88}-a_{44}a_{55}a_{66}a_{77}a_{88}+a_{44}a_{55}a_{61}a_{16}a_{77}\\
&+a_{33}a_{81}a_{22}a_{18}a_{77}-a_{55}a_{61}a_{86}a_{18}a_{77}+a_{33}a_{81}a_{22}a_{18}a_{66}+a_{33}a_{11}a_{76}a_{67}a_{88}-a_{33}a_{11}a_{86}a_{67}a_{78}+a_{33}a_{81}a_{16}a_{67}a_{78}\\
&-a_{33}a_{61}a_{22}a_{86}a_{18}-a_{33}a_{11}a_{22}a_{66}a_{77}-a_{33}a_{11}a_{22}a_{66}a_{88}-a_{33}a_{11}a_{22}a_{77}a_{88}+a_{33}a_{11}a_{22}a_{76}a_{67}-a_{33}a_{81}a_{76}a_{18}a_{67}\\
&+a_{33}a_{81}a_{18}a_{66}a_{77}-a_{33}a_{61}a_{86}a_{18}a_{77}+a_{33}a_{61}a_{16}a_{77}a_{88}-a_{33}a_{11}a_{66}a_{77}a_{88}-a_{33}a_{22}a_{86}a_{67}a_{78}+a_{33}a_{22}a_{76}a_{67}a_{88}\\
&-a_{33}a_{22}a_{66}a_{77}a_{88}+a_{33}a_{61}a_{22}a_{16}a_{77}+a_{33}a_{61}a_{22}a_{16}a_{88}+a_{51}a_{65}a_{86}a_{18}a_{77}+a_{51}a_{15}a_{66}a_{77}a_{88}+a_{51}a_{75}a_{16}a_{67}a_{88}\\
&-a_{51}a_{85}a_{18}a_{66}a_{77}+a_{51}a_{85}a_{76}a_{18}a_{67}-a_{51}a_{85}a_{16}a_{67}a_{78}-a_{51}a_{75}a_{86}a_{18}a_{67}-a_{51}a_{65}a_{16}a_{77}a_{88}-a_{51}a_{15}a_{76}a_{67}a_{88}\\
&+a_{51}a_{15}a_{86}a_{67}a_{78}+a_{51}a_{33}a_{22}a_{15}a_{66}-a_{51}a_{33}a_{22}a_{85}a_{18}+a_{51}a_{33}a_{65}a_{86}a_{18}+a_{51}a_{33}a_{15}a_{66}a_{88}+a_{51}a_{33}a_{75}a_{16}a_{67}
\end{aligned}
$$

$$
\begin{aligned}
& -a_{51}a_{33}a_{85}a_{18}a_{77} - a_{51}a_{33}a_{85}a_{18}a_{66} + a_{51}a_{33}a_{15}a_{66}a_{77} - a_{51}a_{33}a_{65}a_{16}a_{88} - a_{51}a_{33}a_{65}a_{16}a_{77} - a_{51}a_{33}a_{15}a_{76}a_{67} \\
& +a_{51}a_{33}a_{15}a_{77}a_{88} - a_{51}a_{44}a_{22}a_{65}a_{16} + a_{51}a_{44}a_{22}a_{15}a_{77} + a_{51}a_{44}a_{22}a_{15}a_{88} + a_{51}a_{44}a_{22}a_{15}a_{66} - a_{51}a_{44}a_{22}a_{85}a_{18} \\
& +a_{51}a_{44}a_{65}a_{86}a_{18} + a_{51}a_{33}a_{22}a_{15}a_{77} + a_{51}a_{33}a_{22}a_{15}a_{88} - a_{51}a_{33}a_{44}a_{85}a_{18} - a_{51}a_{33}a_{22}a_{65}a_{16} + a_{33}a_{55}a_{81}a_{18}a_{66} \\
& +a_{33}a_{55}a_{81}a_{18}a_{77} + a_{33}a_{55}a_{61}a_{22}a_{16} - a_{33}a_{55}a_{61}a_{86}a_{18} - a_{33}a_{55}a_{11}a_{22}a_{77} - a_{33}a_{55}a_{22}a_{66}a_{77} - a_{33}a_{55}a_{22}a_{66}a_{88} \\
& -a_{33}a_{55}a_{22}a_{77}a_{88} - a_{33}a_{55}a_{86}a_{67}a_{78} + a_{33}a_{55}a_{76}a_{67}a_{88} - a_{33}a_{55}a_{66}a_{77}a_{88} + a_{33}a_{55}a_{61}a_{16}a_{77} + a_{33}a_{55}a_{61}a_{16}a_{88} \\
& -a_{33}a_{55}a_{11}a_{22}a_{66} - a_{33}a_{55}a_{11}a_{22}a_{88} + a_{33}a_{55}a_{11}a_{76}a_{67} - a_{33}a_{55}a_{11}a_{66}a_{77} - a_{33}a_{55}a_{11}a_{66}a_{88} - a_{33}a_{55}a_{11}a_{77}a_{88} \\
& +a_{33}a_{55}a_{22}a_{76}a_{67} + a_{51}a_{22}a_{15}a_{77}a_{88} - a_{51}a_{22}a_{15}a_{76}a_{67} - a_{51}a_{22}a_{65}a_{16}a_{77} - a_{51}a_{22}a_{65}a_{16}a_{88} - a_{51}a_{22}a_{85}a_{18}a_{77} \\
& +a_{51}a_{22}a_{75}a_{16}a_{67} - a_{33}a_{44}a_{55}a_{22}a_{88} - a_{33}a_{44}a_{55}a_{77}a_{88} - a_{33}a_{44}a_{55}a_{11}a_{66} - a_{33}a_{44}a_{55}a_{22}a_{77} + a_{33}a_{44}a_{81}a_{22}a_{18} \\
& +a_{33}a_{44}a_{81}a_{18}a_{66} + a_{33}a_{44}a_{81}a_{18}a_{77} + a_{33}a_{44}a_{61}a_{22}a_{16} - a_{33}a_{44}a_{61}a_{86}a_{18} - a_{33}a_{44}a_{11}a_{22}a_{77} - a_{33}a_{44}a_{22}a_{66}a_{77} \\
& -a_{33}a_{44}a_{22}a_{66}a_{88} - a_{33}a_{44}a_{22}a_{77}a_{88} - a_{33}a_{44}a_{86}a_{67}a_{78} + a_{33}a_{44}a_{76}a_{67}a_{88} - a_{33}a_{44}a_{66}a_{77}a_{88} + a_{33}a_{44}a_{61}a_{16}a_{77} \\
& +a_{33}a_{44}a_{61}a_{16}a_{88} - a_{33}a_{44}a_{11}a_{22}a_{66} - a_{33}a_{44}a_{11}a_{22}a_{88} + a_{33}a_{44}a_{11}a_{76}a_{67} - a_{33}a_{44}a_{11}a_{66}a_{77} - a_{33}a_{44}a_{11}a_{66}a_{88} \\
& -a_{33}a_{44}a_{11}a_{77}a_{88} + a_{33}a_{44}a_{22}a_{76}a_{67} + a_{33}a_{55}a_{81}a_{22}a_{18} + a_{51}a_{44}a_{15}a_{66}a_{88} + a_{51}a_{44}a_{75}a_{16}a_{67} - a_{51}a_{44}a_{85}a_{18}a_{77} \\
& -a_{51}a_{44}a_{85}a_{18}a_{66} + a_{51}a_{44}a_{15}a_{66}a_{77} - a_{51}a_{44}a_{65}a_{16}a_{88} - a_{51}a_{44}a_{65}a_{16}a_{77} - a_{51}a_{44}a_{15}a_{76}a_{67} + a_{51}a_{44}a_{15}a_{77}a_{88} \\
& +a_{51}a_{22}a_{65}a_{86}a_{18} + a_{51}a_{22}a_{15}a_{66}a_{88} - a_{33}a_{44}a_{55}a_{11}a_{88} + a_{33}a_{44}a_{55}a_{76}a_{67} - a_{33}a_{44}a_{55}a_{66}a_{77} - a_{33}a_{44}a_{55}a_{22}a_{66} \\
& -a_{33}a_{44}a_{55}a_{66}a_{88} - a_{33}a_{44}a_{55}a_{11}a_{77} + a_{33}a_{44}a_{55}a_{61}a_{16} - a_{33}a_{44}a_{55}a_{11}a_{22} + a_{33}a_{44}a_{55}a_{81}a_{18} + a_{55}a_{61}a_{22}a_{16}a_{77} \\
& -a_{11}a_{22}a_{66}a_{77}a_{88} + a_{55}a_{61}a_{22}a_{16}a_{88} + a_{61}a_{22}a_{16}a_{77}a_{88} - a_{51}a_{22}a_{85}a_{18}a_{66} + a_{51}a_{22}a_{15}a_{66}a_{77} - a_{61}a_{22}a_{86}a_{18}a_{77} \\
& +a_{55}a_{11}a_{22}a_{76}a_{67} - a_{55}a_{81}a_{76}a_{18}a_{67} + a_{55}a_{81}a_{18}a_{66}a_{77} + a_{55}a_{81}a_{16}a_{67}a_{78} - a_{55}a_{61}a_{22}a_{86}a_{18} - a_{55}a_{11}a_{22}a_{66}a_{77} \\
& -a_{55}a_{11}a_{22}a_{66}a_{88} - a_{55}a_{11}a_{22}a_{77}a_{88} - a_{55}a_{11}a_{86}a_{67}a_{78} + a_{55}a_{11}a_{76}a_{67}a_{88} + a_{55}a_{81}a_{22}a_{18}a_{66} + a_{55}a_{81}a_{22}a_{18}a_{77} \\
& +a_{51}a_{33}a_{44}a_{22}a_{15} - a_{51}a_{33}a_{44}a_{65}a_{16} + a_{51}a_{33}a_{44}a_{15}a_{77} + a_{51}a_{33}a_{44}a_{15}a_{88} + a_{51}a_{33}a_{44}a_{15}a_{66} - a_{11}a_{22}a_{86}a_{67}a_{78} \\
& +a_{11}a_{22}a_{76}a_{67}a_{88} + a_{55}a_{61}a_{16}a_{77}a_{88}, \\
A_6 = {} & a_{51}a_{33}a_{85}a_{16}a_{67}a_{78} + a_{51}a_{33}a_{75}a_{86}a_{18}a_{67} + a_{51}a_{33}a_{22}a_{65}a_{16}a_{88} - a_{51}a_{33}a_{85}a_{76}a_{18}a_{67} - a_{51}a_{33}a_{75}a_{16}a_{67}a_{88} \\
& +a_{51}a_{33}a_{85}a_{18}a_{66}a_{77} + a_{51}a_{33}a_{22}a_{65}a_{16}a_{77} + a_{51}a_{33}a_{22}a_{15}a_{76}a_{67} - a_{51}a_{33}a_{22}a_{15}a_{77}a_{88} - a_{51}a_{33}a_{65}a_{86}a_{18}a_{77} \\
& -a_{51}a_{33}a_{15}a_{66}a_{77}a_{88} - a_{51}a_{33}a_{22}a_{15}a_{66}a_{77} + a_{51}a_{33}a_{22}a_{85}a_{18}a_{66} + a_{51}a_{33}a_{22}a_{85}a_{18}a_{77} - a_{51}a_{33}a_{22}a_{75}a_{16}a_{67} \\
& +a_{51}a_{22}a_{65}a_{16}a_{77}a_{88} + a_{51}a_{22}a_{15}a_{76}a_{67}a_{88} + a_{51}a_{44}a_{22}a_{65}a_{16}a_{88} + a_{51}a_{44}a_{22}a_{65}a_{16}a_{77} - a_{51}a_{33}a_{22}a_{15}a_{66}a_{88} \\
& -a_{51}a_{33}a_{22}a_{65}a_{86}a_{18} - a_{51}a_{33}a_{44}a_{75}a_{16}a_{67} + a_{51}a_{33}a_{44}a_{85}a_{18}a_{77} + a_{51}a_{33}a_{44}a_{85}a_{18}a_{66} - a_{51}a_{33}a_{44}a_{15}a_{66}a_{77} \\
& +a_{51}a_{33}a_{44}a_{65}a_{16}a_{88} + a_{51}a_{33}a_{44}a_{65}a_{16}a_{77} - a_{51}a_{22}a_{75}a_{16}a_{67}a_{88} + a_{51}a_{22}a_{85}a_{18}a_{66}a_{77} + a_{51}a_{44}a_{85}a_{16}a_{67}a_{78} \\
& -a_{51}a_{44}a_{75}a_{16}a_{67}a_{88} + a_{51}a_{44}a_{85}a_{18}a_{66}a_{77} - a_{51}a_{44}a_{85}a_{76}a_{18}a_{67} - a_{51}a_{33}a_{44}a_{65}a_{86}a_{18} - a_{51}a_{44}a_{85}a_{76}a_{18}a_{67} \\
& -a_{51}a_{44}a_{85}a_{76}a_{18}a_{67} - a_{51}a_{33}a_{44}a_{65}a_{86}a_{18} + a_{51}a_{33}a_{44}a_{15}a_{76}a_{67} - a_{51}a_{33}a_{44}a_{15}a_{77}a_{88} - a_{51}a_{33}a_{44}a_{15}a_{66}a_{88} \\
& +a_{51}a_{33}a_{44}a_{22}a_{85}a_{18} - a_{55}a_{81}a_{22}a_{18}a_{66}a_{77} - a_{51}a_{22}a_{15}a_{86}a_{67}a_{78} - a_{51}a_{33}a_{44}a_{22}a_{15}a_{88} - a_{51}a_{33}a_{44}a_{22}a_{15}a_{77} \\
& +a_{51}a_{33}a_{44}a_{22}a_{65}a_{16} - a_{51}a_{33}a_{44}a_{22}a_{15}a_{66} + a_{55}a_{61}a_{22}a_{86}a_{18}a_{77} - a_{55}a_{61}a_{22}a_{16}a_{77}a_{88} + a_{55}a_{11}a_{22}a_{66}a_{77}a_{88} \\
& -a_{55}a_{81}a_{22}a_{16}a_{67}a_{78} + a_{55}a_{81}a_{22}a_{76}a_{18}a_{67} - a_{44}a_{81}a_{22}a_{18}a_{66}a_{77} - a_{55}a_{11}a_{22}a_{76}a_{67}a_{88} + a_{55}a_{11}a_{22}a_{86}a_{67}a_{78} \\
& +a_{44}a_{81}a_{22}a_{76}a_{18}a_{67} + a_{44}a_{11}a_{22}a_{66}a_{77}a_{88} - a_{44}a_{81}a_{22}a_{16}a_{67}a_{78} + a_{44}a_{61}a_{22}a_{86}a_{18}a_{77} - a_{44}a_{61}a_{22}a_{16}a_{77}a_{88} \\
& +a_{44}a_{11}a_{22}a_{86}a_{67}a_{78} - a_{44}a_{11}a_{22}a_{76}a_{67}a_{88} - a_{44}a_{55}a_{81}a_{22}a_{18}a_{77} - a_{44}a_{55}a_{11}a_{76}a_{67}a_{88} - a_{44}a_{55}a_{81}a_{22}a_{18}a_{66} \\
& +a_{44}a_{55}a_{61}a_{22}a_{86}a_{18} + a_{44}a_{55}a_{11}a_{22}a_{66}a_{77} + a_{44}a_{55}a_{11}a_{22}a_{77}a_{88} + a_{44}a_{55}a_{11}a_{22}a_{66}a_{88} + a_{44}a_{55}a_{11}a_{86}a_{67}a_{78} \\
& -a_{44}a_{55}a_{81}a_{16}a_{67}a_{78} - a_{44}a_{55}a_{81}a_{18}a_{66}a_{77} + a_{44}a_{55}a_{81}a_{76}a_{18}a_{67} + a_{44}a_{55}a_{61}a_{86}a_{18}a_{77} - a_{44}a_{55}a_{61}a_{16}a_{77}a_{88} \\
& -a_{44}a_{55}a_{11}a_{22}a_{76}a_{67} + a_{44}a_{55}a_{22}a_{66}a_{77}a_{88} - a_{44}a_{55}a_{61}a_{22}a_{16}a_{77} - a_{44}a_{55}a_{61}a_{22}a_{16}a_{88} + a_{44}a_{55}a_{11}a_{66}a_{77}a_{88} \\
& +a_{44}a_{55}a_{22}a_{86}a_{67}a_{78} - a_{44}a_{55}a_{22}a_{76}a_{67}a_{88} - a_{33}a_{81}a_{22}a_{18}a_{66}a_{77} - a_{33}a_{55}a_{81}a_{22}a_{18}a_{77} + a_{33}a_{11}a_{22}a_{86}a_{67}a_{78} \\
& -a_{33}a_{11}a_{22}a_{76}a_{67}a_{88} + a_{33}a_{61}a_{22}a_{86}a_{18}a_{77} - a_{33}a_{61}a_{22}a_{16}a_{77}a_{88} + a_{33}a_{11}a_{22}a_{66}a_{77}a_{88} - a_{33}a_{81}a_{22}a_{16}a_{67}a_{78} \\
& +a_{33}a_{81}a_{22}a_{76}a_{18}a_{67} + a_{33}a_{55}a_{11}a_{86}a_{67}a_{78} - a_{33}a_{55}a_{11}a_{76}a_{67}a_{88} - a_{33}a_{55}a_{81}a_{22}a_{18}a_{66} + a_{33}a_{55}a_{11}a_{22}a_{66}a_{88} \\
& +a_{33}a_{55}a_{11}a_{22}a_{77}a_{88} + a_{33}a_{55}a_{61}a_{22}a_{86}a_{18} + a_{33}a_{55}a_{11}a_{22}a_{66}a_{77} - a_{33}a_{55}a_{81}a_{16}a_{67}a_{78} + a_{33}a_{55}a_{81}a_{76}a_{18}a_{67}
\end{aligned}
$$

$$
\begin{aligned}
&-a_{33}a_{55}a_{81}a_{18}a_{66}a_{77}-a_{33}a_{55}a_{11}a_{22}a_{76}a_{67}-a_{33}a_{55}a_{61}a_{16}a_{77}a_{88}-a_{33}a_{55}a_{61}a_{22}a_{16}a_{88}+a_{33}a_{55}a_{61}a_{86}a_{18}a_{77}\\
&-a_{33}a_{44}a_{55}a_{22}a_{76}a_{67}-a_{51}a_{44}a_{22}a_{15}a_{77}a_{88}-a_{51}a_{44}a_{65}a_{86}a_{18}a_{77}-a_{51}a_{44}a_{15}a_{66}a_{77}a_{88}+a_{33}a_{55}a_{22}a_{66}a_{77}a_{88}\\
&-a_{33}a_{55}a_{61}a_{22}a_{16}a_{77}-a_{33}a_{44}a_{81}a_{22}a_{18}a_{77}+a_{33}a_{55}a_{11}a_{66}a_{77}a_{88}+a_{33}a_{55}a_{22}a_{86}a_{67}a_{78}-a_{33}a_{55}a_{22}a_{76}a_{67}a_{88}\\
&-a_{33}a_{44}a_{81}a_{22}a_{18}a_{66}+a_{33}a_{44}a_{11}a_{22}a_{77}a_{88}+a_{33}a_{44}a_{11}a_{86}a_{67}a_{78}-a_{33}a_{44}a_{11}a_{76}a_{67}a_{88}+a_{33}a_{44}a_{11}a_{22}a_{66}a_{88}\\
&-a_{33}a_{44}a_{81}a_{16}a_{67}a_{78}+a_{33}a_{44}a_{61}a_{22}a_{86}a_{18}+a_{33}a_{44}a_{11}a_{22}a_{66}a_{77}+a_{33}a_{44}a_{81}a_{76}a_{18}a_{67}-a_{33}a_{44}a_{81}a_{18}a_{66}a_{77}\\
&-a_{33}a_{44}a_{61}a_{16}a_{77}a_{88}-a_{33}a_{44}a_{11}a_{22}a_{76}a_{67}-a_{33}a_{44}a_{61}a_{22}a_{16}a_{77}-a_{33}a_{44}a_{61}a_{22}a_{16}a_{88}+a_{33}a_{44}a_{55}a_{11}a_{22}a_{66}\\
&+a_{33}a_{44}a_{55}a_{66}a_{77}a_{88}-a_{33}a_{44}a_{55}a_{61}a_{16}a_{77}-a_{33}a_{44}a_{55}a_{61}a_{16}a_{88}+a_{33}a_{44}a_{55}a_{11}a_{22}a_{77}+a_{33}a_{44}a_{55}a_{22}a_{66}a_{77}\\
&+a_{33}a_{44}a_{55}a_{22}a_{66}a_{88}+a_{33}a_{44}a_{55}a_{22}a_{77}a_{88}+a_{33}a_{44}a_{55}a_{86}a_{67}a_{78}+a_{33}a_{44}a_{55}a_{61}a_{86}a_{18}-a_{33}a_{44}a_{55}a_{61}a_{22}a_{16}\\
&-a_{33}a_{44}a_{55}a_{81}a_{18}a_{77}-a_{33}a_{44}a_{55}a_{81}a_{22}a_{18}-a_{33}a_{44}a_{55}a_{81}a_{18}a_{66}+a_{33}a_{44}a_{22}a_{66}a_{77}a_{88}+a_{33}a_{44}a_{61}a_{86}a_{18}a_{77}\\
&+a_{33}a_{44}a_{11}a_{66}a_{77}a_{88}+a_{33}a_{44}a_{22}a_{86}a_{67}a_{78}-a_{51}a_{44}a_{22}a_{65}a_{86}a_{18}+a_{51}a_{33}a_{15}a_{76}a_{67}a_{88}-a_{51}a_{44}a_{22}a_{75}a_{16}a_{67}\\
&-a_{51}a_{33}a_{15}a_{86}a_{67}a_{78}+a_{51}a_{33}a_{65}a_{16}a_{77}a_{88}-a_{51}a_{44}a_{22}a_{15}a_{66}a_{88}+a_{33}a_{44}a_{55}a_{11}a_{66}a_{77}+a_{33}a_{44}a_{55}a_{11}a_{22}a_{88}\\
&-a_{33}a_{44}a_{55}a_{11}a_{76}a_{67}+a_{33}a_{44}a_{55}a_{11}a_{66}a_{88}+a_{33}a_{44}a_{55}a_{11}a_{77}a_{88}+a_{51}a_{44}a_{22}a_{15}a_{76}a_{67}+a_{51}a_{44}a_{22}a_{85}a_{18}a_{66}\\
&-a_{51}a_{44}a_{22}a_{15}a_{66}a_{77}+a_{51}a_{44}a_{22}a_{85}a_{18}a_{77}-a_{33}a_{44}a_{55}a_{76}a_{67}a_{88}-a_{33}a_{44}a_{22}a_{76}a_{67}a_{88}+a_{51}a_{44}a_{75}a_{86}a_{18}a_{67}\\
&+a_{51}a_{44}a_{65}a_{16}a_{77}a_{88}+a_{51}a_{44}a_{15}a_{76}a_{67}a_{88}-a_{51}a_{44}a_{15}a_{86}a_{67}a_{78}-a_{51}a_{22}a_{65}a_{86}a_{18}a_{77}-a_{51}a_{22}a_{15}a_{66}a_{77}a_{88}\\
&-a_{51}a_{22}a_{85}a_{76}a_{18}a_{67}+a_{51}a_{22}a_{85}a_{16}a_{67}a_{78}+a_{51}a_{22}a_{75}a_{86}a_{18}a_{67},
\end{aligned}
$$

$$
\begin{aligned}
A_7={}&a_{51}a_{44}a_{22}a_{15}a_{86}a_{67}a_{78}-a_{51}a_{33}a_{44}a_{22}a_{15}a_{76}a_{67}-a_{51}a_{33}a_{44}a_{22}a_{65}a_{16}a_{77}+a_{33}a_{44}a_{55}a_{81}a_{22}a_{18}a_{77}\\
&+a_{33}a_{44}a_{55}a_{81}a_{22}a_{18}a_{66}+a_{33}a_{44}a_{55}a_{11}a_{76}a_{67}a_{88}-a_{33}a_{44}a_{61}a_{22}a_{86}a_{18}a_{77}-a_{33}a_{44}a_{11}a_{22}a_{86}a_{67}a_{78}\\
&+a_{33}a_{44}a_{11}a_{22}a_{76}a_{67}a_{88}-a_{51}a_{44}a_{22}a_{75}a_{86}a_{18}a_{67}+a_{51}a_{33}a_{44}a_{15}a_{66}a_{77}a_{88}-a_{51}a_{44}a_{22}a_{15}a_{76}a_{67}a_{88}\\
&+a_{51}a_{33}a_{22}a_{15}a_{66}a_{77}a_{88}+a_{33}a_{55}a_{81}a_{22}a_{16}a_{67}a_{78}-a_{51}a_{33}a_{22}a_{15}a_{76}a_{67}a_{88}+a_{51}a_{33}a_{44}a_{65}a_{86}a_{18}a_{77}\\
&-a_{33}a_{44}a_{55}a_{11}a_{22}a_{77}a_{88}+a_{44}a_{55}a_{61}a_{22}a_{16}a_{77}a_{88}-a_{44}a_{55}a_{61}a_{22}a_{86}a_{18}a_{77}+a_{51}a_{33}a_{44}a_{22}a_{15}a_{66}a_{88}\\
&+a_{51}a_{33}a_{44}a_{22}a_{75}a_{16}a_{67}+a_{33}a_{44}a_{81}a_{22}a_{18}a_{66}a_{77}-a_{33}a_{44}a_{81}a_{22}a_{76}a_{18}a_{67}+a_{33}a_{44}a_{81}a_{22}a_{16}a_{67}a_{78}\\
&-a_{33}a_{44}a_{11}a_{22}a_{66}a_{77}a_{88}-a_{33}a_{55}a_{11}a_{22}a_{66}a_{77}a_{88}-a_{44}a_{55}a_{81}a_{22}a_{76}a_{18}a_{67}+a_{44}a_{55}a_{81}a_{22}a_{16}a_{67}a_{78}\\
&-a_{44}a_{55}a_{11}a_{22}a_{66}a_{77}a_{88}-a_{51}a_{33}a_{44}a_{22}a_{65}a_{16}a_{88}+a_{51}a_{33}a_{22}a_{65}a_{86}a_{18}a_{77}-a_{51}a_{33}a_{22}a_{85}a_{18}a_{66}a_{77}\\
&-a_{51}a_{33}a_{22}a_{75}a_{86}a_{18}a_{67}+a_{51}a_{33}a_{44}a_{22}a_{15}a_{77}a_{88}+a_{51}a_{33}a_{44}a_{22}a_{65}a_{86}a_{18}-a_{51}a_{33}a_{22}a_{85}a_{16}a_{67}a_{78}\\
&+a_{51}a_{33}a_{22}a_{75}a_{16}a_{67}a_{88}-a_{51}a_{44}a_{22}a_{65}a_{16}a_{77}a_{88}+a_{51}a_{33}a_{44}a_{75}a_{16}a_{67}a_{88}-a_{51}a_{33}a_{44}a_{85}a_{16}a_{67}a_{78}\\
&-a_{51}a_{33}a_{44}a_{22}a_{85}a_{18}a_{77}-a_{51}a_{33}a_{44}a_{22}a_{85}a_{18}a_{66}-a_{51}a_{44}a_{22}a_{85}a_{18}a_{66}a_{77}+a_{51}a_{33}a_{44}a_{85}a_{76}a_{18}a_{67}\\
&+a_{51}a_{33}a_{22}a_{15}a_{86}a_{67}a_{78}+a_{51}a_{44}a_{22}a_{75}a_{16}a_{67}a_{88}-a_{51}a_{44}a_{22}a_{85}a_{16}a_{67}a_{78}+a_{51}a_{33}a_{22}a_{85}a_{76}a_{18}a_{67}\\
&-a_{33}a_{44}a_{55}a_{11}a_{86}a_{67}a_{78}+a_{51}a_{44}a_{22}a_{15}a_{66}a_{77}a_{88}+a_{51}a_{44}a_{22}a_{85}a_{76}a_{18}a_{67}-a_{51}a_{33}a_{44}a_{75}a_{86}a_{18}a_{67}\\
&-a_{51}a_{33}a_{44}a_{65}a_{16}a_{77}a_{88}+a_{44}a_{55}a_{81}a_{22}a_{18}a_{66}a_{77}+a_{51}a_{33}a_{44}a_{22}a_{15}a_{66}a_{77}-a_{33}a_{44}a_{55}a_{11}a_{22}a_{66}a_{77}\\
&-a_{33}a_{44}a_{55}a_{11}a_{22}a_{66}a_{88}+a_{33}a_{44}a_{55}a_{61}a_{22}a_{16}a_{77}-a_{33}a_{44}a_{55}a_{61}a_{22}a_{86}a_{18}+a_{33}a_{44}a_{55}a_{81}a_{16}a_{67}a_{78}\\
&+a_{33}a_{44}a_{55}a_{81}a_{18}a_{66}a_{77}-a_{33}a_{44}a_{55}a_{81}a_{76}a_{18}a_{67}+a_{33}a_{44}a_{55}a_{11}a_{22}a_{76}a_{67}+a_{33}a_{44}a_{55}a_{61}a_{16}a_{77}a_{88}\\
&-a_{33}a_{44}a_{55}a_{61}a_{86}a_{18}a_{77}+a_{33}a_{44}a_{55}a_{61}a_{22}a_{16}a_{88}+a_{33}a_{55}a_{61}a_{22}a_{16}a_{77}a_{88}-a_{33}a_{55}a_{61}a_{22}a_{86}a_{18}a_{77}\\
&+a_{33}a_{55}a_{11}a_{22}a_{76}a_{67}a_{88}-a_{33}a_{55}a_{11}a_{22}a_{86}a_{67}a_{78}-a_{33}a_{44}a_{55}a_{22}a_{66}a_{77}a_{88}+a_{33}a_{44}a_{55}a_{22}a_{76}a_{67}a_{88}\\
&-a_{33}a_{44}a_{55}a_{22}a_{86}a_{67}a_{78}-a_{33}a_{44}a_{55}a_{11}a_{66}a_{77}a_{88}+a_{33}a_{55}a_{81}a_{22}a_{18}a_{66}a_{77}-a_{33}a_{55}a_{81}a_{22}a_{76}a_{18}a_{67}\\
&-a_{51}a_{33}a_{44}a_{15}a_{76}a_{67}a_{88}+a_{51}a_{44}a_{22}a_{65}a_{86}a_{18}a_{77}+a_{51}a_{33}a_{44}a_{15}a_{86}a_{67}a_{78}+a_{33}a_{44}a_{61}a_{22}a_{16}a_{77}a_{88}\\
&+a_{44}a_{55}a_{11}a_{22}a_{76}a_{67}a_{88}-a_{44}a_{55}a_{11}a_{22}a_{86}a_{67}a_{78}-a_{51}a_{33}a_{44}a_{85}a_{18}a_{66}a_{77}-a_{51}a_{33}a_{22}a_{65}a_{16}a_{77}a_{88},
\end{aligned}
$$

$$
\begin{aligned}
A_8={}&-a_{51}a_{33}a_{44}a_{22}a_{85}a_{76}a_{18}a_{67}+a_{51}a_{33}a_{44}a_{22}a_{85}a_{16}a_{67}a_{78}+a_{51}a_{33}a_{44}a_{22}a_{75}a_{86}a_{18}a_{67}+a_{51}a_{33}a_{44}a_{22}a_{65}a_{16}a_{77}a_{88}\\
&+a_{51}a_{33}a_{44}a_{22}a_{15}a_{76}a_{67}a_{88}-a_{51}a_{33}a_{44}a_{22}a_{15}a_{86}a_{67}a_{78}-a_{51}a_{33}a_{44}a_{22}a_{15}a_{66}a_{77}a_{88}-a_{51}a_{33}a_{44}a_{22}a_{75}a_{16}a_{67}a_{88}\\
&+a_{51}a_{33}a_{44}a_{22}a_{85}a_{18}a_{66}a_{77}-a_{51}a_{33}a_{44}a_{22}a_{65}a_{86}a_{18}a_{77}-a_{33}a_{44}a_{55}a_{81}a_{22}a_{16}a_{67}a_{78}+a_{33}a_{44}a_{55}a_{11}a_{22}a_{66}a_{77}a_{88}\\
&-a_{33}a_{44}a_{55}a_{61}a_{22}a_{16}a_{77}a_{88}+a_{33}a_{44}a_{55}a_{81}a_{22}a_{76}a_{18}a_{67}-a_{33}a_{44}a_{55}a_{11}a_{22}a_{76}a_{67}a_{88}+a_{33}a_{44}a_{55}a_{11}a_{22}a_{86}a_{67}a_{78}\\
&-a_{33}a_{44}a_{55}a_{81}a_{22}a_{18}a_{66}a_{77}+a_{33}a_{44}a_{55}a_{61}a_{22}a_{86}a_{18}a_{77},
\end{aligned}
$$

$$B_1 = -b_{32}a_{23},$$

$$B_2 = -b_{32}a_{21}a_{13} + b_{32}a_{23}a_{88} + b_{32}a_{55}a_{23} + b_{32}a_{23}a_{66} + b_{32}a_{23}a_{77} + b_{32}a_{23}a_{11} + b_{32}a_{44}a_{23} - a_{43}b_{32}a_{24},$$

$$\begin{aligned}B_3 = {} & -a_{51}b_{32}a_{13}a_{25} + b_{32}a_{21}a_{13}a_{66} - b_{32}a_{23}a_{11}a_{88} - b_{32}a_{55}a_{23}a_{77} + b_{32}a_{81}a_{23}a_{18} - b_{32}a_{44}a_{23}a_{88} + b_{32}a_{44}a_{21}a_{13} - b_{32}a_{55}a_{23}a_{66} \\ & -b_{32}a_{44}a_{55}a_{23} - b_{32}a_{23}a_{11}a_{66} - b_{32}a_{23}a_{77}a_{88} + b_{32}a_{61}a_{23}a_{16} + a_{51}b_{32}a_{23}a_{15} - b_{32}a_{44}a_{23}a_{11} + b_{32}a_{55}a_{21}a_{13} + b_{32}a_{23}a_{76}a_{67} \\ & +b_{32}a_{21}a_{13}a_{77} - b_{32}a_{55}a_{23}a_{11} - b_{32}a_{23}a_{66}a_{77} - b_{32}a_{23}a_{11}a_{77} - b_{32}a_{44}a_{23}a_{77} - b_{32}a_{23}a_{66}a_{88} + b_{32}a_{21}a_{13}a_{88} - b_{32}a_{55}a_{23}a_{88} \\ & -b_{32}a_{44}a_{23}a_{66} + a_{43}b_{32}a_{24}a_{66} + a_{43}b_{32}a_{24}a_{77} + a_{43}b_{32}a_{24}a_{11} - a_{43}b_{32}a_{21}a_{14} + a_{43}b_{32}a_{55}a_{24} + a_{43}b_{32}a_{24}a_{88},\end{aligned}$$

$$\begin{aligned}B_4 = {} & -b_{32}a_{55}a_{21}a_{13}a_{88} - b_{32}a_{55}a_{21}a_{13}a_{77} - b_{32}a_{44}a_{81}a_{23}a_{18} - b_{32}a_{44}a_{21}a_{13}a_{66} - b_{32}a_{44}a_{61}a_{23}a_{16} + b_{32}a_{44}a_{23}a_{77}a_{88} + b_{32}a_{44}a_{55}a_{23}a_{88} \\ & -a_{43}b_{32}a_{24}a_{11}a_{66} + a_{43}b_{32}a_{21}a_{14}a_{88} + a_{43}b_{32}a_{21}a_{14}a_{77} + a_{43}b_{32}a_{21}a_{14}a_{66} - a_{43}b_{32}a_{24}a_{77}a_{88} - a_{43}b_{32}a_{21}a_{64}a_{16} - a_{43}b_{32}a_{21}a_{84}a_{18} \\ & +a_{43}b_{32}a_{61}a_{24}a_{16} + a_{43}b_{32}a_{81}a_{24}a_{18} - a_{43}b_{32}a_{24}a_{66}a_{88} - a_{43}b_{32}a_{24}a_{66}a_{77} + a_{43}b_{32}a_{24}a_{76}a_{67} - a_{43}b_{32}a_{24}a_{11}a_{88} - a_{43}b_{32}a_{24}a_{11}a_{77} \\ & -a_{43}b_{32}a_{55}a_{24}a_{66} - a_{43}b_{32}a_{55}a_{24}a_{77} - a_{43}b_{32}a_{55}a_{24}a_{88} - a_{43}b_{32}a_{55}a_{24}a_{11} + a_{43}b_{32}a_{55}a_{21}a_{14} - b_{32}a_{23}a_{11}a_{76}a_{67} + b_{32}a_{23}a_{66}a_{77}a_{88} \\ & -b_{32}a_{81}a_{23}a_{18}a_{77} + b_{32}a_{23}a_{11}a_{66}a_{88} + b_{32}a_{61}a_{23}a_{86}a_{18} - b_{32}a_{23}a_{76}a_{67}a_{88} - b_{32}a_{21}a_{13}a_{77}a_{88} + b_{32}a_{21}a_{13}a_{76}a_{67} + b_{32}a_{23}a_{86}a_{67}a_{78} \\ & -b_{32}a_{81}a_{23}a_{18}a_{66} - b_{32}a_{61}a_{23}a_{16}a_{77} - b_{32}a_{44}a_{23}a_{76}a_{67} + b_{32}a_{44}a_{23}a_{11}a_{88} + b_{32}a_{44}a_{23}a_{66}a_{77} + b_{32}a_{44}a_{23}a_{11}a_{77} + b_{32}a_{44}a_{23}a_{11}a_{66} \\ & -b_{32}a_{44}a_{21}a_{13}a_{88} - b_{32}a_{44}a_{21}a_{13}a_{77} + b_{32}a_{44}a_{55}a_{23}a_{77} - b_{32}a_{44}a_{55}a_{21}a_{13} - a_{51}b_{32}a_{23}a_{15}a_{77} - a_{51}b_{32}a_{23}a_{15}a_{66} + a_{51}b_{32}a_{23}a_{65}a_{16} \\ & +a_{51}b_{32}a_{23}a_{85}a_{18} - a_{51}b_{32}a_{44}a_{23}a_{15} + a_{51}b_{32}a_{44}a_{13}a_{25} + b_{32}a_{44}a_{23}a_{66}a_{88} + b_{32}a_{44}a_{55}a_{23}a_{11} + b_{32}a_{44}a_{55}a_{23}a_{66} + b_{32}a_{23}a_{11}a_{66}a_{77} \\ & +b_{32}a_{23}a_{11}a_{77}a_{88} - b_{32}a_{61}a_{23}a_{16}a_{88} - b_{32}a_{21}a_{13}a_{66}a_{77} - b_{32}a_{21}a_{13}a_{66}a_{88} - b_{32}a_{55}a_{81}a_{23}a_{18} - b_{32}a_{55}a_{21}a_{13}a_{66} - b_{32}a_{55}a_{61}a_{23}a_{16} \\ & +a_{51}a_{43}b_{32}a_{24}a_{15} - a_{51}a_{43}b_{32}a_{14}a_{25} + a_{51}b_{32}a_{13}a_{25}a_{88} + a_{51}b_{32}a_{13}a_{25}a_{77} + a_{51}b_{32}a_{13}a_{25}a_{66} - a_{51}b_{32}a_{23}a_{15}a_{88} + b_{32}a_{55}a_{23}a_{77}a_{88} \\ & +b_{32}a_{55}a_{23}a_{66}a_{88} + b_{32}a_{55}a_{23}a_{66}a_{77} - b_{32}a_{55}a_{23}a_{76}a_{67} + b_{32}a_{55}a_{23}a_{11}a_{88} + b_{32}a_{55}a_{23}a_{11}a_{77} + b_{32}a_{55}a_{23}a_{11}a_{66},\end{aligned}$$

$$\begin{aligned}B_5 = {} & -a_{43}b_{32}a_{21}a_{14}a_{66}a_{77} - a_{43}b_{32}a_{21}a_{14}a_{66}a_{88} + a_{43}b_{32}a_{21}a_{14}a_{76}a_{67} - b_{32}a_{55}a_{21}a_{13}a_{76}a_{67} + b_{32}a_{55}a_{61}a_{23}a_{16}a_{88} + b_{32}a_{44}a_{55}a_{21}a_{13}a_{77} \\ & +b_{32}a_{55}a_{23}a_{11}a_{76}a_{67} + b_{32}a_{55}a_{21}a_{13}a_{77}a_{88} + b_{32}a_{55}a_{23}a_{76}a_{67}a_{88} - b_{32}a_{55}a_{23}a_{66}a_{77}a_{88} + b_{32}a_{44}a_{81}a_{23}a_{18}a_{66} - a_{43}b_{32}a_{81}a_{24}a_{18}a_{77} \\ & +a_{43}b_{32}a_{24}a_{86}a_{67}a_{78} - a_{51}b_{32}a_{13}a_{25}a_{66}a_{77} - a_{51}b_{32}a_{13}a_{25}a_{66}a_{88} - b_{32}a_{44}a_{55}a_{23}a_{11}a_{88} + b_{32}a_{44}a_{55}a_{21}a_{13}a_{88} + b_{32}a_{44}a_{55}a_{81}a_{23}a_{18} \\ & -b_{32}a_{44}a_{55}a_{23}a_{11}a_{66} + a_{43}b_{32}a_{55}a_{24}a_{66}a_{88} + b_{32}a_{44}a_{21}a_{13}a_{66}a_{77} + b_{32}a_{44}a_{21}a_{13}a_{77}a_{88} - b_{32}a_{44}a_{23}a_{11}a_{66}a_{77} - a_{51}b_{32}a_{44}a_{23}a_{65}a_{16} \\ & +a_{51}b_{32}a_{44}a_{23}a_{15}a_{66} - b_{32}a_{44}a_{55}a_{23}a_{66}a_{77} - b_{32}a_{81}a_{23}a_{76}a_{18}a_{67} + b_{32}a_{44}a_{55}a_{21}a_{13}a_{66} - b_{32}a_{44}a_{55}a_{23}a_{77}a_{88} - b_{32}a_{23}a_{11}a_{86}a_{67}a_{78} \\ & +a_{51}a_{43}b_{32}a_{14}a_{25}a_{77} - b_{32}a_{55}a_{61}a_{23}a_{86}a_{18} - a_{51}b_{32}a_{44}a_{23}a_{85}a_{18} + b_{32}a_{44}a_{23}a_{76}a_{67}a_{88} - b_{32}a_{44}a_{23}a_{66}a_{77}a_{88} - a_{43}b_{32}a_{55}a_{21}a_{14}a_{77} \\ & -a_{43}b_{32}a_{55}a_{21}a_{14}a_{88} + a_{43}b_{32}a_{55}a_{24}a_{11}a_{66} - a_{43}b_{32}a_{21}a_{74}a_{16}a_{67} + a_{43}b_{32}a_{55}a_{21}a_{84}a_{18} + a_{43}b_{32}a_{55}a_{21}a_{64}a_{16} - a_{43}b_{32}a_{55}a_{61}a_{24}a_{16} \\ & -a_{43}b_{32}a_{55}a_{81}a_{24}a_{18} + a_{43}b_{32}a_{55}a_{24}a_{11}a_{77} + a_{43}b_{32}a_{55}a_{24}a_{11}a_{88} + b_{32}a_{81}a_{23}a_{16}a_{67}a_{78} + b_{32}a_{44}a_{61}a_{23}a_{16}a_{88} - a_{43}b_{32}a_{55}a_{24}a_{76}a_{67} \\ & +b_{32}a_{44}a_{61}a_{23}a_{16}a_{77} - b_{32}a_{44}a_{61}a_{23}a_{86}a_{18} - a_{43}b_{32}a_{24}a_{11}a_{76}a_{67} + a_{51}b_{32}a_{44}a_{23}a_{15}a_{77} + a_{51}b_{32}a_{44}a_{23}a_{15}a_{88} - a_{51}b_{32}a_{13}a_{25}a_{77}a_{88} \\ & -a_{43}b_{32}a_{24}a_{76}a_{67}a_{88} - b_{32}a_{44}a_{23}a_{86}a_{67}a_{78} - a_{51}a_{43}b_{32}a_{84}a_{25}a_{18} + a_{51}b_{32}a_{23}a_{15}a_{66}a_{77} + a_{51}b_{32}a_{23}a_{15}a_{66}a_{88} - b_{32}a_{55}a_{23}a_{11}a_{66}a_{77} \\ & +b_{32}a_{55}a_{61}a_{23}a_{16}a_{77} + a_{43}b_{32}a_{24}a_{11}a_{66}a_{77} + a_{43}b_{32}a_{24}a_{11}a_{66}a_{88} + a_{51}a_{43}b_{32}a_{14}a_{25}a_{88} + a_{43}b_{32}a_{61}a_{24}a_{86}a_{18} + a_{43}b_{32}a_{21}a_{64}a_{16}a_{88} \\ & -a_{43}b_{32}a_{21}a_{64}a_{86}a_{18} + a_{43}b_{32}a_{21}a_{64}a_{16}a_{77} - a_{43}b_{32}a_{55}a_{21}a_{14}a_{66} - b_{32}a_{44}a_{23}a_{11}a_{77}a_{88} - b_{32}a_{21}a_{13}a_{76}a_{67}a_{88} - a_{51}a_{43}b_{32}a_{24}a_{15}a_{88} \\ & +a_{51}a_{43}b_{32}a_{24}a_{65}a_{16} + b_{32}a_{81}a_{23}a_{18}a_{66}a_{77} - b_{32}a_{55}a_{23}a_{11}a_{66}a_{88} - a_{43}b_{32}a_{61}a_{24}a_{16}a_{88} + a_{43}b_{32}a_{21}a_{84}a_{18}a_{66} + a_{43}b_{32}a_{21}a_{84}a_{18}a_{77} \\ & +b_{32}a_{44}a_{23}a_{11}a_{76}a_{67} + b_{32}a_{55}a_{21}a_{13}a_{66}a_{88} - a_{51}b_{32}a_{44}a_{13}a_{25}a_{66} - a_{51}b_{32}a_{44}a_{13}a_{25}a_{77} + b_{32}a_{21}a_{13}a_{86}a_{67}a_{78} - a_{51}a_{43}b_{32}a_{64}a_{25}a_{16} \\ & +a_{51}a_{43}b_{32}a_{24}a_{85}a_{18} + a_{51}a_{43}b_{32}a_{14}a_{25}a_{66} - a_{43}b_{32}a_{21}a_{14}a_{77}a_{88} + b_{32}a_{44}a_{21}a_{13}a_{66}a_{88} + b_{32}a_{55}a_{81}a_{23}a_{18}a_{77} - b_{32}a_{44}a_{55}a_{23}a_{66}a_{88} \\ & -a_{51}a_{43}b_{32}a_{24}a_{15}a_{66} - a_{43}b_{32}a_{61}a_{24}a_{16}a_{77} + a_{51}b_{32}a_{23}a_{15}a_{77}a_{88} + a_{51}b_{32}a_{13}a_{25}a_{76}a_{67} + b_{32}a_{44}a_{55}a_{23}a_{76}a_{67} + b_{32}a_{55}a_{21}a_{13}a_{66}a_{77} \\ & -b_{32}a_{23}a_{11}a_{66}a_{77}a_{88} + a_{51}b_{32}a_{23}a_{75}a_{16}a_{67} + a_{51}b_{32}a_{23}a_{65}a_{86}a_{18} - a_{51}b_{32}a_{44}a_{13}a_{25}a_{88} + a_{43}b_{32}a_{55}a_{24}a_{66}a_{77} - a_{51}b_{32}a_{23}a_{85}a_{18}a_{66} \\ & -a_{51}b_{32}a_{23}a_{85}a_{18}a_{77} + b_{32}a_{21}a_{13}a_{66}a_{77}a_{88} + b_{32}a_{61}a_{23}a_{16}a_{77}a_{88} + a_{43}b_{32}a_{55}a_{24}a_{77}a_{88} - a_{51}a_{43}b_{32}a_{24}a_{15}a_{77} - b_{32}a_{44}a_{23}a_{11}a_{66}a_{88} \\ & +b_{32}a_{44}a_{81}a_{23}a_{18}a_{77} + a_{43}b_{32}a_{24}a_{66}a_{77}a_{88} - a_{43}b_{32}a_{81}a_{24}a_{18}a_{66} - a_{51}b_{32}a_{23}a_{15}a_{76}a_{67} - a_{51}b_{32}a_{23}a_{65}a_{16}a_{77} - a_{51}b_{32}a_{23}a_{65}a_{16}a_{88} \\ & -b_{32}a_{61}a_{23}a_{86}a_{18}a_{77} + b_{32}a_{23}a_{11}a_{76}a_{67}a_{88} + a_{43}b_{32}a_{24}a_{11}a_{77}a_{88} + b_{32}a_{55}a_{81}a_{23}a_{18}a_{66} - b_{32}a_{55}a_{23}a_{86}a_{67}a_{78} + b_{32}a_{44}a_{55}a_{61}a_{23}a_{16} \\ & -b_{32}a_{44}a_{21}a_{13}a_{76}a_{67} - b_{32}a_{44}a_{55}a_{23}a_{11}a_{77} - b_{32}a_{55}a_{23}a_{11}a_{77}a_{88},\end{aligned}$$

$$\begin{aligned}B_6 = {} & -a_{43}b_{32}a_{61}a_{24}a_{86}a_{18}a_{77} + a_{43}b_{32}a_{61}a_{24}a_{16}a_{77}a_{88} + a_{43}b_{32}a_{21}a_{84}a_{76}a_{18}a_{67} + a_{43}b_{32}a_{81}a_{24}a_{16}a_{67}a_{78} + a_{43}b_{32}a_{81}a_{24}a_{18}a_{66}a_{77} \\ & -a_{43}b_{32}a_{81}a_{24}a_{76}a_{18}a_{67} + b_{32}a_{44}a_{55}a_{23}a_{66}a_{77}a_{88} + b_{32}a_{44}a_{55}a_{61}a_{23}a_{86}a_{18} + b_{32}a_{44}a_{55}a_{23}a_{11}a_{66}a_{88} + a_{51}b_{32}a_{23}a_{65}a_{16}a_{77}a_{88} \\ & -a_{51}b_{32}a_{23}a_{65}a_{86}a_{18}a_{77} + a_{51}b_{32}a_{23}a_{75}a_{86}a_{18}a_{67} + a_{51}b_{32}a_{23}a_{85}a_{16}a_{67}a_{78} - a_{51}b_{32}a_{23}a_{75}a_{16}a_{67}a_{88} + a_{51}b_{32}a_{23}a_{85}a_{18}a_{66}a_{77} \\ & -a_{51}b_{32}a_{23}a_{85}a_{76}a_{18}a_{67} + a_{43}b_{32}a_{55}a_{61}a_{24}a_{16}a_{77} - a_{43}b_{32}a_{55}a_{61}a_{24}a_{86}a_{18} + a_{43}b_{32}a_{55}a_{81}a_{24}a_{18}a_{77} + a_{43}b_{32}a_{55}a_{81}a_{24}a_{18}a_{66} \\ & -a_{43}b_{32}a_{55}a_{24}a_{66}a_{77}a_{88} + a_{43}b_{32}a_{55}a_{24}a_{76}a_{67}a_{88} - a_{43}b_{32}a_{55}a_{24}a_{86}a_{67}a_{78} + a_{43}b_{32}a_{55}a_{21}a_{64}a_{86}a_{18} + a_{43}b_{32}a_{55}a_{21}a_{74}a_{16}a_{67}\end{aligned}$$

$$+a_{51}a_{43}b_{32}a_{24}a_{65}a_{86}a_{18}+a_{51}a_{43}b_{32}a_{24}a_{75}a_{16}a_{67}+a_{51}b_{32}a_{44}a_{13}a_{25}a_{77}a_{88}+a_{51}b_{32}a_{44}a_{13}a_{25}a_{66}a_{88}+a_{51}b_{32}a_{44}a_{13}a_{25}a_{66}a_{77}$$
$$-a_{51}b_{32}a_{44}a_{23}a_{15}a_{77}a_{88}-a_{51}b_{32}a_{44}a_{13}a_{25}a_{76}a_{67}-a_{43}b_{32}a_{55}a_{24}a_{11}a_{66}a_{88}-a_{43}b_{32}a_{55}a_{24}a_{11}a_{66}a_{77}+a_{43}b_{32}a_{55}a_{24}a_{11}a_{76}a_{67}$$
$$+a_{43}b_{32}a_{55}a_{21}a_{14}a_{77}a_{88}-a_{51}b_{32}a_{44}a_{23}a_{15}a_{66}a_{88}-a_{51}b_{32}a_{44}a_{23}a_{15}a_{66}a_{77}+a_{51}b_{32}a_{44}a_{23}a_{15}a_{76}a_{67}+a_{51}b_{32}a_{44}a_{23}a_{65}a_{16}a_{88}$$
$$+a_{51}b_{32}a_{44}a_{23}a_{65}a_{16}a_{77}-a_{51}b_{32}a_{44}a_{23}a_{65}a_{86}a_{18}-a_{51}b_{32}a_{44}a_{23}a_{75}a_{16}a_{67}+a_{51}b_{32}a_{44}a_{23}a_{85}a_{18}a_{77}+a_{51}a_{43}b_{32}a_{64}a_{25}a_{16}a_{77}$$
$$+a_{51}b_{32}a_{44}a_{23}a_{85}a_{18}a_{66}+a_{51}a_{43}b_{32}a_{64}a_{25}a_{16}a_{88}+a_{51}b_{32}a_{13}a_{25}a_{66}a_{77}a_{88}-a_{51}a_{43}b_{32}a_{24}a_{15}a_{76}a_{67}-a_{51}b_{32}a_{13}a_{25}a_{76}a_{67}a_{88}$$
$$+a_{51}b_{32}a_{13}a_{25}a_{86}a_{67}a_{78}-a_{51}b_{32}a_{23}a_{15}a_{66}a_{77}a_{88}-a_{43}b_{32}a_{21}a_{84}a_{16}a_{67}a_{78}+a_{51}b_{32}a_{23}a_{15}a_{76}a_{67}a_{88}-a_{51}b_{32}a_{23}a_{15}a_{86}a_{67}a_{78}$$
$$-a_{51}a_{43}b_{32}a_{24}a_{65}a_{16}a_{77}-a_{51}a_{43}b_{32}a_{24}a_{65}a_{16}a_{88}+b_{32}a_{55}a_{61}a_{23}a_{86}a_{18}a_{77}+b_{32}a_{55}a_{81}a_{23}a_{76}a_{18}a_{67}-b_{32}a_{55}a_{81}a_{23}a_{16}a_{67}a_{78}$$
$$-b_{32}a_{55}a_{21}a_{13}a_{86}a_{67}a_{78}+b_{32}a_{55}a_{23}a_{11}a_{66}a_{77}a_{88}-b_{32}a_{55}a_{61}a_{23}a_{16}a_{77}a_{88}+b_{32}a_{55}a_{23}a_{11}a_{86}a_{67}a_{78}+b_{32}a_{55}a_{21}a_{13}a_{76}a_{67}a_{88}$$
$$-b_{32}a_{55}a_{21}a_{13}a_{66}a_{77}a_{88}-b_{32}a_{55}a_{23}a_{11}a_{76}a_{67}a_{88}-b_{32}a_{55}a_{81}a_{23}a_{18}a_{66}a_{77}-b_{32}a_{44}a_{21}a_{13}a_{86}a_{67}a_{78}+a_{51}a_{43}b_{32}a_{14}a_{25}a_{76}a_{67}$$
$$+a_{51}a_{43}b_{32}a_{24}a_{15}a_{77}a_{88}+a_{51}a_{43}b_{32}a_{24}a_{15}a_{66}a_{88}+a_{51}a_{43}b_{32}a_{24}a_{15}a_{66}a_{77}-a_{51}a_{43}b_{32}a_{64}a_{25}a_{86}a_{18}-a_{51}a_{43}b_{32}a_{74}a_{25}a_{16}a_{67}$$
$$+a_{51}a_{43}b_{32}a_{84}a_{25}a_{18}a_{77}+a_{51}a_{43}b_{32}a_{84}a_{25}a_{18}a_{66}-b_{32}a_{44}a_{55}a_{23}a_{76}a_{67}a_{88}-b_{32}a_{44}a_{55}a_{21}a_{13}a_{77}a_{88}+b_{32}a_{44}a_{55}a_{23}a_{86}a_{67}a_{78}$$
$$+b_{32}a_{44}a_{55}a_{21}a_{13}a_{76}a_{67}-b_{32}a_{44}a_{55}a_{81}a_{23}a_{18}a_{66}+b_{32}a_{44}a_{55}a_{23}a_{11}a_{66}a_{77}-b_{32}a_{44}a_{55}a_{61}a_{23}a_{16}a_{77}+b_{32}a_{44}a_{55}a_{23}a_{11}a_{77}a_{88}$$
$$-b_{32}a_{44}a_{55}a_{61}a_{23}a_{16}a_{88}-b_{32}a_{44}a_{55}a_{21}a_{13}a_{66}a_{88}-b_{32}a_{44}a_{55}a_{21}a_{13}a_{66}a_{77}+a_{43}b_{32}a_{55}a_{21}a_{14}a_{66}a_{77}-a_{43}b_{32}a_{55}a_{21}a_{14}a_{76}a_{67}$$
$$-a_{43}b_{32}a_{55}a_{21}a_{64}a_{16}a_{88}-a_{43}b_{32}a_{55}a_{21}a_{64}a_{16}a_{77}-a_{43}b_{32}a_{21}a_{84}a_{18}a_{66}a_{77}-b_{32}a_{44}a_{81}a_{23}a_{16}a_{67}a_{78}+a_{43}b_{32}a_{55}a_{21}a_{14}a_{66}a_{88}$$
$$+a_{43}b_{32}a_{21}a_{14}a_{66}a_{77}a_{88}-a_{43}b_{32}a_{21}a_{14}a_{76}a_{67}a_{88}+a_{43}b_{32}a_{21}a_{14}a_{86}a_{67}a_{78}-a_{43}b_{32}a_{21}a_{64}a_{16}a_{77}a_{88}+a_{43}b_{32}a_{21}a_{64}a_{86}a_{18}a_{77}$$
$$+a_{43}b_{32}a_{21}a_{74}a_{16}a_{67}a_{88}-a_{43}b_{32}a_{21}a_{74}a_{86}a_{18}a_{67}-a_{43}b_{32}a_{55}a_{21}a_{84}a_{18}a_{77}-a_{43}b_{32}a_{55}a_{21}a_{84}a_{18}a_{66}+a_{43}b_{32}a_{55}a_{61}a_{24}a_{16}a_{88}$$
$$-a_{43}b_{32}a_{24}a_{11}a_{66}a_{77}a_{88}+a_{43}b_{32}a_{24}a_{11}a_{76}a_{67}a_{88}-a_{51}a_{43}b_{32}a_{14}a_{25}a_{66}a_{77}+b_{32}a_{44}a_{81}a_{23}a_{76}a_{18}a_{67}-a_{51}a_{43}b_{32}a_{24}a_{85}a_{18}a_{77}$$
$$-a_{51}a_{43}b_{32}a_{24}a_{85}a_{18}a_{66}-a_{51}a_{43}b_{32}a_{14}a_{25}a_{77}a_{88}-a_{51}a_{43}b_{32}a_{14}a_{25}a_{66}a_{88}-a_{43}b_{32}a_{55}a_{24}a_{11}a_{77}a_{88}+b_{32}a_{44}a_{61}a_{23}a_{86}a_{18}a_{77}$$
$$+b_{32}a_{44}a_{23}a_{11}a_{66}a_{77}a_{88}+b_{32}a_{44}a_{21}a_{13}a_{76}a_{67}a_{88}+b_{32}a_{44}a_{23}a_{11}a_{86}a_{67}a_{78}-b_{32}a_{44}a_{81}a_{23}a_{18}a_{66}a_{77}-b_{32}a_{44}a_{61}a_{23}a_{16}a_{77}a_{88}$$
$$-b_{32}a_{44}a_{55}a_{81}a_{23}a_{18}a_{77}-b_{32}a_{44}a_{55}a_{23}a_{11}a_{76}a_{67}-b_{32}a_{44}a_{21}a_{13}a_{66}a_{77}a_{88}-b_{32}a_{44}a_{23}a_{11}a_{76}a_{67}a_{88}-a_{43}b_{32}a_{24}a_{11}a_{86}a_{67}a_{78},$$

$$\begin{aligned}B_7 = {} & -a_{43}b_{32}a_{55}a_{81}a_{24}a_{18}a_{66}a_{77}+a_{43}b_{32}a_{55}a_{81}a_{24}a_{76}a_{18}a_{67}+a_{43}b_{32}a_{55}a_{61}a_{24}a_{86}a_{18}a_{77}+a_{43}b_{32}a_{55}a_{24}a_{11}a_{86}a_{67}a_{78}\\
& -a_{43}b_{32}a_{55}a_{24}a_{11}a_{76}a_{67}a_{88}-a_{43}b_{32}a_{55}a_{21}a_{14}a_{66}a_{77}a_{88}+a_{43}b_{32}a_{55}a_{24}a_{11}a_{66}a_{77}a_{88}+a_{43}b_{32}a_{55}a_{21}a_{84}a_{16}a_{67}a_{78}\\
& +a_{43}b_{32}a_{55}a_{21}a_{84}a_{18}a_{66}a_{77}-a_{43}b_{32}a_{55}a_{21}a_{84}a_{76}a_{18}a_{67}-a_{43}b_{32}a_{55}a_{61}a_{24}a_{16}a_{77}a_{88}+a_{51}b_{32}a_{44}a_{13}a_{25}a_{76}a_{67}a_{88}\\
& -a_{51}b_{32}a_{44}a_{13}a_{25}a_{86}a_{67}a_{78}-b_{32}a_{44}a_{55}a_{61}a_{23}a_{86}a_{18}a_{77}-a_{51}b_{32}a_{44}a_{13}a_{25}a_{66}a_{77}a_{88}-a_{43}b_{32}a_{55}a_{21}a_{64}a_{86}a_{18}a_{77}\\
& -a_{43}b_{32}a_{55}a_{21}a_{74}a_{16}a_{67}a_{88}-a_{43}b_{32}a_{55}a_{21}a_{14}a_{86}a_{67}a_{78}+a_{43}b_{32}a_{55}a_{21}a_{64}a_{16}a_{77}a_{88}+a_{51}a_{43}b_{32}a_{14}a_{25}a_{66}a_{77}a_{88}\\
& +a_{43}b_{32}a_{55}a_{21}a_{14}a_{76}a_{67}a_{88}+a_{51}a_{43}b_{32}a_{24}a_{85}a_{16}a_{67}a_{78}+a_{51}a_{43}b_{32}a_{24}a_{85}a_{18}a_{66}a_{77}-a_{51}a_{43}b_{32}a_{24}a_{75}a_{16}a_{67}a_{88}\\
& +a_{51}a_{43}b_{32}a_{24}a_{75}a_{86}a_{18}a_{67}-a_{51}a_{43}b_{32}a_{24}a_{65}a_{86}a_{18}a_{77}+a_{43}b_{32}a_{55}a_{21}a_{74}a_{86}a_{18}a_{67}+a_{51}a_{43}b_{32}a_{24}a_{65}a_{16}a_{77}a_{88}\\
& +a_{51}b_{32}a_{44}a_{23}a_{75}a_{16}a_{67}a_{88}-a_{51}b_{32}a_{44}a_{23}a_{75}a_{86}a_{18}a_{67}-a_{51}b_{32}a_{44}a_{23}a_{65}a_{16}a_{77}a_{88}+a_{51}b_{32}a_{44}a_{23}a_{65}a_{86}a_{18}a_{77}\\
& +a_{51}b_{32}a_{44}a_{23}a_{15}a_{86}a_{67}a_{78}+a_{51}b_{32}a_{44}a_{23}a_{15}a_{66}a_{77}a_{88}-a_{51}b_{32}a_{44}a_{23}a_{15}a_{76}a_{67}a_{88}-b_{32}a_{44}a_{55}a_{23}a_{11}a_{66}a_{77}a_{88}\\
& +b_{32}a_{44}a_{55}a_{21}a_{13}a_{86}a_{67}a_{78}-b_{32}a_{44}a_{55}a_{21}a_{13}a_{76}a_{67}a_{88}-b_{32}a_{44}a_{55}a_{81}a_{23}a_{76}a_{18}a_{67}+b_{32}a_{44}a_{55}a_{81}a_{23}a_{16}a_{67}a_{78}\\
& +a_{51}a_{43}b_{32}a_{84}a_{25}a_{76}a_{18}a_{67}-a_{51}a_{43}b_{32}a_{84}a_{25}a_{16}a_{67}a_{78}-a_{51}a_{43}b_{32}a_{84}a_{25}a_{18}a_{66}a_{77}+a_{51}a_{43}b_{32}a_{74}a_{25}a_{16}a_{67}a_{88}\\
& -a_{51}a_{43}b_{32}a_{74}a_{25}a_{86}a_{18}a_{67}-a_{51}a_{43}b_{32}a_{64}a_{25}a_{16}a_{77}a_{88}+a_{51}a_{43}b_{32}a_{64}a_{25}a_{86}a_{18}a_{77}+a_{51}a_{43}b_{32}a_{14}a_{25}a_{86}a_{67}a_{78}\\
& -a_{51}a_{43}b_{32}a_{24}a_{15}a_{66}a_{77}a_{88}-a_{51}a_{43}b_{32}a_{24}a_{15}a_{86}a_{67}a_{78}-a_{51}a_{43}b_{32}a_{14}a_{25}a_{76}a_{67}a_{88}+a_{51}a_{43}b_{32}a_{24}a_{15}a_{76}a_{67}a_{88}\\
& -a_{51}a_{43}b_{32}a_{24}a_{85}a_{76}a_{18}a_{67}-a_{43}b_{32}a_{55}a_{81}a_{24}a_{16}a_{67}a_{78}+a_{51}b_{32}a_{44}a_{23}a_{85}a_{76}a_{18}a_{67}-a_{51}b_{32}a_{44}a_{23}a_{85}a_{16}a_{67}a_{78}\\
& -a_{51}b_{32}a_{44}a_{23}a_{85}a_{18}a_{66}a_{77}+b_{32}a_{44}a_{55}a_{81}a_{23}a_{18}a_{66}a_{77}+b_{32}a_{44}a_{55}a_{21}a_{13}a_{66}a_{77}a_{88}+b_{32}a_{44}a_{55}a_{61}a_{23}a_{16}a_{77}a_{88}\\
& +b_{32}a_{44}a_{55}a_{23}a_{11}a_{76}a_{67}a_{88}-b_{32}a_{44}a_{55}a_{23}a_{11}a_{86}a_{67}a_{78},\end{aligned}$$

$$C_1=-b_{42}a_{24},$$

$$C_2=b_{42}a_{24}a_{66}+b_{42}a_{24}a_{88}+b_{42}a_{55}a_{24}+b_{42}a_{24}a_{77}+b_{42}a_{24}a_{11}+b_{42}a_{33}a_{24}-b_{42}a_{21}a_{14},$$

$$\begin{aligned}C_3 = {} & b_{42}a_{21}a_{14}a_{77}+b_{42}a_{81}a_{24}a_{18}-b_{42}a_{24}a_{66}a_{77}-b_{42}a_{21}a_{64}a_{16}+b_{42}a_{21}a_{14}a_{66}-b_{42}a_{24}a_{77}a_{88}+b_{42}a_{24}a_{76}a_{67}-b_{42}a_{24}a_{11}a_{66}\\
& -b_{42}a_{21}a_{84}a_{18}+b_{42}a_{61}a_{24}a_{16}+b_{42}a_{21}a_{14}a_{88}-a_{51}b_{42}a_{14}a_{25}+a_{51}b_{42}a_{24}a_{15}-b_{42}a_{24}a_{11}a_{88}-b_{42}a_{24}a_{11}a_{77}-b_{42}a_{24}a_{66}a_{88}\end{aligned}$$

$$-b_{42}a_{33}a_{24}a_{77}-b_{42}a_{33}a_{24}a_{88}-b_{42}a_{33}a_{24}a_{11}+b_{42}a_{33}a_{21}a_{14}-b_{42}a_{33}a_{55}a_{24}-b_{42}a_{55}a_{24}a_{66}-b_{42}a_{55}a_{24}a_{77}-b_{42}a_{55}a_{24}a_{88}$$
$$-b_{42}a_{55}a_{24}a_{11}+b_{42}a_{55}a_{21}a_{14}-b_{42}a_{33}a_{24}a_{66},$$

$$\begin{aligned}C_4 = {} & b_{42}a_{33}a_{55}a_{24}a_{88}-b_{42}a_{55}a_{81}a_{24}a_{18}+b_{42}a_{55}a_{24}a_{77}a_{88}+b_{42}a_{55}a_{24}a_{66}a_{88}-b_{42}a_{33}a_{21}a_{14}a_{88}-b_{42}a_{33}a_{21}a_{14}a_{77}\\
& -b_{42}a_{21}a_{74}a_{16}a_{67}+b_{42}a_{55}a_{24}a_{11}a_{66}-b_{42}a_{55}a_{21}a_{14}a_{88}-a_{51}b_{42}a_{24}a_{15}a_{77}-b_{42}a_{55}a_{21}a_{14}a_{77}+a_{51}b_{42}a_{14}a_{25}a_{77}\\
& +a_{51}b_{42}a_{14}a_{25}a_{66}-a_{51}b_{42}a_{24}a_{15}a_{88}-a_{51}b_{42}a_{33}a_{24}a_{15}+a_{51}b_{42}a_{14}a_{25}a_{88}-b_{42}a_{33}a_{81}a_{24}a_{18}+b_{42}a_{33}a_{24}a_{11}a_{77}\\
& -b_{42}a_{21}a_{14}a_{77}a_{88}-b_{42}a_{21}a_{14}a_{66}a_{88}-b_{42}a_{21}a_{14}a_{66}a_{77}+b_{42}a_{24}a_{11}a_{66}a_{88}+b_{42}a_{24}a_{11}a_{66}a_{77}-b_{42}a_{24}a_{11}a_{76}a_{67}\\
& -b_{42}a_{33}a_{61}a_{24}a_{16}+b_{42}a_{21}a_{84}a_{18}a_{77}+b_{42}a_{21}a_{84}a_{18}a_{66}-b_{42}a_{61}a_{24}a_{16}a_{88}+b_{42}a_{21}a_{14}a_{76}a_{67}+b_{42}a_{21}a_{64}a_{16}a_{88}\\
& -b_{42}a_{24}a_{76}a_{67}a_{88}+b_{42}a_{24}a_{86}a_{67}a_{78}+b_{42}a_{24}a_{11}a_{77}a_{88}+b_{42}a_{33}a_{21}a_{64}a_{16}+b_{42}a_{33}a_{55}a_{24}a_{11}+b_{42}a_{33}a_{24}a_{66}a_{88}\\
& +b_{42}a_{33}a_{55}a_{24}a_{77}+b_{42}a_{33}a_{55}a_{24}a_{66}-b_{42}a_{21}a_{64}a_{86}a_{18}-b_{42}a_{33}a_{21}a_{14}a_{66}+b_{42}a_{33}a_{21}a_{84}a_{18}-b_{42}a_{55}a_{21}a_{14}a_{66}\\
& +b_{42}a_{55}a_{21}a_{64}a_{16}+b_{42}a_{55}a_{21}a_{84}a_{18}-b_{42}a_{55}a_{61}a_{24}a_{16}+b_{42}a_{21}a_{64}a_{16}a_{77}+a_{51}b_{42}a_{24}a_{65}a_{16}+a_{51}b_{42}a_{24}a_{85}a_{18}\\
& -a_{51}b_{42}a_{64}a_{25}a_{16}-a_{51}b_{42}a_{84}a_{25}a_{18}+a_{51}b_{42}a_{33}a_{14}a_{25}+b_{42}a_{61}a_{24}a_{86}a_{18}-b_{42}a_{81}a_{24}a_{18}a_{77}-b_{42}a_{81}a_{24}a_{18}a_{66}\\
& -b_{42}a_{61}a_{24}a_{16}a_{77}+b_{42}a_{33}a_{24}a_{77}a_{88}-b_{42}a_{33}a_{55}a_{21}a_{14}+b_{42}a_{33}a_{24}a_{11}a_{88}+b_{42}a_{33}a_{24}a_{66}a_{77}-b_{42}a_{33}a_{24}a_{76}a_{67}\\
& +b_{42}a_{24}a_{66}a_{77}a_{88}+b_{42}a_{55}a_{24}a_{11}a_{77}+b_{42}a_{33}a_{24}a_{11}a_{66}+b_{42}a_{55}a_{24}a_{66}a_{77}-b_{42}a_{55}a_{24}a_{76}a_{67}+b_{42}a_{55}a_{24}a_{11}a_{88}\\
& -a_{51}b_{42}a_{24}a_{15}a_{66},\end{aligned}$$

$$\begin{aligned}C_5 = {} & -b_{42}a_{61}a_{24}a_{86}a_{18}a_{77}+b_{42}a_{61}a_{24}a_{16}a_{77}a_{88}+b_{42}a_{21}a_{84}a_{76}a_{18}a_{67}+b_{42}a_{81}a_{24}a_{16}a_{67}a_{78}-b_{42}a_{21}a_{64}a_{16}a_{77}a_{88}\\
& +b_{42}a_{21}a_{14}a_{86}a_{67}a_{78}+b_{42}a_{21}a_{64}a_{86}a_{18}a_{77}-b_{42}a_{21}a_{74}a_{86}a_{18}a_{67}+b_{42}a_{21}a_{74}a_{16}a_{67}a_{88}-b_{42}a_{55}a_{21}a_{84}a_{18}a_{66}\\
& -b_{42}a_{55}a_{21}a_{84}a_{18}a_{77}+b_{42}a_{55}a_{61}a_{24}a_{16}a_{88}-b_{42}a_{21}a_{84}a_{18}a_{66}a_{77}-b_{42}a_{21}a_{84}a_{16}a_{67}a_{78}-b_{42}a_{24}a_{11}a_{86}a_{67}a_{78}\\
& +b_{42}a_{24}a_{11}a_{76}a_{67}a_{88}-b_{42}a_{24}a_{11}a_{66}a_{77}a_{88}-b_{42}a_{21}a_{14}a_{76}a_{67}a_{88}+b_{42}a_{21}a_{14}a_{66}a_{77}a_{88}+b_{42}a_{55}a_{61}a_{24}a_{16}a_{77}\\
& -b_{42}a_{55}a_{61}a_{24}a_{86}a_{18}-b_{42}a_{55}a_{24}a_{86}a_{67}a_{78}+b_{42}a_{55}a_{24}a_{76}a_{67}a_{88}-b_{42}a_{55}a_{24}a_{66}a_{77}a_{88}+b_{42}a_{55}a_{81}a_{24}a_{18}a_{66}\\
& -b_{42}a_{55}a_{24}a_{11}a_{77}a_{88}+b_{42}a_{55}a_{81}a_{24}a_{18}a_{77}-b_{42}a_{55}a_{21}a_{64}a_{16}a_{77}-b_{42}a_{55}a_{24}a_{11}a_{66}a_{88}-b_{42}a_{55}a_{24}a_{11}a_{66}a_{77}\\
& +b_{42}a_{55}a_{24}a_{11}a_{76}a_{67}+b_{42}a_{55}a_{21}a_{14}a_{77}a_{88}+b_{42}a_{55}a_{21}a_{14}a_{66}a_{88}+b_{42}a_{55}a_{21}a_{14}a_{66}a_{77}-b_{42}a_{55}a_{21}a_{64}a_{16}a_{88}\\
& -b_{42}a_{55}a_{21}a_{14}a_{76}a_{67}+a_{51}b_{42}a_{24}a_{15}a_{77}a_{88}+b_{42}a_{55}a_{21}a_{64}a_{86}a_{18}+b_{42}a_{55}a_{21}a_{74}a_{16}a_{67}-b_{42}a_{33}a_{21}a_{84}a_{18}a_{77}\\
& +b_{42}a_{33}a_{61}a_{24}a_{16}a_{88}-b_{42}a_{33}a_{21}a_{84}a_{18}a_{66}+b_{42}a_{33}a_{81}a_{24}a_{18}a_{77}-b_{42}a_{33}a_{61}a_{24}a_{86}a_{18}+b_{42}a_{33}a_{61}a_{24}a_{16}a_{77}\\
& -a_{51}b_{42}a_{33}a_{14}a_{25}a_{66}+b_{42}a_{33}a_{81}a_{24}a_{18}a_{66}-b_{42}a_{33}a_{24}a_{11}a_{66}a_{88}-b_{42}a_{33}a_{24}a_{11}a_{77}a_{88}-b_{42}a_{33}a_{24}a_{86}a_{67}a_{78}\\
& +b_{42}a_{33}a_{24}a_{76}a_{67}a_{88}-b_{42}a_{33}a_{24}a_{66}a_{77}a_{88}-a_{51}b_{42}a_{14}a_{25}a_{66}a_{77}+a_{51}b_{42}a_{14}a_{25}a_{76}a_{67}+a_{51}b_{42}a_{84}a_{25}a_{18}a_{77}\\
& -a_{51}b_{42}a_{14}a_{25}a_{77}a_{88}-a_{51}b_{42}a_{14}a_{25}a_{66}a_{88}+a_{51}b_{42}a_{84}a_{25}a_{18}a_{66}-a_{51}b_{42}a_{33}a_{14}a_{25}a_{88}-b_{42}a_{33}a_{24}a_{11}a_{66}a_{77}\\
& -a_{51}b_{42}a_{74}a_{25}a_{16}a_{67}+b_{42}a_{33}a_{24}a_{11}a_{76}a_{67}-a_{51}b_{42}a_{24}a_{15}a_{76}a_{67}-a_{51}b_{42}a_{24}a_{65}a_{16}a_{88}-a_{51}b_{42}a_{24}a_{65}a_{16}a_{77}\\
& +a_{51}b_{42}a_{24}a_{65}a_{86}a_{18}+a_{51}b_{42}a_{24}a_{75}a_{16}a_{67}+a_{51}b_{42}a_{64}a_{25}a_{16}a_{88}+a_{51}b_{42}a_{64}a_{25}a_{16}a_{77}-a_{51}b_{42}a_{64}a_{25}a_{86}a_{18}\\
& +a_{51}b_{42}a_{24}a_{15}a_{66}a_{77}+b_{42}a_{33}a_{21}a_{14}a_{66}a_{77}+b_{42}a_{33}a_{21}a_{14}a_{66}a_{88}+b_{42}a_{33}a_{21}a_{14}a_{77}a_{88}-b_{42}a_{33}a_{21}a_{64}a_{16}a_{77}\\
& +b_{42}a_{33}a_{21}a_{64}a_{86}a_{18}-b_{42}a_{33}a_{21}a_{64}a_{16}a_{88}-b_{42}a_{33}a_{21}a_{14}a_{76}a_{67}+b_{42}a_{33}a_{55}a_{61}a_{24}a_{16}-b_{42}a_{33}a_{55}a_{21}a_{84}a_{18}\\
& -b_{42}a_{33}a_{55}a_{21}a_{64}a_{16}+b_{42}a_{33}a_{55}a_{21}a_{14}a_{66}+b_{42}a_{33}a_{55}a_{21}a_{14}a_{77}+b_{42}a_{33}a_{55}a_{21}a_{14}a_{88}-b_{42}a_{33}a_{55}a_{24}a_{11}a_{66}\\
& +b_{42}a_{33}a_{21}a_{74}a_{16}a_{67}+b_{42}a_{33}a_{55}a_{81}a_{24}a_{18}-b_{42}a_{33}a_{55}a_{24}a_{77}a_{88}-b_{42}a_{33}a_{55}a_{24}a_{66}a_{88}+a_{51}b_{42}a_{24}a_{15}a_{66}a_{88}\\
& -b_{42}a_{33}a_{55}a_{24}a_{66}a_{77}+b_{42}a_{33}a_{55}a_{24}a_{76}a_{67}-b_{42}a_{33}a_{55}a_{24}a_{11}a_{77}-b_{42}a_{33}a_{55}a_{24}a_{11}a_{88}-a_{51}b_{42}a_{24}a_{85}a_{18}a_{66}\\
& -a_{51}b_{42}a_{33}a_{24}a_{65}a_{16}-a_{51}b_{42}a_{24}a_{85}a_{18}a_{77}+a_{51}b_{42}a_{33}a_{24}a_{15}a_{88}+a_{51}b_{42}a_{33}a_{64}a_{25}a_{16}+a_{51}b_{42}a_{33}a_{24}a_{15}a_{66}\\
& -a_{51}b_{42}a_{33}a_{14}a_{25}a_{77}-b_{42}a_{81}a_{24}a_{76}a_{18}a_{67}+a_{51}b_{42}a_{33}a_{24}a_{15}a_{77}+b_{42}a_{81}a_{24}a_{18}a_{66}a_{77}+a_{51}b_{42}a_{33}a_{84}a_{25}a_{18}\\
& -a_{51}b_{42}a_{33}a_{24}a_{85}a_{18},\end{aligned}$$

$$\begin{aligned}C_6 = {} & -a_{51}b_{42}a_{14}a_{25}a_{76}a_{67}a_{88}-a_{51}b_{42}a_{24}a_{75}a_{16}a_{67}a_{88}+a_{51}b_{42}a_{14}a_{25}a_{86}a_{67}a_{78}-a_{51}b_{42}a_{24}a_{15}a_{66}a_{77}a_{88}-a_{51}b_{42}a_{24}a_{15}a_{86}a_{67}a_{78}\\
& +a_{51}b_{42}a_{24}a_{15}a_{76}a_{67}a_{88}+a_{51}b_{42}a_{24}a_{65}a_{16}a_{77}a_{88}+a_{51}b_{42}a_{24}a_{75}a_{86}a_{18}a_{67}+a_{51}b_{42}a_{24}a_{85}a_{16}a_{67}a_{78}+a_{51}b_{42}a_{24}a_{85}a_{18}a_{66}a_{77}\\
& -a_{51}b_{42}a_{24}a_{85}a_{76}a_{18}a_{67}-a_{51}b_{42}a_{64}a_{25}a_{16}a_{77}a_{88}+a_{51}b_{42}a_{64}a_{25}a_{86}a_{18}a_{77}-a_{51}b_{42}a_{74}a_{25}a_{86}a_{18}a_{67}+a_{51}b_{42}a_{14}a_{25}a_{66}a_{77}a_{88}\\
& -a_{51}b_{42}a_{84}a_{25}a_{16}a_{67}a_{78}-a_{51}b_{42}a_{84}a_{25}a_{18}a_{66}a_{77}+a_{51}b_{42}a_{74}a_{25}a_{16}a_{67}a_{88}-a_{51}b_{42}a_{33}a_{24}a_{65}a_{86}a_{18}+a_{51}b_{42}a_{84}a_{25}a_{76}a_{18}a_{67}\\
& -a_{51}b_{42}a_{33}a_{24}a_{15}a_{77}a_{88}-a_{51}b_{42}a_{33}a_{24}a_{15}a_{66}a_{88}-a_{51}b_{42}a_{33}a_{24}a_{15}a_{66}a_{77}+a_{51}b_{42}a_{33}a_{24}a_{15}a_{76}a_{67}+a_{51}b_{42}a_{33}a_{24}a_{65}a_{16}a_{77}\end{aligned}$$

$$
\begin{aligned}
&+a_{51}b_{42}a_{33}a_{24}a_{65}a_{16}a_{88}-a_{51}b_{42}a_{33}a_{24}a_{75}a_{16}a_{67}+a_{51}b_{42}a_{33}a_{24}a_{85}a_{18}a_{77}+a_{51}b_{42}a_{33}a_{24}a_{85}a_{18}a_{66}-a_{51}b_{42}a_{33}a_{64}a_{25}a_{16}a_{88}\\
&-a_{51}b_{42}a_{33}a_{64}a_{25}a_{16}a_{77}+a_{51}b_{42}a_{33}a_{64}a_{25}a_{86}a_{18}+a_{51}b_{42}a_{33}a_{74}a_{25}a_{16}a_{67}+a_{51}b_{42}a_{33}a_{14}a_{25}a_{77}a_{88}+a_{51}b_{42}a_{33}a_{14}a_{25}a_{66}a_{88}\\
&+a_{51}b_{42}a_{33}a_{14}a_{25}a_{66}a_{77}-a_{51}b_{42}a_{33}a_{14}a_{25}a_{76}a_{67}-a_{51}b_{42}a_{33}a_{84}a_{25}a_{18}a_{77}-a_{51}b_{42}a_{33}a_{84}a_{25}a_{18}a_{66}+b_{42}a_{55}a_{21}a_{84}a_{16}a_{67}a_{78}\\
&+b_{42}a_{55}a_{61}a_{24}a_{86}a_{18}a_{77}-b_{42}a_{55}a_{61}a_{24}a_{16}a_{77}a_{88}-b_{42}a_{55}a_{21}a_{84}a_{76}a_{18}a_{67}+b_{42}a_{55}a_{21}a_{84}a_{18}a_{66}a_{77}+b_{42}a_{33}a_{21}a_{84}a_{16}a_{67}a_{78}\\
&+b_{42}a_{55}a_{21}a_{74}a_{86}a_{18}a_{67}-b_{42}a_{55}a_{21}a_{74}a_{16}a_{67}a_{88}-b_{42}a_{55}a_{21}a_{64}a_{86}a_{18}a_{77}+b_{42}a_{55}a_{21}a_{64}a_{16}a_{77}a_{88}-b_{42}a_{55}a_{21}a_{14}a_{86}a_{67}a_{78}\\
&+b_{42}a_{55}a_{21}a_{14}a_{76}a_{67}a_{88}-b_{42}a_{55}a_{21}a_{14}a_{66}a_{77}a_{88}+b_{42}a_{55}a_{24}a_{11}a_{86}a_{67}a_{78}-b_{42}a_{55}a_{24}a_{11}a_{76}a_{67}a_{88}+b_{42}a_{55}a_{24}a_{11}a_{66}a_{77}a_{88}\\
&+b_{42}a_{55}a_{81}a_{24}a_{76}a_{18}a_{67}-b_{42}a_{55}a_{81}a_{24}a_{18}a_{66}a_{77}+b_{42}a_{33}a_{21}a_{84}a_{18}a_{66}a_{77}-b_{42}a_{33}a_{21}a_{84}a_{76}a_{18}a_{67}-b_{42}a_{33}a_{21}a_{84}a_{76}a_{18}a_{67}\\
&-b_{42}a_{55}a_{81}a_{24}a_{16}a_{67}a_{78}+b_{42}a_{33}a_{21}a_{64}a_{16}a_{77}a_{88}-b_{42}a_{33}a_{21}a_{14}a_{86}a_{67}a_{78}+b_{42}a_{33}a_{21}a_{14}a_{76}a_{67}a_{88}-b_{42}a_{33}a_{21}a_{14}a_{66}a_{77}a_{88}\\
&+b_{42}a_{33}a_{24}a_{11}a_{86}a_{67}a_{78}-b_{42}a_{33}a_{24}a_{11}a_{76}a_{67}a_{88}+b_{42}a_{33}a_{24}a_{11}a_{66}a_{77}a_{88}+b_{42}a_{33}a_{81}a_{24}a_{76}a_{18}a_{67}-b_{42}a_{33}a_{81}a_{24}a_{18}a_{66}a_{77}\\
&-b_{42}a_{33}a_{81}a_{24}a_{16}a_{67}a_{78}+b_{42}a_{33}a_{61}a_{24}a_{86}a_{18}a_{77}-b_{42}a_{33}a_{21}a_{64}a_{86}a_{18}a_{77}-b_{42}a_{33}a_{61}a_{24}a_{16}a_{77}a_{88}-b_{42}a_{33}a_{61}a_{24}a_{16}a_{77}a_{88}\\
&+b_{42}a_{33}a_{21}a_{74}a_{86}a_{18}a_{67}-b_{42}a_{33}a_{21}a_{74}a_{16}a_{67}a_{88}-b_{42}a_{33}a_{55}a_{61}a_{24}a_{16}a_{77}-b_{42}a_{33}a_{55}a_{61}a_{24}a_{16}a_{88}+b_{42}a_{33}a_{55}a_{21}a_{84}a_{18}a_{66}\\
&+b_{42}a_{33}a_{55}a_{21}a_{84}a_{18}a_{77}+b_{42}a_{33}a_{55}a_{61}a_{24}a_{86}a_{18}-b_{42}a_{33}a_{55}a_{81}a_{24}a_{18}a_{66}-b_{42}a_{33}a_{55}a_{81}a_{24}a_{18}a_{77}-b_{42}a_{33}a_{55}a_{24}a_{76}a_{67}a_{88}\\
&+b_{42}a_{33}a_{55}a_{24}a_{66}a_{77}a_{88}+b_{42}a_{33}a_{55}a_{24}a_{11}a_{77}a_{88}+b_{42}a_{33}a_{55}a_{24}a_{86}a_{67}a_{78}+b_{42}a_{33}a_{55}a_{24}a_{11}a_{66}a_{77}+b_{42}a_{33}a_{55}a_{24}a_{11}a_{66}a_{88}\\
&-b_{42}a_{33}a_{55}a_{24}a_{11}a_{76}a_{67}+b_{42}a_{33}a_{55}a_{21}a_{14}a_{76}a_{67}-b_{42}a_{33}a_{55}a_{21}a_{14}a_{66}a_{77}-b_{42}a_{33}a_{55}a_{21}a_{14}a_{66}a_{88}-b_{42}a_{33}a_{55}a_{21}a_{14}a_{77}a_{88}\\
&+b_{42}a_{33}a_{55}a_{21}a_{64}a_{16}a_{77}+b_{42}a_{33}a_{55}a_{21}a_{64}a_{16}a_{88}-b_{42}a_{33}a_{55}a_{21}a_{74}a_{16}a_{67}-b_{42}a_{33}a_{55}a_{21}a_{64}a_{86}a_{18}-a_{51}b_{42}a_{24}a_{65}a_{86}a_{18}a_{77},
\end{aligned}
$$

$$
\begin{aligned}
C_7 = {} & -a_{51}b_{42}a_{33}a_{24}a_{15}a_{76}a_{67}a_{88}+a_{51}b_{42}a_{33}a_{24}a_{65}a_{86}a_{18}a_{77}+a_{51}b_{42}a_{33}a_{24}a_{75}a_{16}a_{67}a_{88}+a_{51}b_{42}a_{33}a_{24}a_{15}a_{86}a_{67}a_{78}\\
&-a_{51}b_{42}a_{33}a_{24}a_{65}a_{16}a_{77}a_{88}-a_{51}b_{42}a_{33}a_{24}a_{85}a_{18}a_{66}a_{77}+a_{51}b_{42}a_{33}a_{24}a_{85}a_{76}a_{18}a_{67}-a_{51}b_{42}a_{33}a_{24}a_{75}a_{86}a_{18}a_{67}\\
&-a_{51}b_{42}a_{33}a_{24}a_{85}a_{16}a_{67}a_{78}-a_{51}b_{42}a_{33}a_{74}a_{25}a_{16}a_{67}a_{88}+a_{51}b_{42}a_{33}a_{74}a_{25}a_{86}a_{18}a_{67}-a_{51}b_{42}a_{33}a_{14}a_{25}a_{66}a_{77}a_{88}\\
&+a_{51}b_{42}a_{33}a_{84}a_{25}a_{16}a_{67}a_{78}+a_{51}b_{42}a_{33}a_{84}a_{25}a_{18}a_{66}a_{77}-a_{51}b_{42}a_{33}a_{84}a_{25}a_{76}a_{18}a_{67}-b_{42}a_{33}a_{55}a_{21}a_{84}a_{16}a_{67}a_{78}\\
&+b_{42}a_{33}a_{55}a_{21}a_{84}a_{76}a_{18}a_{67}-b_{42}a_{33}a_{55}a_{21}a_{84}a_{18}a_{66}a_{77}+b_{42}a_{33}a_{55}a_{81}a_{24}a_{16}a_{67}a_{78}-b_{42}a_{33}a_{55}a_{61}a_{24}a_{86}a_{18}a_{77}\\
&+a_{51}b_{42}a_{33}a_{64}a_{25}a_{16}a_{77}a_{88}-a_{51}b_{42}a_{33}a_{64}a_{25}a_{86}a_{18}a_{77}-b_{42}a_{33}a_{55}a_{81}a_{24}a_{76}a_{18}a_{67}-b_{42}a_{33}a_{55}a_{24}a_{11}a_{66}a_{77}a_{88}\\
&+b_{42}a_{33}a_{55}a_{24}a_{11}a_{76}a_{67}a_{88}-b_{42}a_{33}a_{55}a_{24}a_{11}a_{86}a_{67}a_{78}+b_{42}a_{33}a_{55}a_{21}a_{14}a_{66}a_{77}a_{88}-b_{42}a_{33}a_{55}a_{21}a_{14}a_{76}a_{67}a_{88}\\
&+b_{42}a_{33}a_{55}a_{21}a_{14}a_{86}a_{67}a_{78}-b_{42}a_{33}a_{55}a_{21}a_{64}a_{16}a_{77}a_{88}+b_{42}a_{33}a_{55}a_{21}a_{64}a_{86}a_{18}a_{77}+b_{42}a_{33}a_{55}a_{21}a_{74}a_{16}a_{67}a_{88}\\
&-b_{42}a_{33}a_{55}a_{21}a_{74}a_{86}a_{18}a_{67}+b_{42}a_{33}a_{55}a_{61}a_{24}a_{16}a_{77}a_{88}+b_{42}a_{33}a_{55}a_{81}a_{24}a_{18}a_{66}a_{77}+a_{51}b_{42}a_{33}a_{14}a_{25}a_{76}a_{67}a_{88}\\
&-a_{51}b_{42}a_{33}a_{14}a_{25}a_{86}a_{67}a_{78}+a_{51}b_{42}a_{33}a_{24}a_{15}a_{66}a_{77}a_{88},
\end{aligned}
$$

$$E_1 = -b_{32}a_{25},$$

$$E_2 = b_{32}a_{25}a_{77}+b_{32}a_{33}a_{25}-b_{32}a_{21}a_{15}+b_{32}a_{44}a_{25}+b_{32}a_{25}a_{88}+b_{32}a_{25}a_{11}+b_{32}a_{25}a_{66},$$

$$
\begin{aligned}
E_3 = {} & b_{32}a_{21}a_{15}a_{88}+b_{32}a_{21}a_{15}a_{77}+b_{32}a_{21}a_{15}a_{66}-b_{32}a_{21}a_{65}a_{16}-b_{32}a_{21}a_{85}a_{18}+b_{32}a_{25}a_{76}a_{67}-b_{32}a_{25}a_{11}a_{88}-b_{32}a_{25}a_{11}a_{77}\\
&+b_{32}a_{61}a_{25}a_{16}+b_{32}a_{81}a_{25}a_{18}-b_{32}a_{25}a_{11}a_{66}-b_{32}a_{44}a_{25}a_{77}-b_{32}a_{44}a_{25}a_{11}-b_{32}a_{44}a_{25}a_{66}+b_{32}a_{44}a_{21}a_{15}-b_{32}a_{25}a_{66}a_{77}\\
&-b_{32}a_{25}a_{66}a_{88}-b_{32}a_{44}a_{25}a_{88}-b_{32}a_{33}a_{25}a_{77}-b_{32}a_{33}a_{25}a_{11}-b_{32}a_{33}a_{25}a_{66}+b_{32}a_{33}a_{21}a_{15}-b_{32}a_{33}a_{25}a_{88}-b_{32}a_{33}a_{44}a_{25}\\
&-b_{32}a_{25}a_{77}a_{88},
\end{aligned}
$$

$$
\begin{aligned}
E_4 = {} & -b_{32}a_{44}a_{25}a_{76}a_{67}+b_{32}a_{44}a_{25}a_{11}a_{88}+b_{32}a_{44}a_{25}a_{11}a_{77}-b_{32}a_{44}a_{61}a_{25}a_{16}-b_{32}a_{44}a_{81}a_{25}a_{18}+b_{32}a_{44}a_{25}a_{11}a_{66}\\
&+b_{32}a_{33}a_{25}a_{77}a_{88}+b_{32}a_{33}a_{25}a_{66}a_{88}+b_{32}a_{33}a_{25}a_{66}a_{77}-b_{32}a_{33}a_{21}a_{15}a_{88}-b_{32}a_{33}a_{21}a_{15}a_{77}-b_{32}a_{33}a_{21}a_{15}a_{66}\\
&+b_{32}a_{33}a_{21}a_{65}a_{16}+b_{32}a_{33}a_{21}a_{85}a_{18}-b_{32}a_{33}a_{25}a_{76}a_{67}+b_{32}a_{33}a_{25}a_{11}a_{88}+b_{32}a_{33}a_{25}a_{11}a_{77}-b_{32}a_{33}a_{61}a_{25}a_{16}\\
&-b_{32}a_{33}a_{81}a_{25}a_{18}+b_{32}a_{33}a_{25}a_{11}a_{66}+b_{32}a_{25}a_{11}a_{77}a_{88}+b_{32}a_{33}a_{44}a_{25}a_{11}+b_{32}a_{33}a_{44}a_{25}a_{66}-b_{32}a_{33}a_{44}a_{21}a_{15}\\
&+b_{32}a_{33}a_{44}a_{25}a_{88}-b_{32}a_{25}a_{76}a_{67}a_{88}+b_{32}a_{25}a_{86}a_{67}a_{78}+b_{32}a_{33}a_{44}a_{25}a_{77}+b_{32}a_{25}a_{11}a_{66}a_{88}+b_{32}a_{21}a_{15}a_{76}a_{67}\\
&-b_{32}a_{21}a_{75}a_{16}a_{67}-b_{32}a_{21}a_{65}a_{86}a_{18}+b_{32}a_{21}a_{65}a_{16}a_{77}-b_{32}a_{61}a_{25}a_{16}a_{88}-b_{32}a_{61}a_{25}a_{16}a_{77}+b_{32}a_{21}a_{85}a_{18}a_{77}\\
&+b_{32}a_{25}a_{11}a_{66}a_{77}-b_{32}a_{25}a_{11}a_{76}a_{67}-b_{32}a_{21}a_{15}a_{66}a_{77}-b_{32}a_{21}a_{15}a_{66}a_{88}-b_{32}a_{21}a_{15}a_{77}a_{88}+b_{32}a_{44}a_{25}a_{77}a_{88}\\
&+b_{32}a_{44}a_{25}a_{66}a_{88}+b_{32}a_{44}a_{25}a_{66}a_{77}-b_{32}a_{81}a_{25}a_{18}a_{66}-b_{32}a_{44}a_{21}a_{15}a_{88}-b_{32}a_{44}a_{21}a_{15}a_{77}-b_{32}a_{44}a_{21}a_{15}a_{66}
\end{aligned}
$$

$$
\begin{aligned}
&-b_{32}a_{81}a_{25}a_{18}a_{77}+b_{32}a_{21}a_{65}a_{16}a_{88}+b_{32}a_{21}a_{85}a_{18}a_{66}+b_{32}a_{61}a_{25}a_{86}a_{18}+b_{32}a_{25}a_{66}a_{77}a_{88}+b_{32}a_{44}a_{21}a_{65}a_{16}\\
&+b_{32}a_{44}a_{21}a_{85}a_{18},\\
E_5 ={}& -b_{32}a_{33}a_{21}a_{85}a_{18}a_{77}+b_{32}a_{33}a_{21}a_{15}a_{77}a_{88}+b_{32}a_{81}a_{25}a_{16}a_{67}a_{78}+b_{32}a_{44}a_{25}a_{11}a_{76}a_{67}-b_{32}a_{44}a_{25}a_{11}a_{66}a_{77}\\
&-b_{32}a_{21}a_{75}a_{86}a_{18}a_{67}-b_{32}a_{81}a_{25}a_{76}a_{18}a_{67}+b_{32}a_{33}a_{61}a_{25}a_{16}a_{77}+b_{32}a_{33}a_{25}a_{11}a_{76}a_{67}-b_{32}a_{33}a_{25}a_{11}a_{66}a_{77}\\
&+b_{32}a_{44}a_{25}a_{76}a_{67}a_{88}+b_{32}a_{44}a_{21}a_{75}a_{16}a_{67}-b_{32}a_{44}a_{21}a_{15}a_{76}a_{67}-b_{32}a_{44}a_{25}a_{11}a_{66}a_{88}+b_{32}a_{44}a_{21}a_{15}a_{66}a_{77}\\
&-b_{32}a_{33}a_{44}a_{25}a_{66}a_{88}+b_{32}a_{21}a_{15}a_{66}a_{77}a_{88}+b_{32}a_{21}a_{15}a_{86}a_{67}a_{78}-b_{32}a_{44}a_{25}a_{86}a_{67}a_{78}-b_{32}a_{21}a_{85}a_{18}a_{66}a_{77}\\
&+b_{32}a_{21}a_{85}a_{76}a_{18}a_{67}-b_{32}a_{21}a_{65}a_{16}a_{77}a_{88}-b_{32}a_{25}a_{11}a_{86}a_{67}a_{78}+b_{32}a_{61}a_{25}a_{16}a_{77}a_{88}-b_{32}a_{21}a_{15}a_{76}a_{67}a_{88}\\
&+b_{32}a_{21}a_{65}a_{86}a_{18}a_{77}+b_{32}a_{21}a_{75}a_{16}a_{67}a_{88}+b_{32}a_{25}a_{11}a_{76}a_{67}a_{88}-b_{32}a_{33}a_{21}a_{65}a_{16}a_{88}-b_{32}a_{33}a_{25}a_{66}a_{77}a_{88}\\
&-b_{32}a_{33}a_{61}a_{25}a_{86}a_{18}-b_{32}a_{44}a_{21}a_{85}a_{18}a_{77}+b_{32}a_{44}a_{61}a_{25}a_{16}a_{77}+b_{32}a_{44}a_{21}a_{15}a_{66}a_{88}-b_{32}a_{44}a_{21}a_{65}a_{16}a_{77}\\
&+b_{32}a_{44}a_{21}a_{65}a_{86}a_{18}-b_{32}a_{33}a_{44}a_{25}a_{77}a_{88}+b_{32}a_{81}a_{25}a_{18}a_{66}a_{77}+b_{32}a_{33}a_{21}a_{65}a_{86}a_{18}+b_{32}a_{44}a_{21}a_{15}a_{77}a_{88}\\
&+b_{32}a_{33}a_{81}a_{25}a_{18}a_{66}-b_{32}a_{33}a_{25}a_{86}a_{67}a_{78}-b_{32}a_{33}a_{21}a_{65}a_{16}a_{77}+b_{32}a_{33}a_{44}a_{21}a_{15}a_{77}+b_{32}a_{33}a_{44}a_{21}a_{15}a_{88}\\
&-b_{32}a_{33}a_{44}a_{25}a_{66}a_{77}+b_{32}a_{33}a_{21}a_{15}a_{66}a_{77}+b_{32}a_{33}a_{21}a_{15}a_{66}a_{88}-b_{32}a_{61}a_{25}a_{86}a_{18}a_{77}+b_{32}a_{33}a_{44}a_{61}a_{25}a_{16}\\
&-b_{32}a_{33}a_{44}a_{25}a_{11}a_{77}-b_{32}a_{21}a_{85}a_{16}a_{67}a_{78}-b_{32}a_{25}a_{11}a_{66}a_{77}a_{88}+b_{32}a_{33}a_{44}a_{25}a_{76}a_{67}-b_{32}a_{33}a_{44}a_{21}a_{85}a_{18}\\
&-b_{32}a_{33}a_{44}a_{21}a_{65}a_{16}+b_{32}a_{33}a_{44}a_{21}a_{15}a_{66}-b_{32}a_{33}a_{44}a_{25}a_{11}a_{88}-b_{32}a_{33}a_{44}a_{25}a_{11}a_{66}+b_{32}a_{33}a_{44}a_{81}a_{25}a_{18}\\
&+b_{32}a_{44}a_{61}a_{25}a_{16}a_{88}+b_{32}a_{44}a_{81}a_{25}a_{18}a_{66}+b_{32}a_{44}a_{81}a_{25}a_{18}a_{77}-b_{32}a_{44}a_{25}a_{11}a_{77}a_{88}-b_{32}a_{33}a_{25}a_{11}a_{77}a_{88}\\
&+b_{32}a_{33}a_{25}a_{76}a_{67}a_{88}+b_{32}a_{33}a_{81}a_{25}a_{18}a_{77}-b_{32}a_{33}a_{21}a_{85}a_{18}a_{66}-b_{32}a_{44}a_{25}a_{66}a_{77}a_{88}-b_{32}a_{44}a_{61}a_{25}a_{86}a_{18}\\
&-b_{32}a_{44}a_{21}a_{85}a_{18}a_{66}-b_{32}a_{44}a_{21}a_{65}a_{16}a_{88}+b_{32}a_{33}a_{21}a_{75}a_{16}a_{67}-b_{32}a_{33}a_{21}a_{15}a_{76}a_{67}-b_{32}a_{33}a_{25}a_{11}a_{66}a_{88}\\
&+b_{32}a_{33}a_{61}a_{25}a_{16}a_{88},\\
E_6 ={}& -b_{32}a_{44}a_{21}a_{85}a_{76}a_{18}a_{67}-b_{32}a_{33}a_{25}a_{11}a_{76}a_{67}a_{88}-b_{32}a_{33}a_{44}a_{25}a_{76}a_{67}a_{88}+b_{32}a_{33}a_{44}a_{25}a_{11}a_{66}a_{77}\\
&+b_{32}a_{33}a_{21}a_{15}a_{76}a_{67}a_{88}-b_{32}a_{44}a_{21}a_{15}a_{66}a_{77}a_{88}+b_{32}a_{44}a_{25}a_{11}a_{66}a_{77}a_{88}+b_{32}a_{44}a_{21}a_{65}a_{16}a_{77}a_{88}\\
&+b_{32}a_{33}a_{44}a_{21}a_{85}a_{18}a_{77}-b_{32}a_{33}a_{21}a_{75}a_{16}a_{67}a_{88}+b_{32}a_{33}a_{44}a_{25}a_{66}a_{77}a_{88}-b_{32}a_{33}a_{21}a_{85}a_{76}a_{18}a_{67}\\
&-b_{32}a_{33}a_{81}a_{25}a_{18}a_{66}a_{77}-b_{32}a_{33}a_{44}a_{81}a_{25}a_{18}a_{77}-b_{32}a_{33}a_{21}a_{15}a_{66}a_{77}a_{88}+b_{32}a_{33}a_{44}a_{25}a_{11}a_{77}a_{88}\\
&+b_{32}a_{44}a_{21}a_{15}a_{76}a_{67}a_{88}+b_{32}a_{44}a_{21}a_{85}a_{18}a_{66}a_{77}+b_{32}a_{33}a_{44}a_{21}a_{65}a_{16}a_{77}+b_{32}a_{33}a_{44}a_{21}a_{65}a_{16}a_{88}\\
&-b_{32}a_{33}a_{21}a_{15}a_{86}a_{67}a_{78}-b_{32}a_{44}a_{25}a_{11}a_{76}a_{67}a_{88}+b_{32}a_{33}a_{44}a_{61}a_{25}a_{86}a_{18}+b_{32}a_{33}a_{25}a_{11}a_{66}a_{77}a_{88}\\
&+b_{32}a_{44}a_{25}a_{11}a_{86}a_{67}a_{78}-b_{32}a_{44}a_{81}a_{25}a_{16}a_{67}a_{78}-b_{32}a_{33}a_{44}a_{61}a_{25}a_{16}a_{77}+b_{32}a_{33}a_{21}a_{75}a_{86}a_{18}a_{67}\\
&+b_{32}a_{33}a_{44}a_{21}a_{85}a_{18}a_{66}+b_{32}a_{33}a_{44}a_{25}a_{11}a_{66}a_{88}-b_{32}a_{44}a_{21}a_{65}a_{86}a_{18}a_{77}-b_{32}a_{33}a_{44}a_{61}a_{25}a_{16}a_{88}\\
&-b_{32}a_{44}a_{21}a_{15}a_{86}a_{67}a_{78}-b_{32}a_{33}a_{44}a_{21}a_{75}a_{16}a_{67}+b_{32}a_{33}a_{44}a_{25}a_{86}a_{67}a_{78}+b_{32}a_{44}a_{61}a_{25}a_{86}a_{18}a_{77}\\
&-b_{32}a_{44}a_{21}a_{75}a_{16}a_{67}a_{88}-b_{32}a_{33}a_{81}a_{25}a_{16}a_{67}a_{78}-b_{32}a_{33}a_{61}a_{25}a_{16}a_{77}a_{88}+b_{32}a_{33}a_{44}a_{21}a_{15}a_{76}a_{67}\\
&-b_{32}a_{33}a_{44}a_{81}a_{25}a_{18}a_{66}-b_{32}a_{33}a_{44}a_{21}a_{15}a_{77}a_{88}-b_{32}a_{44}a_{81}a_{25}a_{18}a_{66}a_{77}+b_{32}a_{33}a_{81}a_{25}a_{76}a_{18}a_{67}\\
&-b_{32}a_{44}a_{61}a_{25}a_{16}a_{77}a_{88}+b_{32}a_{44}a_{21}a_{85}a_{16}a_{67}a_{78}-b_{32}a_{33}a_{21}a_{65}a_{86}a_{18}a_{77}+b_{32}a_{33}a_{61}a_{25}a_{86}a_{18}a_{77}\\
&-b_{32}a_{33}a_{44}a_{25}a_{11}a_{76}a_{67}-b_{32}a_{33}a_{44}a_{21}a_{15}a_{66}a_{77}+b_{32}a_{33}a_{21}a_{85}a_{18}a_{66}a_{77}+b_{32}a_{33}a_{21}a_{85}a_{16}a_{67}a_{78}\\
&-b_{32}a_{33}a_{44}a_{21}a_{65}a_{86}a_{18}-b_{32}a_{33}a_{44}a_{21}a_{15}a_{66}a_{88}+b_{32}a_{44}a_{21}a_{75}a_{86}a_{18}a_{67}+b_{32}a_{44}a_{81}a_{25}a_{76}a_{18}a_{67}\\
&+b_{32}a_{33}a_{25}a_{11}a_{86}a_{67}a_{78}+b_{32}a_{33}a_{21}a_{65}a_{16}a_{77}a_{88},\\
E_7 ={}& b_{32}a_{33}a_{44}a_{61}a_{25}a_{16}a_{77}a_{88}-b_{32}a_{33}a_{44}a_{21}a_{85}a_{18}a_{66}a_{77}+b_{32}a_{33}a_{44}a_{21}a_{85}a_{76}a_{18}a_{67}\\
&+b_{32}a_{33}a_{44}a_{25}a_{11}a_{76}a_{67}a_{88}-b_{32}a_{33}a_{44}a_{21}a_{75}a_{86}a_{18}a_{67}-b_{32}a_{33}a_{44}a_{21}a_{65}a_{16}a_{77}a_{88}\\
&+b_{32}a_{33}a_{44}a_{21}a_{15}a_{86}a_{67}a_{78}-b_{32}a_{33}a_{44}a_{81}a_{25}a_{76}a_{18}a_{67}-b_{32}a_{33}a_{44}a_{21}a_{15}a_{76}a_{67}a_{88}\\
&-b_{32}a_{33}a_{44}a_{25}a_{11}a_{66}a_{77}a_{88}-b_{32}a_{33}a_{44}a_{61}a_{25}a_{86}a_{18}a_{77}-b_{32}a_{33}a_{44}a_{21}a_{85}a_{16}a_{67}a_{78}\\
&+b_{32}a_{33}a_{44}a_{21}a_{75}a_{16}a_{67}a_{88}-b_{32}a_{33}a_{44}a_{25}a_{11}a_{86}a_{67}a_{78}+b_{32}a_{33}a_{44}a_{21}a_{15}a_{66}a_{77}a_{88}\\
&+b_{32}a_{33}a_{44}a_{81}a_{25}a_{16}a_{67}a_{78}+b_{32}a_{33}a_{44}a_{21}a_{65}a_{86}a_{18}a_{77}+b_{32}a_{33}a_{44}a_{81}a_{25}a_{18}a_{66}a_{77},
\end{aligned}
\tag{A.1}
$$

Conflicts of Interest

The authors declare that there are no conflicts of interest.

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Research Article

Maximum Likelihood Inference for Univariate Delay Differential Equation Models with Multiple Delays

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This article presents statistical inference methodology based on maximum likelihoods for delay differential equation models in the univariate setting. Maximum likelihood inference is obtained for single and multiple unknown delay parameters as well as other parameters of interest that govern the trajectories of the delay differential equation models. The maximum likelihood estimator is obtained based on adaptive grid and Newton-Raphson algorithms. Our methodology estimates correctly the delay parameters as well as other unknown parameters (such as the initial starting values) of the dynamical system based on simulation data. We also develop methodology to compute the information matrix and confidence intervals for all unknown parameters based on the likelihood inferential framework. We present three illustrative examples related to biological systems. The computations have been carried out with help of mathematical software: MATLAB® 8.0 R2014b.

1. Introduction

Delay differential equations (DDEs) are widely used to model many real life phenomena, especially in science and engineering. Examples include the modeling of spread of infectious diseases, modeling of tumor growth and the growth of blood clots in the brain, population dynamics, traffic monitoring, and price fluctuations of commodities in economics; see [1–4]. A univariate delay differential equation model (DDEM) with multiple delays equates the real valued observations, y_i, as noisy realizations from an underlying DDE:

$$y_i = x(t_i) + \epsilon_i, \quad i = 0, 1, 2, \dots, n, \tag{1}$$

where ϵ_i's are errors assumed to arise from a noise distribution with zero mean and unknown standard deviation $\sigma > 0$. In (1), $x(t_i)$ is the solution, $x(t)$, of the DDE

$$\dot{x}(t) = f(t, x(t), z_1(t), z_2(t), \dots, z_m(t), \boldsymbol{\theta}) \tag{2}$$

evaluated at the n time points, t_i, $i = 0, 1, \dots, n$; in (2), $z_j(t) = x(t - \tau_j)$, $j = 1, 2, \dots, m$, is the jth delay term with delay parameter $\tau_j > 0$, and $\boldsymbol{\theta} = (\theta_1, \theta_2, \dots, \theta_p)$ is a vector of other parameters of interest that govern the trajectories of the underlying DDE in (2). Equations (1) and (2) constitute a univariate DDEM in the most general form. In a DDEM, the parameters θ_r and τ_j are often unknown and have to be estimated based on observations y_i, $i = 0, 1, \dots, n$.

Not many methods appear in the statistical literature on parameter estimation and inference for DDEMs. Among the statistical approaches that have been suggested, many involve restrictions on the form of DDEMs that are being investigated. When such restrictions are relaxed, high computational costs and challenges arise. Typically, further inferential procedures such as obtaining standard errors and confidence intervals associated with parameter estimates involve further computational costs and challenges. We give a brief review of these works and approaches that have been reported in the literature in the following paragraph.

Ellner et al. [5] estimate the derivative of a univariate DDEM, which is assumed to be in an additive form, using nonparametric smoothing. Subsequently, they infer the constant (single) delay parameter, τ, based on fitting a generalized additive model. Ellner's technique, although it unifies previous works, can thus be applied to DDEMs which satisfy the assumed additive form only. Wood [6] developed spline based model fitting techniques in the case when the DDEMs are partially specified. The spline based method involves high computational costs as cross-validation is used to select the smoothing coefficients associated with the penalty term as well as the unknown parameter estimates. A penalized semiparametric method is proposed by Wang and Cao [7] which involves maximizing an objective function consisting of two terms: a likelihood term and a penalty term which measures the discrepancy between an estimate of the derivative, $\dot{x}(t)$, and the right hand side of the DDEM in (1). The selection of smoothing coefficients is done, similar to [6], via cross-validation, whereas standard errors of parameter estimates are obtained by bootstrapping. It follows that the method of [7], like [6], involves high computational costs. Further, Wang and Cao consider only univariate DDEMs with a single delay parameter. An estimation method based on Least Squares Support Vector Machines (LS-SVMs) for approximating constant as well as time-varying parameters in deterministic parameter-affine DDEMs is presented by Mehrkanoon et al. [8]. We note that Mehrkanoon performs parameter estimation only; no standard errors of estimates or confidence intervals are reported. Further, only single delays (either constant or time varying) are considered in [8].

In this paper, we consider parameter estimation and inference for univariate DDEMs with multiple delays based on the maximum likelihood. The method of maximum likelihood, as advocated by Fisher in his important papers [9, 10], has become one of the most significant tools for estimation and inference available to statisticians. Maximum likelihood estimators (MLEs) are well defined once a distributional model is specified for the observations. MLEs have well-behaved and well-understood properties: Huber [11] presents general conditions whereby the MLE is consistent for the true value of the unknown parameters for large sample sizes. Wald [12] and Akaike [13] observed that the maximum likelihood estimator is a natural estimator for the parameters when the true distribution is unknown. The large sample theory and distributional properties of MLEs can be used to perform subsequent inference procedures such as obtaining standard errors and confidence intervals and performing tests of hypotheses at minimal additional computational costs. MLEs are also the basic estimators that are used in subsequent statistical inferential procedures such as model selection using Akaike Information Criteria (AIC), Bayes Information Criteria (BIC), and other model selection criteria. Model selection is an important issue in DDEMs, such as for partially specified DDEMs in [6], where several models can be elicited for an observed physical process, but one model needs to be selected among many which fits the observed data and is simple enough to understand (Occam's razor principle).

MLE can be developed for a large variety of estimation situations and is asymptotically efficient, which means that for large samples it produces the most precise estimates compared to non-MLE based methods (such as [8]). These are the reasons why we preferred using MLE over all other estimators for DDEMs in this paper.

The remainder of this paper is organized as follows: we define univariate DDEMs in Section 2. In Section 3, the MLE approach for DDEMs is outlined and the MLE is obtained computationally using an adaptive grid procedure followed by a gradient descent algorithm. We also develop algorithms for obtaining the information matrix and construct standard errors and confidence intervals for the unknown parameters. Three examples of univariate DDEMs related to biological systems are presented, and the numerical solutions and results based on the proposed methodology are provided based on simulation in Section 4.

2. General Model Formulation

Recall the DDEM defined by (1) and (2). The observation $y_i \in R$ is obtained at the ith sampled time point, t_i, with $T_0 = t_0 < \cdots < t_n = T_1$, where $y_i = x(t_i) + \epsilon_i$, $i = 0, 1, 2, \ldots, n$. In the remainder of this paper, the errors are assumed to be independent and identically distributed according to a normal with mean zero and unknown standard deviation $\sigma > 0$, that is, $\epsilon_i \sim N(0, \sigma^2)$. The underlying dynamical system $x(t)$, $t \in [T_0, T_1] \subset R$, is expressed implicitly in terms of the DDE. The general form of DDE with multiple delays for $x(t) \in R$ is given by (2) as $\dot{x}(t) = f(t, x(t), z_1(t), z_2(t), \ldots, z_m(t), \boldsymbol{\theta})$, where $z_j(t) = \{x(t - \tau_j) : t - \tau_j \geq 0,\ j = 1, 2, \ldots, m\}$, $f(t, x(t), z_1(t), z_2(t), \ldots, z_m(t), \boldsymbol{\theta})$ is 1-dimensional function, and $\dot{x}(t)$ denotes the first derivative of $x(t)$ with respect to time t. The quantities $\boldsymbol{\theta} \in R^p$ and $\boldsymbol{\tau} = (\tau_1, \tau_2, \ldots, \tau_m)$ are unknown parameters of the DDEM, where $\boldsymbol{\theta}$ is a vector of unknown parameters of dimension p and $\boldsymbol{\tau}$ is a vector of time delays of dimension m. The complete trajectory of the function $x(t)$ on $[T_0, T_1]$ will be determined by (2), and initial condition function $\varphi : [t_0 - \max(\tau_1, \tau_2, \ldots, \tau_m), t_0] \to R$, where $\varphi(t) = a$ for all $t \in [t_0 - \max(\tau_1, \tau_2, \ldots, \tau_m), t_0]$, is also unknown in addition to the unknown parameters $\boldsymbol{\theta}$ and $\boldsymbol{\tau}$. For given values of $\boldsymbol{\theta}$, $\boldsymbol{\tau}$, and a, we note that the solution $x(t)$, $x(t) = x(t, \boldsymbol{\theta}, \boldsymbol{\tau}, a)$, is a function of $\boldsymbol{\theta}$, $\boldsymbol{\tau}$, and a; thus, we make it an explicit function of the unknown quantities $\boldsymbol{\theta}$, $\boldsymbol{\tau}$, and a based on the $x(t, \boldsymbol{\theta}, \boldsymbol{\tau}, a)$ notation. The observations $y_0, y_1, \ldots, y_n$ are collected at the $(n+1)$ sampled time points $T_0 = t_0 < t_1 < \cdots < t_n = T_1$, based on the observational model (1). Our goal is to estimate $\boldsymbol{\theta}, \boldsymbol{\tau}$, and a based on the observations $y_0, y_1, \ldots, y_n$. Here, note that a is also unknown and thus appears as a nuisance parameter since properties of the dynamical system are governed by $\boldsymbol{\theta}$ and $\boldsymbol{\tau}$ and not a.

3. The Maximum Likelihood Estimation Approach for DDEMs

The likelihood of the DDEM for parameters $\boldsymbol{\theta}, \boldsymbol{\tau}$, and a, given observations $y_0, y_1, \ldots, y_n$, is

$$L(\boldsymbol{\theta}, \boldsymbol{\tau}, a \mid \mathbf{y}) = \prod_{i=0}^{n} p(y_i \mid \boldsymbol{\theta}, \boldsymbol{\tau}, a), \tag{3}$$

where $\mathbf{y} = (y_0, y_1, \ldots, y_n)$ is the collection of all $(n+1)$ observations on $\mathbf{y}$ with density

$$p(y_i \mid \boldsymbol{\theta}, \boldsymbol{\tau}, a) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{-(1/2\sigma^2)(y_i - x(t_i, \boldsymbol{\theta}, \boldsymbol{\tau}, a))^2}, \tag{4}$$

based on the normality assumption on ϵ_i's in (1). The above expression for the likelihood can be simplified to

$$\begin{aligned} L(\boldsymbol{\theta}, \boldsymbol{\tau}, a \mid \mathbf{y}) &= \prod_{i=0}^{n} \left(\frac{1}{\sqrt{2\pi\sigma^2}} e^{-(1/2\sigma^2)(y_i - x(t_i, \boldsymbol{\theta}, \boldsymbol{\tau}, a))^2} \right) \\ &= \left(2\pi\sigma^2\right)^{-(n+1)/2} e^{-(1/2\sigma^2)\sum_{i=0}^{n}(y_i - x(t_i, \boldsymbol{\theta}, \boldsymbol{\tau}, a))^2}. \end{aligned} \tag{5}$$

We assume for the moment that $\sigma > 0$ is fixed and known; the case when $\sigma > 0$ is unknown is dealt with later. Thus, the above likelihood is taken to be a function of $(\boldsymbol{\theta}, \boldsymbol{\tau}, a)$ for now. The usual practice for statistical inference is to use the natural logarithm of the likelihood function, namely, the log-likelihood function, which is given by

$$\begin{aligned} l(\boldsymbol{\theta}, \boldsymbol{\tau}, a \mid \mathbf{y}) &= \sum_{i=0}^{n} \ln p(y_i \mid \boldsymbol{\theta}, \boldsymbol{\tau}, a) \\ &= -\frac{(n+1)}{2} \ln\left(2\pi\sigma^2\right) \\ &\quad - \frac{1}{2\sigma^2} \sum_{i=0}^{n} (y_i - x(t_i, \boldsymbol{\theta}, \boldsymbol{\tau}, a))^2. \end{aligned} \tag{6}$$

Expressions of the log-likelihood l are often simpler than the likelihood function, L, since they are easier to differentiate and the results are more stable computationally.

Since $\ln(x)$ is a monotonically increasing function of x, it follows that the maximization of (3) and (6) is equivalent in that the same optimized parameter is found. We denote the MLE of $(\boldsymbol{\theta}, \boldsymbol{\tau}, a)$ as $(\widehat{\boldsymbol{\theta}}, \widehat{\boldsymbol{\tau}}, \widehat{a})$. The MLE $(\widehat{\boldsymbol{\theta}}, \widehat{\boldsymbol{\tau}}, \widehat{a})$ is a point estimate such that

$$\left(\widehat{\boldsymbol{\theta}}, \widehat{\boldsymbol{\tau}}, \widehat{a}\right) = \underset{\boldsymbol{\theta}, \boldsymbol{\tau}, a}{\operatorname{argmax}} \{l(\boldsymbol{\theta}, \boldsymbol{\tau}, a)\} \tag{7}$$

and can be viewed as a random vector depending on the distribution of data, $\mathbf{y} = (y_0, y_1, \ldots, y_n)$. We now consider the case when σ^2 is unknown. The MLE of σ^2 is denoted by $\widehat{\sigma}^2$. After finding $(\widehat{\boldsymbol{\theta}}, \widehat{\boldsymbol{\tau}}, \widehat{a})$ as in (7), the log-likelihood equation in (6) is maximized as a function of σ^2. The resulting estimate is available in closed form and is given by

$$\widehat{\sigma}^2 = \frac{1}{n+1} \sum_{i=0}^{n} \left(y_i - x\left(t_i, \widehat{\boldsymbol{\theta}}, \widehat{\boldsymbol{\tau}}, \widehat{a}\right)\right)^2. \tag{8}$$

3.1. A Two-Stage Numerical Procedure for Finding the MLE. To find the MLE numerically, we develop a two-stage numerical procedure consisting of an adaptive grid procedure, then followed by a gradient descent algorithm. Two stages are needed as we wish to utilize the advantages of each algorithm while avoiding the drawbacks of the other in each stage. Grid algorithms are able to find the global maximum of a function over a grid space. First, it evaluates values of the function on the grid space and then finds the grid value that corresponds to the maximum. Provided the grid space is refined enough, the grid value corresponding to this maximum will be close to the domain value that actually corresponds to the global maximum. So by gridding, we are able to ensure that we are close to the global maximum. The adaptive grid algorithm enhances the original gridding algorithm so that we will move closer and closer to the global maximum. However, the main drawback of any grid (and adaptive grid) algorithm is its slowness in convergence.

On the other hand, gradient descent algorithms can converge to maxima of a function sufficiently quickly. The main drawback of gradient descent algorithms is that it will find the nearest local maximum from the starting point. So, if the original starting point is not close to the global maximum, a gradient descent algorithm will not guarantee that the global maximum is found since it might get "stuck" at a local maximum only.

The function to maximize in our case is the log-likelihood in (6) and the domain value corresponding to this maximum is the MLE. Thus, our two-step method uses adaptive grid in the first stage to ensure that we are close to the MLE and then switches to the quasi-Newton algorithm to ensure rapid convergence to the MLE.

3.1.1. Grid Procedure. To find $\widehat{\boldsymbol{\theta}}$ and $\widehat{\boldsymbol{\tau}}$ as in (7), the value with largest (log) likelihood should be chosen. This can be done by an adaptive grid procedure. The gridding is carried out for $\boldsymbol{\theta}$ and $\boldsymbol{\tau}$, and for each pair of $(\boldsymbol{\theta}, \boldsymbol{\tau})$ in the grid space, a Newton-Raphson numerical procedure is used to find the maximum value of a defined as

$$\widehat{a} = \widehat{a}(\boldsymbol{\theta}, \boldsymbol{\tau}) = \underset{a}{\operatorname{argmax}} \{l(\boldsymbol{\theta}, \boldsymbol{\tau}, a)\}. \tag{9}$$

We use the grid space $\Theta = \{(\theta_r, \tau_s),\ r = 1, 2, \ldots, R,\ s = 1, 2, \ldots, S\}$, which covers RS values of (θ_r, τ_s). For every fixed value of θ_r and τ_s in Θ, we find the MLE of a, $\widehat{a}(\boldsymbol{\theta}, \boldsymbol{\tau})$, given by maximizing the log-likelihood above. Since $\widehat{a}(\boldsymbol{\theta}, \boldsymbol{\tau})$ satisfies

$$\frac{\partial l(\boldsymbol{\theta}, \boldsymbol{\tau}, \widehat{a}(\boldsymbol{\theta}, \boldsymbol{\tau}))}{\partial a} = 0, \tag{10}$$

the numerical problem is solved by using Newton-Raphson method:

$$a_{h+1}(\boldsymbol{\theta}, \boldsymbol{\tau}) = a_h(\boldsymbol{\theta}, \boldsymbol{\tau}) - \frac{(\partial l(\boldsymbol{\theta}, \boldsymbol{\tau}, a_h(\boldsymbol{\theta}, \boldsymbol{\tau})) / \partial a)}{(\partial^2 l(\boldsymbol{\theta}, \boldsymbol{\tau}, a_h(\boldsymbol{\theta}, \boldsymbol{\tau})) / \partial a^2)}, \tag{11}$$

where

$$\frac{\partial l(\boldsymbol{\theta}, \boldsymbol{\tau}, a)}{\partial a} = \frac{1}{\sigma^2} \sum_{i=0}^{n} (y_i - x(t_i, \boldsymbol{\theta}, \boldsymbol{\tau}, a)) \frac{\partial x(t_i, \boldsymbol{\theta}, \boldsymbol{\tau}, a)}{\partial a}, \tag{12}$$

$$\frac{\partial^2 l(\boldsymbol{\theta},\boldsymbol{\tau},a)}{\partial a^2} = \frac{1}{\sigma^2}\sum_{i=0}^{n}\left(y_i - x\left(t_i,\boldsymbol{\theta},\boldsymbol{\tau},a\right)\right)\frac{\partial^2 x\left(t_i,\boldsymbol{\theta},\boldsymbol{\tau},a\right)}{\partial a^2} - \frac{1}{\sigma^2}\sum_{i=0}^{n}\left(\frac{\partial x\left(t_i,\boldsymbol{\theta},\boldsymbol{\tau},a\right)}{\partial a}\right)^2; \quad (13)$$

in (12) and (13), $\partial x(t_i,\boldsymbol{\theta},\boldsymbol{\tau},a)/\partial a$ and $\partial^2 x(t_i,\boldsymbol{\theta},\boldsymbol{\tau},a)/\partial a^2$ are, respectively, the first and second partial derivative of $x(t,\boldsymbol{\theta},\boldsymbol{\tau},a)$ with respect to a and then evaluated at $t = t_i$ for $i = 0,1,2,\ldots,n$. As seen from (12) and (13), we need to calculate $\partial x/\partial a$ and $\partial^2 x/\partial a^2$ at each $t = t_i$, $i = 0,1,2,\ldots,n$. This is done recursively as follows.

The first derivative process of $\partial x/\partial a$ is obtained by differentiating (2) with respect to a. Differentiating (2) with respect to a, where $\boldsymbol{\theta}$ and a are independent of each other, gives

$$\frac{\partial \dot{x}}{\partial a} = \frac{\partial f}{\partial x}\frac{\partial x}{\partial a} + \sum_{j=1}^{m}\frac{\partial f}{\partial z_j}\frac{\partial z_j}{\partial a} \quad (14)$$

which implies that the first derivative process $\partial x/\partial a$ satisfies another DDE which is given by (14).

Similarly, the second derivative process $\partial^2 x/\partial a^2$ is obtained by differentiating (14) with respect to a, to obtain

$$\frac{\partial^2 \dot{x}}{\partial a^2} = \frac{\partial^2 f}{\partial x^2}\left(\frac{\partial x}{\partial a}\right)^2 + \sum_{j=1,k=1}^{m}\frac{\partial^2 f}{\partial z_j \partial z_k}\left(\frac{\partial z_j}{\partial a}\right)\left(\frac{\partial z_k}{\partial a}\right) + 2\sum_{j=1}^{m}\frac{\partial^2 f}{\partial x \partial z_j}\frac{\partial x}{\partial a}\frac{\partial z_j}{\partial a} + \frac{\partial^2 x}{\partial a^2}\frac{\partial f}{\partial x} + \sum_{j=1}^{m}\frac{\partial^2 z_j}{\partial a^2}\frac{\partial f}{\partial z_j} \quad (15)$$

which implies that $\partial^2 x/\partial a^2$ satisfies a DDEM depending on $\partial x/\partial a$. The above two DDEs can be solved numerically based on initial conditions that are specified below.

To obtain the initial conditions of the first and second derivative process, we note that

$$x(t) = a \quad \text{for } t \in \left(-\infty, t_0\right]. \quad (16)$$

Thus, $\partial x/\partial a = 1$ and $\partial^2 x/\partial a^2 = 0$ for $t \in (-\infty, t_0]$. Subsequently, we can get the value of $\partial l(\boldsymbol{\theta},\boldsymbol{\tau},a)/\partial a$ and $\partial^2 l(\boldsymbol{\theta},\boldsymbol{\tau},a)/\partial a^2$ numerically at every value of t_i by numerically solving the DDEs using (12) and (13). We divide each $[t_{i-1}, t_i]$ into M equal segments. Here, M is a natural number.

The grid algorithm operates on the grid space of $(\boldsymbol{\theta},\boldsymbol{\tau})$, and the Newton-Raphson procedure is nested within the adaptive grid algorithm. Thus, for every grid value pair (θ_r, τ_s), the Newton-Raphson uses these values of $(\boldsymbol{\theta},\boldsymbol{\tau})$ to find "a" via (11). On convergence of the Newton-Raphson method, we obtain the MLE of a, $\widehat{a}(\theta_r,\tau_s)$, for each point grid (θ_r,τ_s) in Θ. The log-likelihood $l(\boldsymbol{\theta},\boldsymbol{\tau},a)$ is calculated based on (6) using $x_i = x(t_i,\theta_r,\tau_s,\widehat{a}(\theta_r,\tau_s))$. Then the point based maximum is found by finding the maximum $l(\theta_r,\tau_s,\widehat{a}(\theta_r,\tau_s))$ as a function of (θ_r,τ_s). We define the MLE which is obtained from the gridding algorithm as

$$\left(\widehat{\boldsymbol{\theta}}_G, \widehat{\boldsymbol{\tau}}_G\right) = \underset{r,s}{\operatorname{argmax}}\, l\left(\theta_r,\tau_s\right). \quad (17)$$

3.1.2. The Adaptive Grid Procedure. The adaptive grid (AG) algorithm is a repeated application of the generic grid procedure over increasingly finer intervals for $(\boldsymbol{\theta},\boldsymbol{\tau})$. The AG algorithm is as follows:

(1) Choose an initial grid space $\Theta^{(0)}$ consisting of the grid points $({\theta_r}^{(0)}, {\tau_s}^{(0)})$, $r = 1,2,\ldots,R$ and $s = 1,2,\ldots,S$.

(2) Maximize $l(\theta_r,\tau_s,\widehat{a}(\theta_r,\tau_s))$ with respect to r and s as described in the grid procedure above.

(3) Obtain $({\widehat{\boldsymbol{\theta}}_G}^{(0)}, {\widehat{\boldsymbol{\tau}}_G}^{(0)})$ as in (17).

(4) Refine the grid: suppose $({\theta_{r_0}}^{(0)}, {\tau_{s_0}}^{(0)}) \equiv ({\widehat{\boldsymbol{\theta}}_G}^{(0)}, {\widehat{\boldsymbol{\tau}}_G}^{(0)})$ as in #(3). The new grid space $\Theta^{(1)}$ has lower and upper θ-grid points given by $({\theta_{r_0-1}}^{(0)}, {\theta_{r_0+1}}^{(0)})$. The corresponding lower and upper $\boldsymbol{\tau}$-grid points are $({\tau_{s_0-1}}^{(0)}, {\tau_{s_0+1}}^{(0)})$. If either the lower or upper bounds are not found, then the original grip space is enlarged so that the MLE occurs in the interior of $\Theta^{(0)}$.

(5) Repeat steps #(2)–#(4) to obtain $({\widehat{\boldsymbol{\theta}}_G}^{(1)}, {\widehat{\boldsymbol{\tau}}_G}^{(1)})$ based on the generic grid procedure. Repeat to generate the sequence $({\widehat{\boldsymbol{\theta}}_G}^{(k)}, {\widehat{\boldsymbol{\tau}}_G}^{(k)})$, $k = 0,1,2,\ldots$. Stop at k^* when $\|({\widehat{\boldsymbol{\theta}}_G}^{(k^*)}, {\widehat{\boldsymbol{\tau}}_G}^{(k^*)}) - ({\widehat{\boldsymbol{\theta}}_G}^{(k^*-1)}, {\widehat{\boldsymbol{\tau}}_G}^{(k^*-1)})\| < \delta$, a prespecified threshold.

(6) The final MLE based on the adaptive grid technique is

$$\left(\widehat{\boldsymbol{\theta}}_{0,\mathrm{MLE}}, \widehat{\boldsymbol{\tau}}_{0,\mathrm{MLE}}\right) = \left({\widehat{\boldsymbol{\theta}}_G}^{(k^*)}, {\widehat{\boldsymbol{\tau}}_G}^{(k^*)}\right). \quad (18)$$

Remark 1. In step #(1), the initial grid space $\Theta^{(0)}$ is chosen to be a large domain that is likely to contain the MLE. In our simulation experiments, since the true values of $(\boldsymbol{\theta},\boldsymbol{\tau})$ are known, the domain is selected around these true values. In practice, we need to carry out an exhaustive search within the upper and lower bounds of $\boldsymbol{\theta}$ and $\boldsymbol{\tau}$. If the parameters are positive, say, as is usually the case, the lower bounds can be taken to be zero. Next, we can consider a large positive numbers, say B and C, and construct the grid in $[0,B]^p \times [0,C]^m$ consisting of H equidistant marginal grind points. The value of H need not be too large since we only aim to explore the log-likelihood profile. The log-likelihood can be evaluated at these grid points and plotted to visualize properties of the resulting surface. Depending on this plot, we can choose either to fix or increase B and C until we are certain that the MLE is within the selected domain.

After obtaining the first-step approximation to the MLE by the adaptive grid procedure above, we use the MATLAB function `fminunc` to obtain the final MLE by minimizing the negative log-likelihood function viewed as a function of the unknown parameter vector $\boldsymbol{\Gamma} = (\Gamma_1, \Gamma_2, \ldots, \Gamma_J) = (\boldsymbol{\theta}, \boldsymbol{\tau})$. We have $J = p + m$, and the final step MLE is defined as

$$\boldsymbol{\Gamma}_{\mathrm{MLE}} = \underset{\boldsymbol{\Gamma}}{\operatorname{argmin}} \left[-l_0(\boldsymbol{\Gamma})\right], \tag{19}$$

where $l_0(\boldsymbol{\Gamma}) = l_0((\boldsymbol{\theta}, \boldsymbol{\tau})) = l(\boldsymbol{\theta}, \boldsymbol{\tau}, \widehat{a}(\boldsymbol{\theta}, \boldsymbol{\tau}))$ with $\widehat{a}(\boldsymbol{\theta}, \boldsymbol{\tau})$ defined in (9). We require to input the gradient vector for this MATLAB function which is given by

$$\nabla l_0(\boldsymbol{\Gamma}) = \begin{bmatrix} \dfrac{\partial l_0(\boldsymbol{\Gamma})}{\partial \boldsymbol{\Gamma}_1} \\ \dfrac{\partial l_0(\boldsymbol{\Gamma})}{\partial \boldsymbol{\Gamma}_2} \\ \vdots \\ \dfrac{\partial l_0(\boldsymbol{\Gamma})}{\partial \boldsymbol{\Gamma}_j} \end{bmatrix}. \tag{20}$$

The explicit expression of each entry of $\nabla l_0(\boldsymbol{\Gamma})$ is provided in Appendix A. The MATLAB function `fminunc` uses, as an option, a quasi-Newton procedure that does not require the calculation of second derivatives and hence saves computational time.

3.2. Statistical Inference Based on MLEs

3.2.1. Information Matrix. Now we incorporate σ^2 into the estimation procedure as well. Once $(\widehat{\boldsymbol{\theta}}_{\mathrm{MLE}}, \widehat{\boldsymbol{\tau}}_{\mathrm{MLE}}, \widehat{a}_{\mathrm{MLE}})$ is obtained by the above two-stage procedure, the MLE of σ^2 is obtained analytically as

$$\widehat{\sigma}^2_{\mathrm{MLE}} = \frac{1}{(n+1)} \sum_{i=0}^{n} \left(y_i - x\left(t_i, \widehat{\boldsymbol{\theta}}_{\mathrm{MLE}}, \widehat{\boldsymbol{\tau}}_{\mathrm{MLE}}, \widehat{a}_{\mathrm{MLE}}\right)\right)^2. \tag{21}$$

Let $\boldsymbol{\Gamma} = (\Gamma_1, \Gamma_2, \ldots, \Gamma_K) = (\boldsymbol{\theta}, \boldsymbol{\tau}, a, \sigma^2)$ denote the $K \times 1$ vector of all unknown parameters (including σ^2) where $K = J + 2 = p + m + 2$. Subsequent inference based on the MLEs requires the computation of the Fisher information [14, 15]. The Fisher information matrix $I(\boldsymbol{\Gamma})$ is given by the $K \times K$ symmetric matrix whose (u, v)th element is the covariance between uth and vth first partial derivatives of the log-likelihood:

$$I(\boldsymbol{\Gamma})_{(u,v)} = \operatorname{Cov}\left[\frac{\partial l(\boldsymbol{\Gamma} \mid \mathbf{y})}{\partial \Gamma_u}, \frac{\partial l(\boldsymbol{\Gamma} \mid \mathbf{y})}{\partial \Gamma_v}\right]. \tag{22}$$

Based on the expected values of the second partial derivatives, the Fisher information matrix in (22) is equivalent to

$$I(\boldsymbol{\Gamma})_{(u,v)} = -E\left[\frac{\partial^2 l(\boldsymbol{\Gamma} \mid \mathbf{y})}{\partial \Gamma_u \partial \Gamma_v}\right], \quad 1 \le u, v \le K. \tag{23}$$

The observed Fisher information matrix is simply $I(\widehat{\boldsymbol{\Gamma}}_{\mathrm{MLE}})$, the information matrix evaluated at the maximum likelihood estimate, $\widehat{\boldsymbol{\Gamma}}_{\mathrm{MLE}}$, of $\boldsymbol{\Gamma}$. Further, its inverse evaluated at the MLE is an estimate of the asymptotic covariance matrix for $\widehat{\boldsymbol{\Gamma}}_{\mathrm{MLE}}$ which is given by

$$\operatorname{COV}\left(\widehat{\boldsymbol{\Gamma}}_{\mathrm{MLE}}\right) = \left[I\left(\widehat{\boldsymbol{\Gamma}}_{\mathrm{MLE}}\right)\right]^{-1}. \tag{24}$$

Since the log-likelihood function is given by

$$\begin{aligned} l\left(\boldsymbol{\theta}, \boldsymbol{\tau}, a, \sigma^2 \mid \mathbf{y}\right) = {} & -\frac{(n+1)}{2} \ln\left(2\pi\sigma^2\right) \\ & - \frac{1}{2\sigma^2} \sum_{i=0}^{n} \left(y_i - x\left(t_i, \boldsymbol{\theta}, \boldsymbol{\tau}, a\right)\right)^2, \end{aligned} \tag{25}$$

the first-order partial derivative of $l(\boldsymbol{\theta}, \boldsymbol{\tau}, a, \sigma^2 \mid \mathbf{y})$ with respect to each element of $\boldsymbol{\Gamma}$ is given by

$$\begin{aligned} & \frac{\partial l\left(\boldsymbol{\theta}, \boldsymbol{\tau}, a, \sigma^2 \mid \mathbf{y}\right)}{\partial \Gamma_u} \\ & \quad = \frac{1}{\sigma^2} \sum_{i=0}^{n} \left(y_i - x\left(t_i, \boldsymbol{\theta}, \boldsymbol{\tau}, a\right)\right) \left(\frac{\partial x\left(t_i, \boldsymbol{\theta}, \boldsymbol{\tau}, a\right)}{\partial \Gamma_u}\right) \end{aligned} \tag{26}$$

for $1 \le u \le K$. The second-order partial derivative is

$$\begin{aligned} & \frac{\partial^2 l\left(\boldsymbol{\theta}, \boldsymbol{\tau}, a, \sigma^2 \mid \mathbf{y}\right)}{\partial \Gamma_u \partial \Gamma_v} \\ & \quad = \frac{1}{\sigma^2} \left[\sum_{i=0}^{n} \left(y_i - x\left(t_i, \boldsymbol{\theta}, \boldsymbol{\tau}, a\right)\right) \left(\frac{\partial^2 x\left(t_i, \boldsymbol{\theta}, \boldsymbol{\tau}, a\right)}{\partial \Gamma_u \partial \Gamma_v}\right) \right. \\ & \quad \left. - \sum_{i=0}^{n} \left(\frac{\partial x\left(t_i, \boldsymbol{\theta}, \boldsymbol{\tau}, a\right)}{\partial \Gamma_u}\right) \left(\frac{\partial x\left(t_i, \boldsymbol{\theta}, \boldsymbol{\tau}, a\right)}{\partial \Gamma_v}\right)\right], \end{aligned} \tag{27}$$

for $1 \le u, v \le K$,

$$\begin{aligned} & \frac{\partial^2 l}{\partial \Gamma_u \partial \sigma^2} \\ & \quad = \frac{-1}{\left(\sigma^2\right)^2} \sum_{i=0}^{n} \left(y_i - x\left(t_i, \boldsymbol{\theta}, \boldsymbol{\tau}, a\right)\right) \left(\frac{\partial x\left(t_i, \boldsymbol{\theta}, \boldsymbol{\tau}, a\right)}{\partial \Gamma_u}\right) \end{aligned} \tag{28}$$

for $1 \le u \le K$, and

$$\begin{aligned} & \frac{\partial^2 l}{\partial \left(\sigma^2\right)^2} \\ & \quad = \frac{1}{2\sigma^4} \left[(n+1) - \frac{2}{\sigma^2} \sum_{i=0}^{n} \left(y_i - x\left(t_i, \boldsymbol{\theta}, \boldsymbol{\tau}, a\right)\right)^2\right]. \end{aligned} \tag{29}$$

Taking expectations on both sides of the above equations and from (23), we get

$$\begin{aligned} I(\boldsymbol{\Gamma})_{(u,v)} & = -E\left[\frac{\partial^2 l(\boldsymbol{\Gamma} \mid \mathbf{y})}{\partial \Gamma_u \partial \Gamma_v}\right] \\ & = \frac{1}{\sigma^2} \sum_{i=0}^{n} \left(\frac{\partial x\left(t_i, \boldsymbol{\theta}, \boldsymbol{\tau}, a\right)}{\partial \Gamma_u}\right) \left(\frac{\partial x\left(t_i, \boldsymbol{\theta}, \boldsymbol{\tau}, a\right)}{\partial \Gamma_v}\right), \end{aligned} \tag{30}$$

for $1 \le u, v \le K$,

$$I(\boldsymbol{\Gamma})_{(u,\sigma^2)} = -E\left[\frac{\partial^2 l(\boldsymbol{\Gamma} \mid \mathbf{y})}{\partial \Gamma_u \partial \sigma^2}\right] = 0 \tag{31}$$

for $1 \le u \le K$, and

$$I(\boldsymbol{\Gamma})_{(\sigma^2,\sigma^2)} = -E\left[\frac{\partial^2 l(\boldsymbol{\Gamma} \mid \mathbf{y})}{\partial (\sigma^2)^2}\right] = \frac{n+1}{2\sigma^4}. \tag{32}$$

We compute each element (u, v) of the matrix in (23) for DDEMs with single and multiple delays; the explicit expressions are given in Appendices A and B.

3.2.2. Confidence Intervals. A confidence interval for an unknown parameter gives the range of values most likely to cover the true value of the parameter with high probability. The standard form of a confidence interval is

$$\text{estimate} + / - \text{margin of error}. \tag{33}$$

To construct a level C confidence interval for any element of $\boldsymbol{\Gamma} = (\Gamma_1, \Gamma_2, \ldots, \Gamma_K) = (\boldsymbol{\theta}, \boldsymbol{\tau}, a, \sigma^2)$, say, Γ_u, for $1 \le u \le K$, we need to find an estimate of the margin of error. First, the estimated standard error of the maximum likelihood estimate, $\widehat{\Gamma}_{u,\text{MLE}}$, of Γ_u is given by

$$\text{SE}\left(\widehat{\Gamma}_{u,\text{MLE}}\right) = \sqrt{\text{COV}\left(\widehat{\boldsymbol{\Gamma}}_{\text{MLE}}\right)_{(u,u)}}, \tag{34}$$

where $\text{COV}(\widehat{\boldsymbol{\Gamma}}_{\text{MLE}})$ is the covariance matrix as given in (24). The explicit terms of the covariance matrix can be obtained by substituting (30) into (24). The confidence interval for Γ_u is

$$\widehat{\Gamma}_{u,\text{MLE}} \pm z_{\alpha/2}\text{SE}\left(\widehat{\Gamma}_{u,\text{MLE}}\right), \tag{35}$$

where $z_{\alpha/2}$ = `norminv`$(1 - \alpha/2)$, $\alpha = 0.05$, is the desired significance level and $z_{\alpha/2}\text{SE}(\widehat{\Gamma}_{u,\text{MLE}})$ is the margin of error. We can find confidence intervals for all components of $\boldsymbol{\Gamma} = (\Gamma_1, \Gamma_2, \ldots, \Gamma_K) = (\boldsymbol{\theta}, \boldsymbol{\tau}, a, \sigma^2)$ in this way. In some cases, the estimated confidence interval in (35) may include some negative values which is unreasonable for a parameter that is known to be positive. In this case, we perform a logarithmic transformation of the parameter, construct the confidence interval for the log-transformed parameter, and then transform the confidence interval back to the original parameter space. The confidence interval for Γ_u based on this log-transformation procedure is

$$\exp\left(\log\left(\widehat{\Gamma}_{u,\text{MLE}}\right) \pm \frac{z_{\alpha/2}\text{SE}\left(\widehat{\Gamma}_{u,\text{MLE}}\right)}{\widehat{\Gamma}_{u,\text{MLE}}}\right). \tag{36}$$

4. Examples

We present three examples of DDEMS in the univariate case: we consider two models with a single delay and a third one with two delays.

4.1. Example 1. We consider the exponential delay differential equation model (EDDEM) with a single delay (i.e., $p = 1$, $m = 1$) which is the solution to the DDE

$$\dot{x}(t) = \theta x(t - \tau). \tag{37}$$

The EDDEM in (37) is a model for ideal population growth under infinite resources and no deaths, such as a protozoan or bacterial culture dividing under constant environmental conditions. The delay parameter τ can be taken to represent the gestation period or maturity period, that is, the time taken for individuals to be ready for division. The parameter θ represents the growth rate of the population. We numerically solve the DDE in (37) using the MATLAB function `dde23` with fixed parameters $(\theta, \tau, a, \sigma^2)$ values at $(0.5, 1, 5, 0.01)$. Sampled observations from the DDEM as in (1) were obtained at discrete time intervals of width $h = 0.1$ starting from $t_0 = 0$. The endpoint considered is $t_n = 10$ corresponding to $n + 1 = 101$. The aim is to estimate θ, τ, a, and σ^2 based on $y_0, y_1, \ldots, y_n$. Figure 1(a) illustrates the different behaviour of $x(t)$ based on different parameter specifications. Figure 1(b) shows the underlying trajectories of the solution $x(t)$ from the DDE model (37) and the $(n + 1)$ sampled observations.

The initial grid space for the adaptive grid procedure was taken to be $\Theta^{(0)} = \{(\theta_r, \tau_s) : \theta_r = \theta_0 + rh,\ \tau_s = \tau_0 + sh,\ r = 1, 2, \ldots, R;\ s = 1, 2, \ldots, S\}$ with $(\theta_0, \tau_0) = (0.1, 0.6)$, $h = 0.1$, $R = S = 9$; see the remark that is given towards the end of this section regarding the selection of $\Theta^{(0)}$ for this example as well as for the rest. The stopping criteria threshold δ was chosen to be 0.0001. The adaptive grid and Newton-Raphson procedures were run; the results are given in Tables 1 and 2. Recall that M is the number of subdivisions of each interval $[t_{i-1}, t_i]$ needed for calculating the quantities $\partial x(t_i, \theta, \tau, a)/\partial a$ and $\partial^2 x(t_i, \theta, \tau, a)/\partial a^2$; see Section 3.1.1. As M increases, the MLE estimates become more accurate but at the cost of increased computational time. We note that, for $M = 50$ or $M = 100$, satisfactory results are already achieved in terms of closeness to the true parameter values of $(\theta, \tau, a, \sigma^2) = (0.5, 1, 5, 0.01)$. Subsequently, $M = 100$ is considered for finding the maximum of the log-likelihood function, for finding the information matrix and computing the confidence intervals of the parameters.

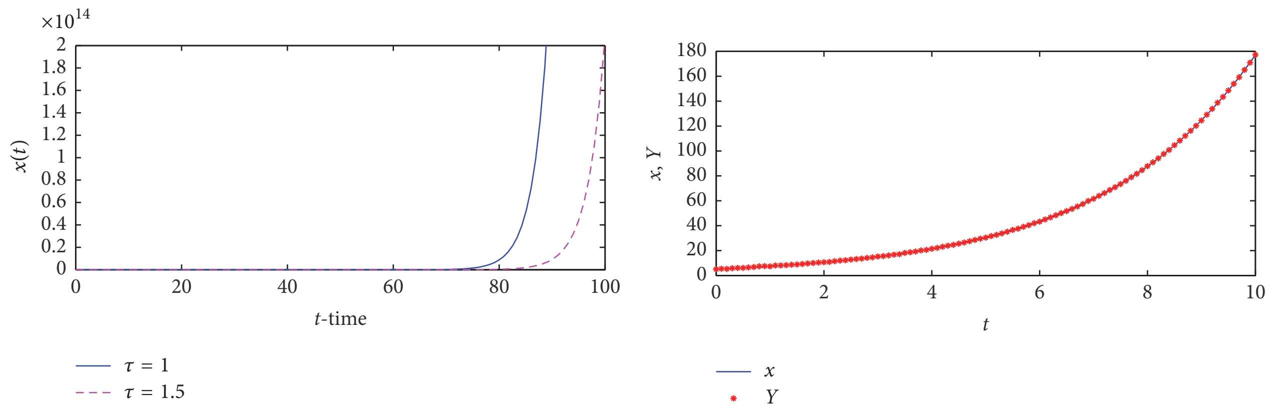
The Fisher information matrix as $h = 0.1$ and $M = 100$ for EDDEM is

$$I(\boldsymbol{\Gamma}) = 10^9 \times \begin{bmatrix} 1.0887 & 0.0404 & 0.0459 & 0 \\ 0.0404 & 0.0015 & 0.0017 & 0 \\ 0.0459 & 0.0017 & 0.0020 & 0 \\ 0 & 0 & 0 & 0.0006 \end{bmatrix}, \tag{38}$$

and variance of $\widehat{\boldsymbol{\Gamma}}$ at the MLE is given by

$$\begin{aligned} &\text{Var}\left(\widehat{\boldsymbol{\Gamma}}\right) \\ &= 10^{-4} \times \begin{bmatrix} 0.0004 & -0.0129 & 0.0015 & 0 \\ -0.0129 & 4.3309 & -3.5029 & 0 \\ 0.0015 & -3.5029 & 3.0445 & 0 \\ 0 & 0 & 0 & 0.0170 \end{bmatrix}. \end{aligned} \tag{39}$$

The 95% confidence intervals for parameters $(\theta, \tau, a, \sigma^2)$ in EDDE with single delay are shown, respectively, in Table 3.



(a) Numerical solution of the EDDEM (37) using the fixed parameter values in $[0, 100]$ by step size $h = 0.1$ with $\theta = 0.5$ and $\tau = 1$ or $\tau = 1.5$

(b) Numerical solution of the EDDEM (37) using the estimated parameter values. The stars are the simulated noisy data from (1) at $n+1 = 101$ equally spaced time points in $[0, 10]$ by step size $h = 0.1$ with $\theta = 0.5$ and $\tau = 1$

FIGURE 1

TABLE 1: Table showing values of Max.Val(l), $\widehat{a}(\widehat{\theta},\widehat{\tau})$, $(\widehat{\theta},\widehat{\tau})$, and $\widehat{\sigma}^2$ for the EDDEM by using the adaptive grid procedure. Here, the number of equally spaced time points in $[0, 10]$ is $n + 1 = 101$ with $h = 0.1$.

M	Max.Val(l)	$\widehat{a}\left(\widehat{\theta},\widehat{\tau}\right)$	$\left(\widehat{\theta},\widehat{\tau}\right)$	$\widehat{\sigma}^2$
10	−0.5817	5.0181	(0.5000, 1.0000)	0.0114
20	−0.5037	5.0091	(0.5000, 1.0000)	0.0099
30	−0.4880	5.0061	(0.5000, 1.0000)	0.0096
40	−0.4821	5.0046	(0.5000, 1.0000)	0.0095
50	−0.4792	5.0037	(0.5000, 1.0000)	0.0094
100	−0.4748	5.0019	(0.5000, 1.0000)	0.0093
1000	−0.4724	5.0002	(0.5000, 1.0000)	0.0093

TABLE 2: Table showing value of Max.Val(l), $\nabla l(\mathbf{\Gamma})$, and $(\widehat{\theta}_{\mathrm{MLE}}, \widehat{\tau}_{\mathrm{MLE}})$ for the EDDEM with $h = 0.1$.

M	Max.Val(l)	$\nabla l(\mathbf{\Gamma})$	$\left(\widehat{\theta}_{0,\mathrm{MLE}}, \widehat{\tau}_{0,\mathrm{MLE}}\right)$	$(\widehat{\theta}_{\mathrm{MLE}}, \widehat{\tau}_{\mathrm{MLE}})$
100	0.4715	$10^{-2} \times \begin{bmatrix} 0.0006 \\ -0.1001 \end{bmatrix}$	(0.5000, 1.000)	(0.5001645, 1.0000017)

TABLE 3: Table showing the 95% confidence intervals for parameters θ, τ, a, and σ^2 in EDDEM.

M	(θ_L, θ_U)	(τ_L, τ_U)	(a_L, a_U)	(σ_L^2, σ_U^2)
100	(0.4996, 0.5004)	(0.9592, 1.0408)	(4.9677, 5.0361)	(0.0068, 0.0119)

4.2. Example 2. A delay differential equation in population ecology given by

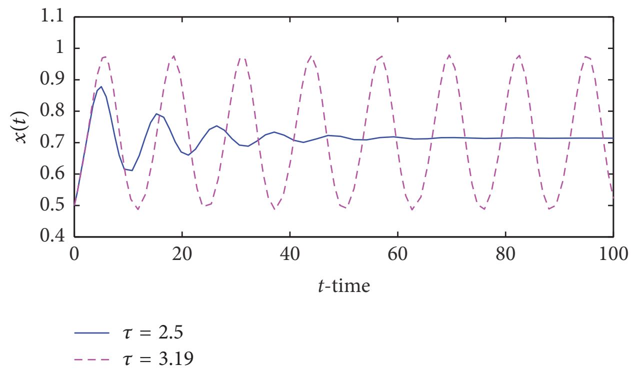
$$\dot{x}(t) = \theta x(t)\left(1 - \frac{x(t-\tau)}{K}\right) \tag{40}$$

is known as Hutchinson's equation [16], where x is the population at that instant, θ is the intrinsic growth rate, and K is the carrying capacity of the population. Both θ and K are positive constants and τ is a positive constant delay parameter.

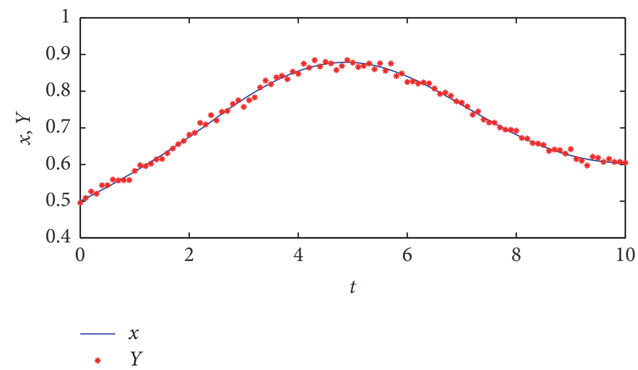
Define $\theta_1 = \theta$ and $\theta_2 = \theta/K$; then (40) can be rewritten as

$$\dot{x}(t) = \theta_1 x(t) - \theta_2 x(t)\, x(t-\tau). \tag{41}$$

The observations $y_0, y_1, \ldots, y_n$ are collected at the $(n+1)$ sampled time points $T_0 = t_0 < t_1 < \cdots < t_n = T_1$, based on the observational model (1), and the aim is to estimate $\theta_1, \theta_2, \tau, a$, and σ^2 based on the observations $y_0, y_1, \ldots, y_n$. The DDE in (41) is solved numerically by using the MATLAB function `dde23` with fixed parameters $(\theta_1, \theta_2, \tau, a, \sigma^2)$ values. Figure 2(a) shows the underlying trajectories (mean function) of the solution $x(t)$ from the DDE model (41). Figure 2(a) illustrates the different behaviour of $x(t)$ based on different parameter specifications which reflect both stable and unstable solutions. Subsequently, we fix the parameter specification at $(\theta_1, \theta_2, \tau, a, \sigma^2) = (0.5, 0.7, 2.5, 0.5, 0.0001)$. Sampled observations from the DDEM as in (1) were obtained



(a) Numerical solution of the DLDEM with two delays (41) using the fixed parameter values in $[0, 100]$ by step size $h = 0.1$ with $\theta_1 = 0.5$ and $\theta_2 = 0.7$. The steady state is stable when $\tau = 2.5$ and becomes unstable when $\tau = 3.19$



(b) Numerical solution of the DLDEM with two delays (41) using the estimated parameter values. The stars are the simulated noisy data by adding noises to the DLDE solutions at $n + 1 = 101$ equally spaced time points in $[0, 10]$ by step size $h = 0.1$ with $\theta_1 = 0.5$, $\theta_2 = 0.7$, and $\tau = 2.5$

Figure 2

Table 4: Table showing values of Max.Val(l), $\widehat{a}(\widehat{\theta}_1, \widehat{\theta}_2, \widehat{\tau})$, $(\widehat{\theta}_1, \widehat{\theta}_2, \widehat{\tau})$, and $\widehat{\sigma}^2$ for the DLDEM with single delay by using an adaptive grid. Here, the number of equally spaced time points in $[0, 10]$ is $n + 1 = 101$ with $h = 0.1$.

M	Max.Val(l)	$\widehat{a}(\theta_1, \theta_2, \tau)$	$(\widehat{\theta}_1, \widehat{\theta}_2, \widehat{\tau})$	$\widehat{\sigma}^2$
10	−0.0049	0.5008	(0.5, 0.7, 2.5)	0.000095
20	−0.0048	0.5005	(0.5, 0.7, 2.5)	0.000095
30	−0.0048	0.5005	(0.5, 0.7, 2.5)	0.000095
40	−0.0048	0.5004	(0.5, 0.7, 2.5)	0.000095
50	−0.0048	0.5004	(0.5, 0.7, 2.5)	0.000095
100	−0.0048	0.5003	(0.5, 0.7, 2.5)	0.000095
1000	−0.0048	0.5003	(0.5, 0.7, 2.5)	0.000095

Table 5: Table showing value of Max.Val(l), $\nabla l(\mathbf{\Gamma})$, and $(\widehat{\theta}_{\mathrm{MLE}}, \widehat{\tau}_{\mathrm{MLE}})$ for the DLDEM with single delay with $h = 0.1$.

M	Max.Val(l)	$\nabla l(\mathbf{\Gamma})$	$(\widehat{\theta}_{10,\mathrm{MLE}}, \widehat{\theta}_{20,\mathrm{MLE}}, \widehat{\tau}_{0,\mathrm{MLE}})$	$(\widehat{\theta}_{1\mathrm{MLE}}, \widehat{\theta}_{2\mathrm{MLE}}, \widehat{\tau}_{\mathrm{MLE}})$
100	0.0048	$10^{-5} \times \begin{bmatrix} -0.4019 \\ -0.2653 \\ 0.9364 \end{bmatrix}$	(0.5, 0.7, 2.5)	(0.5007149, 0.7006367, 2.5004988)

at discrete time intervals of width $h = 0.1$ starting from $t_0 = 0$. The endpoint considered is $t_n = 10$ corresponding to $n = 100$ where the number of sampled time points are $(n + 1)$. Figure 2(b) shows the underlying trajectory of the solution $x(t)$ from the DDE model (41) and the $(n+1)$ sampled observations for the time range selected.

The initial grid space for the adaptive grid procedure was taken to be $\Theta^{(0)} = \{(\theta_{1u}, \theta_{2v}, \tau_r) : \theta_{1u} = \theta_{10} + uh,\ \theta_{2v} = \theta_{20} + vh,\ \tau_r = \tau_0 + rh\}$ with $(\theta_{10}, \theta_{20}, \tau_0) = (0.4, 0.6, 2.4)$, $h = 0.1$ and $U = V = R = 3$. The stopping criteria threshold δ was chosen to be 0.0001. The adaptive grid and Newton-Raphson procedures were run; the results are given in Tables 4 and 5. As in the previous example, as M increases, the $\widehat{a}(\theta_1, \theta_2, \tau)$ becomes more accurate and very close to be the true value $a(\theta_1, \theta_2, \tau) = 0.5$ but at the cost of increased computational time.

The Fisher information matrix as $h = 0.1$ and $M = 100$ for DLDEM with single delay is

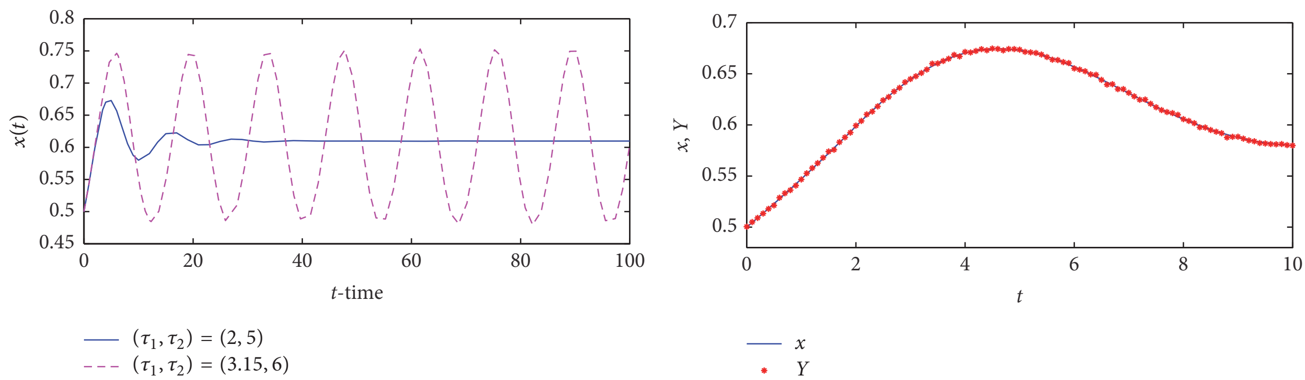
$$I(\mathbf{\Gamma}) = 10^6 \times \begin{bmatrix} 3.7030 & -2.2042 & -0.1819 & -0.5757 & 0 \\ -2.2042 & 1.4665 & 0.2069 & 0.3285 & 0 \\ -0.1819 & 0.2069 & 0.0774 & 0.0059 & 0 \\ -0.5757 & 0.3285 & 0.0059 & 0.3164 & 0 \\ 0 & 0 & 0 & 0 & 5.6613 \times 10^3 \end{bmatrix}, \quad (42)$$

and variance of $\widehat{\mathbf{\Gamma}}$ by using MLE is given by

$$\mathrm{Var}\left(\widehat{\mathbf{\Gamma}}\right) = 10^{-3} \times \begin{bmatrix} 0.0241 & 0.0463 & -0.0669 & -0.0030 & 0 \\ 0.0463 & 0.0907 & -0.1330 & -0.0075 & 0 \\ -0.0669 & -0.1330 & 0.2102 & 0.0125 & 0 \\ -0.0030 & -0.0075 & 0.0125 & 0.0052 & 0 \\ 0 & 0 & 0 & 0 & 1.7664 \times 10^{-7} \end{bmatrix}. \quad (43)$$

TABLE 6: Table showing the 95% confidence intervals for parameters $\theta_1, \theta_2, \tau, a$, and σ^2 in DLDE with single delay.

M	$(\theta_{1L}, \theta_{1U})$	$(\theta_{2L}, \theta_{2U})$	(τ_L, τ_U)	(a_L, a_U)	(σ_L^2, σ_U^2)
100	(0.4904, 0.5096)	(0.6813, 0.7187)	(2.4716, 2.5284)	(0.4959, 0.5048)	(0.00007, 0.00012)



(a) Numerical solution of the DLDEM with two delays (45) using the fixed parameter values in $[0, 100]$ by step size $h = 0.1$ with $\theta_1 = 0.5, \theta_2 = 0.7$, and $\theta_3 = 0.12$. The steady state is stable when $\tau_1 = 2$ and $\tau_2 = 5$ and becomes unstable when $\tau_1 = 3.15$ and $\tau_2 = 6$

(b) Numerical solution of the DLDEM with two delays (45) using the estimated parameter values. The stars are the simulated noisy data by adding noises to the DLDE solutions at $n + 1 = 101$ equally spaced time points in $[0, 10]$ by step size $h = 0.1$ with $\theta_1 = 0.5, \theta_2 = 0.7, \theta_3 = 0.12, \tau_1 = 2$, and $\tau_2 = 5$

FIGURE 3

The 95% confidence intervals for parameters $(\theta_1, \theta_2, \tau, a, \sigma^2)$ in DLDE with single delay are shown in Table 6.

4.3. Example 3. The delayed logistic differential equation model (DLDEM) with two delays proposed by Braddock and van den Driessche [17] is the solution to the DDE

$$\dot{x}(t) = \theta x(t)\left(1 - \frac{x(t-\tau_1)}{k_1} - \frac{x(t-\tau_2)}{k_2}\right), \tag{44}$$

where θ, k_1, k_2, τ_1, and τ_2 are positive constants. DDEs with two delays appear in many applications such as epidemiological models [18], physiological models [19], neurological models [20], and medical models [21]. In such equations [22, 23], very rich dynamics have been observed. Denoting $\theta_1 = \theta$, $\theta_2 = \theta/k_1$, $\theta_3 = \theta/k_2$, $z_1(t) = x(t - \tau_1)$, and $z_2(t) = x(t - \tau_2)$, we obtain

$$\dot{x}(t) = \theta_1 x(t) - \theta_2 z_1(t)\, x(t) - \theta_3 z_2(t)\, x(t). \tag{45}$$

By using the MATLAB function `dde23` with fixed parameters $(\theta_1, \theta_2, \theta_3, \tau_1, \tau_2, a, \sigma^2)$ values, we obtain the trajectories of the solution $x(t)$. As in Example 2, we note the different characteristics of the solution depending on the parameter specifications as shown in Figure 3(a). Subsequently, the parameters are fixed at $(0.5, 0.7, 0.12, 2, 5, 0.5, (0.001)^2)$ and observations $y_0, y_1, \ldots, y_n$ are collected at the $(n+1)$ sampled time points $T_0 = t_0 < t_1 < \cdots < t_n = T_1$, based on the observational model (1) at discrete time intervals of width $h = 0.1$ starting from $t_0 = 0$. The endpoint considered is $t_n = 10$ corresponding to $n + 1 = 101$. Figure 3(b) shows the underlying trajectories of the solution $x(t)$ from the DDE model (41) and the $(n + 1)$sampled observations.

The initial grid space for the adaptive grid procedure is taken to be $\Theta^{(0)} = \{(\theta_{1u}, \theta_{2v}, \theta_{3w}, \tau_{1r}, \tau_{2s}) : \theta_{1u} = \theta_{10} + uh,\ \theta_{2v} = \theta_{20} + vh,\ \theta_{3w} = \theta_{30} + wh,\ \tau_{1r} = \tau_{10} + rh,\ \tau_{2s} = \tau_{20} + sh\}$ with $(\theta_{10}, \theta_{20}, \theta_{30}, \tau_{10}, \tau_{20}) = (0.4, 0.6, 0.02, 1.9, 4.9)$, $h = 0.1$ and $U = V = W = R = S = 3$. The stopping criteria threshold δ was chosen to be 0.0001. The adaptive grid and Newton-Raphson procedures were run; the results are given in Tables 7 and 8.

The Fisher information matrix as $h = 0.1$ for DLDEM with two delays at $M = 100$ is

$$I(\mathbf{\Gamma}) = 10^8 \times \begin{bmatrix} 1.5952 & -0.9359 & -0.8343 & -0.2912 & -0.0098 & -0.2324 & 0 \\ -0.9359 & 0.5630 & 0.4973 & 0.1809 & 0.0074 & 0.1328 & 0 \\ -0.8343 & 0.4973 & 0.4432 & 0.1619 & 0.0063 & 0.1121 & 0 \\ -0.2912 & 0.1809 & 0.1619 & 0.0711 & 0.0033 & 0.0408 & 0 \\ -0.0098 & 0.0074 & 0.0063 & 0.0033 & 0.0003 & 0.0001 & 0 \\ -0.2324 & 0.1328 & 0.1121 & 0.0408 & 0.0001 & 0.1519 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 305361 \end{bmatrix}, \tag{46}$$

Table 7: Table showing value of Max.Val(l), $\widehat{a}(\theta_1,\theta_2,\theta_3,\tau_1,\tau_2)$, $(\widehat{\theta}_1,\widehat{\theta}_2,\widehat{\theta}_3,\widehat{\tau}_1,\widehat{\tau}_2)$, and $\widehat{\sigma}^2$ in DLDEM with two delays by using an adaptive grid for $(\theta_1,\theta_2,\theta_3,\tau_1,\tau_2)=(0.5,0.7,0.12,2,5)$ and $n+1=101$ equally spaced time points in $[0,10]$ at $h=0.1$.

M	Max.Val(l)	$\widehat{a}(\theta_1,\theta_2,\theta_3,\tau_1,\tau_2)$	$(\widehat{\theta}_1,\widehat{\theta}_2,\widehat{\theta}_3,\widehat{\tau}_1,\widehat{\tau}_2)$	$\widehat{\sigma}^2$
10	-6.4697×10^{-5}	0.5007	(0.5, 0.7, 0.12, 2, 5)	1.2686×10^{-6}
20	-6.5220×10^{-5}	0.5006	(0.5, 0.7, 0.12, 2, 5)	1.2788×10^{-6}
30	-6.5478×10^{-5}	0.5005	(0.5, 0.7, 0.12, 2, 5)	1.2839×10^{-6}
40	-6.5622×10^{-5}	0.5005	(0.5, 0.7, 0.12, 2, 5)	1.2867×10^{-6}
50	-6.5714×10^{-5}	0.5005	(0.5, 0.7, 0.12, 2, 5)	1.2885×10^{-6}
100	-6.5910×10^{-5}	0.5005	(0.5, 0.7, 0.12, 2, 5)	1.2923×10^{-6}
1000	-6.6098×10^{-5}	0.5004	(0.5, 0.7, 0.12, 2, 5)	1.2960×10^{-6}

Table 8: Table showing value of Max.Val(l), $\nabla l(\mathbf{\Gamma})$, and $(\widehat{\theta}_{1\text{MLE}},\widehat{\theta}_{2\text{MLE}},\widehat{\theta}_{3\text{MLE}},\widehat{\tau}_{1\text{MLE}},\widehat{\tau}_{2\text{MLE}})$ for DLDEM with two delays with $h=0.1$.

M	Max.Val(l)	$\nabla l(\mathbf{\Gamma})$	$(\widehat{\theta}_{10,\text{MLE}},\widehat{\theta}_{20,\text{MLE}},\widehat{\theta}_{30,\text{MLE}},\widehat{\tau}_{10,\text{MLE}},\widehat{\tau}_{20,\text{MLE}})$	$(\widehat{\theta}_{1\text{MLE}},\widehat{\theta}_{2\text{MLE}},\widehat{\theta}_{3\text{MLE}},\widehat{\tau}_{1\text{MLE}},\widehat{\tau}_{2\text{MLE}})$
100	6.4697×10^{-5}	$10^{-4}\times\begin{bmatrix}0.1600\\-0.1495\\-0.1815\\-0.2596\\-0.0146\end{bmatrix}$	(0.5, 0.7, 0.12, 2, 5)	(0.5001029, 0.6999608, 0.1199824, 2.0000706, 5.0000044)

and variance of $\widehat{\mathbf{\Gamma}}$ by using MLE is given by

$$\operatorname{Var}\left(\widehat{\mathbf{\Gamma}}\right)=10^{-3}\times\begin{bmatrix}0.0642 & 0.0331 & 0.0983 & -0.0161 & -0.6515 & 0.0014 & 0\\ 0.0331 & 0.0215 & 0.0457 & -0.0063 & -0.3586 & 0.0002 & 0\\ 0.0983 & 0.0457 & 0.1569 & -0.0275 & -0.9709 & 0.0027 & 0\\ -0.0161 & -0.0063 & -0.0275 & 0.0066 & 0.1444 & -0.0007 & 0\\ -0.6515 & -0.3586 & -0.9709 & 0.1444 & 6.8315 & -0.0102 & 0\\ 0.0014 & 0.0002 & 0.0027 & -0.0007 & -0.0102 & 0.0002 & 0\\ 0 & 0 & 0 & 0 & 0 & 0 & 3.3000\times10^{-11}\end{bmatrix}. \quad (47)$$

The 95% confidence intervals for parameters $(\theta_1,\theta_2,\theta_3,\tau_1,\tau_2,a,\sigma^2)$ in DLDE with two delays are shown in Table 9.

Remark 2. As mentioned earlier, the adaptive grid procedure in the first stage of our two-step procedure needs to select a sufficiently large domain that is likely to contain the MLE. The MLE should be close to the true parameter values that generated the data as standard MLE theory [11–13] dictates. This has also been established in the three examples considered. Hence, since the true value of $(\boldsymbol{\theta},\boldsymbol{\tau})$ is known in our simulation examples, we selected the initial domain of the grid procedure to contain these true values in its interior. Thus, the notation (θ_0,τ_0) denotes the lower bound of the parameters which is used for the grid procedure. The grid $\Theta^{(0)}=\{(\theta_r,\tau_s):\theta_r=\theta_0+rh,\ \tau_s=\tau_0+sh,\ r=1,2,\ldots,R;\ s=1,2,\ldots,S\}$ is ensured to contain the true parameter values based on selection of R, S, and h in all the examples. Other than this consideration, the true values that were used in the simulation were selected rather arbitrarily, only chosen so as to be representative parameter values that exhibit the typical nature of trajectories of the underlying DDEs as shown in the figures.

5. Conclusion

In this paper, we presented the method of maximum likelihood for estimating parameters in delayed differential equations. As examples we considered the exponential differential equation model, delayed logistic differential equation model with single delay, and delayed logistic differential equation model with two delays; then we estimated the unknown parameters in these models. Two-step approach using an adaptive grid followed by a gradient descent procedure is proposed. Our methodology estimates the delay parameter

Table 9: Table showing the 95% confidence intervals for parameters $\theta_1, \theta_2, \theta_3, \tau_1, \tau_2, a$, and σ^2 in DLDE with two delays.

M	100
$(\theta_{1L}, \theta_{1U})$	(0.4843, 0.5157)
$(\theta_{2L}, \theta_{2U})$	(0.6909, 0.7091)
$(\theta_{3L}, \theta_{3U})$	(0.0955, 0.1445)
(τ_{1L}, τ_{1U})	(1.9950, 2.0050)
(τ_{2L}, τ_{2U})	(4.8380, 5.1620)
(a_L, a_U)	(0.4996, 0.5013)
(σ^2_L, σ^2_U)	(0.0000009, 0.0000016)

as well as the initial starting value of the dynamical system correctly based on simulation data. Confidence intervals and information matrix by using maximum likelihood are obtained and are found to contain the true values of the parameter based on simulation data.

In this paper, we took the initial value function of the DDE as an unknown constant "a". However, it is possible to extend the constant initial value assumption to a more general linear or nonlinear function, say $\varphi(x)$, for $x \in [-\tau, 0]$. Two complications arise here. First, we need additional unknown parameters to represent $\varphi(x)$; for example, if $\varphi(x) = a + bx$ is chosen to be linear, we have to estimate parameter b in addition to a. Higher order functions offer greater flexibility in modeling the initial function but at the expense of estimating extra parameters and slowing down the computational procedure. A second issue that follows the first is the selection of a "best" initial value function—either constant, linear, quadratic, or others. Thus, further research is required to address this concern and we hope to report some results in this direction in the future.

Appendix

A. Quasi-Newton Procedure

As input to the quasi-Newton procedure, we require to compute the gradient vector, $\nabla l_0(\boldsymbol{\Gamma})$, as given in (20), which consists of the partial derivatives of the log-likelihood function with respect to the entries of $\boldsymbol{\Gamma}$. Recall that the DDEM has multiple delays parameters given by $\boldsymbol{\tau} = (\tau_1, \tau_2, \ldots, \tau_m)$, evolution parameters given by $\boldsymbol{\theta} = (\theta_1, \theta_2, \ldots, \theta_p)$, and unknown initial condition a. Based on the log-likelihood

$$l(\boldsymbol{\theta}, \boldsymbol{\tau}, a) = -\frac{1}{2\sigma^2}\sum_{i=0}^{n}\left(y_i - x\left(t_i, \boldsymbol{\theta}, \boldsymbol{\tau}, a\right)\right)^2, \tag{A.1}$$

recall that we define $l(\boldsymbol{\theta}, \boldsymbol{\tau}, \hat{a}(\boldsymbol{\theta}, \boldsymbol{\tau}))$ as

$$\begin{aligned} &l(\boldsymbol{\theta}, \boldsymbol{\tau}, \hat{a}(\boldsymbol{\theta}, \boldsymbol{\tau})) \\ &\quad = -\frac{1}{2\sigma^2}\sum_{i=0}^{n}\left(y_i - x\left(t_i, \boldsymbol{\theta}, \boldsymbol{\tau}, \hat{a}(\boldsymbol{\theta}, \boldsymbol{\tau})\right)\right)^2. \end{aligned} \tag{A.2}$$

Denoting $l_0(\boldsymbol{\theta}, \boldsymbol{\tau}) \equiv l(\boldsymbol{\theta}, \boldsymbol{\tau}, \hat{a}(\boldsymbol{\theta}, \boldsymbol{\tau}))$ and $x_i = x(t_i, \boldsymbol{\theta}, \boldsymbol{\tau}, \hat{a}(\boldsymbol{\theta}, \boldsymbol{\tau}))$, the first-order partial derivatives are as follows:

$$\begin{aligned} \frac{\partial l_0}{\partial \theta_u} &= \frac{1}{\sigma^2}\sum_{i=0}^{n}\left(y_i - x_i\right)\left[\frac{\partial x_i}{\partial \theta_u} + \frac{\partial x_i}{\partial a}\frac{\partial \hat{a}}{\partial \theta_u}\right], \\ \frac{\partial l_0}{\partial \tau_v} &= \frac{1}{\sigma^2}\sum_{i=0}^{n}\left(y_i - x_i\right)\left[\frac{\partial x_i}{\partial \tau_v} + \frac{\partial x_i}{\partial a}\frac{\partial \hat{a}}{\partial \tau_v}\right]. \end{aligned} \tag{A.3}$$

The above equations involve derivatives of x_i with respect to the parameters. Each derivative expression of $\partial x_i/\partial \theta_u$, $\partial x_i/\partial \tau_v$, and $\partial x_i/\partial a$ for $i = 0, 1, 2, \ldots, n$ can be numerically obtained from respective DDEs which are derived from the initial model in (2) by differentiating it with respect to the quantity of interest. In the case of $\partial x_i/\partial \theta_u$, differentiating (2) with respect to θ_u gives a new DDE for $\partial x/\partial \theta_u$:

$$\dot{\left(\frac{\partial x}{\partial \theta_u}\right)} = \frac{\partial f}{\partial x}\frac{\partial x}{\partial \theta_u} + \sum_{j=1}^{m}\frac{\partial f}{\partial z_j}\frac{\partial z_j}{\partial \theta_u} + \frac{\partial f}{\partial \theta_u}, \tag{A.4}$$

where $(\dot{\partial x/\partial \theta_u})$ is the derivative of $\partial x/\partial \theta_u$ with respect to t and $\partial z_j/\partial \theta_u$ is the delayed version of $\partial x/\partial \theta_u$; that is,

$$\frac{\partial z_j}{\partial \theta_u}(t) = \frac{\partial x}{\partial \theta_u}\left(t - \tau_j\right). \tag{A.5}$$

The initial condition for the DDE in (A.4) is $\partial x/\partial \theta_u = 0$ since the derivative of the initial value a with respect to θ_u is 0. Based on this initial condition, the above DDE model can be numerically solved and the values of $\partial x_i/\partial \theta_u$ can be obtained from $\partial x(t)/\partial \theta_u$ for each $t = t_i$, $i = 0, 1, 2, \ldots, n$.

In a similar way, each value of $\partial x_i/\partial \tau_v$ can be determined by differentiating (2) with respect to τ_v. The new DDE for $\partial x/\partial \tau_v$ is

$$\begin{aligned} \dot{\left(\frac{\partial x}{\partial \tau_v}\right)} &= \frac{\partial f}{\partial x}\frac{\partial x}{\partial \tau_v} + \sum_{j=1}^{m}\frac{\partial f}{\partial z_j}\left[\frac{\partial x\left(t - \tau_j\right)}{\partial \tau_v} - f\left(t - \tau_v,\right.\right. \\ &\quad x\left(t - \tau_v\right), z_1\left(t - \tau_v\right), z_2\left(t - \tau_v\right), \ldots, z_m\left(t - \tau_v\right), \\ &\quad \left.\left.\boldsymbol{\theta}\right)\right], \end{aligned} \tag{A.6}$$

where $(\dot{\partial x/\partial \tau_v})$ is the derivative of $\partial x/\partial \tau_v$ with respect to t and $\partial z_j/\partial \tau_v$ is the delayed version of $\partial x/\partial \tau_v$; that is,

$$\begin{aligned} \frac{\partial z_j}{\partial \tau_v}(t) &= \frac{\partial x\left(t - \tau_j\right)}{\partial \tau_v} - f\left(t - \tau_v, x\left(t - \tau_v\right),\right. \\ &\quad \left. z_1\left(t - \tau_v\right), z_2\left(t - \tau_v\right), \ldots, z_m\left(t - \tau_v\right), \boldsymbol{\theta}\right). \end{aligned} \tag{A.7}$$

The initial condition for the DDE in (A.6) is $\partial x/\partial \tau_v = 0$ since, again, the derivative of the initial value a with respect to τ_v is 0. Based on this initial condition, the above DDE model can be numerically solved and the values of $\partial x_i/\partial \tau_v$ can be obtained from $\partial x(t)/\partial \tau_v$ for each $t = t_i$, $i = 0, 1, 2, \ldots, n$. The case of $\partial x_i/\partial a$ is similar and has been discussed in the main text when presenting the Newton-Raphson procedure.

The expressions in (A.3) also involve $\partial\hat{a}/\partial\theta_u$ and $\partial\hat{a}/\partial\tau_v$. They can be obtained from differentiating the equation satisfied by $\hat{a}(\boldsymbol{\theta},\boldsymbol{\tau})$ in (10) for every pair $(\boldsymbol{\theta},\boldsymbol{\tau})$:

$$\frac{\partial l(\boldsymbol{\theta},\boldsymbol{\tau},\hat{a}(\boldsymbol{\theta},\boldsymbol{\tau}))}{\partial a} = 0 \quad \forall \boldsymbol{\theta},\boldsymbol{\tau}. \tag{A.8}$$

Differentiating with respect to θ_u, we get

$$\frac{\partial^2 l}{\partial\theta_u \partial a} + \frac{\partial^2 l}{\partial a^2}\frac{\partial\hat{a}}{\partial\theta_u} = 0; \tag{A.9}$$

thus

$$\frac{\partial\hat{a}}{\partial\theta_u} = -\frac{\partial^2 l/\partial\theta_u\partial a}{\partial^2 l/\partial a^2} \tag{A.10}$$

for $1 \le u \le p$. Similarly, from differentiating (10) with respect to τ_v, we get

$$\frac{\partial^2 l}{\partial\tau_v \partial a} + \frac{\partial^2 l}{\partial a^2}\frac{\partial\hat{a}}{\partial\tau_v} = 0, \tag{A.11}$$

and hence,

$$\frac{\partial\hat{a}}{\partial\tau_v} = -\frac{\partial^2 l/\partial\tau_v\partial a}{\partial^2 l/\partial a^2}, \tag{A.12}$$

for $1 \le v \le m$. We give the explicit expressions for the second-order derivatives of l with respect to its arguments in Appendix B (as given by (B.6), (B.7), and (B.11) in Appendix B).

B. Information Matrix

For the DDE in (2) with multiples delays $\boldsymbol{\tau} = (\tau_1,\tau_2,\ldots,\tau_m)$ and $\boldsymbol{\theta} = (\theta_1,\theta_2,\ldots,\theta_p)$, recall that $l(\boldsymbol{\theta},\boldsymbol{\tau},a,\sigma^2) = -((n+1)/2)\ln(2\pi\sigma^2) - (1/2\sigma^2)\sum_{i=0}^{n}(y_i - x_i)^2$, where $x_i = x(t_i,\boldsymbol{\theta},\boldsymbol{\tau},a)$. The first-order partial derivatives of $l(\boldsymbol{\theta},\boldsymbol{\tau},a,\sigma^2)$ are as follows:

$$\begin{aligned}
\frac{\partial l}{\partial\theta_u} &= \frac{1}{\sigma^2}\sum_{i=0}^{n}(y_i - x_i)\left(\frac{\partial x_i}{\partial\theta_u}\right),\\
\frac{\partial l}{\partial\tau_v} &= \frac{1}{\sigma^2}\sum_{i=0}^{n}(y_i - x_i)\left(\frac{\partial x_i}{\partial\tau_v}\right),\\
\frac{\partial l}{\partial a} &= \frac{1}{\sigma^2}\sum_{i=0}^{n}(y_i - x_i)\left(\frac{\partial x_i}{\partial a}\right)
\end{aligned} \tag{B.1}$$

for $1 \le u \le p$, $1 \le v \le m$. As mentioned in Appendix A, these partial derivatives of $l(\boldsymbol{\theta},\boldsymbol{\tau},a,\sigma^2)$ can be evaluated numerically from the derivative expression of $\partial x_i/\partial\theta_u$, $\partial x_i/\partial\tau_v$, and $\partial x_i/\partial a$ for $i = 0,1,2,\ldots,n$, since each of them forms an additional DDE derived from (2) by differentiating it with respect to the quantity of interest. Further we have

$$\frac{\partial l}{\partial\sigma^2} = -\frac{1}{2\sigma^2}\left[(n+1) - \frac{1}{\sigma^2}\sum_{i=0}^{n}(y_i - x_i)^2\right]. \tag{B.2}$$

Differentiating the above again with respect to the arguments of $l(\boldsymbol{\theta},\boldsymbol{\tau},a,\sigma^2)$, the second-order partial derivatives have the general forms

$$\begin{aligned}
\frac{\partial^2 l}{\partial\theta_u\partial\theta_{u^*}} = \frac{1}{\sigma^2}&\left[\sum_{i=0}^{n}(y_i - x_i)\left(\frac{\partial^2 x_i}{\partial\theta_u\partial\theta_{u^*}}\right)\right.\\
&\left.-\sum_{i=0}^{n}\left(\frac{\partial x_i}{\partial\theta_u}\right)\left(\frac{\partial x_i}{\partial\theta_{u^*}}\right)\right],
\end{aligned} \tag{B.3}$$

$$\begin{aligned}
\frac{\partial^2 l}{\partial\theta_u\partial\tau_{v^*}} = \frac{1}{\sigma^2}&\left[\sum_{i=0}^{n}(y_i - x_i)\left(\frac{\partial^2 x_i}{\partial\theta_u\partial\tau_{v^*}}\right)\right.\\
&\left.-\sum_{i=0}^{n}\left(\frac{\partial x_i}{\partial\theta_u}\right)\left(\frac{\partial x_i}{\partial\tau_{v^*}}\right)\right],
\end{aligned} \tag{B.4}$$

$$\begin{aligned}
\frac{\partial^2 l}{\partial\tau_v\partial\tau_{v^*}} = \frac{1}{\sigma^2}&\left[\sum_{i=0}^{n}(y_i - x_i)\left(\frac{\partial^2 x_i}{\partial\tau_v\partial\tau_{v^*}}\right)\right.\\
&\left.-\sum_{i=0}^{n}\left(\frac{\partial x_i}{\partial\tau_v}\right)\left(\frac{\partial x_i}{\partial\tau_{v^*}}\right)\right],
\end{aligned} \tag{B.5}$$

$$\begin{aligned}
\frac{\partial^2 l}{\partial\theta_u\partial a} = \frac{1}{\sigma^2}&\left[\sum_{i=0}^{n}(y_i - x_i)\left(\frac{\partial^2 x_i}{\partial\theta_u\partial a}\right)\right.\\
&\left.-\sum_{i=0}^{n}\left(\frac{\partial x_i}{\partial\theta_u}\right)\left(\frac{\partial x_i}{\partial a}\right)\right],
\end{aligned} \tag{B.6}$$

$$\begin{aligned}
\frac{\partial^2 l}{\partial\tau_v\partial a} = \frac{1}{\sigma^2}&\left[\sum_{i=0}^{n}(y_i - x_i)\left(\frac{\partial^2 x_i}{\partial\tau_v\partial a}\right)\right.\\
&\left.-\sum_{i=0}^{n}\left(\frac{\partial x_i}{\partial\tau_v}\right)\left(\frac{\partial x_i}{\partial a}\right)\right],
\end{aligned} \tag{B.7}$$

$$\frac{\partial^2 l}{\partial\theta_u\partial\sigma^2} = \frac{-1}{(\sigma^2)^2}\sum_{i=0}^{n}(y_i - x_i)\left(\frac{\partial x_i}{\partial\theta_u}\right), \tag{B.8}$$

$$\frac{\partial^2 l}{\partial\tau_v\partial\sigma^2} = \frac{-1}{(\sigma^2)^2}\sum_{i=0}^{n}(y_i - x_i)\left(\frac{\partial x_i}{\partial\tau_v}\right), \tag{B.9}$$

$$\frac{\partial^2 l}{\partial a\partial\sigma^2} = \frac{-1}{(\sigma^2)^2}\sum_{i=0}^{n}(y_i - x_i) \tag{B.10}$$

$$\frac{\partial^2 l}{\partial a^2} = \frac{1}{\sigma^2}\left[\sum_{i=0}^{n}(y_i - x_i)\left(\frac{\partial^2 x_i}{\partial a^2}\right) - \sum_{i=0}^{n}\left(\frac{\partial x_i}{\partial a}\right)^2\right], \tag{B.11}$$

$$\frac{\partial^2 l}{\partial(\sigma^2)^2} = \frac{1}{2(\sigma^2)^2}\left[(n+1) - \frac{2}{\sigma^2}\sum_{i=0}^{n}(y_i - x_i)^2\right]. \tag{B.12}$$

Equations (B.6), (B.7), and (B.10) are required for the quasi-Newton procedure in Appendix A.

To obtain the information matrix, we need to take the expectation of the negative of the second-order derivatives of $l(\boldsymbol{\theta}, \boldsymbol{\tau}, a, \sigma^2) = l(\boldsymbol{\Gamma} \mid \mathbf{y})$ with respect to its arguments:

$$I(\boldsymbol{\Gamma})_{(u,v)} = -E\left[\frac{\partial^2 l(\boldsymbol{\Gamma} \mid \mathbf{y})}{\partial \Gamma_u \partial \Gamma_v}\right]. \tag{B.13}$$

Taking negative on the LHS of (B.3)–(B.12), followed by expectation under the sampling distribution of each y_i, we note that the general terms of the form

$$\sum_{i=0}^{n} (y_i - x_i)\left(\frac{\partial^2 x_i}{\partial \Gamma_u \partial \Gamma_v}\right) \tag{B.14}$$

or

$$\sum_{i=0}^{n} (y_i - x_i)\left(\frac{\partial^2 x_i}{\partial \Gamma_u}\right) \tag{B.15}$$

on the RHS become zero since the expectation of y_i equals x_i. Hence we get

$$\begin{aligned} I(\boldsymbol{\Gamma})_{(u,v)} &= -E\left[\frac{\partial^2 l(\boldsymbol{\Gamma} \mid \mathbf{y})}{\partial \Gamma_u \partial \Gamma_v}\right] \\ &= \frac{1}{\sigma^2}\sum_{i=0}^{n}\left(\frac{\partial x(t_i, \boldsymbol{\theta}, \boldsymbol{\tau}, a)}{\partial \Gamma_u}\right)\left(\frac{\partial x(t_i, \boldsymbol{\theta}, \boldsymbol{\tau}, a)}{\partial \Gamma_v}\right) \end{aligned} \tag{B.16}$$

as in (30) as well as

$$I(\boldsymbol{\Gamma})_{(u,\sigma^2)} = -E\left[\frac{\partial^2 l(\boldsymbol{\Gamma} \mid \mathbf{y})}{\partial \Gamma_u \partial \sigma^2}\right] = 0. \tag{B.17}$$

Finally, taking expectation in (B.12),

$$\begin{aligned} &E\left(-\frac{\partial^2 l}{\partial (\sigma^2)^2}\right) \\ &= -\frac{1}{2(\sigma^2)^2}\left[(n+1) - \frac{2}{\sigma^2}\sum_{i=0}^{n} E(y_i - x_i)^2\right] \\ &= -\frac{1}{2(\sigma^2)^2}\left[(n+1) - \frac{2}{\sigma^2}(n+1)\sigma^2\right] = \frac{(n+1)}{2(\sigma^2)^2}. \end{aligned} \tag{B.18}$$

Conflicts of Interest

The authors declare that there are no conflicts of interest with respect to the research, authorship, and/or publication of this paper.

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Research Article

Impact of Time Delay in Perceptual Decision-Making: Neuronal Population Modeling Approach

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Impairments in decision-making are frequently observed in neurodegenerative diseases, but the mechanisms underlying such pathologies remain elusive. In this work, we study, on the basis of novel time-delayed neuronal population model, if the delay in self-inhibition terms can explain those impairments. Analysis of proposed system reveals that there can be up to three positive steady states, with the one having the lowest neuronal activity being always locally stable in nondelayed case. We show, however, that this steady state becomes unstable above a critical delay value for which, in certain parameter ranges, a subcritical Hopf bifurcation occurs. We then apply psychometric function to translate model-predicted ring rates into probabilities that a decision is being made. Using numerical simulations, we demonstrate that for small synaptic delays the decision-making process depends directly on the strength of supplied stimulus and the system correctly identifies to which population the stimulus was applied. However, for delays above the Hopf bifurcation threshold we observe complex impairments in the decision-making process; that is, increasing the strength of the stimulus may lead to the change in the neuronal decision into a wrong one. Furthermore, above critical delay threshold, the system exhibits ambiguity in the decision-making.

1. Introduction

Gamma-Aminobutyric Acid (GABA) is the most prevalent inhibitory neurotransmitter in the human brain [1, 2]. There is a body of evidence that aging has a major influence on the effectiveness of the GABAergic synapses [3]. Moreover, as found in the recent studies with the use of magnetic resonance spectroscopy (MRS, [4, 5]), local GABA concentrations in the frontal areas influence cognitive performance in aging adults. Taken together, aging can cause a reduced release of GABA to the intersynaptic cleft and decrease the quality of the synaptic transmission. This can result in an increase of the synaptic delays in the local inhibition.

On the other hand, in the aging process, the sensory capacity is declining, which affects the cognitive functions [6–8]. In particular, the working memory—which involves active manipulation of information—is affected, and this effect can further influence the perceptual decision-making [9]. (One important note here is that there is a difference between perceptual decision-making and making the abstract complex choices: the latter was reported not to be impaired in the elderly subjects [10], and some studies even report that elderly subjects are actually more efficient at making complex decisions [11, 12]. Therefore, in the paper we refer to the perceptual decision-making.).

In 1996, Salthouse [13] proposed a processing-speed theory of age-related deficits in cognition, for example, in working memory and perceptual decision-making. According to this theory, reduction in the processing speed can cause impairments in the cognitive functions for two major reasons. Cognitive functions can decline either because necessary logic operations cannot be executed within the time limit, or because the higher-order operations are blocked by slow execution of lower-order operations. This subject-matter was further experimentally investigated from different angles [14–16], but the consensus in the field is that, in general, the elderly subjects are slower in perceptual decision-making than youngsters.

In this work, we propose a mechanism linking the two aspects of aging in cortical networks: the neurodegeneration in the local inhibitory synapses and the processing-speed related impairments in perceptual decision-making. This mechanism is based on a neuronal population model of decision-making based on a winner-take-all mechanism. The novelty lies in combining a winner-take-all mechanism well routed in the decision-making neuroscience, with the system of delayed differential equations representing the local inhibition within the two competing populations. With the use of this model, we are able to demonstrate that, for small synaptic delays in the local inhibition within the competing populations, the decision-making process depends directly on the strength of the stimulus, and the network is able to correctly identify the direction the stimulus came from. However, large delays can lead to a subcritical Hopf bifurcation resulting in complex decision-making process impairments. In particular, we demonstrate that, above the Hopf bifurcation point, increasing the strength of the stimulus can confuse the network and cause a wrong decision to be made. Furthermore, for delay values above critical threshold the system exhibits ambiguity in the decision-making. This effect can explain how the experimentally found difficulties in decision-making in elderly adults can be caused by loss in cognitive capacities [14].

The paper is organized in the following way. In Section 2, we introduce the model. In Section 3, qualitative analysis of the model, focusing on the stability analysis and Hopf bifurcation appearance, is made. Firstly, we present the analytic results for a symmetric model with no delay (Section 3.1) and then with positive delay (Section 3.2). In Section 4, we present the simulations undertaken to explore the dynamic repertoire of the model. In Section 5, we critically discuss the results and give recommendations for the future research.

2. Perceptual Decision-Making Model

The famous perceptual experiment on rhesus monkeys [17] by Shadlen and Newsome, involved a binary classification task: the monkeys had to assess whether the majority of the moving dots on the screen moved to the left or to the right. In the literature, one model proposed to model the decision-making in this experiment was the slow reverberation mechanism by Wang [18]. In Wang's model, two populations of densely interconnected, spiking neurons compete with each other once being supplied by noisy inputs. This model involves simulations of two competing pools of stochastic spiking neurons. Since Wang's work was published, some rodent [19] and computational [20] models were proposed to study perceptual choices.

In this work, we focus on modeling the most basic perceptual decision-making in neuronal networks. In such conditions, the network needs to disambiguate between two sensory stimuli. We consider changes in the firing rates $r(t)$ of two positively interconnected self-inhibiting neuronal populations that receive external inputs $I_1(t)$ and $I_2(t)$, respectively (Figure 1).

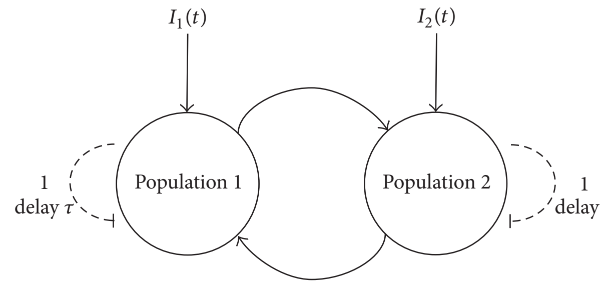

Figure 1: A neuronal population model of decision-making. Neurons in the first population project to the neurons in the second population and vice versa. Both neuronal populations receive self-inhibition with delay (τ, dashed arrows with flat heads). In addition, they receive external inputs $I_1(t)$ and $I_2(t)$, respectively. The dynamics of this system is described by (1).

In order to describe the temporal dynamics of considered system (Figure 1), we introduce a system of delay differential equations (DDEs [21]) in the following form:

$$\begin{aligned}\dot{r}_1(t) &= \alpha\left(I_1(t) - r_1(t-\tau) + \epsilon f\left(r_1(t)\, r_2(t)\right) r_2(t)\right),\\ \dot{r}_2(t) &= \alpha\left(I_2(t) - r_2(t-\tau) + \epsilon f\left(r_1(t)\, r_2(t)\right) r_1(t)\right),\end{aligned} \tag{1}$$

where $\alpha = 1/\tau_r$, τ_r denotes a model time scale, τ denotes the delay in self-inhibition, and ϵ is a coefficient describing the maximal capacity of a synapse, related to its anatomy. The function f characterizes interactions between populations through synaptic plasticity which undergoes a Hebbian rule [22]; that is, the dynamics of synaptic weights is firing rate-dependent. For in-depth analytical and numerical investigations we have chosen a biologically plausible [23] sigmoid function $f(x) = x^2/(1+x^2)$.

In reality both populations considered in the proposed model are embedded in a larger network; therefore even in the absence of the population-specific sensory stimulus, they receive a constant input. Therefore, in the resting state, this system receives equal constant inputs $I_1(t) = I_2(t) \equiv I$ to both nodes and, due to the system's symmetry, both populations will be firing with the same rates. The symmetry breaks down if one of the populations receives an additional, external stimulation. The decision-making in this system means decoding *which* of the two populations received an additional stimulus (without estimation of the stimulus magnitude). The decoding is based on the difference between the two firing rates: the larger the difference $r_1(t) - r_2(t)$, the more likely the decision that the population 1 received the stimulation. The evidence behind each of the two options accumulates over time; therefore the psychometric function for the first population takes the integral form of

$$p_1(t) = \frac{1}{1 + \exp\left(-\beta \int_0^t \left(r_1(\xi) - r_2(\xi)\right) d\xi\right)}, \tag{2}$$

where β is a parameter influencing the slope of the sigmoid function with respect to the cumulative difference $\int_0^t (r_1(\xi) - r_2(\xi))d\xi$. Similarly, we define the psychometric function for the second population as

$$p_2(t) = \frac{1}{1 + \exp\left(-\beta \int_0^t (r_2(\xi) - r_1(\xi))\, d\xi\right)}. \tag{3}$$

Values $p_1(t)$ and $p_2(t)$ can only asymptotically approach 1; therefore we add a condition that if, at a given time point t, $p_1(t)$ exceeds the threshold value of $1-\gamma$ (where γ is a given precision), the decision is made.

3. Qualitative Behavior of the Model

In this section, we provide the analytical results regarding the behavior of solutions of (1) for $\alpha = 1$ and constant symmetric input I. Notice that the qualitative dynamics of (1) does not depend on α.

3.1. Behavior of the Model for $\tau = 0$ and Constant Symmetric Input I. In this subsection, we present a detailed analysis of the model dynamics for $\tau = 0$ and $I_1(t) = I_2(t) \equiv I$, as it is a crucial first step in the analysis of time-delayed models. While looking for steady states of (1), we need to solve the system of equations

$$\begin{aligned} I - r_1 + \epsilon r_2 f(r_1 r_2) &= 0, \\ I - r_2 + \epsilon r_1 f(r_1 r_2) &= 0, \end{aligned} \tag{4}$$

which yields $r_1 - r_2 + \epsilon(r_1 - r_2) f(r_1 r_2) = 0$. It is then obvious that both coordinates of any steady state are the same. Let us denote a steady state by $(\bar{r}, \bar{r})$. Clearly, $I - \bar{r} + \epsilon \bar{r} f(\bar{r}^2) = 0$, and the number of steady states depends on the shape of the graph of $h_\epsilon(r) = (1-\epsilon)r + \epsilon(r/(1+r^4))$. Notice that the reference case $\epsilon = 1$ is specific, as for $\epsilon \neq 1$ the function h is asymptotically linear $\sim (1-\epsilon)r$, while for $\epsilon = 1$ it tends to 0 as $r \to \infty$.

Let us consider $\epsilon = 1$. Then we have $h_1'(r) = (1 - 3r^4)/(1+r^4)^2$, and therefore h_1 is increasing for $r \in [0, \sqrt[4]{27}/3]$, achieves its maximum $h_1^m = \sqrt[4]{27}/4 \approx 0.5699$ at $r^m = \sqrt[4]{27}/3$, and decreases to 0 for $r > r^m$. This implies that there are two steady states for $0 < I < h_1^m$ and no steady state for $I > h_1^m$, while for $I = h_1^m$ there is a bifurcation. The reference value $I = 0.4 < h_1^m$, so there exist two steady states, $\bar{r} \approx 0.4115$ and $\bar{\bar{r}} \approx 1.1827$.

For $\epsilon \neq 1$, we have $h_\epsilon'(r) = 1 - \epsilon + \epsilon((1-3r^4)/(1+r^4)^2)$, and looking for zeros of h_ϵ' we obtain $(1-\epsilon)r^8 + (2-5\epsilon)r^4 + 1 = 0$, and we see that this quadratic equation has two positive solutions for $\epsilon \in (16/25, 1)$, no real solution for $\epsilon < 16/25$, and one positive solution for $\epsilon > 1$. This means that for $\epsilon < 16/25$ the function h_ϵ is increasing, for $\epsilon \geq 1$ it has one maximum and tends either to 0 (for $\epsilon = 1$) or to $-\infty$ (for $\epsilon > 1$), while for $\epsilon \in (16/25, 1)$ it is first increasing, then decreasing, and eventually increasing linearly to $+\infty$.

Corollary 1. *For $\epsilon < 16/25$ there is one steady state of (1); for $\epsilon \geq 1$ there are two steady states for small values of I and no steady state for larger I values; for $\epsilon \in (16/25, 1)$ there is one steady state for small and sufficiently large values of I, while for intermediate I values 3 steady states exist.*

Notice that due to its symmetric structure the system described by (1) always has solutions lying within a straight line $r_2 = r_1$. Clearly, assuming $r_1 = r_2 = r$ from both equations of (1) we obtain

$$\dot{r} = I - r + \epsilon r f(r^2). \tag{5}$$

The number of steady states determines the dynamics of (5). Let us assume that $\epsilon < 16/25$. Then there is only one steady state $\bar{r}$ and the right-hand side of (5) is positive for $r < \bar{r}$ and negative for $r > \bar{r}$. Therefore, $\bar{r}$ is globally attractive. If $\epsilon \geq 1$, then there are two steady states $\bar{r} < \bar{\bar{r}}$ for small I, and the right-hand side is positive for $r < \bar{r}$ and $r > \bar{\bar{r}}$ and negative for $r \in (\bar{r}, \bar{\bar{r}})$. This means that $\bar{r}$ is locally stable, while $\bar{\bar{r}}$ is unstable. Moreover, solutions for $r(0) > \bar{\bar{r}}$ tends to ∞. If there is no steady state, then all solutions tend to $+\infty$, as they are increasing and unbounded. For $\epsilon \in (16/25, 1)$ there can be up to three steady states. Assume that there are three steady states $\bar{r} < \bar{\bar{r}} < \bar{\bar{\bar{r}}}$. In this case $\bar{r}$ and $\bar{\bar{\bar{r}}}$ are stable, while $\bar{\bar{r}}$ is unstable. Moreover, for $r(0) > \bar{\bar{\bar{r}}}$ solutions tend to $\bar{\bar{\bar{r}}}$.

It is obvious that the symmetry of (1) implies that the phase space is divided into two symmetric subspaces by the straight line $r_2 = r_1$. Moreover, the dynamics of (5) is crucial in determining the whole model dynamics. Notice that $\dot{r}_1 = I - r_1 + \epsilon r_2 f(r_1 r_2) < I - r_1 + \epsilon r_2$ and for $r_2 < (r_1 - I)/\epsilon$ we have $\dot{r}_1 < 0$. Similarly, for $r_2 > I + \epsilon r_1$ we have $\dot{r}_2 < 0$. Moreover, these straight lines are asymptotes for null-clines of (1). Therefore, asymptotic dynamics for large values of r_1, r_2 is related to the dynamics of (5) for large r, as it determines the direction of the vector-field in the region between the null-clines. Three generic types of the model dynamics when at least one steady state exists are presented in Figure 2.

3.2. Model Behavior for $\tau > 0$ and Constant Symmetric Input I. Now, we aim to study the influence of the delay on the dynamics of the model. Our main goal is to show that there exists such time delay $\tau_{th} > 0$ for which the steady state $(\bar{r}, \bar{r})$ loses stability and a Hopf bifurcation occurs. Moreover, we would like to analyze the type of this bifurcation.

Before starting the analysis, we first state some general results that will be useful in this section. Let us consider a general DDE

$$\begin{aligned} \dot{x} &= g(x_t), \\ g(0) &= 0, \end{aligned} \tag{6}$$

with a smooth function g. Let $W(\lambda, \tau)$ denote a characteristic function for (6) at $\bar{x} = 0$. Assume that

$$\begin{aligned} W(\lambda, \tau) &= W_I(\lambda, \tau) \cdot W_{II}(\lambda, \tau), \\ W_I(\lambda, \tau) &= P(\lambda) + Q(\lambda) e^{-\lambda\tau}, \end{aligned} \tag{7}$$

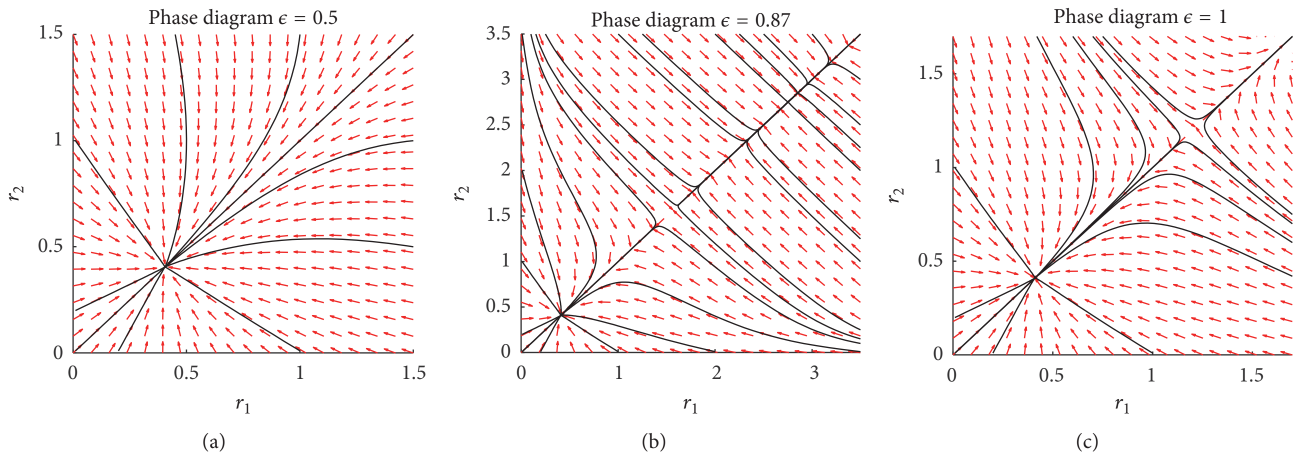

FIGURE 2: Examples of the phase space portrait of (1) for $I = 0.4$ and $\epsilon = 0.5$ (a) (there is only one steady state, stable node at around $(0.41, 0.41)$); $\epsilon = 0.87$ (b) (there are three steady states: stable nodes at around $(0.41, 0.41)$ and $(2.77, 2.77)$ and a saddle at around $(1.55, 1.55)$); $\epsilon = 1$ (c) (there are two steady states: a stable node at around $(0.41, 0.41)$ and a saddle at around $(1.18, 1.18)$).

where P and Q are polynomials, $\deg P > \deg Q$. Together with (6) we consider

$$\dot{x} = g_1(x_t), \quad g_1(0) = 0, \tag{8}$$

for which W_I is a characteristic function.

Lemma 2. *Assume that P and Q have no common imaginary root and W_I has a pair of purely imaginary simple eigenvalues $\pm i\omega_0$ ($\omega_0 > 0$) for some critical value $\tau = \tau_0 > 0$, and moreover these eigenvalues satisfy transversality condition $(d/d\tau)\operatorname{Re}\lambda(\tau)|_{\tau=\tau_0} \neq 0$. If $W_{II}(i\omega_0, \tau) \neq 0$, then $\pm i\omega_0$ is a pair of simple eigenvalues of $W(\lambda, \tau)$ for $\tau = \tau_0$ which satisfies transversality condition. Moreover, the eigenvalues of (6) cross imaginary axis in the same direction as the eigenvalues of (8).*

Proof. We only need to check transversality condition. The derivative $(d/d\tau)\operatorname{Re}\lambda(\tau)|_{\tau=\tau_0}$ for (6) is obtained from the relation

$$\frac{d}{d\tau}(W_I(\lambda,\tau))\Big|_{\tau=\tau_0} \cdot W_{II}(\lambda,\tau)|_{\tau=\tau_0} + W_I(\lambda,\tau)|_{\tau=\tau_0} \cdot \frac{d}{d\tau}(W_{II}(\lambda,\tau))\Big|_{\tau=\tau_0} = 0. \tag{9}$$

As $W_I(\lambda,\tau)|_{\tau=\tau_0} = 0$ while $W_{II}(\lambda,\tau)|_{\tau=\tau_0} \neq 0$, this implies $(d/d\tau)(W_I(\lambda,\tau))|_{\tau=\tau_0} \neq 0$ which is the relation determining transversality condition for (8). □

Lemma 2 holds under weaker assumptions, that is, for P and Q being analytic functions, not only polynomials; compare [24] for more details. However, for our analysis, it is sufficient to consider the presented version.

The next lemma is a simple consequence of Proposition 1 from [24].

Lemma 3. *Let $W_I(\lambda,\tau) = \lambda + \gamma + e^{-\lambda\tau}$, $|\gamma| < 1$. Then there exists a pair of purely imaginary eigenvalues $\pm i\omega_0$, $\omega_0 = \sqrt{1-\gamma^2}$, for $\tau_0 = \arccos(-\gamma)/\omega_0$ for which eigenvalues cross imaginary axis from left to right. Moreover, a steady state $\overline{x} = 0$ loses stability for $\tau = \tau_0$ and cannot gain it again for $\tau > \tau_0$.*

Proof. Following [24] we define an auxiliary function $F_A(\omega) = |P(i\omega)|^2 - |Q(i\omega)|^2 = \omega^2 + \gamma^2 - 1$. It is obvious that $\omega_0 = \sqrt{1-\gamma^2}$ is a simple zero of F_A. Looking for critical delay related to this pair of eigenvalues $\pm i\omega_0$, we need to solve a system of equations

$$\cos(\omega_0\tau) = -\gamma, \quad \sin(\omega_0\tau) = \omega_0 > 0. \tag{10}$$

It is obvious that we obtain a sequence of critical delays $\tau_n = (1/\omega_0)(\arccos(-\gamma) + 2n\pi)$, $n \in \mathbb{N}$. However, as the derivative of the auxiliary function is positive, eigenvalues always cross imaginary axis from left to right (independently of n), which means that a switch of stability appears only at $\tau = \tau_0$. □

Now, we turn to the main topic of this subsection that is analysis of (1) for $\tau > 0$. While studying a Hopf bifurcation, we follow the ideas introduced in [25]. Let us rewrite the system described by (1) in its functional form (cf. [26, 27]); that is,

$$\dot{X} = L(X_t) + G(X_t), \tag{11}$$

where $X = (x, y) = (r_1 - \overline{r}, r_2 - \overline{r})$ and $X_t(h) = X(t+h)$ for $h \in [-\tau, 0]$, L is a linear part, and G is nonlinear part of the system. Hence,

$$L(x_t, y_t) = (L_1(x_t, y_t), L_2(x_t, y_t)) = (-x_t(-\tau) + \eta x_t(0) + (\eta+\beta) y_t(0), -y_t(-\tau) + \eta y_t(0) + (\eta+\beta) x_t(0))^T,$$

$$
\begin{aligned}
G(x_t, y_t) &= (G_1(x_t, y_t), G_2(x_t, y_t)) \\
&= ((y_t(0) + \overline{r})(F(x_t, y_t) - \beta) - \eta(x_t(0) + y_t(0)), (x_t(0) + \overline{r})(F(x_t, y_t) - \beta) - \eta(x_t(0) + y_t(0)))^T,
\end{aligned} \tag{12}
$$

where $F(x_t, y_t) = F(x(t), y(t)) = \epsilon f((x(t) + \overline{r})(y(t) + \overline{r}))$, $\eta = \epsilon f'(\overline{r}^2)\overline{r}^2 > 0$, and $\beta = \epsilon f(\overline{r}^2) > 0$. With the linear operator L we are able to associate an operator $T(t)X_0 = X_t$ which is a solution to (1) for initial data X_0. In this way we obtain a strongly continuous semigroup generated by an infinitesimal generator A (cf. [26, 27]). If for some critical value τ_0 the generator A has an eigenvalue $\lambda = i\omega_0$, then a Hopf bifurcation occurs under the assumptions that the eigenvalues $\pm i\omega_0$ are simple and cross imaginary axis with nonzero speed when τ crosses τ_0.

Let us denote a characteristic matrix by $\Delta(\lambda, \tau)$; that is,

$$
\Delta(\lambda, \tau) = \begin{pmatrix} \lambda + \exp(-\lambda\tau) - \eta & -(\beta + \eta) \\ -(\beta + \eta) & \lambda + \exp(-\lambda\tau) - \eta \end{pmatrix}. \tag{13}
$$

Looking for eigenvalues, we need to find zeros of the characteristic function

$$
\begin{aligned}
W(\lambda, \tau) &= \det \Delta(\lambda, \tau) \\
&= (\lambda + \exp(-\lambda\tau) - \eta)^2 - (\eta + \beta)^2.
\end{aligned} \tag{14}
$$

It is obvious that

$$
\begin{aligned}
W(\lambda, \tau) &= W_I(\lambda, \tau) \cdot W_{II}(\lambda, \tau), \\
W_I(\lambda, \tau) &= \lambda - 2\eta - \beta + e^{-\lambda\tau}, \\
W_{II}(\lambda, \tau) &= \lambda + \beta + e^{-\lambda\tau}.
\end{aligned} \tag{15}
$$

Clearly, we can use Lemmas 2 and 3 in the analysis of stability switches for the steady state $(\overline{r}, \overline{r})$. In the considered case, the steady state $(\overline{r}, \overline{r})$ is stable for $\tau = 0$; that is, $W(\lambda, 0) = (\lambda - 2\eta - \beta + 1)(\lambda + \beta + 1)$ has negative zeros, yielding $1 > 2\eta + \beta$. Hence, both quasi-polynomials W_I and W_{II} satisfy assumptions of Lemma 3. This means that there are two sequences of critical delays $(\tau_n^I)_{n\in\mathbb{N}}$ and $(\tau_n^{II})_{n\in\mathbb{N}}$ associated with W_I and W_{II}, respectively. However, the switch of stability can occur only for τ_0^I or τ_0^{II}, depending on the magnitude of those delays. Clearly, according to Lemma 2 eigenvalues cross imaginary axis in the same direction for both W_I and W_{II}, which means that they cross from left to right, and therefore the steady state $(\overline{r}, \overline{r})$ loses stability for the smallest critical delay.

As a result, we can state the following theorem.

Theorem 4. *Let $\tau_0 = \arccos(2\eta + \beta)/\sqrt{1 - (2\eta + \beta)^2}$. The steady state $(\overline{r}, \overline{r})$ of (1) is locally asymptotically stable for $\tau < \tau_0$ and unstable for $\tau > \tau_0$, and at $\tau = \tau_0$ a Hopf bifurcation occurs.*

Proof. We only need to check that $\tau_0 = \tau_0^I < \tau_0^{II}$. Notice that $\tau_0^{II} = \arccos(-\beta)/\sqrt{1 - \beta^2}$. Moreover, the function $\arccos(x)/\sqrt{1 - x^2}$, $x \in (-1, 1)$ is decreasing. As $\arccos(-\beta) > \arccos(\beta)$ we obtain

$$
\begin{aligned}
\tau_0^{II} &= \frac{\arccos(-\beta)}{\sqrt{1 - \beta^2}} > \frac{\arccos(\beta)}{\sqrt{1 - \beta^2}} > \frac{\arccos(2\eta + \beta)}{\sqrt{1 - (2\eta + \beta)^2}} \\
&= \tau_0^I.
\end{aligned} \tag{16}
$$

□

For the reference values of parameters for $\overline{r} \approx 0.4115$ we obtain $\beta \approx 0.02787$ and $\eta \approx 0.05418$. Considering W_I we obtain $\omega_0^I \approx 0.9907$ and $\tau_0^I \approx 1.4476$. For W_{II} we have $\omega_0^{II} \approx 0.9996$ and $\tau_0^{II} = \arccos(-\beta)/\sqrt{1 - \beta^2} \approx 1.5993$.

Hence, we study the bifurcation at $\tau_0 = \tau_0^I$ and corresponding $\omega_0 = \sqrt{1 - (2\eta + \beta)^2}$. Let us denote $\beta_1 = 2\eta + \beta$ to shorten the notation. Therefore, $\omega_0 = \sqrt{1 - \beta_1^2}$. Notice that from the form of W_I we obtain $i\omega_0 + e^{-i\omega_0\tau_0} = \beta_1$.

In the following, we base on the ideas presented in [25]. We know that $\lambda = i\omega_0$ is a purely imaginary eigenvalue of the infinitesimal generator A for $\tau = \tau_0$ if there exists a vector $\mathbf{p} \in \mathbb{C}^2$ such that $\Delta(i\omega_0, \tau_0)\mathbf{p} = 0$ and then $\Phi(h) = e^{i\omega_0 h}\mathbf{p}$ is an eigenvector for A at τ_0. Moreover, $i\omega_0$ is also an eigenvalue for the adjoint operator A^* for $\tau = \tau_0$ and $\Psi(h) = \mathbf{q}e^{i\omega_0 h}$ is an eigenvector, where $\mathbf{q}\Delta(i\omega_0, \tau_0) = 0$. In the considered case, we are able to choose $\mathbf{q}$ such that $\mathbf{q}d_1\Delta(i\omega_0, \tau_0)\mathbf{p} = 1$, where d_1 is the derivative with respect to the first variable, here λ.

When looking for $\mathbf{p} = (a, b)^T$ we obtain

$$
\begin{aligned}
\Delta(\lambda, \tau)\mathbf{p} &= \begin{pmatrix} \lambda + \exp(-\lambda\tau) - \eta & -(\beta + \eta) \\ -(\beta + \eta) & \lambda + \exp(-\lambda\tau) - \eta \end{pmatrix} \\
&\quad \cdot \begin{pmatrix} a \\ b \end{pmatrix} = \begin{pmatrix} \eta + \beta & -(\eta + \beta) \\ -(\eta + \beta) & \eta + \beta \end{pmatrix} \cdot \begin{pmatrix} a \\ b \end{pmatrix} \\
&= (0, 0)^T,
\end{aligned} \tag{17}
$$

and therefore

$$
(\beta + \eta)a - (\beta + \eta)b = 0. \tag{18}
$$

Clearly, $a = b$ and we can choose $\mathbf{p} = (1, 1)^T$. Hence, $\Phi(h) = e^{i\omega_0 h}(1, 1)^T$ is the eigenvector for the eigenvalue $i\omega_0$.

Next, we need to find a vector $\mathbf{q}$ that satisfies

$$
\mathbf{q}\Delta(\lambda, \tau) = (a, b) \cdot \begin{pmatrix} \eta + \beta & -(\eta + \beta) \\ -(\eta + \beta) & \eta + \beta \end{pmatrix} = (0, 0), \tag{19}
$$

which means that coordinates of $\mathbf{q}$ satisfy the same relation as for $\mathbf{p}$, that is, $a = b$. Next, calculating

$$d_1\Delta(i\omega_0, \tau_0) = \begin{pmatrix} 1 - \tau_0 \exp(-i\omega_0\tau_0) & 0 \\ 0 & 1 - \tau_0 \exp(-i\omega_0\tau_0) \end{pmatrix} \quad (20)$$

we obtain $2a(1 - \tau_0 \exp(-i\omega_0\tau_0)) = 1$, that is, $a = 1/2(1 + \tau_0(i\omega_0 - \beta_1))$, and eventually

$$a = \frac{1}{2}\frac{1 - \tau_0\beta_1 - i\omega_0\tau_0}{(1 - \tau_0\beta_1)^2 + \omega_0^2\tau_0^2}. \quad (21)$$

The type of the studied bifurcation is determined by a coefficient μ_2 of the third term in Taylor expansion of an orbit. This coefficient reads

$$\mu_2 = \frac{\operatorname{Re}(c)}{\operatorname{Re}(\mathbf{q}d_2\Delta(i\omega_0, \tau_0)\mathbf{p})}, \quad (22)$$

where d_2 denotes a first derivative with respect to the second variable τ, while $c = c_I + c_{II} + c_{III}$, and

$$\begin{aligned} c_I &= \frac{1}{2}\mathbf{q}d_1^3 G(0, \tau_0)(\Phi, \Phi, \overline{\Phi}), \\ c_{II} &= \mathbf{q}d_1^2 G(0, \tau_0)(\Psi_1, \Phi), \\ c_{III} &= \frac{1}{2}\mathbf{q}d_1^2 G(0, \tau_0)(\Psi_2, \overline{\Phi}), \end{aligned} \quad (23)$$

where d_1^i, $i = 2, 3$, denotes ith derivative with respect to the first variable, $\Psi_1(h) = (\Delta(0, \tau_0))^{-1} d_1^2 G(0, \tau_0)(\Phi, \overline{\Phi})$ (in fact Ψ_1 is a constant function as it does not depend on h), and $\Psi_2(h) = e^{2i\omega_0 h}(\Delta(2i\omega_0, \tau_0))^{-1} d_1^2 G(0, \tau_0)(\Phi, \Phi)$.

If $\mu_2 > 0$, then the bifurcation is supercritical; that is, periodic solutions appear for $\tau > \tau_0$ and are stable in such a case. If $\mu_2 < 0$, then the bifurcation is subcritical: periodic solutions exist for $\tau < \tau_0$, and as the steady state is stable in this case, periodic orbits are necessarily unstable.

First, we calculate the denominator of μ_2. We have

$$\begin{aligned} d_2\Delta(i\omega_0, \tau_0) &= \begin{pmatrix} -i\omega_0 \exp(-i\omega_0\tau_0) & 0 \\ 0 & -i\omega_0 \exp(-i\omega_0\tau_0) \end{pmatrix} \\ &= \begin{pmatrix} -\omega_0^2 - i\omega_0\beta_1 & 0 \\ 0 & -\omega_0^2 - i\omega_0\beta_1 \end{pmatrix}, \end{aligned} \quad (24)$$

$$\mathbf{q} \cdot d_2\Delta(i\omega_0, \tau_0) \cdot \mathbf{p} = -2a(\omega_0^2 + i\omega_0\beta_1),$$

and we easily check that the real part of this expression is equal to $-\omega_0^2/((1 - \tau_0\beta_1)^2 + \omega_0^2\tau_0^2) < 0$.

Next, we would like to calculate the numerator of μ_2. To this end, we need to calculate the derivatives of the nonlinear part G necessary to calculate c, and we omit bar in the notation $\bar{r}$. Denoting by u, v, and w test functions from $\mathbf{C}([-\tau, 0], \mathbb{R}^2)$, we obtain

$$\begin{aligned}
d_1G_1(x_t, y_t)(u) &= \left((y(t) + r) F'_x(x(t), y(t)) - \eta\right) \\
&\quad \cdot u_1(0) + \left(F(x(t), y(t))\right. \\
&\quad \left. + (y(t) + r) F'_y(x(t), y(t)) - \beta - \eta\right) u_2(0), \\
d_1G_2(x_t, y_t)(u) &= \left(F(x(t), y(t))\right. \\
&\quad \left. + (x(t) + r) F'_x(x(t), y(t)) - \beta - \eta\right) u_1(0) \\
&\quad + \left((x(t) + r) F'_y(x(t), y(t)) - \eta\right) u_2(0), \\
d_1^2G_1(x_t, y_t)(u, v) &= \left(y(t + r) F''_{xx}(x(t), y(t))\right) \\
&\quad \cdot u_1(0) v_1(0) + \left(F'_x(x(t), y(t))\right. \\
&\quad \left. + (y(t) + r) F''_{xy}(x(t), y(t))\right)(u_1(0) v_2(0) \\
&\quad + u_2(0) v_1(0)) + \left(2F'_y(x(t), y(t))\right. \\
&\quad \left. + (y(t) + r) F''_{yy}(x(t), y(t))\right) u_2(0) v_2(0), \\
d_1^2G_2(x_t, y_t)(u, v) &= \left(2F'_x(x(t), y(t))\right. \\
&\quad \left. + (x(t) + r) F''_{xx}(x(t), y(t))\right) u_1(0) v_1(0) \\
&\quad + \left(F'_y(x(t), y(t)) + (x(t) + r) F''_{xy}(x(t), y(t))\right) \\
&\quad \cdot (u_1(0) v_2(0) + u_2(0) v_1(0)) \\
&\quad + \left((x(t) + \bar{r}) F''_{yy}(x(t), y(t))\right) u_2(0) v_2(0), \\
d_1^3G_1(x_t, y_t)(u, v, w) & \\
&= \left((y(t) + r) F'''_{xxx}(x(t), y(t))\right) u_1(0) v_1(0) w_1(0) \\
&\quad + \left(F''_{xx}(x(t), y(t))\right. \\
&\quad \left. + (y(t) + r) F'''_{xxy}(x(t), y(t))\right) \\
&\quad \cdot (u_1(0) v_1(0) w_2(0) + u_1(0) v_2(0) w_1(0) \\
&\quad + u_2(0) v_1(0) w_1(0)) + \left(2F''_{xy}(x(t), y(t))\right. \\
&\quad \left. + (y(t) + r) F'''_{xyy}(x(t), y(t))\right)(u_1(0) v_2(0) w_2(0) \\
&\quad + u_2(0) v_1(0) w_2(0) + u_2(0) v_2(0) w_1(0)) \\
&\quad + \left(3F''_{yy}(x(t), y(t))\right. \\
&\quad \left. + (y(t) + r) F'''_{yyy}(x(t), y(t))\right) u_2(0) v_2(0) w_2(0), \\
d_1^3G_2(x_t, y_t)(u, v, w) &= \left(3F''_{xx}(x(t), y(t))\right. \\
&\quad \left. + (x(t) + r) F'''_{xxx}(x(t), y(t))\right) u_1(0) v_1(0) w_1(0) \\
&\quad + \left(2F''_{xy}(x(t), y(t))\right.
\end{aligned}$$

$$+ (x(t)+r) F'''_{xxy}(x(t), y(t))\big) (u_1(0) v_1(0) w_2(0)$$
$$+ u_1(0) v_2(0) w_1(0) + u_2(0) v_1(0) w_1(0))$$
$$+ \big(F''_{yy}(x(t), y(t))$$
$$+ (x(t)+r) F'''_{xyy}(x(t), y(t))\big) (u_1(0) v_2(0) w_2(0)$$
$$+ u_2(0) v_1(0) w_2(0) + u_2(0) v_2(0) w_1(0))$$
$$+ \big((x(t)+r) F'''_{yyy}(x(t), y(t))\big) u_2(0) v_2(0) w_2(0). \quad (25)$$

Evaluating the second and third derivative at $(0,0)$ we obtain

$$\begin{aligned}
d_1^2 G_1(u,v) &= \frac{2\epsilon r^3}{(1+r^4)^3} \big((1-3r^4) u_1(0) v_1(0) + (3 - r^4)(u_1(0) v_2(0) + u_2(0) v_1(0)) + (3-r^4) u_2(0) \cdot v_2(0)\big), \\
d_1^2 G_2(u,v) &= \frac{2\epsilon r^3}{(1+r^4)^3} \big((3-r^4) u_1(0) v_1(0) + (3 - r^4)(u_1(0) v_2(0) + u_2(0) v_1(0)) + (1-3r^4) \cdot u_2(0) v_2(0)\big), \\
d_1^3 G_1(u,v,w) &= \frac{2\epsilon r^2}{(1+r^4)^4} \big(12r^4(r^4-1) u_1(0) v_1(0) \cdot w_1(0) + 3(1-6r^4+r^8)(u_1(0) v_1(0) w_2(0) + u_1(0) v_2(0) w_1(0) + u_2(0) v_1(0) w_1(0)) + 2(3 - 8r^4 + r^8)(u_1(0) v_2(0) w_2(0) + u_2(0) v_1(0) w_2(0) + u_2(0) v_2(0) w_1(0)) + 3(1 - 6r^4 + r^8) u_2(0) v_2(0) w_2(0)\big), \\
d_1^3 G_2(u,v,w) &= \frac{2\epsilon r^2}{(1+r^4)^4} \big(3(1-6r^4+r^8) u_1(0) \cdot v_1(0) w_1(0) + 2(3-8r^4+r^8) \cdot (u_1(0) v_1(0) w_2(0) + u_1(0) v_2(0) w_1(0) + u_2(0) v_1(0) w_1(0)) + 3(1-6r^4+r^8) \cdot (u_1(0) v_2(0) w_2(0) + u_2(0) v_1(0) w_2(0) + u_2(0) v_2(0) w_1(0)) + 12r^4(r^4-1) u_2(0) v_2(0) \cdot w_2(0)\big),
\end{aligned} \quad (26)$$

where $d_1^j G_i(0,0)$, $i = 1,2$, $j = 2,3$, is denoted by $d_1^j G_i$, to shorten the notation.

Using the formula above, we calculate

$$\begin{aligned}
c_I &= \frac{1}{2} \mathbf{q} \cdot d_1^3 G(\Phi, \Phi, \overline{\Phi}) \\
&= \frac{1}{2}(a,a) \cdot \begin{pmatrix} \dfrac{12\epsilon r^2 (5r^8 - 22r^4 + 5)}{(1+r^4)^4} \\ \dfrac{12\epsilon r^2 (5r^8 - 22r^4 + 5)}{(1+r^4)^4} \end{pmatrix} \\
&= \frac{12\epsilon r^2 (5r^8 - 22r^4 + 5)}{(1+r^4)^4} a.
\end{aligned} \quad (27)$$

To calculate c_{II} we need to evaluate $(\Delta(0,\tau_0))^{-1}$. We have

$$(\Delta(0,\tau_0))^{-1} = \frac{1}{(1+\beta)(1-\beta_1)} \begin{pmatrix} 1-\eta & \eta+\beta \\ \eta+\beta & 1-\eta \end{pmatrix}. \quad (28)$$

Moreover,

$$d_1^2 G(\Phi, \overline{\Phi}) = \begin{pmatrix} \dfrac{4\epsilon r^3 (5-3r^4)}{(1+r^4)^3} \\ \dfrac{4\epsilon r^3 (5-3r^4)}{(1+r^4)^3} \end{pmatrix}, \quad (29)$$

and therefore

$$\begin{aligned}
\Psi_1 &= (\Delta(0,\tau_0))^{-1} d_1^2 G(\Phi, \overline{\Phi}) \\
&= \frac{4\epsilon r^3 (5-3r^4)}{(1+r^4)^3 (1-\beta_1)} \begin{pmatrix} 1 \\ 1 \end{pmatrix}.
\end{aligned} \quad (30)$$

Finally,

$$\begin{aligned}
c_{II} &= \mathbf{q} \cdot d_1^2 G(\Psi_1, \Phi) \\
&= \frac{4\epsilon r^3 (5-3r^4)}{(1+r^4)^3 (1-\beta_1)} (u,u) \cdot \begin{pmatrix} \dfrac{4\epsilon r^3 (5-3r^4)}{(1+r^4)^3} \\ \dfrac{4\epsilon r^3 (5-3r^4)}{(1+r^4)^3} \end{pmatrix} \\
&= \frac{32\epsilon^2 r^6 (5-3r^4)^2}{(1+r^4)^6 (1-\beta_1)} u.
\end{aligned} \quad (31)$$

To obtain the last parameter c_{III} we first need to calculate $(\Delta(2i\omega_0, \tau_0))^{-1}$.

Let us denote $M = \Delta(2i\omega_0, \tau_0)$ and calculate the first term of this matrix; that is,

$$\begin{aligned}
2i\omega_0 + e^{-2i\omega_0\tau_0} - \eta &= 2i\omega_0 + (\beta_1 - i\omega_0)^2 - \eta \\
&= \beta_1^2 - \omega_0^2 - \eta + 2i\omega_0 (1-\beta_1).
\end{aligned} \quad (32)$$

Hence,

$$\det M = \left(\beta_1^2 - \omega_0^2 - \eta + 2i\omega_0(1-\beta_1)\right)^2 - (\eta+\beta)^2 = \left(\beta_1^2 - \omega_0^2 + \beta + 2i\omega_0(1-\beta_1)\right) \cdot \left(\beta_1^2 - \omega_0^2 - \beta_1 + 2i\omega_0(1-\beta_1)\right),$$
$$M^{-1} = \frac{1}{\det M} \cdot \begin{pmatrix} \beta_1^2 - \omega_0^2 - \eta + 2i\omega_0(1-\beta_1) & \eta+\beta \\ \eta+\beta & \beta_1^2 - \omega_0^2 - \eta + 2i\omega_0(1-\beta_1) \end{pmatrix}. \quad (33)$$

Next we calculate $\Psi_2(h) = e^{2i\omega_0 h}V$, where

$$V = M^{-1} d_1^2 G(\Phi,\Phi) = M^{-1} \begin{pmatrix} \dfrac{4\epsilon r^3(5-3r^4)}{(1+r^4)^3} \\ \dfrac{4\epsilon r^3(5-3r^4)}{(1+r^4)^3} \end{pmatrix} = \frac{\left(4\epsilon r^3(5-3r^4)/(1+r^4)^3\right)\left(\beta_1^2-\omega_0^2+\beta+2i\omega_0(1-\beta_1)\right)}{\det M} \cdot \begin{pmatrix}1\\1\end{pmatrix} = \frac{4\epsilon r^3(5-3r^4)}{(1+r^4)^3(\beta_1^2-\omega_0^2-\beta_1+2i\omega_0(1-\beta_1))}\begin{pmatrix}1\\1\end{pmatrix}. \quad (34)$$

Finally, we evaluate

$$d_1^2 G(\Psi_2, \overline{\Phi}) = \frac{4\epsilon r^3(5-3r^4)}{(1+r^4)^3(\beta_1^2-\omega_0^2-\beta_1+2i\omega_0(1-\beta_1))} \cdot \begin{pmatrix} \dfrac{4\epsilon r^3(5-3r^4)}{(1+r^4)^3} \\ \dfrac{4\epsilon r^3(5-3r^4)}{(1+r^4)^3} \end{pmatrix} = \frac{16\epsilon^2 r^6(5-3r^4)^2}{(1+r^4)^6(\beta_1^2-\omega_0^2-\beta_1+2i\omega_0(1-\beta_1))}\begin{pmatrix}1\\1\end{pmatrix}, \quad (35)$$

and therefore

$$c_{III} = \frac{1}{2}(a,a)\cdot d_1^2 G(\Psi_2,\overline{\Phi}) = \frac{16\epsilon^2 r^6(5-3r^4)^2}{(1+r^4)^6(\beta_1^2-\omega_0^2-\beta_1+2i\omega_0(1-\beta_1))}a. \quad (36)$$

Now, we are in a position to check the sign of $\operatorname{Re} c$, where $c = c_I + c_{II} + c_{III}$. Clearly,

$$c = \frac{4\epsilon r^2}{(1+r^4)^4}\Bigg(3(5r^8-22r^4+5) + \frac{8\epsilon r^4(5-3r^4)^2}{(1+r^4)^2(1-\beta_1)} + \frac{4\epsilon r^4(5-3r^4)^2(\beta_1^2-\omega_0^2-\beta_1-2i\omega_0(1-\beta_1))}{(1+r^4)^2\left((\beta_1^2-\omega_0^2-\beta_1)^2+4\omega_0^2(1-\beta_1)^2\right)}\Bigg) \cdot a, \quad (37)$$

and therefore

$$\frac{(1+r^4)^4}{4\epsilon r^2}\operatorname{Re} c = \Bigg(3(5r^8-22r^4+5) + \frac{8\epsilon r^4(5-3r^4)^2}{(1+r^4)^2(1-\beta_1)} + \frac{4\epsilon r^4(5-3r^4)^2(\beta_1^2-\omega_0^2-\beta_1)}{(1+r^4)^2\left((\beta_1^2-\omega_0^2-\beta_1)^2+4\omega_0^2(1-\beta_1)^2\right)}\Bigg) \cdot \operatorname{Re} a + \frac{8\omega_0\epsilon r^4(5-3r^4)^2(1-\beta_1)}{(1+r^4)^2\left((\beta_1^2-\omega_0^2-\beta_1)^2+4\omega_0^2(1-\beta_1)^2\right)}\operatorname{Im} a, \quad (38)$$

where $\operatorname{Re} a = (1-\tau_0\beta_1)/2((1-\tau_0\beta_1)^2+\omega_0^2\tau_0^2)$ and $\operatorname{Im} a = -\omega_0\tau_0/2((1-\tau_0\beta_1)^2+\omega_0^2\tau_0^2)$.

Notice that, for small ϵ, the first term of the expression above is dominating, and therefore in the range of parameters we are interested in the fact that, as $\overline{r} < 0.5$, the first term is positive and of the order of units, suggesting that $\operatorname{Re} c > 0$. This implies that the bifurcation we study is subcritical, which therefore yields instability of appearing periodic orbits. However, in general it is necessary to calculate the exact value of $\operatorname{Re} c$, as it is difficult to guess its sign.

Now, we calculate $\operatorname{Re} c$ for the reference parameters with $\epsilon = 1$. Let us recall that $r = 0.4115$, $\beta = 0.02787$, $\eta = 0.05418$, $\omega_0 = 0.9907$, $\tau_0 = 1.4476$, and moreover $\beta_1 = 2\eta + \beta = 0.13623$. We obtain $\operatorname{Re} a \approx 0.1486$ and $\operatorname{Im} a \approx -0.2655$. Consecutive terms in the brackets are equal to 13.11988735, 6.060143781, and −0.6953365688, while the last fraction is 1.082692850. Eventually,

$$\operatorname{Re} c \approx 0.6049083964\,(18.48469456 \cdot 0.1486 - 1.082692850 \cdot 0.2655) \approx 1.487693962 > 0, \quad (39)$$

which means that, in our reference case, the bifurcation is *subcritical*.

In order to complement the analysis above, we can also show that in the reference case the second bifurcation appearing for τ_0^{II} is subcritical as well. We again denote τ_0^{II} by τ_0, to shorten the notation. Now, the pair ω_0, τ_0 satisfies $i\omega_0 + \beta + \exp(-i\omega_0\tau_0) = 0$ yielding $i\omega_0 + \exp(-i\omega_0\tau_0) = -\beta$, and from this relation we obtain the vector $\mathbf{p} = (1,-1)^T$. Hence, $\Phi(h) = \exp(i\omega_0 h)(1,-1)^T$ is the eigenvector for the eigenvalue $i\omega_0$. Next, we find $\mathbf{q}$ such that $\mathbf{q}d_1\Delta(i\omega_0,\tau_0)\mathbf{p} = 1$. As before, coordinates of $\mathbf{q}$ satisfies the same relation as for $\mathbf{p}$, that is, $\mathbf{q} = (a,a)$, $a == (1/2)((1+\tau_0\beta - i\omega_0\tau_0)/((1+\tau_0\beta)^2 + \omega_0^2\tau_0^2))$. Calculating the denominator of μ_2 we obtain

$$d_2\Delta(i\omega_0,\tau_0) = \begin{pmatrix} -\omega_0^2 + i\omega_0\beta & 0 \\ 0 & -\omega_0^2 + i\omega_0\beta \end{pmatrix}, \tag{40}$$

next

$$\begin{aligned} \mathbf{q}\cdot d_2\Delta(i\omega_0,\tau_0)\cdot\mathbf{p} &= 2a\left(-\omega_0^2 + i\omega_0\beta\right) \\ &= \frac{i\omega_0\tau_0 - (\tau_0\beta+1)}{\omega_0^2\tau_0^2 + (\tau_0\beta+1)^2}\left(\omega_0^2 - i\omega_0\beta\right) \\ &= \frac{-\omega_0 + i\left(\beta + \tau_0\left(\beta^2+\omega_0^2\right)\right)}{\omega_0^2\tau_0^2 + (\tau_0\beta+1)^2}\omega_0, \end{aligned} \tag{41}$$

and we easily see that the real part of this expression is negative.

Next, we calculate

$$\begin{aligned} c_I &= \frac{1}{2}\mathbf{q}\cdot d_1^3 G\left(\Phi,\Phi,\overline{\Phi}\right) \\ &= \frac{1}{2}(a,-a)\cdot\begin{pmatrix} \dfrac{12\epsilon r^2}{(1+r^4)^2} \\ -\dfrac{12\epsilon r^2}{(1+r^4)^2} \end{pmatrix} = \frac{12\epsilon r^2}{(1+r^4)^2}a, \\ c_{II} &= -\frac{4\epsilon r^3}{(1+r^4)^2}\frac{1}{(1-\beta_1)}(a,-a)\cdot\begin{pmatrix} -\dfrac{4\epsilon r^3}{(1+r^4)^2} \\ \dfrac{4\epsilon r^3}{(1+r^4)^2} \end{pmatrix} \\ &= \frac{(4\epsilon r^3)^2}{(1+r^4)^4}\frac{2a}{(1-\beta_1)}, \\ c_{III} &= \frac{(4r^3\epsilon)^2 u}{(1+r^4)^4\left(2i\omega_0(\beta+1) + \beta^2 - \omega_0^2 - \beta_1\right)}. \end{aligned} \tag{42}$$

Eventually,

$$\begin{aligned} c = \frac{4\epsilon r^2}{(1+r^4)^4}&\left(3\left(1+r^4\right)^2 + \frac{8\epsilon r^4}{1-\beta_1}\right. \\ &\left.+ \frac{4\epsilon r^4\left(\beta^2 - \omega_0^2 - \beta_1 - 2i\omega_0(\beta+1)\right)}{4\omega_0^2(\beta+1)^2 + \left(\beta^2 - \omega_0^2\beta_1\right)^2}\right)a, \end{aligned} \tag{43}$$

and hence,

$$\begin{aligned} \operatorname{sign}\operatorname{Re} c = \operatorname{sign}&\left(\left(1+\tau_0\beta\right)\left(3\left(1+r^4\right)^2 + \frac{8\epsilon r^4}{1-\beta_1}\right.\right. \\ &\left.+ \frac{4\epsilon r^4\left(\beta^2 - \omega_0^2 - \beta_1\right)}{4\omega_0^2(\beta+1)^2 + \left(\beta^2 - \omega_0^2 - \beta_1\right)^2}\right) \\ &\left.- \frac{8\epsilon r^2\tau_0\omega_0^2(\beta+1)}{4\omega_0^2(\beta+1)^2 + \left(\beta^2 - \omega_0^2 - \beta_1\right)^2}\right). \end{aligned} \tag{44}$$

For our reference values the expression in the brackets equals $3.146913951 > 0$.

At the end we sum up the results of the Hopf bifurcation analysis in the following corollary.

Corollary 5. *For reference parameter values the system described by (1) undergoes two subsequent subcritical Hopf bifurcations.*

4. Numerical Simulations

In order to simulate the decision-making process, we assume a transient change in one of the inputs to the nodes; that is, we start from the resting state of the network and then solve (1) with $I_2(t) \equiv I$ and

$$I_1(t) = \begin{cases} I + \sigma, & \text{for } 0 \le t \le T_{\text{stim}}, \\ I, & \text{for } t \ge T_{\text{stim}}, \end{cases} \tag{45}$$

where T_{stim} is the stimulation duration time. In a properly working decision-making network, we should expect that the bigger the value of σ is, that is, the stimulus, the faster the decision in favor of population 1 according to the psychometric function (2) will be.

In all the numerical experiments, we have chosen $\epsilon = 1$ and $\alpha = 3$ (for this value the time scale τ_r allows to reproduce delays present in real systems). Note that the qualitative dynamics of the system described by (1) does not depend on α. Moreover, we choose a reference value $I = 0.4$ to reflect that there is a certain baseline input to the network. Other parameter values fixed across all simulations were $\beta = 100$, $\gamma = 0.001$, and $T_{\text{stim}} = 0.5$ s. We perform numerical simulations of the model with respect to the magnitude of delay τ and stimulus strength σ. For all of the simulations we use the built-in MATLAB delayed differential equation solver dde23 [28] with lowered default tolerances (*RelTol* and *AbsTol* equal to $1e-8$). We performed the simulations on the Neuroscience Gateway platform [29].

One important aspect of the considered (1) is that we cannot guarantee the nonnegativity of solutions as the delayed self-inhibition term has a negative sign. It is obvious, however, that the firing rate cannot have a negative value and, in order for the model to be physiologically valid, we need to impose a barrier for the firing rates at zero. Thus, in the simulations, whenever one of the coordinates reaches value of zero, we stop the simulation and solve the reduced system with one

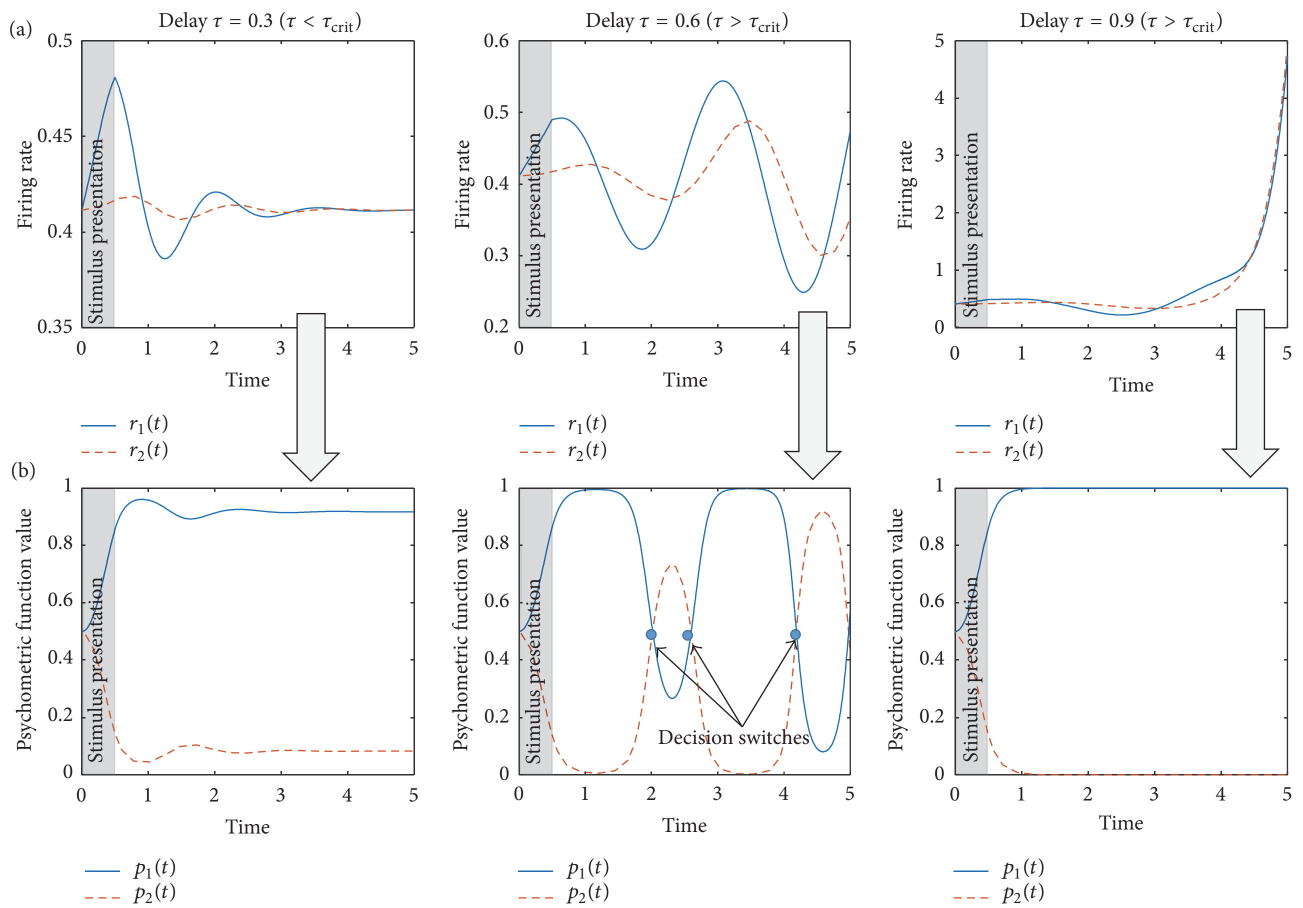

Figure 3: Comparison of the model solutions ((a); (1)) together with the corresponding psychometric function values ((b); (2) and (3)) for different values of time delay and stimulus strength $\sigma = 0.05$. For small delays, that is, in the stability regime, we observe vanishing oscillations with no certain decision being made ($p_1 < 1$). Interestingly, for $\tau = 0.6$ which is above critical destabilizing delay value we observe multiple preference switches (middle column). For $\tau = 0.9$ certain decision is being made ($p_1 = 1$).

of the coordinates equal to zero until its derivative becomes positive again; that is, its delayed value becomes lower than I.

We start our numerical experiments from simulations in which stimulus of a fixed magnitude $\sigma = 0.05$ is applied to the network with different delay τ in the self-inhibition terms. As it can be expected from the analysis, for small delays, that is, below the Hopf bifurcation threshold, the solutions exhibit vanishing oscillations around the stable steady state; see left panel in Figure 3(a). The stimulus in this particular case is too small for any certain decision to be made, and both psychometric functions remain separated from the value of 1; see left panel in Figure 3(b). It is clear, however, that if the stimulus was stronger, then a certain decision would be made, that is, p_1 would cross the threshold of $1 - \gamma$ at some point.

Interestingly, for delays above the critical value at which first Hopf bifurcation occurs, we observe very nonintuitive behavior; see middle panels in Figures 3(a) and 3(b). Namely, the psychometric function value shows multiple perceptual switches; that is, there are multiple time points in which there is a change from $p_1 > p_2$ into $p_2 < p_1$. For even larger delays we observe that a certain decision has been made for the same stimulus of $\sigma = 0.05$ magnitude that was insufficient to make a certain decision in the case of small delays; see right panels Figures 3(a) and 3(b).

Because of the observed nonintuitive behavior of the psychometric function, we decided to calculate a decision map; that is, to evaluate the psychometric function values on the model solutions for different values of delay τ and the stimulus strength σ, see Figure 4. As expected, for delay values below the critical Hopf bifurcation threshold, the certainty of the decision depends directly on the strength of the stimulus, and the networks is always able to correctly identify that the stimulus was applied to population 1. Interestingly, this is not the case for larger delays and we observe that for the same value of delay above the critical first bifurcation threshold the decision can be opposite depending on the stimulus strength, compare Figure 4(a). Moreover, above the bifurcation threshold we can have more than 10 transient decision switches before any certain decision is made; compare Figure 4(b).

In Figure 5, in order to complete presentation of the numerical experiments, we show the solution for which decision made by the network is in favor of the population 2 instead of the population 1 to which the stimulus was applied.

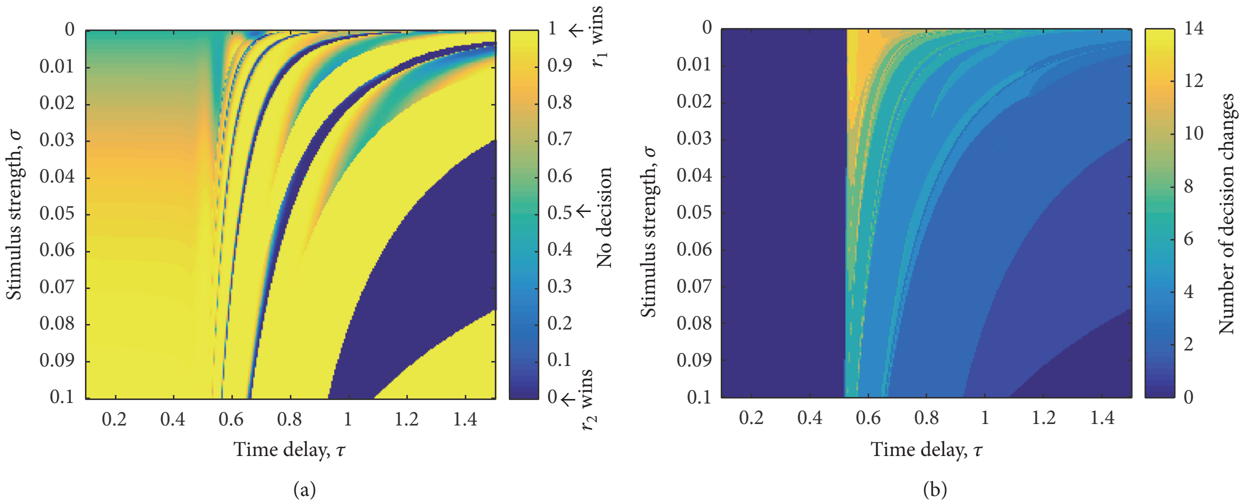

FIGURE 4: (a) Decision map resulting from the psychometric function evaluation on solutions to (1) for different values of time delay τ and stimulus strengths σ. Yellow regions indicate values for which certain decision is being made in favor of population r_1, that is, $p_1 = 1$ after breaching critical γ distance first. Dark blue regions indicate values for which certain decision is being made in favor of population 2, that is, $p_2 = 1$ after breaching critical γ distance first. Values in other places are $p_1(T)$ for $T = 15$. (b) Number of decision switches (see a particular example in middle panel Figure 3(b)) for different delay values τ and stimulus strengths σ.

5. Discussion

In this study, we model perceptual decision-making in elderly individuals. Although there is an extensive evidence that the cognitive impairments in aging relate to the slow processing of information [13, 16, 30, 31], the cortical mechanisms underlying cognitive impairments in aging remain elusive. In principle, the decision-making experiments in humans are mostly performed in young and healthy individuals [32, 33], which is one of the reasons behind the lack of knowledge upon the cortical mechanisms of aging.

In order to bridge this gap, we propose to study the influence of synaptic delays on making perceptual choices with use of a population model of decision-making based on a winner-take-all mechanism. In this simple model, the network needs to make a binary choice between the two options. The inspiration for this model was a spiking neuronal network model with a slow reverberation mechanism by Wang [18], created to explain Shadlen and Newsome's experiments on perceptual decision-making in rhesus monkeys [17]. Unlike Wang, we do not use simulations of stochastic spiking neuronal networks in our study though, but we take an analytic approach instead. This allows us to study the rich dynamic repertoire of networks with delay and the influence of the delay on the outcome decisions.

We achieve two main results that can contribute to the understanding of the associations between the delayed GABA-signaling and the cognitive impairments during aging. Firstly, the decision-making performance is dependent on the synaptic delays in the local inhibition. For the delays below the critical value, we observe a clear association between the magnitude of the stimulus and the probability of making the correct decision (Figure 4). This result is concordant with classic experiments on perceptual decision-making, as typically, a monotonic psychometric curve links the strength of the stimulus with the decision accuracy [17, 34]. However, for the synaptic delays exceeding the critical threshold, the system falls into a new dynamical regime and is no longer precise in making decisions. Dependent on both the synaptic delays and the signal magnitude, it can even achieve an accuracy of zero, by always choosing the wrong option. As known from experiments on reversal learning in rhesus monkeys [35] and humans [36], aging subjects exhibit habitual behaviors and are reluctant to relearn rules. Therefore in some cases, falling into a behavioral schema in which the wrong decision is being taken in repetitive fashion is possible in elderly subjects.

The second important result from our study is that, for delay values above critical threshold, the system exhibits ambiguity in decision-making, reflected by decision switches. This result can account for the slow reaction times in perceptual decision-making in the elderly [37–41]; however the subsequent experimental validation is necessary in order to test this hypothesis.

Our model predicts that impairment in the local inhibition in the cortex can result in the impaired decision-making. Although GABA concentration in prefrontal cortex and perceptual decision-making are both affected by aging, there is a lack of computational models characterizing the causal link between the two. Therefore, the model should be validated in laboratory conditions. The prediction given by the model is hard to test in the human cohorts because recordings from interneurons in the cortex are invasive. However, there are now tools in translational psychiatry that make this validation viable. For instance, the decision-making quality can be evaluated in mice in multiple experimental paradigms [19] and that results can be than correlated with the speed of synaptic transmission evaluated postmortem in an in vitro experiment [42].

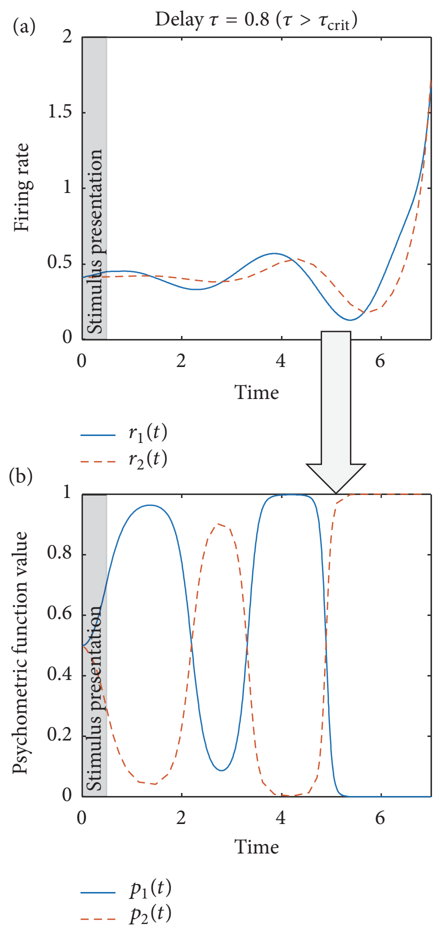

FIGURE 5: Exemplary solution of (1) in which stimulus is being applied to the population 1, but certain decision is being made in favor of the population 2, that is, $p_2 = 1$ after breaching γ distance at some point.

One remark to make is that our model is qualitative rather than quantitative, and the same mechanism can be encountered at different time scales of inhibition and for different configurations of inputs and stimuli. There are multiple GABAergic receptors in the cortex, and they have their own characteristic timescales. In example, the fast mode of inhibition is related to the GABA-A receptors [43, 44] which give synaptic delays lasting for several tens of milliseconds (excluding the afterdepolarizations lasting for several tens of milliseconds as well [45–49]). On the other hand, the slowest mode of inhibition is related to the metabotropic GABA-B receptors which have a time scale of a few hundred milliseconds [50]. Still little is known about the structure and functions of these receptors [51]. In practice, the local inhibition in the nodes of the cortical network is most probably a combination of the multiple interacting processes at different time scales. Our model is a demonstration of the principle and does not require specification of GABAergic receptors that lead a primary role in the oscillatory mechanisms considered in this work.

As a summary, the model proposed in this work yields new insights into the mechanisms of aging in cortical circuits, mediated by neurodegeneration in the local inhibitory synapses.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Authors' Contributions

The authors developed the model as a team. Urszula Foryś conducted the derivations in a collaboration with Martyna Płomecka and Katarzyna Piskała. Jan Poleszczuk performed and visualized numerical simulations. Natalia Z. Bielczyk formulated the introduction and the discussion part of the manuscript.

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Research Article

On Coupled p-Laplacian Fractional Differential Equations with Nonlinear Boundary Conditions

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This paper is related to the existence and uniqueness of solutions to a coupled system of fractional differential equations (FDEs) with nonlinear p-Laplacian operator by using fractional integral boundary conditions with nonlinear term and also to checking the Hyers-Ulam stability for the proposed problem. The functions involved in the proposed coupled system are continuous and satisfy certain growth conditions. By using topological degree theory some conditions are established which ensure the existence and uniqueness of solution to the proposed problem. Further, certain conditions are developed corresponding to Hyers-Ulam type stability for the positive solution of the considered coupled system of FDEs. Also, from applications point of view, we give an example.

1. Introduction

Due to high profile accuracy and usability, FDEs become an area of interest for various fields of scientists and mathematicians. In last few years, some physical phenomenons were described through FDEs and compared with integer order differential equations which have better results, that is why researchers of different areas have paid great attention to study FDEs. The applications of FDEs can be studied in several disciplines including aerodynamics, engineering, electrical circuits, plasma physics, chemical reaction design, turbulent filtration in porous media, and signal and image processing; for further details we refer to [1–5].

Nonlinear operators have vital roles in differential equations; one of the most important operators used in FDEs is the classical nonlinear p-Laplacian operator, which is defined as

$$\begin{gathered}\frac{1}{p}+\frac{1}{q}=1,\\ \phi_p(s)=|s|^{p-2}s,\\ p\ge 1,\\ \phi_q(\tau)=\phi_p^{-1}.\end{gathered}\tag{1}$$

For further details and applications of the nonlinear p-Laplacian operators, reader should study [6].

Researchers study different aspects of FDEs involving p-Laplacian operators like the existence theory, which has been extensively investigated by using classical fixed point theory. The mentioned theory has been investigated very well for the aforesaid equations of ordinary and partial fractional differential equations. Since p-Laplacian operators have been greatly applied in the mathematical modeling of large numbers of real world phenomenons devoted to physics, mechanics, dynamical systems, electrodynamics, and so forth, therefore researchers paid much attention to study such type of differential equation dealing with p-Laplacian operators from different aspects including existence theory, multiplicity results, and stability analysis. For instance, Lu et al. [7] discussed Sturm-Liouville boundary value problems (BVP) of FDEs with p-Laplacian operator for existence of two or three positive solutions by using fixed point theory. By applying Leggett-William fixed point theorem, the mentioned author studied the following problem:

$$\begin{gathered}\mathrm{D}^{\beta}\left(\phi_p\left((D)^{\alpha}\mu(x)\right)\right)+\mathfrak{F}(x,\mu(x))=0,\quad 0<x<1,\\ \jmath\mu(0)-\eta\mu'(0)=0,\end{gathered}$$

$$\gamma\mu(1)+\delta\mu'(1)=0,$$
$$D^{\alpha}\mu(0)=0 \quad (2)$$

and also he provided proper example, where D^{α} and D^{β} denote standard Caputo fractional derivatives with $1<\alpha\le 2$, $0<\beta\le 1$, $1/p+1/q=1$, $\phi_p(\tau)=|s|^{p-2}s$, $p>1$, $\phi_q(\tau)=\phi_p^{-1}$, $\rho=\jmath\gamma+\jmath\delta+\eta\gamma>0$, $\jmath,\eta,\delta,\gamma\ge 0$, and $\mathfrak{F}$ is continuous.

Hu and Zhang [8] have investigated a nonlinear FDE with p-Laplacian operator for existence of solution as given by

$$\begin{aligned} &D^{\beta}\left(\phi_p\left((D)^{\alpha}\mu(x)\right)\right)+\mathfrak{F}\left(x,\mu(x),D^{\alpha}\mu(x)\right)=0, \\ &\qquad\qquad x\in(0,1), \\ &D^{\alpha}\mu(0)=0=D^{\alpha}\mu(1), \end{aligned} \quad (3)$$

where $0<\alpha,\beta<1$, $1<\alpha+\beta<2$, D^{α} and D^{β} represent standard Caputo fractional derivatives, $\mathfrak{F}$ is continuous and $1/p+1/q=1$, $\phi_p(\tau)=|s|^{p-2}s$, $p>1$, and $\phi_q(\tau)=\phi_p^{-1}$. Zhi et al. [9] have investigated the existence of positive solutions for the nonlocal BVP of FDEs with p-Laplacian operator and illustrated the problem with expressive example. The corresponding problem is given by

$$\begin{aligned} &\left(\phi_p\left(D^{\alpha}\mu(x)\right)\right)''=\mathfrak{F}\left(x,\mu(x),D^{\beta}\mu(x)\right), \\ &\qquad\qquad x\in(0,1), \\ &\mu(x)\big|_{x=0}=\mu''(x)\big|_{x=0}=0, \\ &\mu(1)=\int_0^1 g(\tau)\mu(\tau)\,d\tau, \\ &\left(\phi_p\left(D^{\alpha}\right)\mu(0)\right)'=\xi_1\left(\phi_p\left(D^{\alpha}\right)\mu(\jmath_1)\right)', \\ &\left(\phi_p\left(D^{\alpha}\right)\mu(1)\right)=\xi_2\left(\phi_p\left(D^{\alpha}\right)\mu(\jmath_2)\right), \end{aligned} \quad (4)$$

where ϕ_p is p-Laplacian operator and $2<\alpha\le 3$, $1<\beta<\alpha-1<2$, $0<\jmath_1\le\jmath_2<1$, $0\le\xi_1,\xi_2<1$, and D^{α} expresses Caputo derivative of order α. For further study about the existence theory and multiplicity results of p-Laplacian operator involved in differential equations, see [10–14].

Using classical fixed point theory needs strong conditions to establish conditions for existence and uniqueness of solutions to FDEs and therefore restrict the applicability to certain classes of FDEs and their systems. To relax the criteria degree theory plays excellent roles for the existence of solutions to FDEs and their systems. Various degree theories including Brouwer and Leray-Schauder were established to deal with the existence theory of differential equations. An important degree theory known as topological degree theory which was introduced by Stamova [15] and later on extended by Isaia [16] has been used to establish existence theory for solutions to nonlinear differential and integral equations. The mentioned method is called prior-estimate method which needs no compactness of the operator and relaxes much the condition for existence and uniqueness of solutions to differential and integral equations. Recently, the aforesaid degree theory has been applied to investigate certain classes of FDEs with boundary conditions; see [17–19].

In recent years another aspect of FDEs which has greatly attracted the attentions of researchers is devoted to the stability analysis of the mentioned equations. Stability analysis plays significant roles in the optimization and numerical analysis of the aforesaid equations. Different kinds of stability have been studied for fractional differential equations including exponential, Mittag-Leffler, and Lyapunov stabilities; see [15, 20, 21]. An important stability was pointed out by Ulam [22], in 1940, which was formally introduced by Hyers [23], in 1941. The aforesaid stability has now been considered in many papers for classical differential equations; see [24–26]. For instance, Urs [27] has investigated the Hyers-Ulam stability for the following coupled periodic BVPs given as

$$\begin{aligned} &\mu''(x)-\mathfrak{F}_1(x,\mu(x))=\mathfrak{F}_2(x,\nu(x)), \quad x\in[0,T], \\ &\nu''(x)-\mathfrak{F}_1(x,\nu(x))=\mathfrak{F}_2(x,\mu(x)), \\ &\mu(x)\big|_{x=0}=\mu(x)\big|_{x=T}, \\ &\nu(x)\big|_{x=0}=\nu(x)\big|_{x=T}. \end{aligned} \quad (5)$$

The Hyers-Ulam stability has been investigated for certain FDEs with boundary and initial conditions; see [28–30]. In many situations, Lyapunov type stability and its investigation are very difficult and time-consuming for certain nonlinear fractional differential equations. This is due to the predefined Lyapunov function which is often very difficult to construct for FDEs. Therefore, Hyers-Ulam type stability plays important roles in such a situation. Inspired from the above-mentioned work, in this paper, we study a coupled system of FDEs with nonlinear p-Laplacian operator by using topological degree theory. Further, we also investigated some conditions for the Hyers-Ulam stability of the solution to the proposed problem. The proposed problem is given by

$$\begin{aligned} &D^{\beta_1}\phi_p\left(D^{\alpha_1}\mu(x)\right)+\mathfrak{F}_1(x,\nu(x))=0, \quad x\in(0,1), \\ &D^{\beta_2}\phi_p\left(D^{\alpha_2}\nu(x)\right)+\mathfrak{F}_2(x,\mu(x))=0, \quad x\in(0,1), \\ &D^{\alpha_1}\mu(x)\big|_{x=0}=0=\mu(x)\big|_{x=0}=\mu''(x)\big|_{x=0}, \\ &\mu'(x)\big|_{x=1}=\eta_1 I_P^{\gamma_1}\psi_1(\mu) \\ &\quad=\frac{\eta_1}{\Gamma(\gamma_1)}\int_0^P(P-\tau)^{\gamma_1-1}\psi_1(\mu(\tau))\,d\tau, \\ &D^{\alpha_2}\nu(x)\big|_{x=0}=\nu(x)\big|_{x=0}=\nu''(x)\big|_{x=0}=0, \\ &\nu'(x)\big|_{x=1}=\eta_2 I_P^{\gamma_2}\psi_2(\nu) \\ &\quad=\frac{\eta_2}{\Gamma(\gamma_2)}\int_0^P(P-\tau)^{\gamma_2-1}\psi_2(\nu(\tau))\,d\tau, \end{aligned} \quad (6)$$

where $2<\alpha_i<3$, $0<\beta_i<1$, $P,\eta_i,\gamma_i>0$, $\psi_1,\psi_2\in L[0,1]$, and D^{α_i} and D^{β_i} where $i=1,2$ stand for Caputo fractional derivative, $\phi_p(\kappa) = |\kappa|^{p-2}\kappa$ is p-Laplacian operator, where $1/p + 1/q = 1$, ϕ_q denotes inverse of p-Laplacian, and $\mathfrak{F}_i : [0,1] \times [0,\infty) \to (0,\infty)$, $i = 1,2$, are continuous functions. Here, we remark that applying degree method to deal with existence and uniqueness and to find conditions for Hyers-Ulam stability to a coupled system of FDEs with p-Laplacian operator has not been investigated properly to the best of our knowledge. Therefore thanks to the coincidence degree theory and nonlinear functional analysis greatly developed by Deimling [31], we establish necessary and sufficient conditions for existence and uniqueness as well as for Hyers-Ulam stability corresponding to the aforementioned problem considered by us. We also demonstrate our result through expressive example.

2. Axillary Results

Here we recall some special definitions, theorems, and Hyers-Ulam stability results from the literature [1–4] which have important applications throughout this paper.

Definition 1. The integral with fractional order $\alpha > 0$ of Riemann-Liouville type is defined for the function $\mathfrak{F}$ as

$$I_0^{\alpha}\mathfrak{F}(x) = \frac{1}{\Gamma(\alpha)}\int_0^x (x-\tau)^{\alpha-1}\mathfrak{F}(\tau)\,d\tau, \tag{7}$$

provided that the integral on the right converges pointwise on $(0,\infty)$.

Definition 2. The derivative with fractional order $\alpha > 0$ of Caputo type is defined for the function $\mathfrak{F}$ as

$$D_0^{\alpha}\mathfrak{F}(x) = \frac{1}{\Gamma(m-\alpha)}\int_0^x (x-\tau)^{m-\alpha-1}\mathfrak{F}^{(m)}(\tau)\,d\tau, \tag{8}$$

where $m = [\alpha] + 1$, $[\alpha]$ is the integer part of α such that the integral on the right converges pointwise on $(0,\infty)$.

Lemma 3. *Let $\alpha > 0$ and $\mu \in C(0,1) \cap L^1(0,1)$, and then the general solution of FDE*

$$D_0^{\alpha}\mu(x) = y(x) \tag{9}$$

is given by

$$\mu(x) = I_0^{\alpha}y(x) + A_0 + A_1x + A_2x^2 + \cdots + A_{m-1}x^{m-1}, \tag{10}$$

for some $A_i \in \mathbb{R}$, $i = 0,1,2,\ldots,m-1$ and m is smallest integer such that $m \geq \alpha$.

Let $\mathscr{L}$ be the space of all continuous functions $\mu : [0,1] \to \mathbb{R}$ endowed with a norm $\sup_{x\in[0,1]}\{|\mu(x)| : \mu \in C[0,1]\}$ which is obviously a Banach space. Then the product space denoted by $\mathscr{L} = \mathscr{L}_1 \times \mathscr{L}_2$ under the norms $\|(\mu,\nu)\| = \|\mu\| + \|\nu\|$ is also a Banach space which will be used throughout this paper. For the coincidence degree theory and nonlinear functional analysis, we recall the following definitions which can be traced in [15, 16, 31] as follows.

Definition 4. Let the class of all bounded set of $P(\mathscr{L})$ be denoted by $\aleph$. Then the mapping $\jmath : \aleph \to (0,\infty)$ for Kuratowski measure of noncompactness is defined as

$$\jmath(\hbar) = \inf\{d > 0 : \hbar \text{ is the finite cover for sets of diameter } \leq d\}, \tag{11}$$

where $\hbar \in \aleph$.

Proposition 5. *The following are the characteristics of Kuratowski measure $\jmath$:*

(1) *For relative compact $\hbar$, then Kuratowski measure $\jmath(\hbar) = 0$.*
(2) *For seminorm $\jmath$, $\jmath(\kappa\hbar) = |\kappa|\jmath(\hbar)$, $\kappa \in \mathbb{R}$, and $\jmath(\hbar_1 + \hbar_2) \leq \jmath(\hbar_1) + \jmath(\hbar_2)$.*
(3) *$\hbar_1 \subset \hbar_2$ yields $\jmath(\hbar_1)$; $\jmath(\hbar_1 \cup \hbar_2) = \sup\{\jmath(\hbar_1), \jmath(\hbar_2)\}$.*
(4) *$\jmath(\operatorname{conv}\hbar) = \jmath(\hbar)$.*
(5) *$\jmath(\overline{\hbar}) = \jmath(\hbar)$.*

Definition 6. Assume that $\varphi : \vartheta \to \mathscr{U}$ is bounded and continuous mapping such that $\vartheta \subset \mathscr{U}$. Then φ is a $\jmath$-Lipschitz, where $\zeta \geq 0$ such that

$$\jmath(\varphi(\hbar)) \leq \zeta\jmath(\hbar) \quad \text{for all bounded } \hbar \subset \vartheta. \tag{12}$$

Then φ is called strict $\jmath$-contraction under the condition $\zeta < 1$.

Definition 7. The function φ is $\jmath$-condensing if

$$\jmath(\varphi(\hbar)) < \jmath(\hbar), \quad \text{for all bounded } \hbar \subset \vartheta \text{ such that } \jmath(\hbar) > 0. \tag{13}$$

Therefore $\jmath(\varphi(\hbar)) \geq \jmath(\hbar)$ yields $\jmath(\hbar) = 0$.

Further we have $\varphi : \vartheta \to \mathscr{U}$ which is Lipschitz for $\zeta > 0$, such that

$$\|\varphi(\upsilon) - \varphi(\overline{\upsilon})\| \leq \zeta\|\upsilon - \overline{\upsilon}\|, \quad \text{for all } \upsilon, \overline{\upsilon} \in \vartheta. \tag{14}$$

The condition $\zeta < 1$ yields that φ is a strict contraction.

Proposition 8. *The mapping φ is $\jmath$-Lipschitz with constant $\zeta = 0$ if and only if $\varphi : \vartheta \to \mathscr{U}$, which is said to be compact.*

Proposition 9. *The operator φ is $\jmath$-Lipschitz for some constant ζ if and only if $\varphi : \vartheta \to \mathscr{U}$, which is Lipschitz with constant ζ.*

Theorem 10. *Let $\varphi : \mathscr{L} \to \mathscr{L}$ be a $\jmath$-contraction and*

$$\mathscr{G} = \{z \in \mathscr{L}: \text{there exist } 0 \leq \lambda \leq 1 \text{ such that } z = \lambda\varphi(z)\}. \tag{15}$$

Under the conditions $\mathscr{G} \subset \mathscr{L}$ is bounded for $r > 0$ and $\mathscr{G} \subset \hbar_r(0)$, with degree

$$\deg(I - \lambda\varphi, \hbar_r(0), 0) = 1, \quad \text{for every } \lambda \in [0,1]. \tag{16}$$

Then, φ has at least one fixed point.

Lemma 11 (see [10]). *Let ϕ_p be a p-Laplacian operator. Then*

(i) *if* $1 < p \le 2$, $\kappa_1\kappa_2 > 0$, *and* $|\kappa_1|, |\kappa_2| \ge m > 0$, *then*

$$\left|\phi_p(\kappa_1) - \phi_p(\kappa_2)\right| \le (p-1)\, m^{p-2} \left|\kappa_1 - \kappa_2\right|; \tag{17}$$

(ii) *if* $p > 2$ *and* $|\kappa_1|, |\kappa_2| \le M$, *then*

$$\left|\phi_p(\kappa_1) - \phi_p(\kappa_2)\right| \le (p-1)\, M^{p-2} \left|\kappa_1 - \kappa_2\right|. \tag{18}$$

Definition 12. Let $\mathbb{T} : \mathscr{L} \to \mathscr{L}$. Then the operator equation given by

$$\mathbb{T}\mu(x) = \mu(x), \quad x \in [0,1] \tag{19}$$

is called Hyers-Ulam stable if, for any $\xi > 0$, the inequality given as

$$\|\mu - \mathbb{T}\mu\| \le \xi, \quad x \in [0,1] \tag{20}$$

has a unique fixed point say μ^* with constant $D > 0$ such that $\|\mu - \mu^*\| \le D\xi$, for all $x \in [0,1]$ holds.

In view of Definition 12, we give the following definition.

Definition 13. The system of Hammerstein type integral equations

$$\begin{aligned}
\mu(x) &= \int_0^1 \Omega_{\alpha_1}(x,\tau)\, \phi_q\left(I^{\beta_1}\mathfrak{F}_1(\tau, \nu(\tau))\right) d\tau \\
&\quad + \frac{\eta_1 x}{\Gamma(\gamma_1)} \int_0^P (P-\tau)^{\gamma_1 - 1} \psi_1(\mu(\tau))\, d\tau, \\
\nu(x) &= \int_0^1 \Omega_{\alpha_2}(x,\tau)\, \phi_q\left(I^{\beta_2}\mathfrak{F}_2(\tau, \mu(\tau))\right) d\tau \\
&\quad + \frac{\eta_2 x}{\Gamma(\gamma_2)} \int_0^P (P-\tau)^{\gamma_2 - 1} \psi_2(\nu(\tau))\, d\tau
\end{aligned} \tag{21}$$

is called Hyers-Ulam stable such that, for $D_i > 0\ (i = 1,2,3,4)$ and for all $\xi_1, \xi_2 > 0$ and for every solution (μ^*, ν^*) to the system

$$\begin{aligned}
&\left|\mu^*(x) - \int_0^1 \Omega_{\alpha_1}(x,\tau)\, \phi_q\left(I^{\beta_1}\mathfrak{F}_1(\tau, \nu(\tau))\right) d\tau \right.\\
&\left.\quad + \frac{\eta_1 x}{\Gamma(\gamma_1)} \int_0^P (P-\tau)^{\gamma_1 - 1} \psi_1(\mu(\tau))\, d\tau\right| \le \xi_1, \\
&\left|\nu^*(x) - \int_0^1 \Omega_{\alpha_2}(x,\tau)\, \phi_q\left(I^{\beta_2}\mathfrak{F}_2(\tau, \mu(\tau))\right) d\tau \right.\\
&\left.\quad + \frac{\eta_2 x}{\Gamma(\gamma_2)} \int_0^P (P-\tau)^{\gamma_2 - 1} \psi_2(\nu(\tau))\, d\tau\right| \le \xi_2,
\end{aligned} \tag{22}$$

there exists a unique solution (λ_1, λ_2) of (21) satisfying the following system of inequalities:

$$\begin{aligned}
\|\lambda_1 - \mu^*\| &\le D_1\xi_1 + D_2\xi_2, \quad x \in [0,1], \\
\|\lambda_2 - \nu^*\| &\le D_3\xi_1 + D_4\xi_2, \quad x \in [0,1].
\end{aligned} \tag{23}$$

3. Some Data Dependence Assumptions

To proceed further, let the following hypothesis hold:

($\mathbb{A}_1$) The nonlocal functions ψ_1 and ψ_2 where $\omega, \mu, \nu, \upsilon \in \mathbb{R}$ satisfy the following:

$$\begin{aligned}
\left|\psi_1(\omega) - \psi_1(\mu)\right| &\le \mathbb{K}_{\psi_1} \left|\omega - \mu\right|, \\
\left|\psi_2(\nu) - \psi_2(\upsilon)\right| &\le \mathbb{K}_{\psi_2} \left|\nu - \upsilon\right|,
\end{aligned} \tag{24}$$

where $\mathbb{K}_{\psi_1}, \mathbb{K}_{\psi_2} \in [0,1)$.

($\mathbb{A}_2$) To satisfy the following growth conditions by the constants $\mathbb{C}_{\psi_1}, \mathbb{C}_{\psi_2}, \mathbb{M}_{\psi_1}, \mathbb{M}_{\psi_2} > 0$ and $q_1 \in [0,1)$ for $\mu, \nu \in \mathbb{R}$ with the nonlocal functions ψ_1 and ψ_2 we have

$$\begin{aligned}
\left|\psi_1(\mu)\right| &\le \mathbb{C}_{\psi_1} |\mu|^{q_1} + \mathbb{M}_{\psi_1}, \\
\left|\psi_2(\nu)\right| &\le \mathbb{C}_{\psi_2} |\nu|^{q_1} + \mathbb{M}_{\psi_2}.
\end{aligned} \tag{25}$$

($\mathbb{A}_3$) The functions $\mathfrak{F}_1$ and $\mathfrak{F}_2$ satisfy the following growth conditions under the constants $a, b, \mathbb{M}_1^*, \mathbb{M}_2^*$, $p_1 \in (0,1]$:

$$\begin{aligned}
\left|\mathfrak{F}_1(x, \mu)\right| &\le a |\mu|^{p_1} + \mathbb{M}^*_{\mathfrak{F}_1}, \\
\left|\mathfrak{F}_2(x, \upsilon)\right| &\le b |\upsilon|^{p_1} + \mathbb{M}^*_{\mathfrak{F}_2}.
\end{aligned} \tag{26}$$

($\mathbb{A}_4$) There exist real valued constants $\mathbb{L}_{\mathfrak{F}_1}$ and $\mathbb{L}_{\mathfrak{F}_2}$, and for all $\mu, \upsilon, \omega_1, \omega_2 \in \mathbb{R}$,

$$\begin{aligned}
\left|\mathfrak{F}_1(x, \upsilon) - \psi_1(x, \omega_1)\right| &\le \mathbb{L}_{\mathfrak{F}_1} \left|\upsilon - \omega_1\right|, \\
\left|\mathfrak{F}_2(x, \mu) - \psi_2(x, \omega_2)\right| &\le \mathbb{L}_{\mathfrak{F}_1} \left|\mu - \omega_2\right|.
\end{aligned} \tag{27}$$

4. Main Results

Theorem 14. *Let* $\mathfrak{F}_1(x) \in C[0,1]$ *be integrable function for FDEs and with integral boundary conditions; then the solution of*

$$\begin{aligned}
&\mathrm{D}^{\beta_1}\phi_p\left(\mathrm{D}^{\alpha_1}\mu(x)\right) + \mathfrak{F}_1(x) = 0, \\
&\qquad 0 < \beta_1 \le 1,\ 2 < \alpha_1 \le 3,\ x \in [0,1], \\
&\mathrm{D}^{\alpha_1}\mu(x)\big|_{x=0} = \mu(x)\big|_{x=0} = \mu''(x)\big|_{x=0} = 0, \\
&\mu'(x)\big|_{x=1} = \eta_1 I_T^{\gamma_1}\psi_1(\mu) \\
&\quad = \frac{\eta_1}{\Gamma(\gamma_1)} \int_0^P (P-\tau)^{\gamma_1 - 1} \psi_1(\mu(\tau))\, d\tau
\end{aligned} \tag{28}$$

is provided by

$$\begin{aligned}
\mu(x) &= \int_0^1 \Omega_{\alpha_1}(x,\tau)\, \phi_q\left(I^{\beta_1}\mathfrak{F}_1(\tau)\right) d\tau \\
&\quad + \frac{\eta_1 x}{\Gamma(\gamma_1)} \int_{0q}^P (P-\tau)^{\gamma_1 - 1} \psi_1(\mu(\tau))\, d\tau,
\end{aligned} \tag{29}$$

where $\Omega_{\alpha_1}(x,\tau)$ is Green's function, given by

$$\Omega_{\alpha_1}(x,\tau) = \begin{cases} \dfrac{x(1-\tau)^{\alpha_1-2}}{\Gamma(\alpha_1-1)} - \dfrac{(x-\tau)^{\alpha_1-1}}{\Gamma(\alpha_1)}, & 0 \le \tau \le x \le 1, \\ \dfrac{x(1-\tau)^{\alpha_1-2}}{\Gamma(\alpha_1-1)}, & 0 \le x \le \tau \le 1. \end{cases} \tag{30}$$

Proof. Applying the operator I^{β_1} on (28) and using Lemma 3, we get from problem (28) the following equivalent integral form as

$$\phi_p\left(\mathrm{D}^{\alpha_1}\mu(x)\right) = -I^{\beta_1}\mathfrak{F}_1(x) + A_0. \tag{31}$$

By using conditions $\mathrm{D}^{\alpha_1}\mu(x)|_{x=0} = 0$, we get $A_0 = 0$. From (31), we have

$$\mathrm{D}^{\alpha_1}\mu(x) = -\phi_q\left(I^{\beta_1}\mathfrak{F}_1(x)\right). \tag{32}$$

Applying the operator I^{α_1} on (32) and using Lemma 3 again, we get from problem (32) the following equivalent integral form given by

$$\mu(x) = -\mathcal{I}^{\alpha_1}\left(\phi_q I^{\beta_1}\mathfrak{F}_1(x)\right) + A_1 + A_2 x + A_3 x^2. \tag{33}$$

By using the condition $\mu(x)|_{x=0} = \mu''(x)|_{x=0} = 0$ in (33), we obtain $A_1 = A_3 = 0$. Also in view of condition $\mu'(x)|_{x=1} = \eta_1 I_T^{\gamma}\psi_1(\mu)$ in (33), we get

$$\begin{aligned} A_2 &= \frac{1}{\Gamma(\alpha_1-1)}\int_0^1 (1-\tau)^{\alpha_1-2}\phi_q\left(I^{\beta_1}\mathfrak{F}_1(x)\right)d\tau \\ &\quad + \frac{\eta_1}{\Gamma\gamma_1}\int_0^P (P-\tau)^{\gamma_1-1}\psi_1(\mu(\tau))\,d\tau. \end{aligned} \tag{34}$$

By substituting the values of A_1, A_2, and A_3 in (33), we get the following integral equation:

$$\begin{aligned} \mu(x) &= \left[\frac{1}{\Gamma(\alpha_1-1)}\int_0^1 x(1-\tau)^{\alpha_1-2} \right. \\ &\quad \left. - \frac{1}{\Gamma(\alpha_1)}\int_0^x (x-\tau)^{\alpha_1-1}\right]\phi_q\left(I^{\beta_1}\mathfrak{F}_1(\tau)\right)d\tau \\ &\quad + \frac{\eta_1 x}{\Gamma(\gamma_1)}\int_0^P (P-\tau)^{\gamma_1-1}\psi_1(\mu(\tau))\,d\tau \\ &= \int_0^1 \Omega_{\alpha_1}(x,\tau)\phi_q\left(I^{\beta_1}\mathfrak{F}_1(\tau)\right)d\tau + \frac{\eta_1 x}{\Gamma(\gamma_1)} \\ &\quad \cdot \int_0^P (P-\tau)^{\gamma_1-1}\psi_1(\mu(\tau))\,d\tau. \end{aligned} \tag{35}$$

□

According to Theorem 14, the equivalent system of Hammerstein type integral equations corresponding to coupled system (6) is given by

$$\begin{aligned} \mu(x) &= \int_0^1 \Omega_{\alpha_1}(x,\tau)\phi_q\left(I^{\beta_1}\mathfrak{F}_1(\tau,\nu(\tau))\right)d\tau \\ &\quad + \frac{\eta_1 x}{\Gamma(\gamma_1)}\int_0^P (P-\tau)^{\gamma_1-1}\psi_1(\mu(\tau))\,d\tau, \\ \upsilon(x) &= \int_0^1 \Omega_{\alpha_2}(x,\tau)\phi_q\left(I^{\beta_2}\mathfrak{F}_2(\tau,\mu(\tau))\right)d\tau \\ &\quad + \frac{\eta_2 x}{\Gamma(\gamma_2)}\int_0^P (P-\tau)^{\gamma_2-1}\psi_2(\upsilon(\tau))\,d\tau, \end{aligned} \tag{36}$$

where $\Omega_{\alpha_2}(x,\tau)$ is defined as

$$\Omega_{\alpha_2}(x,\tau) = \begin{cases} \dfrac{x(1-\tau)^{\alpha_2-2}}{\Gamma(\alpha_2-1)} - \dfrac{(x-\tau)^{\alpha_2-1}}{\Gamma(\alpha_2)}, & 0 \le \tau \le x \le 1, \\ \dfrac{x(1-\tau)^{\alpha_2-2}}{\Gamma(\alpha_2-1)}, & 0 \le x \le \tau \le 1. \end{cases} \tag{37}$$

From $\Omega_{\alpha_1}(x,\tau)$ and $\Omega_{\alpha_2}(x,\tau)$ clearly,

$$\begin{aligned} \max_{x\in J}\left|\Omega_{\alpha_1}(x,\tau)\right| &= \frac{(1-\tau)^{\alpha_1-2}}{\Gamma(\alpha_1-1)}, \\ \max_{t\in J}\left|\Omega_{\alpha_2}(x,\tau)\right| &= \frac{(1-\tau)^{\alpha_2-2}}{\Gamma(\alpha_2-1)}. \end{aligned} \tag{38}$$

Further, we define the operators $\varphi_1 : \mathscr{L}_1 \to \mathscr{L}_1$ and $\varphi_2 : \mathscr{L}_2 \to \mathscr{L}_2$ by

$$\begin{aligned} \varphi_1\mu(x) &= \frac{\eta_1 x}{\Gamma(\gamma_1)}\int_0^P (P-\tau)^{\gamma_1-1}\psi_1(\mu(\tau))\,d\tau, \\ &\qquad x \in [0,1], \\ \varphi_2\upsilon(x) &= \frac{\eta_2 x}{\Gamma(\gamma_2)}\int_0^P (P-\tau)^{\gamma_2-1}\psi_2(\upsilon(\tau))\,d\tau, \\ &\qquad x \in [0,1], \end{aligned} \tag{39}$$

and $\Upsilon_i : \mathscr{L} \to \mathscr{L}$ for $(i = 1, 2)$ by

$$\begin{aligned} \Upsilon_1\upsilon(x) &= \int_0^1 \Omega_{\alpha_1}(x,\tau)\phi_q\left(I^{\beta_1}\mathfrak{F}_1(\tau,\nu(\tau))\right)d\tau, \\ &\qquad x \in [0,1] \\ \Upsilon_2\mu(x) &= \int_0^1 \Omega_{\alpha_2}(x,\tau)\phi_q\left(I^{\beta_2}\mathfrak{F}_2(\tau,\mu(\tau))\right)d\tau, \\ &\qquad x \in [0,1]. \end{aligned} \tag{40}$$

Hence we have $\varphi(\mu,\nu) = (\varphi_1,\varphi_2)(\mu,\nu)$, $\Upsilon(\mu,\nu) = (\Upsilon_1,\Upsilon_2)(\mu,\nu)$, and $\mathbb{T}(\mu,\nu) = \varphi(\mu,\nu) + \Upsilon(\mu,\nu)$. Therefore the operator equation of Hammerstein type integral equations (36) is given by

$$(\mu,\nu)=\mathbb{T}(\mu,\nu)=\varphi(\mu,\nu)+\Upsilon(\mu,\nu). \tag{41}$$

Thus the solution of Hammerstein type equation (36) is the fixed points of operator equation (41).

Theorem 15. *In view of hypotheses $(\mathbb{A}_1)$ and $(\mathbb{A}_4)$, the operator φ is $\jmath$-Lipschitz and satisfies the growth condition given by*

$$\|\varphi(\mu,v)\|\le\mathbb{C}_\varphi\|(\mu,v)\|^{q_1}+\mathbb{M}_\varphi,\quad\forall(\mu,v)\in\mathscr{L}. \tag{42}$$

Proof. From condition $(\mathbb{A}_1)$ and using $x\le 1$, we get

$$\begin{aligned}&|\varphi_1(\mu)(x)-\varphi_1(\overline{\mu})(x)|\\&=\left|\frac{\eta_1}{\Gamma(\gamma_1)}\int_0^P(P-\tau)^{\gamma_1-1}[\psi_1(\mu)-\psi_1(\overline{\mu})]\,d\tau\right|\\&\le\frac{\eta_1}{\Gamma(\gamma_1)}\int_0^P(P-\tau)^{\gamma_1-1}|\psi_1(\mu)-\psi_1(\overline{\mu})|\,d\tau,\end{aligned} \tag{43}$$

which implies that $|\varphi_1(\mu)(x)-\varphi_2(\overline{\mu})(x)|\le\overline{\mathbb{K}}_{\psi_1}\|\mu-\overline{\mu}\|$, where $\overline{\mathbb{K}}_{\psi_1}=\mathbb{K}_{\psi_1}P^{\gamma_1}/\Gamma(\gamma_1+1)\in[0,1)$. To obtain the growth condition we have

$$\begin{aligned}|\varphi_1(\mu)(x)|&=\left|\frac{\eta_1}{\Gamma(\gamma_1)}\int_0^P(P-\tau)^{\gamma_1-1}\psi_1(\mu(\tau))\,d\tau\right|\\&\le\frac{\eta_1}{\Gamma(\gamma_1)}\int_0^P(P-\tau)^{\gamma_1-1}|\psi_1(\mu(\tau))|\,d\tau.\end{aligned} \tag{44}$$

Upon simplification, we get from (44)

$$\|\varphi_1\mu\|\le\frac{\eta_1P^{\gamma_1}}{\Gamma(\gamma_1+1)}\left[\mathbb{C}_{\psi_1}\|\mu\|^{q_1}+\mathbb{M}_{\psi_1}\right]. \tag{45}$$

Similarly, we get

$$\|\varphi_2v\|\le\frac{\eta_2P^{\gamma_2}}{\Gamma(\gamma_2+1)}\left[\mathbb{C}_{\psi_2}\|v\|^{q_1}+\mathbb{M}_{\psi_2}\right]. \tag{46}$$

Now

$$\begin{aligned}&\|\varphi(\mu,v)\|\\&\le\frac{\eta_1P^{\gamma_1}}{\Gamma(\gamma_1+1)}\left[\mathbb{C}_{\psi_1}\|\mu\|^{q_1}+\mathbb{M}_{\psi_1}\right]\\&\quad+\frac{\eta_2P^{\gamma_2}}{\Gamma(\gamma_2+1)}\left[\mathbb{C}_{\psi_2}\|v\|^{q_1}+\mathbb{M}_{\psi_2}\right]\\&\le\left(\frac{\eta_1P^{\gamma_1}}{\Gamma(\gamma_1+1)}\mathbb{C}_{\psi_1}\|\mu\|^{q_1}+\frac{\eta_2P^{\gamma_2}}{\Gamma(\gamma_2+1)}\mathbb{C}_{\psi_2}\|v\|^{q_1}\right)\\&\quad+\left(\frac{\eta_1P^{\gamma_1}\mathbb{M}_{\psi_1}}{\Gamma(\gamma_1+1)}+\frac{\eta_2P^{\gamma_2}\mathbb{M}_{\psi_2}}{\Gamma(\gamma_2+1)}\right)\\&\le\mathbb{C}_\varphi\left[\|\mu\|^{q_1}+\|v\|^{q_1}\right]+\mathbb{M}_\varphi=\mathbb{C}_\varphi\|(\mu,v)\|^{q_1}+\mathbb{M}_\varphi,\end{aligned} \tag{47}$$

where

$$\begin{aligned}&\max\left\{\frac{\eta_1P^{\gamma_1}}{\Gamma(\gamma_1+1)}\mathbb{C}_{\psi_1},\frac{\eta_2P^{\gamma_2}}{\Gamma(\gamma_2+1)}\mathbb{C}_{\psi_2}\right\}=\mathbb{C}_\varphi,\\&\mathbb{M}_\varphi=\frac{\eta_1P^{\gamma_1}\mathbb{M}_{\psi_1}}{\Gamma(\gamma_1+1)}+\frac{\eta_2P^{\gamma_2}\mathbb{M}_{\psi_2}}{\Gamma(\gamma_2+1)}.\end{aligned} \tag{48}$$

□

Theorem 16. *In view of hypothesis $(\mathbb{A}_3)$, the operator Υ is continuous and satisfies the growth condition given by*

$$\|\Upsilon(\mu,v)\|^{p_1}\le\digamma\|(\mu,v)\|^{p_1}+\Xi, \tag{49}$$

where $\digamma=\wp(a+b)$, $\wp=\max\{((q-1)m_1^{q-2}/\Gamma(\beta_1+1))(1/\Gamma(\alpha_1+1)),((q-1)m_2^{q-2}/\Gamma(\beta_2+1))(1/\Gamma(\alpha_2+1))\}$, and $\Xi=\wp(\mathbb{M}_1^*+\mathbb{M}_2^*)$ for each $(\mu,v)\in\mathscr{L}$.

Proof. Consider bounded set $\mathbb{B}_r=\{(\mu,v)\in\mathscr{L}:\|(\mu,v)\|\le r\}$ with sequence (μ_n,v_n) converging to (μ,v) in $\mathbb{B}_r$. We have to show that $\|\Upsilon(\mu_n,v_n)-\Upsilon(\mu,v)\|\to 0$ as $n\to\infty$. Therefore, we have to consider

$$\begin{aligned}&|\Upsilon_1(v_n(x))-\Upsilon(v(x))|\le\left|\frac{x}{\Gamma(\alpha_1-1)}\int_0^1(1-\tau)^{\alpha_1-2}\right.\\&\cdot\left[\phi_q\left(I^\beta\mathfrak{F}_1(\tau,v_n(\tau))\right)\right.\\&\left.\left.-\phi_q\left(I^\beta\mathfrak{F}_1(\tau,v(\tau))\right)\right]d\tau\right|+\left|\frac{1}{\Gamma(\alpha_1)}\int_0^x(x\right.\\&-\tau)^{\alpha_1-1}\left[\phi_q\left(I^\beta\mathfrak{F}_1(\tau,v_n(\tau))\right)\right.\\&\left.\left.-\phi_q\left(I^\beta\mathfrak{F}_1(\tau,v(\tau))\right)\right]d\tau\right|\le(q-1)\\&\cdot m_1^{q-2}\left[\frac{1}{\Gamma(\alpha_1-1)}\int_0^1(1-\tau)^{\alpha_1-2}-\frac{1}{\Gamma(\alpha_1)}\int_0^x(x\right.\\&\left.-\tau)^{\alpha_1-1}\right]\times\left|I^\beta\mathfrak{F}_1(\tau,v_n(\tau))-I^\beta\mathfrak{F}_1(\tau,v(\tau))\right|d\tau.\end{aligned} \tag{50}$$

Due to continuity of $\mathfrak{F}_1$, one has $\mathfrak{F}_1(\tau,v_n(\tau))\to\mathfrak{F}_1(\tau,v(\tau))$ as $n\to\infty$. Thus in view of Lebesgue dominated convergent theorem, we have $|I^\beta\mathfrak{F}_1(x,v_n(x))-I^\beta\mathfrak{F}_1(x,v(x))|\to 0$ as $n\to\infty$. Thus $|\Upsilon_1(v_n(x))-\Upsilon(v(x))|\to 0$, as $n\to\infty$. Hence Υ_1 is continuous. Now for growth condition (49), we have

$$\begin{aligned}|\Upsilon_1v(x)|&=\left|\int_0^1\Omega_{\alpha_1}(x,\tau)\phi_q\left(I^{\beta_1}\mathfrak{F}_1(\tau,v(\tau))\right)d\tau\right|\\&\le(q-1)m_1^{q-2}\left|\int_0^1\Omega_{\alpha_1}(x,\tau)\left(I^{\beta_1}\mathfrak{F}_1(\tau,v(\tau))\right)d\tau\right|,\end{aligned}$$

$$\begin{aligned}&\|\Upsilon_1v\|^{p_1}\\&\le\frac{(q-1)m_1^{q-2}}{\Gamma(\beta_1+1)}\left[\frac{1}{\Gamma(\alpha_1+1)}\right]\left(a\|v\|^{p_1}+\mathbb{M}_1^*\right),\end{aligned}$$

$$\begin{aligned}
\left|\Upsilon_2\mu(x)\right| &= \left|\int_0^1 \Omega_{\alpha_2}(x,\tau)\,\phi_q\left(I^{\beta_2}\mathfrak{F}_2(\tau,\mu(\tau))\right)ds\right| \\
&\le (q-1)\,m_2^{q-2}\left|\int_0^1 \Omega_{\alpha_2}(x,\tau)\left(I^{\beta_2}\mathfrak{F}_1(\tau,v(\tau))\right)ds\right|, \\
\left\|\Upsilon_2\mu\right\|^{p_1} & \\
&\le \frac{(q-1)\,m_2^{q-2}}{\Gamma(\beta_2+1)}\left[\frac{1}{\Gamma(\alpha_2+1)}\right]\left(b\left\|\mu\right\|^{p_1}+\mathbb{M}_2^*\right).
\end{aligned} \tag{51}$$

From, (51), we obtain the following result

$$\begin{aligned}
\left\|\Upsilon(\mu,v)\right\|^{p_1} &= \left\|\Upsilon_1(v)\right\|^{p_1}+\left\|\Upsilon_2(\mu)\right\|^{p_1} \\
&\le \wp\left(a\left\|v\right\|^{p_1}+\mathbb{M}_1^*\right)+\wp\left(b\left\|\mu\right\|^{p_1}+\mathbb{M}_2^*\right) \\
&\le \wp(a+b)\left(\left\|v\right\|^{p_1}+\left\|\mu\right\|^{p_1}\right) \\
&\quad+\wp\left(\mathbb{M}_1^*+\mathbb{M}_2^*\right)=F\left\|(\mu,v)\right\|^{p_1}+\Xi.
\end{aligned} \tag{52}$$

□

Theorem 17. *The operator $\Upsilon : \mathscr{L} \to \mathscr{L}$ is compact and $\jmath$-Lipschitz with constant zero.*

Proof. Consider a sequence $\{\mathfrak{F}_n\}$ in bounded set D such that D is subset of $\mathbb{B}_r$; in view of (49), we see

$$\left\|\Upsilon(\mu_n,v_n)\right\|^{p_1} \le F\left\|(\mu_n,v_n)\right\|^{p_1}+\Xi, \quad \text{for every } (\mu,v)\in\mathscr{L}. \tag{53}$$

Thus Υ is bounded for $(\mu_n,v_n)\in D$. Let us, for any $x_1,x_2\in[0,1]$, consider

$$\begin{aligned}
&\left|\Upsilon v_n(x_1)-\Upsilon v_n(x_2)\right| \\
&= \left|\int_0^1 \Omega_{\alpha_1}(x_1,\tau)\,\phi_q\left(I^{\beta_1}\mathfrak{F}_1(\tau,v_n(\tau))\right)d\tau\right. \\
&\quad\left.-\int_0^1 \Omega_{\alpha_1}(x_2,\tau)\,\phi_q\left(I^{\beta_1}\mathfrak{F}_1(\tau,v_n(\tau))\right)d\tau\right| \le (q \\
&\quad-1)\,m_1^{q-2}\left|\int_0^1 \Omega_1(x_1,\tau)-\int_0^1 \Omega_1(x_2,\tau)\right| \\
&\quad\cdot\left|\left(I^{\beta_1}\mathfrak{F}_1(\tau,v_n(\tau))\right)\right|d\tau \\
&\le \frac{(q-1)\,m_1^{q-2}}{\Gamma(\beta_1+1)}\left[\frac{(x_1-x_2)}{\Gamma(\alpha_1-1)}\int_0^1(1-\tau)^{\alpha_1-2}d\tau\right. \\
&\quad+\frac{1}{\Gamma(\alpha_1)}\left(\int_0^{x_1}(x_1-\tau)^{\alpha_1-1}d\tau\right. \\
&\quad\left.\left.-\int_0^{x_2}(x_2-\tau)^{\alpha_1-1}d\tau\right)\right]\left(a\left\|v_n\right\|^{p_1}+\mathbb{M}_1^*\right).
\end{aligned} \tag{54}$$

By simplification, we get the following result:

$$\begin{aligned}
&\left|\Upsilon_1 v_n(x_1)-\Upsilon_1 v_n(x_2)\right| \\
&\quad\le \frac{(q-1)\,m_1^{q-2}}{\Gamma(\beta_1+1)}\left[\frac{\left|x_1-x_2\right|}{\Gamma(\alpha_1)}+\frac{\left|x_1^{\alpha_1}-x_2^{\alpha_1}\right|}{\Gamma(\alpha_1+1)}\right] \\
&\quad\cdot\left(a\left\|\mu_n\right\|^{p_1}+\mathbb{M}_1^*\right).
\end{aligned} \tag{55}$$

And also in same fashion, one has

$$\begin{aligned}
&\left|\Upsilon_2\mu_n(x_1)-\Upsilon_2\mu_n(x_2)\right| \\
&\quad\le \frac{(q-1)\,m_2^{q-2}}{\Gamma(\beta_2+1)}\left[\frac{\left|x_1-x_2\right|}{\Gamma(\alpha_2)}+\frac{\left|x_1^{\alpha_2}-x_2^{\alpha_2}\right|}{\Gamma(\alpha_2+1)}\right] \\
&\quad\cdot\left(b\left\|v\right\|^{p_2}+\mathbb{M}_2^*\right).
\end{aligned} \tag{56}$$

Therefore if $x_1 \to x_2$, then the right hand side of both sides of (55) and (56) tends to zero. Thus Υ_1,Υ_2 are equicontinuous, and therefore $\Upsilon = (\Upsilon_1,\Upsilon_2)$ is equicontinuous on D. Hence, thanks to the Arzelá-Ascoli theorem, $\Upsilon(D)$ is compact. Also, by proposition Υ is $\jmath$-Lipschitz with constant zero. □

Remark 18. The results of Theorems 15, 16, and 17 are also hold for using $q_1 = p_1 = 1$.

Theorem 19. *In view of assumptions $(\mathbb{A}_1)$–$(\mathbb{A}_4)$ such that $\mathbb{C}_\varphi + F \le 1$, then the coupled system (6) has at least one solution $(\mu,v)\in\mathscr{L}$ together with condition that the set of the solutions $\mathscr{B}$ is bounded in $\mathscr{L}$.*

Proof. φ and Υ are continuous and $\jmath$-Lipschitz with constant $\mathbb{C}_\varphi$ and 0, respectively. Thanks to Theorem 10, $\mathbb{T}$ is strict $\jmath$-contraction, and then consider a set

$$\mathscr{B} = \left\{(\mu,v)\in\mathscr{L}\colon \lambda\in[0,1] \mid (\mu,v)=\lambda\mathbb{T}(\mu,v)\right\}. \tag{57}$$

To prove that $\mathscr{B}$ is bounded, let

$$\begin{aligned}
\left\|(\mu,v)\right\| &= \left\|\lambda\mathbb{T}(\mu,v)\right\| \le \left\|\lambda\varphi(\mu,v)\right\|+\left\|\lambda\Upsilon(\mu,v)\right\| \\
&\le \mathbb{C}_\varphi\left\|(\mu,v)\right\|+\mathbb{M}_\varphi+F\left\|(\mu,v)\right\|+\Xi \\
&= \left(\mathbb{C}_\varphi+F\right)\left\|(\mu,v)\right\|+\mathbb{M}_\varphi+\Xi.
\end{aligned} \tag{58}$$

Therefore, the set of solutions $\mathscr{B}$ is bounded. □

Theorem 20. *Assume that hypotheses $(\mathbb{A}_1)$–$(\mathbb{A}_4)$ hold. Then system (6) has a unique solution if and only if $\Theta < 1$, where*

$$\begin{aligned}
\Theta &= \frac{\eta_1\mathbb{K}_{\psi_1}P^{\gamma_1}}{\Gamma(\gamma_1+1)}+\frac{\eta_2\mathbb{K}_{\psi_2}T^{\gamma_2}}{\Gamma(\gamma_2+1)}+\frac{(q-1)\,m_1^{q-2}\mathbb{L}_{\mathfrak{F}_1}}{\Gamma(\beta_1+1)\,\Gamma(\alpha_1)} \\
&\quad+\frac{(q-1)\,m_2^{q-2}\mathbb{L}_{\mathfrak{F}_2}}{\Gamma(\beta_2+1)\,\Gamma\alpha_2}.
\end{aligned} \tag{59}$$

Proof. Let (μ,v) and $(\overline{\mu},\overline{v})\in\mathscr{L}$ be two solutions; then

$$\begin{aligned}
\left|\mathbb{T}(\mu,v)-\mathbb{T}(\overline{\mu},\overline{v})\right| &\le \left|\varphi(\mu,v)-\varphi(\overline{\mu},\overline{v})\right| \\
&\quad+\left|\Upsilon(\mu,v)-\Upsilon(\overline{\mu},\overline{v})\right|;
\end{aligned} \tag{60}$$

therefore by simplification (60), we get the following result:

$$\begin{aligned}\left\|\mathbb{T}(\mu,v)-\mathbb{T}(\bar{\mu},\bar{v})\right\| &\leq \left(\frac{\eta_1\mathbb{K}_{\psi_1}P^{\gamma_1}}{\Gamma(\gamma_1+1)}+\frac{\eta_2\mathbb{K}_{\psi_2}T^{\gamma_2}}{\Gamma(\gamma_2+1)}\right.\\ &\left.+\frac{(q-1)m_1^{q-2}\mathbb{L}_{\mathfrak{F}_1}}{\Gamma(\beta_1+1)\Gamma\alpha_1}+\frac{(q-1)m_2^{q-2}\mathbb{L}_{\mathfrak{F}_2}}{\Gamma(\beta_2+1)\Gamma\alpha_2}\right)\|(\mu,v)\\ &-(\bar{\mu},\bar{v})\|\leq\Theta\left\|(\mu,v)-(\bar{\mu},\bar{v})\right\|.\end{aligned}\tag{61}$$

Thus the operator $\mathbb{T}$ is a contraction. Hence the uniqueness of solution to system (6) follows due to the Banach fixed point theorem. □

5. Hyers-Ulam Stability of Coupled System

In the present section, we derive the Hyers-Ulam type stability for the solution of the considered problem.

Theorem 21. *By assumptions* $(\mathbb{A}_1)$–$(\mathbb{A}_4)$, *system (6) is Hyers-Ulam stable.*

Proof. By Theorem 20 and Definition 13, let (λ_1,λ_2) be the exact solution, and let (μ^*,v^*) be any other solution of system (36). Then from equation of (36) we have

$$\begin{aligned}\left|\lambda_1(x)-\mu^*(x)\right| &\leq \left|\int_0^1\Omega_{\alpha_1}(x,\tau)\,\phi_q\right.\\ &\cdot\left[I^{\beta_1}\left(\mathfrak{F}_1(\tau,y(\tau))-\mathfrak{F}_1(\tau,v^*(\tau))\right)\right]d\tau+\frac{\eta_1 x}{\Gamma(\gamma_1)}\\ &\left.\cdot\int_0^P(P-\tau)^{\gamma_1-1}\left(\psi_1(x)-\psi_1(\mu^*)\right)d\tau\right|\end{aligned}\tag{62}$$

$$\begin{aligned}\text{implies that }\left\|\lambda_1-\mu^*\right\| &\leq \frac{(q-1)m_1^{q-2}\mathbb{L}_{\mathfrak{F}_1}}{\Gamma(\beta_1+1)\Gamma(\alpha_1)}\left\|x-v^*\right\|\\ &+\frac{\eta_1P^{\gamma_1}\mathbb{K}_{\psi_1}}{\Gamma(\gamma_1+1)}\left\|y-\mu^*\right\|\leq D_1\xi_1+D_2\xi_2,\end{aligned}\tag{63}$$

where $D_1=(q-1)m_1^{q-2}\mathbb{L}_{\mathfrak{F}_1}/\Gamma(\beta_1+1)\Gamma(\alpha_1)$ and $D_2=\eta_1P^{\gamma_1}\mathbb{K}_{\psi_1}/\Gamma(\gamma_1+1)$. By the same process we also get that

$$\left\|\lambda_2-v^*\right\|\leq D_3\xi_1+D_4\xi_2,\tag{64}$$

where $D_3=(q-1)m_1^{q-2}\mathbb{L}_{\mathfrak{F}_2}/\Gamma(\beta_2+1)\Gamma(\alpha_2)$ and $D_4=\eta_2P^{\gamma_2}\mathbb{K}_{\psi_2}/\Gamma(\gamma_2+1)$.

Hence in view of (62) and (64), the system of integral equation (36) is Hyers-Ulam stable, and consequently, the solution of system (6) is Hyers-Ulam stable. □

6. Illustrative Examples

Example 1. Consider the following coupled system of FDEs with p-Laplacian operator and fractional order differential and integral boundary conditions of the type

$$\begin{aligned}&D^{1/2}\phi_p\left(D^{5/2}\mu(x)\right)+\left(\frac{x}{99}+19\sin|v(x)|\right)=0,\\ &D^{1/2}\phi_p\left(D^{5/2}v(x)\right)+\left(\frac{x}{100}+3\sin|\mu(x)|+75\right)=0,\end{aligned}\tag{65}$$

$$\begin{aligned}&D^{5/2}\,\mu(x)|_{x=0}=0=\mu(x)|_{x=0}=\mu''(x)\big|_{x=0},\\ &\mu'(x)\big|_{x=1}=\frac{1}{3\Gamma(3/2)}\int_0^1(1-\tau)^{1/2}\cos(\mu)\,d\tau,\\ &D^{5/2}\,v(x)|_{x=0}=0=v(x)|_{x=0}=v''(x)\big|_{x=0},\\ &v'(x)\big|_{x=1}=\frac{1}{3\Gamma(3/2)}\int_0^1(1-\tau)^{1/2}\cos(v)\,d\tau,\end{aligned}\tag{66}$$

where $x\in[0,1]$, $P=1$, $p=3$, $\alpha_i=5/2$, $\beta_i=1/2$, $\eta_i=1/3$, $\gamma_i=3/2$, where $i=1,2$, $\mathbb{K}_{\psi_1},\mathbb{K}_{\psi_2}=1/5$, $\mathbb{M}_i=2$, and $\mathbb{L}_{\mathfrak{F}_i}=1/6$. By simple calculation we obtain the following:

$$\begin{aligned}&\frac{(1/3)(1/5)}{\Gamma(3/2+1)}+\frac{(1/3)(1/5)}{\Gamma(3/2+1)}+\frac{(3/2-1)2^{-1/2}(1/6)}{\Gamma(1/2+1)\Gamma(5/2)}\\ &\quad+\frac{(3/2-1)2^{-1/2}(1/6)}{\Gamma(1/2+1)\Gamma(5/2)}<1.\end{aligned}\tag{67}$$

Therefor from Theorem 20, we concluded that (65) has unique solution. Similarly, the conditions of Theorem 21 can be verified easily. Thus the solution of system (65) is Hyers-Ulam stable.

7. Conclusion

We have investigated sufficient conditions for existence and uniqueness of solutions to a coupled system of nonlinear FDEs with fractional integral boundary conditions with nonlinear p-Laplacian operator by using topological degree method. Further, we have established some adequate conditions for the Hyers-Ulam stability to the proposed problem.

Conflicts of Interest

The authors declare that no conflicts of interest exist regarding this manuscript.

Authors' Contributions

All authors equally contributed to this paper and approved the final version.

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Research Article

Analytical Solution of the Fractional Fredholm Integrodifferential Equation Using the Fractional Residual Power Series Method

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We study the solution of fractional Fredholm integrodifferential equation. A modified version of the fractional power series method (RPS) is presented to extract an approximate solution of the model. The RPS method is a combination of the generalized fractional Taylor series and the residual functions. To show the efficiency of the proposed method, numerical results are presented.

1. Introduction

Fractional Fredholm integrodifferential equations have several applications in sciences and engineering. The closed form of the exact solution of such problems is difficult to find and in most of the cases is not available. For this reason, researchers are looking for the numerical solutions of such problems. Irandoust-Pakchin and Abdi-mazraeh [1] used the variational iteration method for solving fractional integrodifferential equations with the nonlocal boundary conditions. Adomian decomposition method is used in [2, 3] while the homotopy perturbation method is used in [4, 5]. Wazwaz [6–8] studied the Fredholm integral equations of the form

$$u(x) = f(x) + \lambda \int_a^b K(x,t)\, u(t)\, dt, \tag{1}$$

where a and b are constants, λ is a parameter, $u(x)$ is a smooth function as the discussion required, and $K(x,t) \in C(\mathbb{R} \times [a,b])$ is the kernel. In this paper, we study the generalization of the above problem. We study the following class of fractional Fredholm integrodifferential equations of the form

$$D^{\alpha} u(x) = f(x) + \lambda \int_a^b K(x,t)\, u^m(t)\, dt, \qquad 0 < \alpha \le 1,\ x \in \mathbb{R},\ a \le t \le b, \tag{2}$$

subject to

$$u(a) = a_0. \tag{3}$$

The fractional derivative in (2) is in the Caputo sense. If $\alpha = 0$, we do not need the initial condition (3) and we return back to the problem which is discussed by Wazwaz [8]. In the following definition and theorem, we write the definition of Caputo derivative as well as the power rule which we are using in this paper. For more details on the geometric and physical interpretation for Caputo fractional derivatives, see [9].

Definition 1. For m to be the smallest integer that exceeds α, the Caputo fractional derivatives of order $\alpha > 0$ are defined as

$$D^{\alpha} u(x) = \begin{cases} \dfrac{1}{\Gamma(m-\alpha)} \displaystyle\int_0^x (x-\tau)^{m-\alpha-1} \frac{d^m u(\tau)}{d\tau^m} d\tau, & m-1 < \alpha < m, \\ \dfrac{d^m u(x)}{dx^m}, & \alpha = m \in \mathbb{N}. \end{cases} \tag{4}$$

Theorem 2. *The Caputo fractional derivative of the power function satisfies*

$$D^{\alpha} x^p = \begin{cases} \dfrac{\Gamma(p+1)}{\Gamma(p-\alpha+1)} x^{p-\alpha}, & m-1 < \alpha < m,\ p > m-1,\ p \in \mathbb{R}, \\ 0, & m-1 < \alpha < m,\ p \le m-1,\ p \in \mathbb{N}. \end{cases} \tag{5}$$

Definition 3. The Riemann-Liouville fractional integral operator of order α of $u(x) \in C_\gamma$, $\gamma > -1$, is defined as

$$I^\alpha u(x) = \begin{cases} \dfrac{1}{\Gamma(\alpha)} \displaystyle\int_0^x (x-\tau)^{\alpha-1} u(\tau)\, d\tau, & 0 \le m-1 < \alpha < m, \\ u(x), & \alpha = m \in \mathbb{N}, \end{cases} \quad (6)$$

where C_γ is the space of real functions $u(x)$, $x \in \mathfrak{R}$, such that, for each $u(x)$, there exists a real number $\rho > \gamma$ such that $u(x) = x^\rho u_1(x)$ where $u_1(x) \in C(\mathfrak{R})$.

In addition, $u(x) \in C_\gamma^m$ if $u^{(m)}(x) \in C_\gamma$ where $m \in \mathbb{N}$. We present the following definition and some properties of the fractional power series which are used in this paper. More details can be found in [10].

Definition 4. A power series expansion of the form

$$\sum_{m=0}^{\infty} c_m (x-x_0)^{m\alpha} = c_0 + c^1 (x-x_0)^\alpha + c^2 (x-x_0)^{2\alpha} + \cdots, \quad (7)$$

where $0 \le m-1 < \alpha \le m$, is called fractional power series FPS about. $x = x_0$.

Theorem 5. *Suppose that f has a fractional FPS representation at $x = x_0$ of the form*

$$g(x) = \sum_{m=0}^{\infty} c_m (x-x_0)^{m\alpha}, \quad x_0 \le x < x_0 + \beta. \quad (8)$$

If $D^{m\alpha} g(x)$, $m = 0, 1, 2, \ldots$, are continuous on $\mathbb{R}$, then $c_m = D^{m\alpha} g(x_0))/\Gamma(1 + m\alpha)$.

Theorem 6. *Let $u(x) \in C([x_0, x_0 + R))$ and $D^{i\alpha} u(x) \in C((x_0, x_0 + R))$ for $i = 0, 1, \ldots, m+1$ where $0 \le m-1 < \alpha \le m$. Then,*

$$I^{(m+1)\alpha} D^{(m+1)\alpha} u(x) = \frac{D^{(m+1)\alpha}(\varpi)}{\Gamma((m+1)\alpha + 1)} (x-x_0)^{(m+1)\alpha+1}, \quad x_0 \le \varpi \le x < x_0 + R. \quad (9)$$

Theorem 7. *Let $u(x) \in C([x_0, x_0 + R))$, $D^{i\alpha} u(x) \in C((x_0, x_0 + R))$, and $D^{i\alpha} u(x)$ can differentiate $(m-1)$ with respect to x for $i = 0, 1, \ldots, m+1$ where $0 \le m-1 < \alpha \le m$. Then,*

$$u(x) = \sum_{k=0}^{m} \frac{D^{k\alpha}(\varpi)}{\Gamma(k\alpha + 1)} (x-x_0)^{k\alpha} + \frac{D^{(m+1)\alpha}(\varpi)}{\Gamma((m+1)\alpha + 1)} (x-x_0)^{(m+1)\alpha+1}, \quad x_0 \le \varpi \le x < x_0 + R. \quad (10)$$

Theorem 8. *Let $|D^{(m+1)\alpha} u(x)| \in A$ on $x_0 \le x < s$ where $m-1 < \alpha \le m$. Then, the reminder R_m satisfies*

$$|R_m| \le \frac{A}{\Gamma((m+1)\alpha + 1)} (x-x_0)^{(m+1)\alpha}, \quad x_0 \le x < s. \quad (11)$$

This paper is organized as follows. A description of the modified fractional power series method (MFPS) for approximating the fractional Fredholm integrodifferential equations problem (2)-(3) is presented in Section 2. Several numerical examples are discussed in Section 3. Conclusions and closing remarks are given in Section 4.

2. Algorithm of the MFPS Method

Consider the following class of fractional Fredholm integrodifferential equations of the form

$$u(x) = f(x) + \lambda \int_a^b K(x,t)\, u(t)\, dt, \quad 0 < \alpha \le 1 \quad (12)$$

subject to

$$u(a) = a_0. \quad (13)$$

Using the MFPS method, the solution problem (2)-(3) can be written the fractional power series form as

$$u(x) = \sum_{n=0}^{\infty} f_n \frac{(x-a)^{n\alpha}}{\Gamma(1+n\alpha)}. \quad (14)$$

To obtain the approximate values of the above series (14), the kth truncated series $u_k(x)$ is written in the form

$$u_k(x) = \sum_{n=0}^{k} f_n \frac{(x-a)^{n\alpha}}{\Gamma(1+n\alpha)}. \quad (15)$$

Since $u(a) = f_0 = a_0$, we rewrite (14) as

$$u_k(x) = a_0 + \sum_{n=1}^{k} f_n \frac{(x-a)^{n\alpha}}{\Gamma(1+n\alpha)}, \quad k = 1, 2, \ldots, \quad (16)$$

where $u_0(x) = a_0$ is considered to be the 0th MRPS approximate solution of $u(x)$. To find the values of the MFPS-coefficients f_k, $k = 1, 2, 3, \ldots$, we solve the fractional differential equation

$$D^{(k-1)\alpha} \mathrm{Res}_k(u(a)) = 0, \quad k = 1, 2, 3, \ldots, \quad (17)$$

where $\mathrm{Res}_k(u(a))$ is the kth residual function and is defined by

$$\mathrm{Res}_k(u(x)) = D^\alpha u_k(x) - f(x) - \lambda \int_a^b K(x,t)\, u_k(t)\, dt. \quad (18)$$

To determine the coefficient f_1 in the expansion (15), we substitute the 1st RPS approximate solution

$$u_1(x) = a_0 + f_1 \frac{(x-a)^{\alpha}}{\Gamma(1+\alpha)} \tag{19}$$

into (18) to get

$$\begin{aligned}
&\operatorname{Res}_1(u(a)) \\
&= \left(D^{\alpha} u_1(x) - f(x) - \lambda \int_a^b K(x,t)\, u_1(t)\, dt\right)_{x=a} \\
&= f_1 - f(a) - \lambda \int_a^b a_0 K(a,t)\, dt \\
&\quad - \lambda f_1 \int_a^b \frac{(t-a)^{\alpha}}{\Gamma(1+\alpha)} K(x,t)\, dt = 0.
\end{aligned} \tag{20}$$

Then, we solve $\operatorname{Res}_1(a) = 0$ to get

$$f_1 = \frac{f(a) + \lambda \int_a^b a_0 K(a,t)\, dt}{1 - \lambda \int_a^b \left((t-a)^{\alpha}/\Gamma(1+\alpha)\right) K(a,t)\, dt}. \tag{21}$$

To find f_2, we substitute the 2nd RPS approximate solution

$$u_2(x) = a_0 + f_1 \frac{(x-a)^{\alpha}}{\Gamma(1+\alpha)} + f_2 \frac{(x-a)^{2\alpha}}{\Gamma(1+2\alpha)} \tag{22}$$

into the 2nd residual function $\operatorname{Res}_2(u(x))$ such that

$$\begin{aligned}
&\operatorname{Res}_2(u(x)) = D^{\alpha} u_2(x) - f(x) - \lambda \int_a^b K(x,t) \\
&\quad \cdot u_2(t)\, dt = f_1 + f_2 \frac{(x-a)^{\alpha}}{\Gamma(1+\alpha)} - f(x) \\
&\quad - \lambda \int_a^b K(x,t) \\
&\quad \cdot \left(a_0 + f_1 \frac{(t-a)^{\alpha}}{\Gamma(1+\alpha)} + f_2 \frac{(t-a)^{2\alpha}}{\Gamma(1+2\alpha)}\right) dt.
\end{aligned} \tag{23}$$

Then, we solve $D^{\alpha}\operatorname{Res}_2(u(a)) = 0$ to get

$$f_2 = \frac{D^{\alpha} f(a) + \lambda a_0 \int_a^b D_x^{\alpha} K(a,t)\, dt + \lambda f_1 \int_a^b \left((t-a)^{\alpha}/\Gamma(1+\alpha)\right) D_x^{\alpha} K(a,t)\, dt}{1 - \lambda \int_a^b \left((t-a)^{2\alpha}/\Gamma(1+2\alpha)\right) D_x^{\alpha} K(x,t)\, dt}. \tag{24}$$

To find f_3, we substitute the 3rd RPS approximate solution

$$\begin{aligned}
u_3(x) &= a_0 + f_1 \frac{(x-a)^{\alpha}}{\Gamma(1+\alpha)} + f_2 \frac{(x-a)^{2\alpha}}{\Gamma(1+2\alpha)} \\
&\quad + f_3 \frac{(x-a)^{3\alpha}}{\Gamma(1+3\alpha)}
\end{aligned} \tag{25}$$

into the 3rd residual function $\operatorname{Res}_3(u(x))$ such that

$$\begin{aligned}
&\operatorname{Res}_3(u(x)) = D^{\alpha} u_3(x) - f(x) - \lambda \int_a^b K(x,t) \\
&\quad \cdot u_3(t)\, dt = f_1 + f_2 \frac{(x-a)^{\alpha}}{\Gamma(1+\alpha)} + f_3 \frac{(x-a)^{2\alpha}}{\Gamma(1+2\alpha)} \\
&\quad - f(x) - \lambda \int_a^b K(x,t) \left(a_0 + f_1 \frac{(t-a)^{\alpha}}{\Gamma(1+\alpha)}\right. \\
&\quad \left. + f_2 \frac{(t-a)^{2\alpha}}{\Gamma(1+2\alpha)} + f_3 \frac{(t-a)^{3\alpha}}{\Gamma(1+3\alpha)}\right) dt.
\end{aligned} \tag{26}$$

Then, we solve $D^{2\alpha}\operatorname{Res}_3(u(a)) = 0$ to get

$$f_3 = \frac{f_2 + D^{2\alpha} f(a) + \lambda \sum_{k=0}^{2} f_k \int_a^b \left((t-a)^{k\alpha}/\Gamma(1+k\alpha)\right) D_x^{2\alpha} K(a,t)\, dt}{1 - \lambda \int_a^b \left((t-a)^{3\alpha}/\Gamma(1+3\alpha)\right) D_x^{2\alpha} K(a,t)\, dt}. \tag{27}$$

To find f_4, we substitute the 4th RPS approximate solution

$$\begin{aligned}
u_4(x) &= a_0 + f_1 \frac{(x-a)^{\alpha}}{\Gamma(1+\alpha)} + f_2 \frac{(x-a)^{2\alpha}}{\Gamma(1+2\alpha)} \\
&\quad + f_3 \frac{(x-a)^{3\alpha}}{\Gamma(1+3\alpha)} + f_4 \frac{(x-a)^{4\alpha}}{\Gamma(1+4\alpha)}
\end{aligned} \tag{28}$$

into the 4th residual function $\operatorname{Res}_4(u(x))$ such that

$$\begin{aligned}
&\operatorname{Res}_4(u(x)) = D^{\alpha} u_4(x) - f(x) - \lambda \int_a^b K(x,t) \\
&\quad \cdot u_4(t)\, dt = f_1 + f_2 \frac{(x-a)^{\alpha}}{\Gamma(1+\alpha)} + f_3 \frac{(x-a)^{2\alpha}}{\Gamma(1+2\alpha)}
\end{aligned}$$

$$+ f_4\frac{(x-a)^{4\alpha}}{\Gamma(1+4\alpha)} - f(x) - \lambda\int_a^b K(x,t)\left(a_0 + f_1\frac{(x-a)^{\alpha}}{\Gamma(1+\alpha)} + f_2\frac{(x-a)^{2\alpha}}{\Gamma(1+2\alpha)} + f_3\frac{(x-a)^{3\alpha}}{\Gamma(1+3\alpha)} + f_4\frac{(x-a)^{4\alpha}}{\Gamma(1+4\alpha)}\right)dt. \tag{29}$$

Then, we solve $D^{3\alpha}\mathrm{Res}_4(u(a)) = 0$ to get

$$f_4 = \frac{f_3 + D^{3\alpha}f(a) + \lambda\sum_{k=0}^{3} f_k\int_a^b\left((t-a)^{k\alpha}/\Gamma(1+k\alpha)\right)D_x^{2\alpha}K(a,t)\,dt}{1-\lambda\int_a^b\left((t-a)^{4\alpha}/\Gamma(1+4\alpha)\right)D_x^{2\alpha}K(a,t)\,dt}. \tag{30}$$

Using similar argument, we find that

$$f_n = \frac{f_{n-1} + D^{(n-1)\alpha}f(a) + \lambda\sum_{k=0}^{n-1} f_k\int_a^b\left((t-a)^{k\alpha}/\Gamma(1+k\alpha)\right)D_x^{(n-1)\alpha}K(a,t)\,dt}{1-\lambda\int_a^b\left((t-a)^{n\alpha}/\Gamma(1+n\alpha)\right)D_x^{(n-1)\alpha}K(a,t)\,dt}, \quad n = 1, 2, 3, \ldots. \tag{31}$$

Thus,

$$u_k(x) = a_0 + \sum_{n=1}^{k}\left(\frac{f_{n-1} + D^{(n-1)\alpha}f(a) + \lambda\sum_{k=0}^{n-1} f_k\int_a^b\left((t-a)^{k\alpha}/\Gamma(1+k\alpha)\right)D_x^{(n-1)\alpha}K(a,t)\,dt}{1-\lambda\int_a^b\left((t-a)^{n\alpha}/\Gamma(1+n\alpha)\right)D_x^{(n-1)\alpha}K(a,t)\,dt}\right)\frac{(x-a)^{n\alpha}}{\Gamma(1+n\alpha)}. \tag{32}$$

For $k = 1, 2, \ldots$.

3. Numerical Results

In this section, we present three examples to show the efficiency of the proposed method. We use Mathematica software to generate the results in this section.

Example 1. Consider the following fractional Fredholm integrodifferential equation:

$$D^{1/2}u(x) = \frac{32}{3\sqrt{\pi}}x^{1.5} + \frac{16}{3\sqrt{\pi}}x^{2.5} - 2x + \int_0^1 xtu(t), \quad x \in \mathbb{R} \tag{33}$$

subject to

$$u(0) = 0. \tag{34}$$

The exact solution is

$$u(x) = 4x^2 + 5x^3. \tag{35}$$

Using the same argument described in the previous section, we find that

$$\begin{aligned} &f_0 = f_1 = f_2 = f_3 = 0,\\ &f_4 = 8,\\ &f_5 = 0,\\ &f_6 = 30,\\ &f_n = 0, \quad n = 7, 8, \ldots. \end{aligned} \tag{36}$$

Thus,

$$u_6(x) = 4x^2 + 5x^3 \tag{37}$$

which is the exact solution.

Example 2. Consider the following fractional Fredholm integrodifferential equation:

$$D^{1/4}u(x) = \sum_{k=0}^{\infty}\frac{x^{k+3/4}}{2^{k+1}\Gamma(k-1/4)} - \left(4-2\sqrt{e}\right)x^2 + \int_0^1 x^2tu(t), \quad x \in \mathbb{R} \tag{38}$$

subject to

$$u(0) = 1. \tag{39}$$

The exact solution is

$$u(x) = e^{(1/2)x}. \tag{40}$$

Using the same argument described in the previous section, we find the first few terms which are

$$\begin{aligned} f_0 &= 1, \\ f_1 &= f_2 = f_3 = 0, \\ f_4 &= \frac{1}{2}, \\ f_5 &= f_6 = f_7 = 0, \\ f_8 &= \frac{1}{4}. \end{aligned} \quad (41)$$

Continuing in this process, we find that

$$f_n = \begin{cases} \frac{1}{2^k}, & n = 4k, \ k = 0, 1, 2, \ldots, \\ 0, & \text{otherwise}. \end{cases} \quad (42)$$

Thus, if $n = 4k$ for some positive integer k,

$$\begin{aligned} u_n(x) &= \sum_{m=0}^{n} f_m \frac{x^{m/4}}{\Gamma(1 + m/4)} = \sum_{m=0}^{k} \frac{1}{2^m} \frac{x^{4m/4}}{\Gamma(1 + 4m/4)} \\ &= \sum_{m=0}^{k} \frac{1}{2^m} \frac{x^m}{m!}. \end{aligned} \quad (43)$$

Hence,

$$\lim_{n\to\infty} u_n(x) = \lim_{n\to\infty} \sum_{m=0}^{k} \frac{1}{2^m} \frac{x^m}{m!} = \sum_{m=0}^{\infty} \frac{1}{2^m} \frac{x^m}{m!} = e^{(1/2)x} \quad (44)$$

which is the exact solution.

Example 3. Consider the following fractional Fredholm integrodifferential equation:

$$D^{1/3}u(x) = \frac{\Gamma(4/3)}{\Gamma(11/3)} - 5e^x + 4\int_0^1 e^x t u(t)\, dt, \quad x \in \mathbb{R} \quad (45)$$

subject to

$$u(0) = 1. \quad (46)$$

The exact solution is

$$u(x) = 1 + x^3. \quad (47)$$

Using the same argument described in the previous section, we find that the first few terms are

$$\begin{aligned} f_0 &= 1, \\ f_1 &= f_2 = f_3 = f_4 = 0, \\ f_5 &= f_6 = f_7 = f_8 = 0, \\ f_9 &= 6, \\ f_9 &= f_{10} = 0. \end{aligned} \quad (48)$$

Continuing in this process, we find that

$$f_n = \begin{cases} 1, & n = 0, \\ 6, & n = 9, \\ 0, & \text{otherwise}. \end{cases} \quad (49)$$

Thus,

$$u_9(x) = 1 + x^3 \quad (50)$$

which is the exact solution.

4. Conclusions and Closing Remarks

In this paper we employed the MFPS method to handle the fractional Fredholm integrodifferential problems. The method showed reliability in handling these ill-posed problems. It is worth mentioning that we get the exact solution in the above three examples. We test the prosed method and we get very accurate results. Although the MRPS method is not commonly used for such problems, it gives us very accurate results. This technique can be extended to other applications in science and engineering.

Conflicts of Interest

The author declares that there are no conflicts of interest regarding the publication of this paper.

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Research Article

Hybrid Adaptive Pinning Control for Function Projective Synchronization of Delayed Neural Networks with Mixed Uncertain Couplings

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This paper presents the function projective synchronization problem of neural networks with mixed time-varying delays and uncertainties asymmetric coupling. The function projective synchronization of this model via hybrid adaptive pinning controls and hybrid adaptive controls, composed of nonlinear and adaptive linear feedback control, is further investigated in this study. Based on Lyapunov stability theory combined with the method of the adaptive control and pinning control, some novel and simple sufficient conditions are derived for the function projective synchronization problem of neural networks with mixed time-varying delays and uncertainties asymmetric coupling, and the derived results are less conservative. Particularly, the control method focuses on how to determine a set of pinned nodes with fixed coupling matrices and strength values and randomly select pinning nodes. Based on adaptive control technique, the parameter update law, and the technique of dealing with some integral terms, the control may be used to manipulate the scaling functions such that the drive system and response systems could be synchronized up to the desired scaling function. Finally, numerical examples are given to illustrate the effectiveness of the proposed theoretical results.

1. Introduction

Presently, neural networks are under extensive consideration because of their significant application in various fields such as image processing, pattern recognition, and associative memories because the switching speed of information processing and the inherent neuron communication is limited [1, 2]. Global asymptotic stability of a general class of recurrent neural networks with time-varying delays is discussed in [3]. Zhang and Han [4] investigated the global asymptotical stability analysis for delayed neural networks using a matrix-based quadratic convex approach. It is well know that the time delay is continually necessarily existent in neural networks because it might lead to inconstancy or considerably inferior performances. So, the neural networks with time delays have attracted considerable attention of many researchers [5–7].

In addition, much attention has been paid to the potential applications of the synchronization of coupled neural networks, for example, secure communication [8–10]. The synchronization criteria for coupled stochastic neural networks with time-varying delays and leakage delay were discussed in [11]. Chen and Cao [12] suggested projective synchronization of neural networks with mixed time-varying delays and parameter mismatch. Moreover, there is synchronization problem that is called function projective synchronization that has received increasing attention in [13–15]. FPS is the driver and response system that can be synchronized up to a scaling function. Many researches mentioned that function projective synchronization (FPS) is the greater general definition of chaotic synchronization [16–18]. It is obvious that the definition of FPS includes comprehensive synchronization and projective synchronization. In order for scaling function to achieve unity or be constant, only one complete synchronization or projective synchronization could be obtained since the unpredictability of the scaling function in FPS can also raise the security of communication. Thus, FPS has drawn the attention of many researchers in various fields. In Gao et al. [19] the generalized function projective synchronization of weighted cellular neural networks with multiple time-varying coupling delays was studied. Adaptive projective synchronization in complex networks with time-varying coupling delay discussed in [20]. Tang and Wong [21] studied on the distributed synchronization problem of coupled neural networks by randomly occurring control method. Hu et al. [22] suggested a pinning synchronization control scheme for a class of linearly coupled neural networks. Huang et al. [23] investigated the stabilization of delayed chaotic neural networks by periodically intermittent control. Further, Cai et al. [24] considered the outer synchronization between two hybrid-coupled delayed dynamical networks via aperiodically adaptive intermittent pinning control. However, not all of the neural networks could synchronize by themselves. So, they need to bring the suitable controllers in order to make them synchronize. One of the most important existing control methods is the pinning control.

Pinning control is the strategy that employs the local feedback injection to a small fraction of nodes to carry out the global performances of the total networks. It is a competent and useful strategy especially for the large size networks. The pinning synchronization of neural networks has been generally examined at the present [25–33]. Meanwhile, various selection rules of pinned nodes have been introduced in the existing literatures. The pinned nodes selection rules according to the out-degree and in-degree of the nodes and the synchronization problem were studied for undirected and directed networks which was presented in [25, 26, 34]. The pinning control problem of neural networks was considered and then some unexceptional pinning conditions were found out [27–29], while Chen et al. [35] expressed that, even applying one single pinned node, the whole networks could be controlled as long as the coupling strength was large enough. Furthermore, Wang and Chen [36] summarized that the most highly connected nodes are pinned in order to get the better performance for the undirected networks.

As discussions mentioned above, hybrid adaptive pinning control for FPS of neural networks with mixed time-varying delays and uncertainties asymmetric coupling is an interesting topic for investigating. Therefore, this paper will be focused on this topic in order to facilitate clear comprehension and the purposes of this paper are given as follows:

(i) The mixed time-varying delays with discrete and distributed time-varying delays are considered in the dynamical nodes and in uncertainties asymmetric coupling, simultaneously, which are different from time-delay case in [23, 27–29]. So, our systems are general ones.

(ii) For the control method, FPS is studied by using the nonlinear and adaptive pinning controls and using the nonlinear and adaptive controls which contain error linear term, time-varying delay error linear term, and distributed time-varying delay error linear term.

(iii) The FPS of this paper focuses on how to determine a set of pinned nodes for a linearly coupled delayed neural network with fixed coupling matrices and strength values. Moreover, this paper used random selection of pinning nodes which is different from the pinning control method in [13, 37].

Based on constructing a novel Lyapunov-Krasovskii functional, adaptive control technique, the parameter update law, and the technique of dealing with Jensen's and Cauchy inequalities, some novel sufficient conditions for guaranteeing the existence of the FPS of neural networks with mixed time-varying delays and uncertainties asymmetric coupling are derived. Finally, numerical examples are included to show the effectiveness of using the nonlinear and adaptive pinning controls and the nonlinear and adaptive controls.

The rest of the paper is organized as follows. Section 2 provides some mathematical preliminaries and network model. Section 3 presents FPS of neural network with mixed time-varying delays and hybrid uncertainties asymmetric coupling by hybrid adaptive control and hybrid adaptive pinning control, respectively. In Section 4, some numerical examples illustrate given theoretical results. The paper ends with conclusions in Section 5 and cited references.

2. Model Description and Preliminaries

Notations. The following notation will be used in this paper: $\mathscr{R}^n$ denotes the n-dimensional space and $\|\cdot\|$ denotes the Euclidean vector norm; A^T denotes the transpose of matrix A; A is symmetric if $A = A^T$; I_N denotes an N-dimensional identity matrix; for the matrix $A \in \mathscr{R}^N \times \mathscr{R}^N$, the ith row and the ith column of A are called the ith row-column pair of A. $A_l \in \mathscr{R}^{(N-l)\times(N-l)}$ is the minor matrix of $A \in \mathscr{R}^{N\times N}$ by removing arbitrary l $(1 \le l \le N)$ row-column pairs of A. The symbol $\otimes$ denotes the Kronecker product.

Consider an array of delayed neural networks consisting of N identical nodes with uncertainties asymmetric coupling

$$\begin{aligned}\dot{x}_i(t) = {}& -Ax_i(t) + W_1 f_1(x_i(t)) + W_2 f_2(x_i(t-h(t))) \\ & + W_3 \int_{t-k(t)}^{t} f_3(x_i(\theta))\,d\theta \\ & + c_1 \sum_{j=1}^{N} G_{1_{ij}} (\Gamma_1 + \Delta\Gamma_1) x_j(t) \\ & + c_2 \sum_{j=1}^{N} G_{2_{ij}} (\Gamma_2 + \Delta\Gamma_2) x_j(t-h(t)) \\ & + c_3 \sum_{j=1}^{N} G_{3_{ij}} (\Gamma_3 + \Delta\Gamma_3) \int_{t-k(t)}^{t} x_j(\theta)\,d\theta + \mathscr{U}_i(t), \\ & \qquad i = 1, 2, \ldots, N,\end{aligned} \tag{1}$$

where N is the number of coupled nodes, $x_i(t) = (x_{i1}(t), x_{i2}(t), \ldots, x_{in}(t))^T \in \mathscr{R}^n$ is the neuron state vector of the ith node, n denotes the number of neurons in a neural network, $A = \operatorname{diag}(a_1, a_2, \ldots, a_n) > 0$ denote the rate with which the cell i resets its potential to the resting state when being isolated from other cells and inputs, W_1, W_2, and W_3 are connection weight matrices, $h(t)$ and $k(t)$ are the time-varying delays, $f_r(x_i(\cdot)) = [f_{r1}(x_{i1}(\cdot)), \ldots, f_{rn}(x_{in}(\cdot))]^T$, $r = 1, 2, 3$, denote the neuron activation function vector, the positive constants c_1, c_2, and c_3 are the strength values for the constant coupling and delayed couplings, respectively, $\mathscr{U}_i(t) \in \mathscr{R}^m$ are the control input of the node i, Γ_1, Γ_2, and $\Gamma_3 \in \mathscr{R}^{n\times n}$ are constant inner-coupling matrices and it is assumed that Γ_1, Γ_2, and Γ_3 are positive definite matrix, $\Delta\Gamma_1, \Delta\Gamma_2$, and $\Delta\Gamma_3$ are the uncertainties of inner-coupling matrices, and $G_r = (G_{r_{ij}})_{N\times N}$ $(r = 1, 2, 3)$ are the outer-coupling matrices and satisfy the following conditions:

$$\begin{aligned} &G_{r_{ij}} \geq 0, \quad i \neq j, \ r = 1, 2, 3, \\ &G_{r_{ii}} = -\sum_{j=1, j\neq i}^{N} G_{r_{ij}}, \quad i, j = 1, 2, \ldots, N. \end{aligned} \tag{2}$$

Assumption 1. The time-varying delay function $h(t)$ is differential function and $k(t)$ satisfies the conditions $0 \leq h(t) \leq h$, $0 \leq k(t) \leq k$, and $0 \leq \dot{h}(t) \leq \mu < 1$.

Assumption 2. The activation functions $f_{ri}(\cdot)$, $r = 1, 2, 3$, $i = 1, 2, \ldots, n$, satisfy the Lipschitz constants $f_{ri} > 0$:

$$\begin{aligned} &\left\|f_{1i}(x(t)) - f_{1i}(\alpha(t) y(t))\right\| \leq F_1 \left\|x(t) - \alpha(t) y(t)\right\|, \\ &\left\|f_{2i}(x(t-h(t))) - f_{2i}(\alpha(t) y(t-h(t)))\right\| \\ &\quad \leq F_2 \left\|x(t-h(t)) - \alpha(t) y(t-h(t))\right\|, \\ &\left\|f_{3i}(x(\theta)) - f_{3i}(\alpha(t) y(\theta))\right\| \\ &\quad \leq F_3 \left\|x(\theta) - \alpha(t) y(\theta)\right\|, \end{aligned} \tag{3}$$

where F_r $(r = 1, 2, 3)$ are positive constant matrices and we denote

$$\begin{aligned} F_1 &= \operatorname{diag}\{f_{1i}, \ i = 1, 2, \ldots, n\}, \\ F_2 &= \operatorname{diag}\{f_{2i}, \ i = 1, 2, \ldots, n\}, \\ F_3 &= \operatorname{diag}\{f_{3i}, \ i = 1, 2, \ldots, n\}. \end{aligned} \tag{4}$$

Assumption 3. The parameter uncertainties are assumed to satisfy the following conditions:

$$\left[\Delta\Gamma_1(t) \ \ \Delta\Gamma_2(t) \ \ \Delta\Gamma_3(t)\right] = M\nabla(t)\left[E_1 \ \ E_2 \ \ E_3\right], \tag{5}$$

where M, E_1, E_2, and E_3 are known real constant matrices and $\nabla(t)$ is and unknown time-varying matrix function satisfying $\nabla^T(t)\nabla(t) \leq I$.

The isolated dynamic network is

$$\begin{aligned} \dot{s}(t) = &-As(t) + W_1 f_1(s(t)) + W_2 f_2(s(t-h(t))) \\ &+ W_3 \int_{t-k(t)}^{t} f_3(s(\theta))\, d\theta, \end{aligned} \tag{6}$$

where $s(t) = (s_1(t), s_2(t), \ldots, s_n(t))^T \in \mathscr{R}^n$ with $x_0 \in \mathscr{R}^n$ and the parameters A, W_1, W_2, and W_3 and the nonlinear functions $f(\cdot)$ have the same definitions as in (1).

Definition 4 (FPS). Network (1) with time delay is said to achieve function projective synchronization if there exists a continuously differentiable scaling function $\alpha(t)$ such that

$$\begin{aligned} \lim_{t\to\infty} \left\|e_i(t)\right\| = \lim_{t\to\infty} \left\|x_i(t) - \alpha(t) s(t)\right\|, \\ i = 1, 2, \ldots, N, \end{aligned} \tag{7}$$

where $\|\cdot\|$ stands for the Euclidean vector norm and $s(t) \in \mathscr{R}^n$ can be an equilibrium point, or a (quasi-)periodic orbit, or an orbit of a chaotic attractor.

To investigate the stability of the synchronized states (1), we set the synchronization error $e_i(t)$ in the form $e_i(t) = x_i(t) - \alpha(t)s(t)$, $i = 1, \ldots, N$. Then, substituting it into (1), it is easy to get the following:

$$\begin{aligned} \dot{e}_i(t) &= \dot{x}_i(t) - \dot{\alpha}(t) s(t) - \alpha(t) \dot{s}(t) \\ &= -Ae_i(t) + W_1\left[f_1(x_i(t)) - \alpha(t) f_1(s(t))\right] \\ &\quad + W_2\left[f_2(x_i(t-h(t))) - \alpha(t) f_2(s(t-h(t)))\right] \\ &\quad + W_3 \int_{t-k(t)}^{t} \left[f_3(x_i(\theta)) - \alpha(t) f_3(s(\theta))\right] d\theta \\ &\quad + c_1 \sum_{j=1}^{N} G_{1_{ij}}\left(\Gamma_1 + \Delta\Gamma_1\right) e_j(t) \\ &\quad + c_2 \sum_{j=1}^{N} G_{2_{ij}}\left(\Gamma_2 + \Delta\Gamma_2\right) e_j(t-h(t)) \\ &\quad + c_3 \sum_{j=1}^{N} G_{3_{ij}}\left(\Gamma_3 + \Delta\Gamma_3\right) \int_{t-k(t)}^{t} e_j(\theta)\, d\theta - \dot{\alpha}(t) s(t) \\ &\quad + \mathscr{U}_i(t). \end{aligned} \tag{8}$$

The initial condition of (8) is defined by

$$e_i(r) = \phi_i(r), \quad -\tau \leq r \leq 0, \tag{9}$$

where $\tau = \max\{k, h\}$ and $\phi_i(r) \in \mathscr{C}([-\tau, 0], \mathscr{R}^n)$, $i = 1, 2, \ldots, N$.

Remark 5. If neural networks (1) are without parameter uncertainties and $c_3 = 0$, the networks model turns into the neural networks proposed in [27–29]:

$$\begin{aligned} \dot{x}_i(t) = &-Ax_i(t) + W_1 f_1(x_i(t)) \\ &+ W_2 f_2(x_i(t-h(t))) \\ &+ W_3 \int_{t-k(t)}^{t} f_3(x_i(\theta))\, d\theta + c_1 \sum_{j=1}^{N} G_{1_{ij}} \Gamma_1 x_j(t) \\ &+ c_2 \sum_{j=1}^{N} G_{2_{ij}} \Gamma_2 x_j(t-h(t)), \quad i = 1, 2, \ldots, N. \end{aligned} \tag{10}$$

Hence, our network model (1) includes previous network model, which can be regarded as a special case of neural network (1).

Lemma 6 (see [5] (Cauchy inequality)). *For any symmetric positive definite matrixes $N \in M^{n\times n}$ and $x, y \in \mathscr{R}^n$ we have*

$$\pm 2x^T y \leq x^T N x + y^T N^{-1} y. \tag{11}$$

Lemma 7 (see [5]). *For any constant symmetric matrixes $M \in \mathscr{R}^{m\times m}$, $M = M^T > 0$, and $\gamma > 0$, vector function $\omega : [0,\gamma] \rightarrow \mathscr{R}^m$ such that the integrations concerned are well defined, and then*

$$\begin{aligned} &\left(\int_0^\gamma \omega^T(\theta)\, d\theta\right)^T M \left(\int_0^\gamma \omega(\theta)\, d\theta\right) \\ &\quad \leq \gamma \int_0^\gamma \omega^T(s) M \omega(\theta)\, d\theta. \end{aligned} \tag{12}$$

Lemma 8 (see [38]). *Let $c \in \mathscr{R}$ and A, B, C, and D be matrices with appropriate dimensions. Then*

(i) $c(A \otimes B) = (cA) \otimes B = A \otimes (cB)$,

(ii) $(A \otimes B)^T = A^T \otimes B^T$,

(iii) $(A \otimes B)(C \otimes D) = (AC) \otimes (BD)$,

(iv) $A \otimes (B + C) = (A \otimes B) + (A \otimes C)$,

(v) $A \otimes B \otimes C = (A \otimes B) \otimes C = A \otimes (B \otimes C)$.

Lemma 9 (see [25]). *Assume that A and B are the $N \times N$ Hermitian matrices. Suppose that $\alpha_1 \geq \alpha_2 \geq \cdots \geq \alpha_N$, $\beta_1 \geq \beta_2 \geq \cdots \geq \beta_N$, and $\gamma_1 \geq \gamma_2 \geq \cdots \geq \gamma_N$ are eigenvalues of matrices A, B, and A + B, respectively. Then one has $\alpha_i + \beta_N \leq \gamma_i \leq \alpha_i + \beta_1$, $i = 1, 2, \ldots, N$.*

Lemma 10 (see [35]). *If $A = (a_{ij})_{N\times N}$ is irreducible and satisfies $a_{ij} = a_{ji} \geq 0$, $i \neq j$, $a_{ii} = -\sum_{j=1, i\neq j}^{N} a_{ij}$, $i, j = 1, 2, \ldots, N$. Then, for any constant $\xi > 0$, all eigenvalues of the matrix $A - \Xi$ are negative definite, where $\Xi = \mathrm{diag}(\xi, 0, \ldots, 0)$.*

Lemma 11 (see [25]). *For a symmetric matrix $M \in \mathscr{R}^{N\times N}$ and a diagonal matrix $D = \mathrm{diag}(d_1, \ldots, d_l, \underbrace{0, \ldots, 0}_{N-l})$ with $d_i > 0$, $i = 1, 2, \ldots, l$ $(1 \leq l < N)$, let*

$$M - D = \begin{bmatrix} A - \widetilde{D} & B \\ B^T & M_l \end{bmatrix}, \tag{13}$$

where M_l is the minor matrix of M by removing its first l row-column pairs, A and B are matrices with appropriate dimensions, and $\widetilde{D} = \mathrm{diag}(d_1, \ldots, d_l)$. If $d_i > \lambda_{\max}(A - BM_l^{-1}B^T)$, $i = 1, \ldots, l$, $M - D < 0$ is equivalent to $M_l < 0$.

3. Main Results

In this section, we present hybrid control scheme to synchronize neural networks (1) to the homogenous trajectory (6). Then, we will give some sufficient conditions in FPS of neural networks with mixed time-varying delays and uncertainties asymmetric coupling.

3.1. FPS under Hybrid Adaptive Pinning Control. We design nonlinear and adaptive pinning controls to realize FPS of neural networks with mixed time-varying delays and uncertainties asymmetric coupling. In order to stabilize the origin of neural networks (1) by means of nonlinear and adaptive pinning controls $\mathscr{U}_i(t)$ such as

$$\mathscr{U}_i(t) = u_{i1}(t) + u_{i2}(t), \quad i = 1, 2, \ldots, N, \tag{14}$$

where

$$\begin{aligned} u_{i1}(t) &= \dot{\alpha}(t) s(t) - W_1 \left[\alpha(t) f_1(s(t)) + f_1(\alpha(t) s(t))\right] - W_2 \left[\alpha(t) f_2(s(t - h(t))) + f_2(\alpha(t) s(t - h(t)))\right] \\ &\quad - W_3 \int_{t-k(t)}^{t} \left[\alpha(t) f_3(s(\theta)) - f_3(\alpha(t) s(\theta))\right] d\theta, \quad i = 1, 2, \ldots, N, \\ u_{i2}(t) &= \begin{cases} -c_1 d_{1i}(t) \Gamma_1 e_i(t) - c_2 d_{2i}(t) \Gamma_2 e_i(t - h(t)) - c_3 d_{3i}(t) \Gamma_3 \displaystyle\int_{t-k(t)}^{t} e_i(\theta)\, d\theta, & i = 1, 2, \ldots, l, \\ 0 & i = l+1, l+2, \ldots, N, \end{cases} \end{aligned} \tag{15}$$

the updating laws are

$$\begin{aligned} \dot{d}_{1i}(t) &= \beta_{i1} e_i^T(t) \Gamma_1 e_i(t), \\ \dot{d}_{2i}(t) &= \beta_{i2} e_i^T(t) \Gamma_2 e_i(t - h(t)), \\ \dot{d}_{3i}(t) &= \beta_{i3} e_i^T(t) \Gamma_3 \int_{t-k(t)}^{t} e_i(\theta)\, d\theta, \end{aligned} \tag{16}$$

where β_{i1}, β_{i2}, and β_{i3} are positive constants and $s(t)$ is a solution of an isolated node. The controller $\mathscr{U}_i(t)$ is different type of controller, and $u_{i1}(t)$ is the nonlinear control and $u_{i2}(t)$ is the adaptive linear pinning control. Then, substituting (14) into (8), it can be derived that

$$\begin{aligned} \dot{e}_i(t) &= -Ae_i(t) + W_1 \widetilde{f}_1(e_i(t)) \\ &\quad + W_2 \widetilde{f}_2(e_i(t - h(t))) \end{aligned}$$

$$
\begin{aligned}
&+ W_3 \int_{t-k(t)}^{t} \tilde{f}_3(e_i(\theta))\,d\theta \\
&+ c_1 \sum_{j=1}^{N} G_{1_{ij}} (\Gamma_1 + \Delta\Gamma_1) e_j(t) \\
&+ c_2 \sum_{j=1}^{N} G_{2_{ij}} (\Gamma_2 + \Delta\Gamma_2) e_j(t - h(t)) \\
&+ c_3 \sum_{j=1}^{N} G_{3_{ij}} (\Gamma_3 + \Delta\Gamma_3) \int_{t-k(t)}^{t} e_j(\theta)\,d\theta \\
&- c_1 d_{1i}(t) \Gamma_1 e_i(t) \\
&- c_2 d_{2i}(t) \Gamma_2 e_i(t - h(t)) \\
&- c_3 d_{3i}(t) \Gamma_3 \int_{t-k(t)}^{t} e_i(\theta)\,d\theta, \\
&\qquad i = 1, 2, \ldots, l, \\
\dot{e}_i(t) &= -A e_i(t) + W_1 \tilde{f}_1(e_i(t)) \\
&+ W_2 \tilde{f}_2(e_i(t - h(t))) \\
&+ W_3 \int_{t-k(t)}^{t} \tilde{f}_3(e_i(\theta))\,d\theta \\
&+ c_1 \sum_{j=1}^{N} G_{1_{ij}} (\Gamma_1 + \Delta\Gamma_1) e_j(t) \\
&+ c_2 \sum_{j=1}^{N} G_{2_{ij}} (\Gamma_2 + \Delta\Gamma_2) e_j(t - h(t)) \\
&+ c_3 \sum_{j=1}^{N} G_{3_{ij}} (\Gamma_3 + \Delta\Gamma_3) \int_{t-k(t)}^{t} e_j(\theta)\,d\theta, \\
&\qquad i = l+1, l+2, \ldots, N, \\
\dot{d}_{1i}(t) &= \beta_{i1} e_i^T(t) \Gamma_1 e_i(t), \quad i = 1, 2, \ldots, l, \\
\dot{d}_{2i}(t) &= \beta_{i2} e_i^T(t) \Gamma_2 e_i(t - h(t)), \quad i = 1, 2, \ldots, l, \\
\dot{d}_{3i}(t) &= \beta_{i3} e_i^T(t) \Gamma_3 \int_{t-k(t)}^{t} e_i(\theta)\,d\theta, \quad i = 1, 2, \ldots, l,
\end{aligned}
\tag{17}
$$

where

$$
\begin{aligned}
\tilde{f}_1(e_i(t)) &= f_1(x_i(t)) - f_1(\alpha(t) s(t)), \\
\tilde{f}_2(e_i(t - h(t))) &= f_2(x_i(t - h(t))) \\
&\quad - f_2(\alpha(t) s(t - h(t))), \\
\tilde{f}_3(e_i(\theta)) &= f_3(x_i(\theta)) - f_3(\alpha(t) s(\theta)),
\end{aligned}
\tag{18}
$$

and, for convenience, we denote

$$
\begin{aligned}
\Pi_1 = \frac{1}{\lambda_{\min}(I_N \otimes \Gamma_1)} \Bigg[&-\lambda_{\max}(I_N \otimes A) \\
&+ \frac{1}{2\varepsilon_1} \lambda_{\max}\left(I_N \otimes W_1 W_1^T\right) + \frac{\varepsilon_1}{2} \lambda_{\max}\left(I_N \otimes F_1^T F_1\right) \\
&+ \frac{c_3 k^2}{2} \lambda_{\max}(I_N \otimes \Gamma_3) + \frac{1}{2\varepsilon_2} \lambda_{\max}\left(I_N \otimes W_2 W_2^T\right) \\
&+ \frac{1}{2\varepsilon_3} \lambda_{\max}\left(I_N \otimes W_3 W_3^T\right) + \frac{c_1 \varepsilon_6}{2} \lambda_{\max}\left(I_N \otimes E_1^T E_1\right) \\
&+ \frac{c_1}{2\varepsilon_6} \lambda_{\max}\left(G_1 G_1^T\right) \lambda_{\max}\left(M M^T\right) \\
&+ \frac{c_2}{2\varepsilon_7} \lambda_{\max}\left(G_2 G_2^T\right) \lambda_{\max}\left(\Gamma_2 \Gamma_2^T\right) \\
&+ \frac{c_2}{2\varepsilon_8} \lambda_{\max}\left(G_2 G_2^T\right) \lambda_{\max}\left(M M^T\right) \\
&+ \frac{c_3}{2\varepsilon_9} \lambda_{\max}\left(G_3 G_3^T\right) \lambda_{\max}\left(\Gamma_3 \Gamma_3^T\right) \\
&+ \frac{c_3}{2\varepsilon_{10}} \lambda_{\max}\left(G_3 G_3^T\right) \lambda_{\max}\left(M M^T\right) \\
&+ \frac{c_2}{2(1-\mu)} \lambda_{\max}(I_N \otimes \Gamma_2) \\
&+ \frac{c_2 \overline{d}_2^*}{2\varepsilon_4} \lambda_{\max}\left(I_N \otimes \Gamma_2 \Gamma_2^T\right) \\
&+ \frac{c_3 \overline{d}_3^*}{2\varepsilon_5} \lambda_{\max}\left(I_N \otimes \Gamma_3 \Gamma_3^T\right) \Bigg], \\
\Pi_2 = \frac{1}{2\lambda_{\min}(I_N \otimes \Gamma_2)} \Big[&\varepsilon_2 \lambda_{\max}\left(I_N \otimes F_2^T F_2\right) + c_2 \varepsilon_7 \\
&+ c_2 \varepsilon_8 \lambda_{\max}\left(I_N \otimes E_2^T E_2\right) + c_2 \overline{d}_2^* \varepsilon_4 \Big], \\
\Pi_3 = \frac{1}{2\lambda_{\min}(I_N \otimes \Gamma_3)} \Big[&\varepsilon_3 \lambda_{\max}\left(I_N \otimes F_3^T F_3\right) + c_3 \varepsilon_9 \\
&+ c_3 \varepsilon_{10} \lambda_{\max}\left(I_N \otimes E_3^T E_3\right) + c_3 \overline{d}_3^* \varepsilon_5 \Big], \\
\xi(t) = \Bigg(&e^T(t), e^T(t - h(t)), \left(\int_{t-k(t)}^{t} e(\theta)\,d\theta \right)^T \Bigg)^T.
\end{aligned}
\tag{19}
$$

Theorem 12. *For some given synchronization scaling function $\alpha(t)$, neural networks (1) satisfying Assumptions 1, 2, and 3, and target system can realize function projective synchronization by the nonlinear and adaptive pinning control law as shown in (14) if there exist positive constants ε_i, $i = 1, 2, \ldots, 10$, and by taking appropriate d_{1i}^* $(i = 1, 2, \ldots, l)$, $\overline{d}_2^*$, and $\overline{d}_3^*$ such that*

$$
\lambda_{\max}\left(\frac{G_1 + G_1^T}{2}\right)_l < -\frac{\Pi_1}{c_1},
\tag{20}
$$

$$\overline{d}_2^* - \frac{1}{c_2\varepsilon_4}\left[\varepsilon_2\lambda_{\max}\left(I_N\otimes F_2^TF_2\right)+c_2\varepsilon_7 + c_2\varepsilon_8\lambda_{\max}\left(I_N\otimes E_2^TE_2\right)-\lambda_{\min}\left(I_N\otimes\Gamma_2\right)\right]>0, \tag{21}$$

$$\overline{d}_3^* - \frac{1}{c_3\varepsilon_5}\left[\varepsilon_3\lambda_{\max}\left(I_N\otimes F_3^TF_3\right)+c_3\varepsilon_9 + c_3\varepsilon_{10}\lambda_{\max}\left(I_N\otimes E_3^TE_3\right)-\lambda_{\min}\left(I_N\otimes\Gamma_3\right)\right]>0. \tag{22}$$

Then controlled neural network (1) is function projective synchronization.

Proof. Construct the following Lyapunov-Krasovskii functional candidate:

$$V(t)=V_1(t)+V_2(t)+V_3(t)+V_4(t), \tag{23}$$

where

$$\begin{aligned}
V_1(t)&=\frac{1}{2}\sum_{i=1}^N e_i^T(t)\,e_i(t),\\
V_2(t)&=\frac{c_2}{2(1-\mu)}\sum_{i=1}^N\int_{t-h(t)}^t e_i^T(\theta)\,\Gamma_2e_i(\theta)\,d\theta,\\
V_3(t)&=\frac{c_3k}{2}\sum_{i=1}^N\int_{-k}^0\int_{t+s}^t e_i^T(\theta)\,\Gamma_3e_i(\theta)\,d\theta\,ds,\\
V_4(t)&=\frac{c_1}{2}\sum_{i=1}^l\frac{1}{\beta_{i1}}\left(d_{1i}(t)-d_{1i}^*\right)^2 + \frac{c_2}{2}\sum_{i=1}^l\frac{1}{\beta_{i2}}\left(d_{2i}(t)-d_{2i}^*\right)^2 + \frac{c_3}{2}\sum_{i=1}^l\frac{1}{\beta_{i3}}\left(d_{3i}(t)-d_{3i}^*\right)^2.
\end{aligned} \tag{24}$$

By taking the derivative of $V(t)$ along the trajectories of system (17), we have the following:

$$\begin{aligned}
\dot{V}_1(t)&=-\sum_{i=1}^N e_i^T(t)\,Ae_i(t)+\sum_{i=1}^N e_i^T(t)\,W_1\widetilde{f}_1\left(e_i(t)\right) + \sum_{i=1}^N e_i^T(t)\,W_2\widetilde{f}_2\left(e_i(t-h(t))\right)\\
&\quad+\sum_{i=1}^N e_i^T(t)\,W_3\int_{t-k(t)}^t\widetilde{f}_3\left(e_i(\theta)\right)d\theta + c_1\sum_{i=1}^N\sum_{j=1}^N e_i^T(t)\,G_{1_{ij}}\left(\Gamma_1+\Delta\Gamma_1\right)e_j(t)\\
&\quad+c_2\sum_{i=1}^N\sum_{j=1}^N e_i^T(t)\,G_{2_{ij}}\left(\Gamma_2+\Delta\Gamma_2\right)e_j(t-\tau(t)) + c_3\sum_{i=1}^N\sum_{j=1}^N e_i^T(t)\,G_{3_{ij}}\left(\Gamma_3+\Delta\Gamma_3\right)\int_{t-k(t)}^{\mathrm{t}} e_j(\theta)\,d\theta\\
&\quad-\sum_{i=1}^N e_i^T(t)\,c_1d_{1i}(t)\,\Gamma_1e_i(t) - \sum_{i=1}^N e_i^T(t)\,c_2d_{2i}(t)\,\Gamma_2e_i(t-h(t)) - \sum_{i=1}^N e_i^T(t)\,c_3d_{3i}(t)\,\Gamma_3\int_{t-k(t)}^t e_i(\theta)\,d\theta.\\
\dot{V}_2(t)&=\frac{c_2}{2(1-\mu)}\sum_{i=1}^N e_i^T(t)\,\Gamma_2e_i(t) - \frac{c_2\left(1-\dot{h}(t)\right)}{2(1-\mu)}\sum_{i=1}^N e_i^T(t-h(t))\,\Gamma_2e_i(t-h(t)).\\
\dot{V}_3(t)&=\frac{c_3k^2}{2}\sum_{i=1}^N e_i^T(t)\,\Gamma_3e_i(t) - \frac{c_3k}{2}\sum_{i=1}^N\int_{t-k(t)}^t e_i^T(\theta)\,\Gamma_3e_i(\theta)\,d\theta.\\
\dot{V}_4(t)&=\sum_{i=1}^l\frac{c_1}{\beta_{i1}}\left(d_{1i}(t)-d_{1i}^*\right)\beta_{i1}e_i^T(t)\,\Gamma_1e_i(t) + \sum_{i=1}^l\frac{c_2}{\beta_{i2}}\left(d_{2i}(t)-d_{2i}^*\right)\beta_{i2}e_i^T(t)\,\Gamma_2e_i(t-h(t))\\
&\quad+\sum_{i=1}^l\frac{c_3}{\beta_{i3}}\left(d_{3i}(t)-d_{3i}^*\right)\beta_{i3}e_i^T(t)\,\Gamma_3\int_{t-k(t)}^t e_i(\theta)\,d\theta.
\end{aligned} \tag{25}$$

After $V(t)$ were calculated, we will get that

$$\begin{aligned}
\dot{V}(t)&\le-\sum_{i=1}^N e_i^T(t)\,Ae_i(t)+\sum_{i=1}^N e_i^T(t)\,W_1\widetilde{f}_1\left(e_i(t)\right) + \sum_{i=1}^N e_i^T(t)\,W_2\widetilde{f}_2\left(e_i(t-h(t))\right)+\sum_{i=1}^N e_i^T(t)\,W_3\\
&\quad\cdot\int_{t-k(t)}^t\widetilde{f}_3\left(e_i(\theta)\right)d\theta + c_1\sum_{i=1}^N\sum_{j=1}^N e_i^T(t)\,G_{1_{ij}}\left(\Gamma_1+\Delta\Gamma_1\right)e_j(t)\\
&\quad+c_2\sum_{i=1}^N\sum_{j=1}^N e_i^T(t)\,G_{2_{ij}}\left(\Gamma_2+\Delta\Gamma_2\right)e_j(t-\tau(t)) + c_3\sum_{i=1}^N\sum_{j=1}^N e_i^T(t)\,G_{3_{ij}}\left(\Gamma_3+\Delta\Gamma_3\right)\times\int_{t-k(t)}^t e_j(\theta)\,d\theta\\
&\quad+\frac{c_2}{2(1-\mu)}\sum_{i=1}^N e_i^T(t)\,\Gamma_2e_i(t)-\frac{c_2}{2(1-\mu)}
\end{aligned}$$

$$
\begin{aligned}
&\cdot \sum_{i=1}^{N} e_i^T(t-h(t))\,\Gamma_2 e_i(t-h(t)) + \frac{c_3 k^2}{2} \\
&\cdot \sum_{i=1}^{N} e_i^T(t)\,\Gamma_3 e_i(t) - \frac{c_3 k}{2}\sum_{i=1}^{N}\int_{t-k(t)}^{t} e_i^T(\theta)\,\Gamma_3 e_i(\theta)\,d\theta \\
&- c_1 \sum_{i=1}^{l} d_{1i}^* e_i^T(t)\,\Gamma_1 e_i(t) \\
&- c_2 \sum_{i=1}^{l} d_{2i}^* e_i^T(t)\,\Gamma_2 e_i(t-h(t))\,ds \\
&- c_3 \sum_{i=1}^{l} d_{3i}^* e_i^T(t)\,\Gamma_3 \int_{t-k(t)}^{t} e_i(\theta)\,d\theta \\
\le{} & -e^T(t)(I_N\otimes A)e(t) + e^T(t)(I_N\otimes W_1)\tilde f_1(e(t)) \\
&+ e^T(t)(I_N\otimes W_2)\tilde f_2(e(t-h(t))) + e^T(t)\big(I_N \\
&\otimes W_3\big)\int_{t-k(t)}^{t}\tilde f_3(e(\theta))\,d\theta + c_1 e^T(t)\big(G_1 \\
&\otimes(\Gamma_1+\Delta\Gamma_1)\big)e(t) + c_2 e^T(t)\big(G_2\otimes(\Gamma_2+\Delta\Gamma_2)\big)e(t \\
&- h(t)) + c_3 e^T(t)\big(G_3\otimes(\Gamma_3+\Delta\Gamma_3)\big)\int_{t-k(t)}^{t} e(\theta)\,d\theta \\
&+ \frac{c_2}{2(1-\mu)}e^T(t)(I_N\otimes\Gamma_2)e(t) - \frac{c_2}{2(1-\mu)}e^T(t \\
&- h(t))(I_N\otimes\Gamma_2)e(t-h(t)) + \frac{c_3 k^2}{2}e^T(t)(I_N\otimes\Gamma_3) \\
&\cdot e(t) - \frac{c_3 k}{2}\int_{t-k(t)}^{t} e^T(\theta)(I_N\otimes\Gamma_3)e(\theta)\,d\theta \\
&- c_1 e^T(t)(D_1^*\otimes\Gamma_1)e(t) - c_2\overline{d}_2^* e^T(t)(I_N\otimes\Gamma_2) \\
&\cdot e(t-h(t)) - c_3\overline{d}_3^* e^T(t)(I_N\otimes\Gamma_3)\int_{t-k(t)}^{t} e(\theta)\,d\theta,
\end{aligned}
\tag{26}
$$

where $e(t) = (e_1(t),\dots,e_N(t)) \in \mathscr{R}^{n\times N}$, $e(t-h(t)) = (e_1(t-h(t)),\dots,e_N(t-h(t))) \in \mathscr{R}^{n\times N}$, $\int_{t-k(t)}^{t} e(\theta)d\theta = \int_{t-k(t)}^{t}(e_1(\theta),e_2(\theta),\dots,e_N(\theta))d\theta \in \mathscr{R}^{n\times N}$, $D_1^* = \mathrm{diag}(d_{11}^*, d_{12}^*,\dots,d_{1l}^*,0,\dots,0) \in \mathscr{R}^{N\times N}$, $\overline{d}_2^* = \max_{1\le i\le l}\{d_{2i}^*\}$, and $\overline{d}_3^* = \max_{1\le i\le l}\{d_{3i}^*\}$.

From Assumption 2, we obtain the following three inequalities:

$$
\begin{aligned}
&\left\|\tilde f_{1i}(e_i(t))\right\| = \left\|\tilde f_{1i}(x(t)) - \tilde f_{1i}(\alpha(t)s(t))\right\| \\
&\quad \le F_{1i}\left\|e_i(t)\right\|, \\
&\left\|\tilde f_{2i}(e_i(t-h(t)))\right\| \\
&\quad = \left\|\tilde f_{2i}(x(t-h(t))) - \tilde f_{2i}(\alpha(t)s(t-h(t)))\right\| \\
&\quad \le F_{2i}\left\|e_i(t-h(t))\right\|, \\
&\left\|\tilde f_{3i}(e_i(\theta))\right\| = \left\|\tilde f_{3i}(x(\theta)) - \tilde f_{3i}(\alpha(t)s(\theta))\right\| \\
&\quad \le F_{3i}\left\|e_i(\theta)\right\|.
\end{aligned}
\tag{27}
$$

Applying Lemmas 6 and 7, we have

$$
\begin{aligned}
&e^T(t)(I_N\otimes W_1)\tilde f_1(e(t)) \le \frac{1}{2\varepsilon_1}e^T(t)\left(I_N\otimes W_1W_1^T\right) \\
&\quad \cdot e(t) + \frac{\varepsilon_1}{2}\tilde f_1^T(e(t))(I_N\otimes I_n)\tilde f_1(e(t)), \\
&\le \frac{1}{2\varepsilon_1}e^T(t)\left(I_N\otimes W_1W_1^T\right)e(t) + \frac{\varepsilon_1}{2}e^T(t) \\
&\quad \cdot\left(I_N\otimes F_1^TF_1\right)e(t), \\
&e^T(t)(I_N\otimes W_2)\tilde f_2(e(t-h(t))) \le \frac{1}{2\varepsilon_2}e^T(t) \\
&\quad \cdot\left(I_N\otimes W_2W_2^T\right)e(t) + \frac{\varepsilon_2}{2}\tilde f_2^T((t-h(t)))(I_N\otimes I_n) \\
&\quad \cdot\tilde f_2(e(t-h(t))), \\
&\le \frac{1}{2\varepsilon_2}e^T(t)\left(I_N\otimes W_2W_2^T\right)e(t) + \frac{\varepsilon_2}{2}e^T(t-h(t)) \\
&\quad \cdot\left(I_N\otimes F_2^TF_2\right)e(t-h(t)), \\
&e^T(t)(I_N\otimes W_3)\int_{t-k(t)}^{t}\tilde f_3(e(\theta))\,d\theta \le \frac{1}{2\varepsilon_3}e^T(t) \\
&\quad \cdot\left(I_N\otimes W_3W_3^T\right)e(t) + \frac{\varepsilon_3}{2}\left(\int_{t-k(t)}^{t}\tilde f_3^T(e(\theta))\,d\theta\right)^T \\
&\quad \cdot(I_N\otimes I_n)\left(\int_{t-k(t)}^{t}\tilde f_3^T(e(\theta))\,d\theta\right), \\
&\le \frac{1}{2\varepsilon_3}e^T(t)\left(I_N\otimes W_3W_3^T\right)e(t) + \frac{\varepsilon_3}{2} \\
&\quad \times\left(\int_{t-k(t)}^{t}e^T(\theta)\,d\theta\right)^T\left(I_N\otimes F_3^TF_3\right) \\
&\quad \cdot\left(\int_{t-k(t)}^{t}e^T(\theta)\,d\theta\right), \\
&- c_2\overline{d}_2^* e^T(t)(I_N\otimes\Gamma_2)e(t-h(t)) \le \frac{c_2\overline{d}_2^*}{2\varepsilon_4}e^T(t) \\
&\quad \cdot\left(I_N\otimes\Gamma_2\Gamma_2^T\right)e(t) + \frac{c_2\overline{d}_2^*\varepsilon_4}{2}e^T(t-h(t))(I_N\otimes I_n) \\
&\quad \cdot e(t-h(t)), \\
&- c_3\overline{d}_3^* e^T(t)(I_N\otimes\Gamma_3)\int_{t-k(t)}^{t} e(\theta)\,d\theta \le \frac{c_3\overline{d}_3^*}{2\varepsilon_5}e^T(t)
\end{aligned}
$$

$$\cdot\left(I_N\otimes\Gamma_3\Gamma_3^T\right)e(t)+\frac{c_3\overline{d}_3^*\varepsilon_5}{2}\times\left(\int_{t-k(t)}^t e^T(\theta)\,d\theta\right)^T$$
$$\cdot\left(I_N\otimes I_n\right)\left(\int_{t-k(t)}^t e^T(\theta)\,d\theta\right),$$
$$c_1e^T(t)\left(G_1\otimes(\Gamma_1+\Delta\Gamma_1)\right)e(t)=c_1e^T(t)\left(G_1\otimes\Gamma_1\right)$$
$$\cdot e(t)+c_1e^T(t)\left(G_1\otimes M\nabla(t)E_1\right)e(t),$$
$$\leq c_1e^T(t)\left(G_1\otimes\Gamma_1\right)e(t)+\frac{c_1}{2\varepsilon_6}e^T(t)\left(G_1G_1^T\otimes MM^T\right)$$
$$\cdot e(t)+\frac{c_1\varepsilon_6}{2}e^T(t)\left(I_N\otimes E_1^TE_1\right)e(t),$$
$$c_2e^T(t)\left(G_2\otimes(\Gamma_2+\Delta\Gamma_2)\right)e(t-h(t))=c_2e^T(t)$$
$$\cdot\left(G_2\otimes\Gamma_2\right)e(t-h(t))+c_2e^T(t)\left(G_2\otimes M\nabla(t)E_2\right)$$
$$\cdot e(t-h(t)),$$
$$\leq\frac{c_2}{2\varepsilon_7}e^T(t)\left(G_2G_2^T\otimes\Gamma_2\Gamma_2^T\right)e(t)+\frac{c_2\varepsilon_7}{2}e^T(t-h(t))$$
$$\cdot\left(I_N\otimes I_n\right)e(t-h(t))+\frac{c_2}{2\varepsilon_8}e^T(t)$$
$$\cdot\left(G_2G_2^T\otimes MM^T\right)e(t)+\frac{c_2\varepsilon_8}{2}e^T(t-h(t))$$
$$\cdot\left(I_N\otimes E_2^TE_2\right)(t-h(t)),$$
$$c_3e^T(t)\left(G_3\otimes(\Gamma_3+\Delta\Gamma_3)\right)\int_{t-k(t)}^t e(\theta)\,d\theta=c_3e^T(t)$$
$$\cdot\left(G_3\otimes\Gamma_3\right)\int_{t-k(t)}^t e(\theta)\,d\theta+c_3e^T(t)$$
$$\cdot\left(G_3\otimes M\nabla(t)E_3\right)\int_{t-k(t)}^t e(\theta)\,d\theta,$$
$$\leq\frac{c_3}{2\varepsilon_9}e^T(t)\left(G_3G_3^T\otimes\Gamma_3\Gamma_3^T\right)e(t)$$
$$+\frac{c_3\varepsilon_9}{2}\left(\int_{t-k(t)}^t e^T(\theta)\,d\theta\right)^T\left(I_N\otimes I_n\right)$$
$$\cdot\left(\int_{t-k(t)}^t e^T(\theta)\,d\theta\right)+\frac{c_3}{2\varepsilon_{10}}e^T(t)\left(G_3G_3^T\otimes MM^T\right)$$
$$\cdot e(t)+\frac{c_3\varepsilon_{10}}{2}\times\left(\int_{t-k(t)}^t e^T(\theta)\,d\theta\right)^T\left(I_N\otimes E_3^TE_3\right)$$
$$\cdot\left(\int_{t-k(t)}^t e^T(\theta)\,d\theta\right). \tag{28}$$

Therefore, we have

$$e^T(t)\Bigg[-c_1\left(D_1^*\otimes\Gamma_1\right)+c_1\left(G_1\otimes\Gamma_1\right)+\frac{c_3k^2}{2}\left(I_N\otimes\Gamma_3\right)$$
$$+\frac{1}{2\varepsilon_2}\left(I_N\otimes W_2W_2^T\right)+\frac{1}{2\varepsilon_3}\left(I_N\otimes W_3W_3^T\right)$$
$$+\frac{c_1}{2\varepsilon_6}\left(G_1G_1^T\otimes MM^T\right)+\frac{c_1\varepsilon_6}{2}\left(I_N\otimes E_1^TE_1\right)$$
$$+\frac{c_2}{2\varepsilon_7}\left(G_2G_2^T\otimes\Gamma_2\Gamma_2^T\right)+\frac{c_2}{2\varepsilon_8}\left(G_2G_2^T\otimes MM^T\right)$$
$$+\frac{c_3}{2\varepsilon_9}\left(G_3G_3^T\otimes\Gamma_3\Gamma_3^T\right)+\frac{c_3}{2\varepsilon_{10}}\left(G_3G_3^T\otimes MM^T\right)$$
$$+\frac{c_2\overline{d}_2^*}{2\varepsilon_4}\left(I_N\otimes\Gamma_2\Gamma_2^T\right)+\frac{c_3\overline{d}_3^*}{2\varepsilon_5}\left(I_N\otimes\Gamma_3\Gamma_3^T\right)\Bigg]e(t)$$
$$-e^T(t-h(t))\left[\frac{c_2}{2}\left(I_N\otimes\Gamma_2\right)-\Pi_2\left(I_N\otimes\Gamma_2\right)\right]e(t$$
$$-h(t))-\int_{t-k(t)}^t e^T(\theta)$$
$$\cdot\left[\frac{c_3k}{2}\left(I_N\otimes\Gamma_3\right)-\Pi_3\left(I_N\otimes\Gamma_3\right)\right]e(\theta)\,d\theta,$$
$$\leq e^T(t)\left[\left(\Pi_1I_N+c_1G_1-c_1D_1^*\right)\otimes\Gamma_1\right]e(t)-e^T(t$$
$$-h(t))\left[\left(\frac{c_2}{2}-\Pi_2\right)\left(I_N\otimes\Gamma_2\right)\right]e(t-h(t))$$
$$-\int_{t-k(t)}^t e^T(\theta)\left[\left(\frac{c_3k}{2}-\Pi_3\right)\left(I_N\otimes\Gamma_3\right)\right]e(\theta)\,d\theta,$$
$$=e^T(t)\left[\left(\mathscr{M}-c_1D_1^*\right)\otimes\Gamma_1\right]e(t)-e^T(t-h(t))$$
$$\cdot\left[\left(\frac{c_2}{2}-\Pi_2\right)\left(I_N\otimes\Gamma_2\right)\right]e(t-h(t))-\int_{t-k(t)}^t e^T(\theta)$$
$$\cdot\left[\left(\frac{c_3k}{2}-\Pi_3\right)\left(I_N\otimes\Gamma_3\right)\right]e(\theta)\,d\theta, \tag{29}$$

where $\mathscr{M}=\Pi_1I_N+c_1G_1$. Note that the matrix $\mathscr{M}$ is symmetric. Let

$$\mathscr{M}-D_1^*=\begin{bmatrix}\widetilde{\mathscr{M}}_1-\widetilde{D}_{1l}^* & \widetilde{\mathscr{M}}_3\\ \widetilde{\mathscr{M}}_3^T & \widetilde{\mathscr{M}}_2\end{bmatrix}, \tag{30}$$

where $\widetilde{\mathscr{M}}_2$ is the minor matrix of $\mathscr{M}$ by removing its first l $(1\leq l<N)$ row-column pairs, $\widetilde{\mathscr{M}}_1$ and $\widetilde{\mathscr{M}}_3$ are matrices with appropriate dimensions, and $\widetilde{D}_{1l}^*=\mathrm{diag}(d_{11}^*, d_{12}^*,\ldots,d_{1l}^*)$. If $\lambda_{\max}((G_1+G_1^T)/2)_l<-\Pi_1/c_1$ and with Lemma 9, we have $\widetilde{\mathscr{M}}_2<0$. Therefore, one can choose suitable positive constants $d_{1i}^*>0$, $i=1,2,\ldots,l$, such that $d_{1i}^*>\lambda_{\max}(\widetilde{\mathscr{M}}_1-\widetilde{\mathscr{M}}_3\widetilde{\mathscr{M}}_2^{-1}\widetilde{\mathscr{M}}_3^T)$. It follows from Lemma 11 and $\widetilde{\mathscr{M}}_2<0$ that $\mathscr{M}-c_1D_1^*<0$. Then, by $\Gamma_1>0$ and (29), we can conclude that

$$\dot{V}(t)\leq-e^T(t-h(t))\left(\left(\frac{c_2}{2}-\Pi_2\right)\left(I_N\otimes\Gamma_2\right)\right)$$

$$\cdot e(t-h(t)) - \left(\int_{t-k(t)}^{t} e(\theta)\,d\theta\right)^{T} \cdot \left(\left(\frac{c_3 k}{2} - \Pi_3\right)(I_N \otimes \Gamma_3)\right) \cdot \left(\int_{t-k(t)}^{t} e(\theta)\,d\theta\right). \tag{31}$$

We only need to choose the suitable positive constants $\overline{d}_2^*$ and $\overline{d}_3^*$ such that

$$\overline{d}_2^* - \frac{1}{c_2\varepsilon_4}\left[\varepsilon_2\lambda_{\max}\left(I_N \otimes F_2^T F_2\right) + c_2\varepsilon_7 + c_2\varepsilon_8\lambda_{\max}\left(I_N \otimes E_2^T E_2\right) - \lambda_{\min}\left(I_N \otimes \Gamma_2\right)\right] > 0, \tag{32}$$

$$\overline{d}_3^* - \frac{1}{c_3\varepsilon_5}\left[\varepsilon_3\lambda_{\max}\left(I_N \otimes F_3^T F_3\right) + c_3\varepsilon_9 + c_3\varepsilon_{10}\lambda_{\max}\left(I_N \otimes E_3^T E_3\right) - \lambda_{\min}\left(I_N \otimes \Gamma_3\right)\right] > 0. \tag{33}$$

We can choose $\overline{d}_2^*$ and $\overline{d}_3^*$ satisfying (32) and (33), respectively. Since Γ_1, Γ_2, and Γ_3 are positive definite matrix, we know that $\dot{V}(t) \leq 0$. Therefore, pinning controlled delayed neural networks (1) globally asymptotically synchronize to trajectory (6) if conditions (20), (21), and (22) hold. Then the controlled neural networks (1) are function projective synchronization. □

Remark 13. If there are no uncertain parameters in coupled delayed neural networks (1), $\Delta\Gamma_1 = \Delta\Gamma_2 = \Delta\Gamma_3 = 0$. One can obtain similar synchronization results.

Remark 14. The nodes pinned for directed networks are chosen as follows.

Step 1. Choose some appropriate parameters ε_i, $i = 1, 2, \ldots, 10$, by taking appropriate $\overline{d}_{1i}^*$, $i = 1, 2, \ldots, l$, $\overline{d}_2^*$, and $\overline{d}_3^*$ such that the conditions in Theorem 12 are feasible.

Step 2. The l pinned nodes are sorted according to the pinned-node selection scheme studied [26], for the pinning controlled error neural network (17); so, the nodes to be pinned are chosen in the particular order. Let $l = 1$, if the first inequalities of Theorem 12 are satisfied, and then the least number is 1; otherwise, go to the next step.

Step 3. If condition (20) is not satisfied, increase l ($l = l + 1$) gradually with more network nodes to the pinned node based on the order in Step 2 particularly until condition (20) holds.

For undirected networks, for example, the small-world network [31], the scale-free network [32], and the Watts-Strogatz network [39], we can randomly choose a set of pinned nodes to satisfy condition (20) by increasing the number of pinned nodes l.

3.2. FPS under Hybrid Adaptive Control. The nonlinear and adaptive controls are designed to realize FPS of neural networks with mixed time-varying delays and uncertainties asymmetric coupling. Then we have the following controlled form:

$$\mathscr{U}_i(t) = u_{i1}(t) + u_{i2}(t), \quad i = 1, 2, \ldots, N, \tag{34}$$

where

$$\begin{aligned} u_{i1}(t) &= \dot{\alpha}(t)s(t) - W_1\left[\alpha(t) f_1(s(t)) + f_1(\alpha(t)s(t))\right] - W_2\left[\alpha(t) f_2(s(t-h(t))) + f_2(\alpha(t)s(t-h(t)))\right] \\ &\quad - W_3\int_{t-k(t)}^{t}\left[\alpha(t) f_3(s(\theta)) - f_3(\alpha(t)s(\theta))\right]d\theta, \quad i = 1, 2, \ldots, N, \\ u_{i2}(t) &= -c_1 d_{1i}(t)\Gamma_1 e_i(t) - c_2 d_{2i}(t)\Gamma_2 e_i(t-h(t)) - c_3 d_{3i}(t)\Gamma_3\int_{t-k(t)}^{t} e_i(\theta)\,d\theta, \quad i = 1, 2, \ldots, N. \end{aligned} \tag{35}$$

Then, substituting (34) into (8), we have

$$\begin{aligned} \dot{e}_i(t) &= -Ae_i(t) + W_1\widetilde{f}_1(e_i(t)) + W_2\widetilde{f}_2(e_i(t-h(t))) + W_3\int_{t-k(t)}^{t}\widetilde{f}_3(e_i(\theta))\,d\theta \\ &\quad + c_1\sum_{j=1}^{N} G_{1_{ij}}(\Gamma_1 + \Delta\Gamma_1)e_j(t) + c_2\sum_{j=1}^{N} G_{2_{ij}}(\Gamma_2 + \Delta\Gamma_2)e_j(t-h(t)) \\ &\quad + c_3\sum_{j=1}^{N} G_{3_{ij}}(\Gamma_3 + \Delta\Gamma_3)\int_{t-k(t)}^{t} e_j(\theta)\,d\theta - c_1 d_{1i}(t)\Gamma_1 e_i(t) - c_2 d_{2i}(t)\Gamma_2 e_i(t-h(t)) \\ &\quad - c_3 d_{3i}(t)\Gamma_3\int_{t-k(t)}^{t} e_i(\theta)\,d\theta, \quad i = 1, 2, \ldots, N, \\ \dot{d}_{1i}(t) &= \beta_{i1}e_i^T(t)\Gamma_1 e_i(t), \quad i = 1, 2, \ldots, N, \\ \dot{d}_{2i}(t) &= \beta_{i2}e_i^T(t)\Gamma_2 e_i(t-h(t)), \quad i = 1, 2, \ldots, N, \\ \dot{d}_{3i}(t) &= \beta_{i3}e_i^T(t)\Gamma_3\int_{t-k(t)}^{t} e_i(\theta)\,d\theta, \quad i = 1, 2, \ldots, N, \end{aligned} \tag{36}$$

where

$$\Omega_1 = \frac{1}{\lambda_{\min}(I_N \otimes \Gamma_1)} \Big[-\lambda_{\max}(I_N \otimes A) + \frac{1}{2\varepsilon_1}\lambda_{\max}(I_N \otimes W_1 W_1^T) + \frac{\varepsilon_1}{2}\lambda_{\max}(I_N \otimes F_1^T F_1) + c_1 \lambda_{\max}(G_1)\lambda_{\max}(\Gamma_1) + \frac{c_3 k^2}{2}\lambda_{\max}(I_N \otimes \Gamma_3) + \frac{1}{2\varepsilon_2}\lambda_{\max}(I_N \otimes W_2 W_2^T) + \frac{1}{2\varepsilon_3}\lambda_{\max}(I_N \otimes W_3 W_3^T) + \frac{c_1 \varepsilon_6}{2}\lambda_{\max}(I_N \otimes E_1^T E_1) + \frac{c_1}{2\varepsilon_6}\lambda_{\max}(G_1 G_1^T)\lambda_{\max}(MM^T) + \frac{c_2}{2\varepsilon_7}\lambda_{\max}(G_2 G_2^T)\lambda_{\max}(\Gamma_2 \Gamma_2^T) + \frac{c_2}{2\varepsilon_8}\lambda_{\max}(G_2 G_2^T)\lambda_{\max}(MM^T) + \frac{c_3}{2\varepsilon_9}\lambda_{\max}(G_3 G_3^T)\lambda_{\max}(\Gamma_3 \Gamma_3^T) + \frac{c_3}{2\varepsilon_{10}}\lambda_{\max}(G_3 G_3^T)\lambda_{\max}(MM^T) + \frac{c_2}{2(1-\mu)}\lambda_{\max}(I_N \otimes \Gamma_2) + \frac{c_2 d_2^*}{2\varepsilon_4}\lambda_{\max}(I_N \otimes \Gamma_2 \Gamma_2^T) + \frac{c_3 d_3^*}{2\varepsilon_5}\lambda_{\max}(I_N \otimes \Gamma_3 \Gamma_3^T) \Big],$$

$$\Omega_2 = \frac{1}{2\lambda_{\min}(I_N \otimes \Gamma_2)} \left[\varepsilon_2 \lambda_{\max}(I_N \otimes F_2^T F_2) + c_2 \varepsilon_7 + c_2 \varepsilon_8 \lambda_{\max}(I_N \otimes E_2^T E_2) + c_2 d_2^* \varepsilon_4 \right],$$

$$\Omega_3 = \frac{1}{2\lambda_{\min}(I_N \otimes \Gamma_3)} \left[\varepsilon_3 \lambda_{\max}(I_N \otimes F_3^T F_3) + c_3 \varepsilon_9 + c_3 \varepsilon_{10} \lambda_{\max}(I_N \otimes E_3^T E_3) + c_3 d_3^* \varepsilon_5 \right],$$

$$\xi(t) = \left(e^T(t), e^T(t-h(t)), \left(\int_{t-k(t)}^{t} e(\theta)\, d\theta \right)^T \right)^T. \tag{37}$$

By using adaptive controlling method, we get the following theorem.

Theorem 15. *For some given synchronization scaling function $\alpha(t)$, neural networks (1) satisfying Assumptions 1, 2, and 3, and target system can realize function projective synchronization by the adaptive control law as shown in (34) if there exist positive constants ε_i, $i = 1, 2, \ldots, 10$, and by taking appropriate d_1^*, d_2^*, and d_3^* such that*

$$\begin{aligned} & d_1^* - \frac{\Omega_1}{c_1} > 0, \\ & d_2^* - \frac{1}{c_2 \varepsilon_4} \left[\varepsilon_2 \lambda_{\max}(I_N \otimes F_2^T F_2) + c_2 \varepsilon_7 + c_2 \varepsilon_8 \lambda_{\max}(I_N \otimes E_2^T E_2) - \lambda_{\min}(I_N \otimes \Gamma_2) \right] > 0, \\ & d_3^* - \frac{1}{c_3 \varepsilon_5} \left[\varepsilon_3 \lambda_{\max}(I_N \otimes F_3^T F_3) + c_3 \varepsilon_9 + c_3 \varepsilon_{10} \lambda_{\max}(I_N \otimes E_3^T E_3) - \lambda_{\min}(I_N \otimes \Gamma_3) \right] > 0. \end{aligned} \tag{38}$$

Then controlled neural networks (1) are function projective synchronization.

Proof. Construct the following Lyapunov-Krasovskii functional candidate:

$$V(t) = V_1(t) + V_2(t) + V_3(t) + V_4(t), \tag{39}$$

where

$$\begin{aligned} V_1(t) &= \frac{1}{2}\sum_{i=1}^{N} e_i^T(t) e_i(t), \\ V_2(t) &= \frac{c_2}{2(1-\mu)} \sum_{i=1}^{N} \int_{t-h(t)}^{t} e_i^T(\theta)\Gamma_2 e_i(\theta)\, d\theta, \\ V_3(t) &= \frac{c_3 k}{2} \sum_{i=1}^{N} \int_{-k}^{0} \int_{t+s}^{t} e_i^T(\theta)\Gamma_3 e_i(\theta)\, d\theta\, ds, \\ V_4(t) &= \frac{c_1}{2}\sum_{i=1}^{N} \frac{1}{\beta_{i1}} (d_{1i}(t) - d_1^*)^2 + \frac{c_2}{2}\sum_{i=1}^{N} \frac{1}{\beta_{i2}} (d_2(t) - d_{2i}^*)^2 + \frac{c_3}{2}\sum_{i=1}^{N} \frac{1}{\beta_{i3}} (d_3(t) - d_{3i}^*)^2. \end{aligned} \tag{40}$$

By taking the derivative of $V(t)$ along the trajectories of system (36) that is similar to the proof of Theorem 12, we obtain

$$\dot{V}(t) \le e^T(t) \Big[-(I_N \otimes A) + \frac{1}{2\varepsilon_1}(I_N \otimes W_1 W_1^T) + \frac{\varepsilon_1}{2}(I_N \otimes F_1^T F_1) + \frac{c_2}{2(1-\mu)}(I_N \otimes \Gamma_2) - c_1 d_1^* (I_N \otimes \Gamma_1) + c_1 (G_1 \otimes \Gamma_1) + \frac{c_3 k^2}{2}(I_N \otimes \Gamma_3) + \frac{1}{2\varepsilon_2}(I_N \otimes W_2 W_2^T) + \frac{1}{2\varepsilon_3}(I_N \otimes W_3 W_3^T)$$

$$
\begin{aligned}
&+\frac{c_1}{2\varepsilon_6}\left(G_1G_1^T\otimes MM^T\right)+\frac{c_1\varepsilon_6}{2}\left(I_N\otimes E_1^TE_1\right)\\
&+\frac{c_2}{2\varepsilon_7}\left(G_2G_2^T\otimes\Gamma_2\Gamma_2^T\right)+\frac{c_2}{2\varepsilon_8}\left(G_2G_2^T\otimes MM^T\right)\\
&+\frac{c_3}{2\varepsilon_9}\left(G_3G_3^T\otimes\Gamma_3\Gamma_3^T\right)+\frac{c_3}{2\varepsilon_{10}}\left(G_3G_3^T\otimes MM^T\right)\\
&+\frac{c_2d_2^*}{2\varepsilon_4}\left(I_N\otimes\Gamma_2\Gamma_2^T\right)+\frac{c_3d_3^*}{2\varepsilon_5}\left(I_N\otimes\Gamma_3\Gamma_3^T\right)\Bigg]e(t)\\
&-e^T(t-h(t))\left[\frac{c_2}{2}\left(I_N\otimes\Gamma_2\right)-\Omega_2\left(I_N\otimes\Gamma_2\right)\right]e(t\\
&-h(t))-\int_{t-k(t)}^{t}e^T(\theta)\\
&\cdot\left[\frac{c_3k}{2}\left(I_N\otimes\Gamma_3\right)-\Omega_3\left(I_N\otimes\Gamma_3\right)\right]e(\theta)\,d\theta,\\
\le{}& e^T(t)\left[\left(\Omega_1-c_1d_1^*\right)\left(I_N\otimes\Gamma_1\right)\right]e(t)-e^T(t-h(t))\\
&\cdot\left[\left(\frac{c_2}{2}-\Omega_2\right)\left(I_N\otimes\Gamma_2\right)\right]e(t-h(t))\\
&-\left(\int_{t-k(t)}^{t}e(\theta)\,d\theta\right)^T\left[\left(\frac{c_3k}{2}-\Omega_3\right)\left(I_N\otimes\Gamma_3\right)\right]\\
&\cdot\left(\int_{t-k(t)}^{t}e(\theta)\,d\theta\right).
\end{aligned}
\tag{41}
$$

It is obvious that there exist sufficiently large positive constants d_1^*, d_2^*, and d_3^* such that

$$d_1^*-\frac{\Omega_1}{c_1}>0, \tag{42}$$

$$
\begin{aligned}
d_2^*-\frac{1}{c_2\varepsilon_4}&\left[\varepsilon_2\lambda_{\max}\left(I_N\otimes F_2^TF_2\right)+c_2\varepsilon_7\right.\\
&\left.+c_2\varepsilon_8\lambda_{\max}\left(I_N\otimes E_2^TE_2\right)-\lambda_{\min}\left(I_N\otimes\Gamma_2\right)\right]>0,
\end{aligned}
\tag{43}
$$

$$
\begin{aligned}
d_3^*-\frac{1}{c_3\varepsilon_5}&\left[\varepsilon_3\lambda_{\max}\left(I_N\otimes F_3^TF_3\right)+c_3\varepsilon_9\right.\\
&\left.+c_3\varepsilon_{10}\lambda_{\max}\left(I_N\otimes E_3^TE_3\right)-\lambda_{\min}\left(I_N\otimes\Gamma_3\right)\right]>0.
\end{aligned}
\tag{44}
$$

We can choose d_1^*, d_2^*, and d_3^* satisfying (42), (43), and (44), respectively. The remaining proof is similar to Theorem 12 and omitted. □

4. Numerical Simulations

In this section, we provide several numerical examples to demonstrate the feasibility of the proposed method.

Example 16. Consider a two-dimensional neural network with time-varying delay presented in the following system:

$$
\begin{aligned}
\dot{s}(t)={}&-As(t)+W_1f_1(s(t))+W_2f_2(s(t-h(t)))\\
&+W_3\int_{t-k(t)}^{t}f_3(s(\theta))\,d\theta,
\end{aligned}
\tag{45}
$$

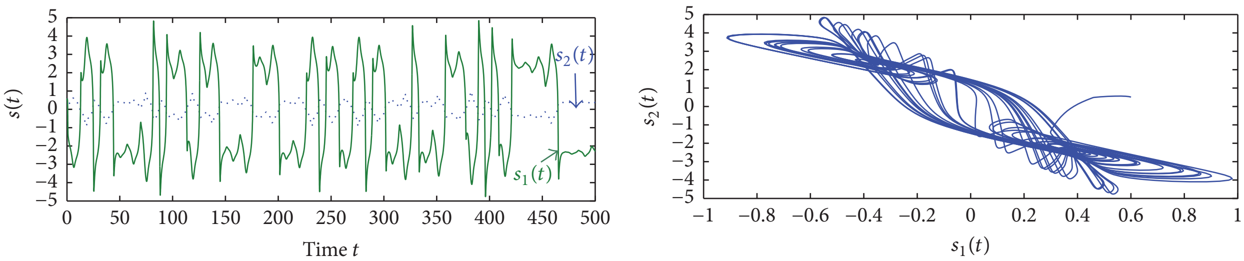
where $s(t)=\left[s_1(t)\ \ s_2(t)\right]^T\in\mathscr{R}^2$ is the state vector of the network, the activation function $f_j(x_i(t))=\tanh(x_i(t))$, $(i=1,2,\ j=1,2,3)$, the delays $h(t)=1-0.9\sin(t)$ and $k(t)=0.2\sin(t)$, and the other matrices are as follows:

$$
\begin{aligned}
A&=\begin{bmatrix}1&0\\0&1\end{bmatrix},\\
W_1&=\begin{bmatrix}2&-0.1\\-5&4.5\end{bmatrix},\\
W_2&=\begin{bmatrix}-1.5&-0.1\\-0.2&-4\end{bmatrix},\\
W_3&=\begin{bmatrix}-0.3&0.1\\0.1&-0.2\end{bmatrix}.
\end{aligned}
\tag{46}
$$

The dynamical chaotic trajectory of neural network (45) with initial conditions $s_1(r)=0.6$ and $s_2(r)=0.5$, $\forall r\in[-2,0]$, is shown in Figure 1.

Afterwards, the FPS problems for the nonlinear and adaptive pinning controlled network consisting of N two-dimensional neural networks are described as follows:

$$
\begin{aligned}
\dot{x}_i(t)={}&-Ax_i(t)+W_1f_1(x_i(t))\\
&+W_2f_2(x_i(t-h(t)))\\
&+W_3\int_{t-k(t)}^{t}f_3(x_i(\theta))\,d\theta\\
&+c_1\sum_{j=1}^{N}G_{1_{ij}}\left(\Gamma_1+\Delta\Gamma_1\right)x_j(t)\\
&+c_2\sum_{j=1}^{N}G_{2_{ij}}\left(\Gamma_2+\Delta\Gamma_2\right)x_j(t-h(t))\\
&+c_3\sum_{j=1}^{N}G_{3_{ij}}\left(\Gamma_3+\Delta\Gamma_3\right)\int_{t-k(t)}^{t}x_j(\theta)\,d\theta\\
&+\mathscr{U}_i(t),\quad i=1,2,\ldots,N,
\end{aligned}
\tag{47}
$$



(a) (b)

Figure 1: (a) Chaotic trajectory of neural network (45). (b) Phase portrait of the strange attractor.

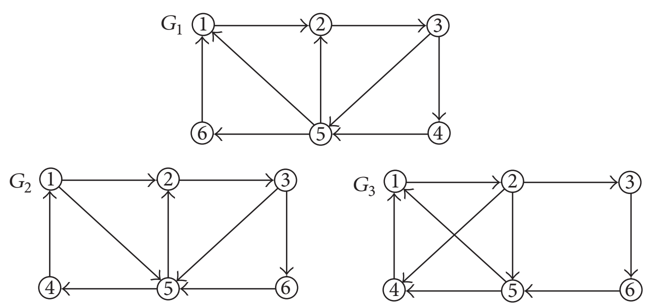


Figure 2: Simple directed neural network with 6 nodes.

where $x_i(t) = [x_{i1}(t), x_{i2}(t)]^T \in \mathscr{R}^2$ is the state variable of the ith node. The inner-coupling matrices with uncertainties are

$$\Gamma_1 = \begin{bmatrix} 5 & 0 \\ 0 & 5 \end{bmatrix},$$
$$\Gamma_2 = \begin{bmatrix} 2 & 0 \\ 0 & 2 \end{bmatrix},$$
$$\Gamma_3 = \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix},$$
$$M = \begin{bmatrix} 0.2 & 0 \\ 0 & 0.2 \end{bmatrix}, \quad (48)$$
$$\nabla(t) = \begin{bmatrix} \sin(t) & 0 \\ 0 & \cos(t) \end{bmatrix},$$
$$E_r = \begin{bmatrix} 0.1 & 0 \\ 0 & 0.1 \end{bmatrix} \quad (r = 1, 2, 3),$$

and the other parameters are the same as those in (45).

Directed Neural Network. We consider the directed neural networks as shown in Figure 2.

Choose the following parameters: the time-varying scaling function $\alpha(t) = 1.3\sin(2\pi/15)$, the coupling strength values $c_1 = 16$, $c_2 = 1$, and $c_3 = 1$, and the positive constants $\varepsilon_1 = 12.5$, $\varepsilon_2 = 4.5$, $\varepsilon_3 = 0.8$, $\varepsilon_4 = 0.7$, $\varepsilon_5 = 0.8$, $\varepsilon_6 = 7.2$, $\varepsilon_7 = 3.7$, $\varepsilon_8 = 5$, $\varepsilon_9 = 5$, and $\varepsilon_{10} = 12$. According to Figure 2, the controller networks with 6 nodes are described with the outer-coupling matrices by

$$G_1 = \begin{bmatrix} -2 & 0 & 0 & 0 & 1 & 1 \\ 1 & -2 & 0 & 0 & 1 & 0 \\ 0 & 1 & -1 & 0 & 0 & 0 \\ 0 & 0 & 1 & -1 & 0 & 0 \\ 0 & 0 & 1 & 1 & -2 & 0 \\ 0 & 0 & 0 & 0 & 1 & -1 \end{bmatrix},$$
$$G_2 = \begin{bmatrix} -1 & 0 & 0 & 1 & 0 & 0 \\ 1 & -2 & 0 & 0 & 1 & 0 \\ 0 & 1 & -1 & 0 & 0 & 0 \\ 0 & 0 & 0 & -1 & 1 & 0 \\ 1 & 0 & 1 & 0 & -3 & 1 \\ 0 & 0 & 1 & 0 & 0 & -1 \end{bmatrix}, \quad (49)$$
$$G_3 = \begin{bmatrix} -2 & 0 & 0 & 1 & 1 & 0 \\ 1 & -1 & 0 & 0 & 0 & 0 \\ 0 & 1 & -1 & 0 & 0 & 0 \\ 0 & 1 & 0 & -2 & 1 & 0 \\ 0 & 1 & 0 & 0 & -2 & 1 \\ 0 & 0 & 1 & 0 & 0 & -1 \end{bmatrix}.$$

Solution. As presented in Figure 2, there are the out-degrees and the in-degree of nodes. According to the pinned-node selection scheme, we rearrange the nodes in G_1 and the new

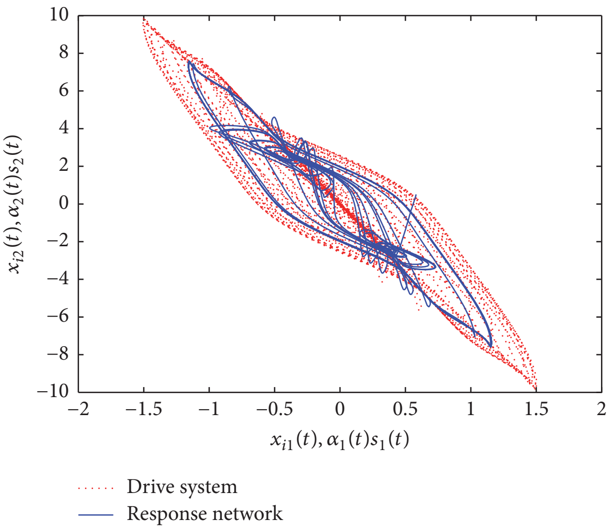


FIGURE 3: Chaotic behavior of isolate node $\alpha(t)s(t)$ (45) and node $x_i(t)$ (47) with the time-varying scaling function $\alpha(t)$.

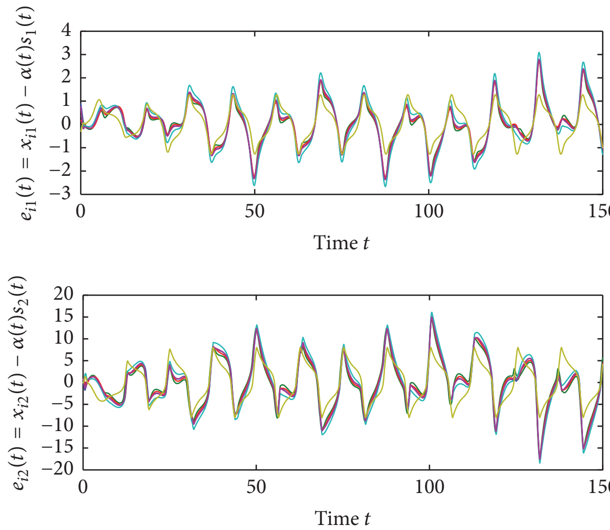


FIGURE 4: The FPS errors between the states of isolate node $\alpha(t)s(t)$ (45) and node $x_i(t)$ (47) without nonlinear and adaptive pinning control (14).

order is 3, 5, 4, 6, 1, 2. When node 3 is chosen as pinned node with $l = 1$, we obtain $d_{1l} = 5$, $\overline{d}_2^* = 2.0125$, and $\overline{d}_3^* = 3.4560$. Thus, it is confirmed that pinning conditions (20)–(22) in Theorem 12 hold:

$$\lambda_{\max}\left(\frac{G_1 + G_1^T}{2}\right)_l = -0.2989 < -\frac{\Pi_1}{c_1} = -\frac{4.5659}{15} = -0.2854. \tag{50}$$

Figure 3 shows the chaotic behavior of isolate node $\alpha(t)s(t)$ (45) and node $x_i(t)$ (47), with the time-varying scaling function $\alpha(t)$. Figure 4 shows the FPS errors between the states of isolate node $\alpha(t)s(t)$ (45) and node $x_i(t)$ (47), where $e_{ij}(t) = x_{ij}(t) - \alpha_j(t)s_j(t)$ for $i = 1, \ldots, 6$, $j = 1, 2$, without nonlinear and adaptive pinning control (14). Figure 5 shows the FPS errors between the states of isolate node $\alpha(t)s(t)$ (45) and node $x_i(t)$ (47) where $e_{ij}(t) = x_{ij}(t) - \alpha_j(t)s_j(t)$ for $i = 1, \ldots, 6$, $j = 1, 2$ with nonlinear and adaptive pinning control (14). Figure 6 gives the evolution of adaptive pinning feedback gains $d_{11}(t)$, $d_{21}(t)$, and $d_{31}(t)$.

Undirected Neural Network. We consider the FPS for a large-scale undirected Watts-Strogatz network with 30 identical nodes of the isolated dynamic network with mixed time-varying delays which is given in (47). Choose the time-varying scaling function $\alpha(t) = 1.3\sin(2\pi/15)$ and the coupling strength values $c_1 = 12$, $c_2 = 1$, and $c_3 = 1$. For a Watts-Strogatz network here, we set the parameters $[N = 30, K = 2, \text{and } \rho = 0.65]$, $[N = 30, K = 1, \text{and } \rho = 1]$, and $[N = 30, K = 1, \text{and } \rho = 0.8]$, respectively. Then, the coupling matrices G_1, G_2, and G_3 can be randomly generated by the Watts-Strogatz models and are shown in Figures 7–9, respectively.

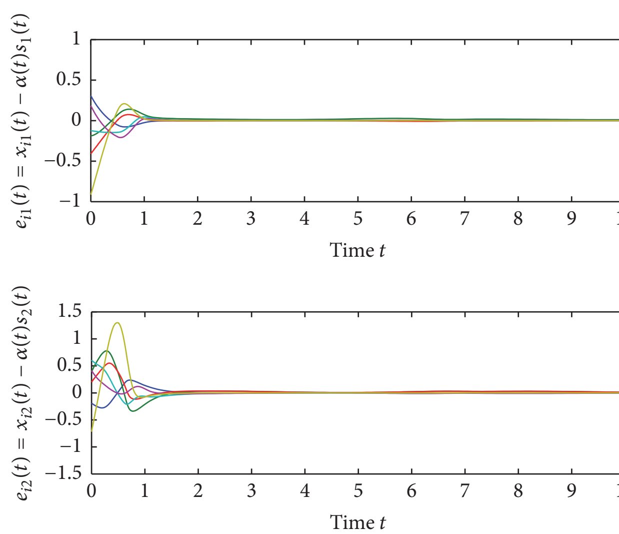


FIGURE 5: The FPS errors between the states of isolate node $\alpha(t)s(t)$ (45) and node $x_i(t)$ (47) with nonlinear and adaptive pinning control (14).

Solution. From conditions (20)–(22) in Theorem 12 and the positive constants $\varepsilon_1 = 12.5$, $\varepsilon_2 = 4.5$, $\varepsilon_3 = 0.8$, $\varepsilon_4 = 0.7$, $\varepsilon_5 = 0.8$, $\varepsilon_6 = 7.2$, $\varepsilon_7 = 3.7$, $\varepsilon_8 = 5$, $\varepsilon_9 = 5$, and $\varepsilon_{10} = 12$, one can check that the last three conditions in Theorem 12 are satisfied. We study how to select pinned nodes of network. As G_1 is an undirected Watts-Strogatz network, the pinned nodes can be randomly chosen for the convenience of practical applications by randomly choosing ten network nodes; that is, $l = 10$, and the feedback control gains are chosen as $d_{1i} = 30$ $(i = 1, 2, \ldots, 10)$, $\overline{d}_2^* = 2.0125$, and $\overline{d}_3^* = 3.4560$. From simple numerical calculation, it can

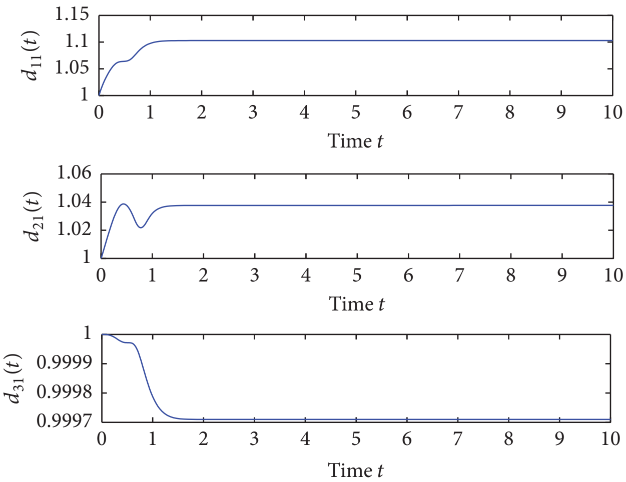


FIGURE 6: The evolution of adaptive pinning feedback gains $d_{11}(t)$, $d_{21}(t)$, and $d_{31}(t)$.

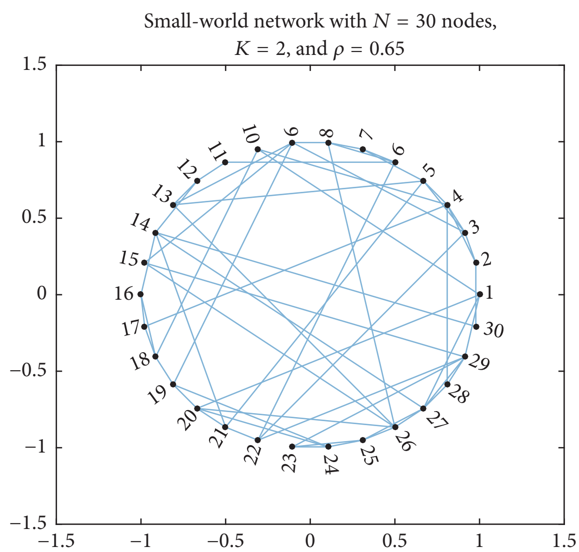


FIGURE 7: The topology structure of Watts-Strogatz neural network with $N = 30$, $K = 2$, and $\rho = 0.65$.

be seen that pinning condition (20) holds:

$$\lambda_{\max}\left(\frac{G_1 + G_1^T}{2}\right)_l = -0.6407 < -\frac{\Pi_1}{c_1} = -\frac{7.1110}{12} = -0.5926. \tag{51}$$

Figure 10 shows the FPS errors between the states of isolate node $\alpha(t)s(t)$ (45) and node $x_i(t)$ (47), where $e_{ij}(t) = x_{ij}(t) - \alpha_j(t)s_j(t)$ for $i = 1, \ldots, 6$, $j = 1, 2$, without nonlinear and adaptive pinning control (14). Figure 11 shows the FPS errors between the states of isolate node $\alpha(t)s(t)$ (45) and node $x_i(t)$ (47), where $e_{ij}(t) = x_{ij}(t) - \alpha_j(t)s_j(t)$ for $i = 1, \ldots, 6$, $j = 1, 2$, with nonlinear and adaptive pinning control (14). Figure 12 gives the evolution of adaptive pinning feedback gains $d_{1i}(t)$, $d_{2i}(t)$, and $d_{3i}(t)$ $(i = 1, 2, \ldots, 10)$.

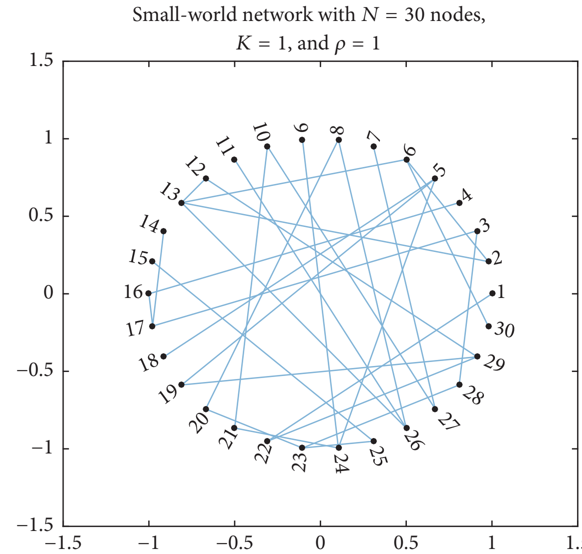


FIGURE 8: The topology structure of Watts-Strogatz neural network with $N = 30$, $K = 1$, and $\rho = 1$.

Example 17. We consider the FPS problems for the nonlinear and adaptive controlled network consisting of N two-dimensional neural networks (36). The directed neural networks are shown in Figure 13, where the constant coupling matrix is determined to be

$$G_1 = \begin{bmatrix} -1 & 0 & 0 & 0 & 1 \\ 1 & -2 & 0 & 0 & 1 \\ 0 & 1 & -1 & 0 & 0 \\ 0 & 0 & 1 & -1 & 0 \\ 0 & 0 & 1 & 1 & -2 \end{bmatrix},$$
$$G_2 = \begin{bmatrix} -2 & 0 & 0 & 1 & 1 \\ 1 & -1 & 0 & 0 & 0 \\ 0 & 0 & -1 & 0 & 1 \\ 0 & 1 & 1 & -2 & 0 \\ 0 & 1 & 0 & 1 & -2 \end{bmatrix}, \tag{52}$$
$$G_3 = \begin{bmatrix} -1 & 0 & 0 & 1 & 0 \\ 1 & -1 & 0 & 0 & 0 \\ 1 & 1 & -2 & 0 & 0 \\ 0 & 0 & 1 & -2 & 1 \\ 0 & 1 & 0 & 0 & -1 \end{bmatrix}.$$

The inner-coupling matrices with uncertainties are the same as in (47), and the other parameters are the same as those in (45). Choose the time-varying scaling function $\alpha(t) = 1.3\sin(2\pi/15)$ and the coupling strength values $c_1 = 2.5$, $c_2 = 0.2$, and $c_3 = 0.5$.

Solution. From conditions (38) in Theorem 15 and the positive constants $\varepsilon_1 = 0.1$, $\varepsilon_2 = 10.5$, $\varepsilon_3 = 3.5$, $\varepsilon_4 = 0.5$, $\varepsilon_5 = 0.7$, $\varepsilon_6 =$

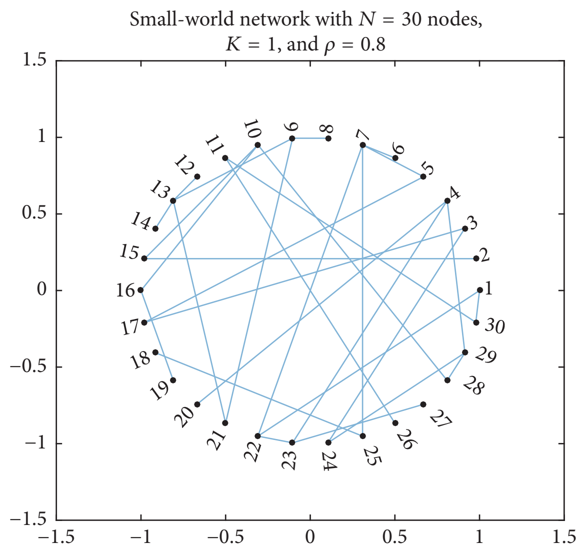


Figure 9: The topology structure of Watts-Strogatz neural network with $N = 30$, $K = 1$, and $\rho = 0.8$.

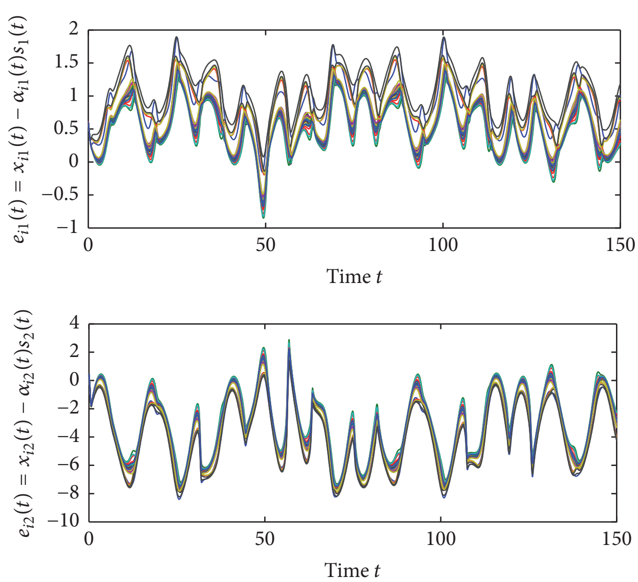


Figure 10: The FPS errors between the states of isolate node $\alpha(t)s(t)$ (45) and node $x_i(t)$ (47) without nonlinear and adaptive pinning control (14).

10, $\varepsilon_7 = 3.7$, $\varepsilon_8 = 6$, $\varepsilon_9 = 4.2$, and $\varepsilon_{10} = 5$, one can check that the last three conditions in Theorem 15 are satisfied. Then, we obtain $d_1^* > 3.4425$, $d_2^* > 2.8000$, and $d_3^* > 5.5199$.

Figure 14 shows the FPS errors between the states of isolate node $\alpha(t)s(t)$ of (45) and node $x_i(t)$ of (47), where $e_{ij}(t) = x_{ij}(t) - \alpha_j(t)s_j(t)$ for $i = 1, 2$, $j = 1, 2, 3$, without nonlinear and adaptive control (34). Figure 15 shows the FPS errors between the states of isolate node $\alpha(t)s(t)$ of (45) and node $x_i(t)$ of (47), where $e_{ij}(t) = x_{ij}(t) - \alpha_j(t)s_j(t)$ for $i = 1, 2$, $j = 1, 2, 3$, with nonlinear and adaptive control (34). Figure 16 gives the evolution of adaptive feedback gains $d_{11}(t)$, $d_{21}(t)$, and $d_{31}(t)$.

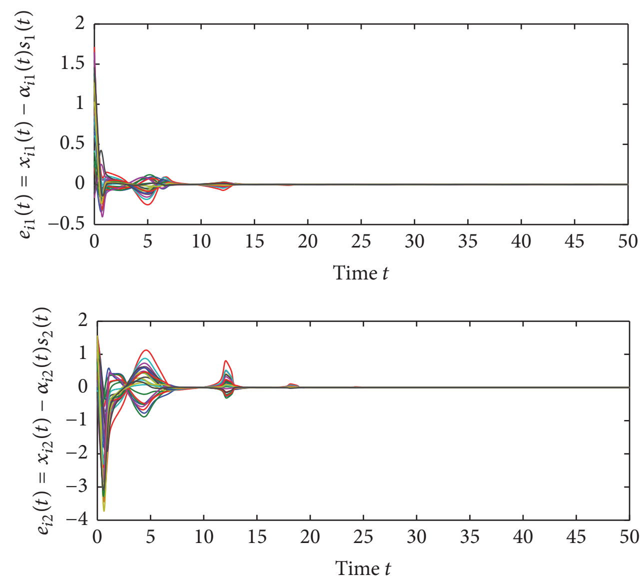


Figure 11: The FPS errors between the states of isolate node $\alpha(t)s(t)$ (45) and node $x_i(t)$ (47) with nonlinear and adaptive pinning control (14).

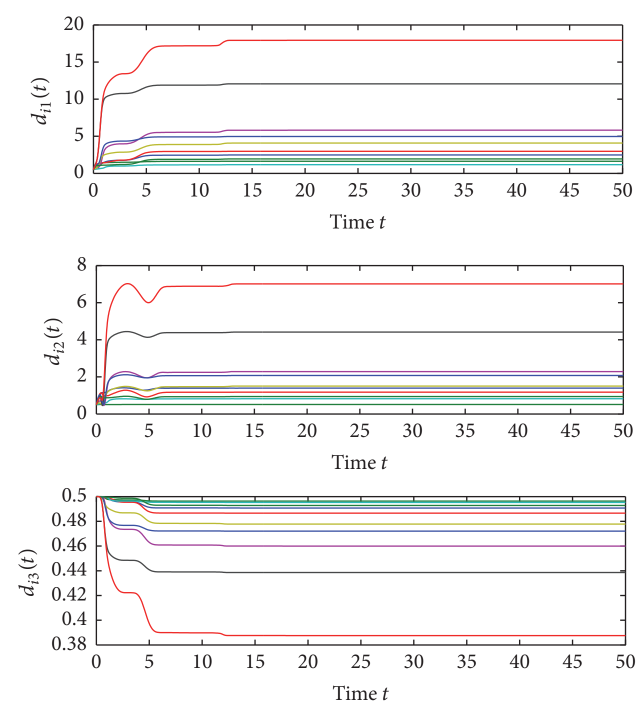


Figure 12: The evolution of adaptive pinning feedback gains $d_{i1}(t)$, $d_{i2}(t)$, and $d_{i3}(t) (i = 1, 2, \ldots, 10)$.

5. Conclusions

In this paper, the hybrid adaptive pinning control for FPS of neural networks with mixed time-varying delays and uncertainties asymmetric coupling were investigated. We have applied the use of nonlinear and adaptive pinning controls and the nonlinear and adaptive controls. Some sufficient conditions are derived to guarantee the FPS by

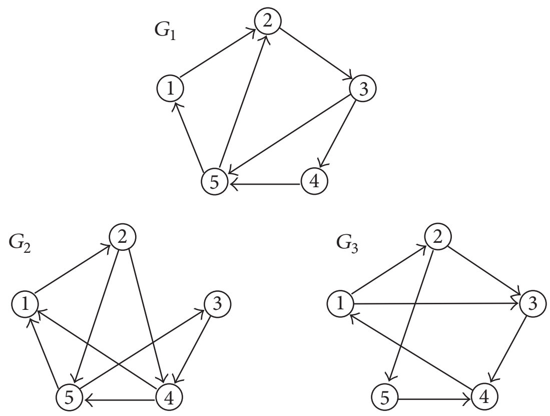


FIGURE 13: Simple directed neural network with 5 nodes.

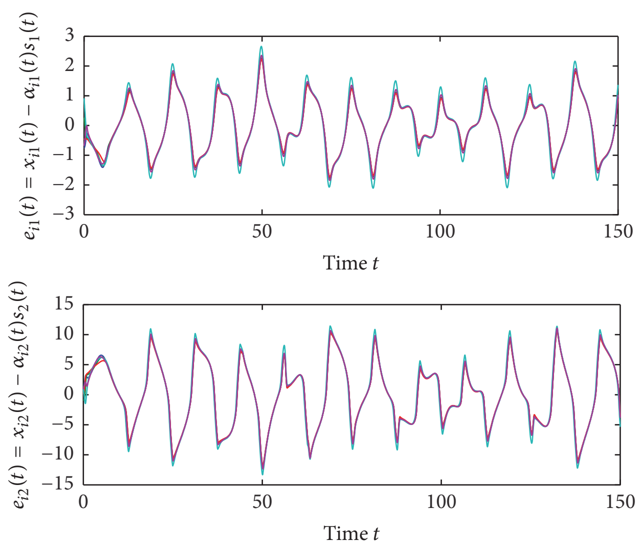


FIGURE 14: The FPS errors between the states of isolate node $\alpha(t)s(t)$ (45) and node $x_i(t)$ (47) without nonlinear and adaptive control (14).

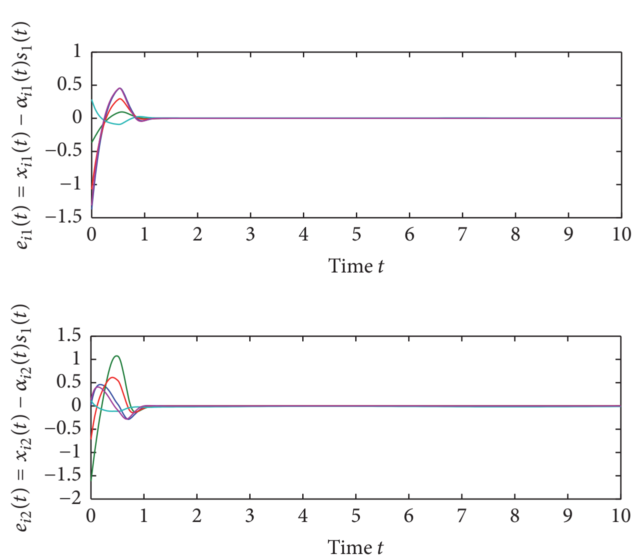


FIGURE 15: The FPS errors between the states of isolate node $\alpha(t)s(t)$ (45) and node $x_i(t)$ (47) with nonlinear and adaptive control (14).

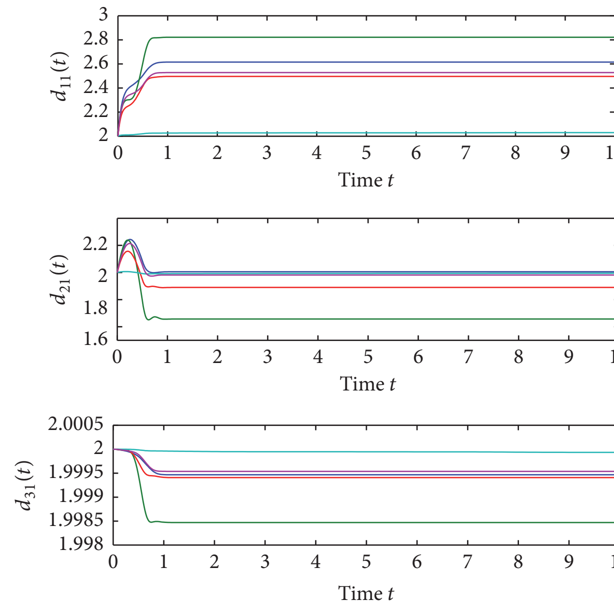


FIGURE 16: The evolution of adaptive feedback gains $d_{11}(t)$, $d_{21}(t)$, and $d_{31}(t)$.

use of the Lyapunov-Krasovskii function method. Moreover, the drive and response systems could be synchronized up to the desired scaling functions based on the adaptive control technique. Furthermore, numerical examples are given to illustrate the effectiveness of the proposed theoretical results in this paper as well.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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Research Article

Numerical Study for Time Delay Multistrain Tuberculosis Model of Fractional Order

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A novel mathematical fractional model of multistrain tuberculosis with time delay memory is presented. The proposed model is governed by a system of fractional delay differential equations, where the fractional derivative is defined in the sense of the Grünwald–Letinkov definition. Modified parameters are introduced to account for the fractional order. The stability of the equilibrium points is investigated for any time delay. Nonstandard finite deference method is proposed to solve the resulting system of fractional-order delay differential equations. Numerical simulations show that nonstandard finite difference method can be applied to solve such fractional delay differential equations simply and effectively.

1. Introduction

It is known that tuberculosis (TB) is one of the most important infectious diseases and is considered as the second largest cause of mortality by infectious diseases and a challenging disease to control [1]. Time delays required to treatment of active TB present a major obstacle to the control of a TB epidemic [2]; it worsens the disease, increases the risk of death, and enhances tuberculosis transmission to the community [3, 4]. Both patient and the health system may be responsible for the treatment delay [3]. On the other hand, mathematical models are quite important and efficient tool to describe and investigate TB diseases; see [5–9]. In [10], Silva et al. presented TB model with time-delay memory. Herein, we consider a general model of multistrain TB diseases with time-delay memory. A discrete time delay is incorporated, in the variables of active TB infection of two and three strains, to represent the required time to commencement of treatment and diagnosis [11].

The multistrain TB model incorporates three strains: *extensively drug-resistant* (XDR), emerging *multidrug resistant* (MDR), and drug sensitive, and has been developed by Arino and Soliman [12] in 2015. Several factors of spreading TB such as the exogenous reinfection, the fast infection, and secondary infection are included in this model. Sweilam et al. introduced some numerical studies for this model in [13–16].

Fractional differential equations have been the focus of many studies due to their frequent appearance in various sciences [13–20]. The general theory of differential equations with delays (DDEs) is widely developed and discussed in the literature [21–25]. *Delayed fractional differential equations* (DFDEs) are also used to describe dynamical systems [26–28]. Recently, DFDEs begin to raise the attention of many researchers [29–33]. Relatable and efficient numerical techniques for DFDEs are very necessary and important [34]. *Nonstandard finite difference method* (NSFDM) was firstly proposed by Mickens [35] in 1980s to solve numerically the *ordinary differential equations* (ODEs) and *partial differential*

Table 1: Interpretation of the variable states of system (1).

Variable	Interpretation
$S(t)$	Individuals have never encountered TB.
$L_s(t)$	The individuals infected with drug-sensitive TB but not infectious.
$L_m(t)$	Infected with MDR-TB but not infectious.
$L_x(t)$	Infected with XDR-TB but not infectious.
$I_s(t)$	Able to infect others with drug sensitive strain.
$I_m(t)$	Able to infect others with MDR strain.
$I_x(t)$	Able to infect others with XDR strain.
$R(t)$	Recovered by getting a successful treatment.
$N(t)$	The variable of population size. $N(t) = S(t) + L_s(t) + L_m(t) + L_x(t) + I_s(t) + I_m(t) + I_x(t) + R(t)$.

Table 2: All adapted parameters and their interpretation of system (1).

Parameter	Interpretation
d^α	Natural death rate
b^α	Birth rate
λ_j^α	Rate of infected individuals move to L_j with strain $j \in \{s, m, x\}$
$1 - \lambda_j^\alpha$	Rate of newly infected individuals progressing to active TB with strain $j \in \{s, m, x\}$
β_j^α	Transmission coefficient with strain $j \in \{s, m, x\}$
ε_j^α	Rate of endogenous reactivation of L_j
γ_j^α	Rate of natural recovery to the latent stage L_j
δ_j^α	Rate of death due to TB of strain j
α_{j1}^α, α_{j2}^α	Rate of exogenous reinfection of L_{j1} due to contact with I_{j2}
$1 - \sigma_j^\alpha$	Efficiency of treatment in preventing infection with strain j
P_1^α	Probability of treatment success for L_s
$1 - P_1^\alpha$	Proportion of treated L_s moved to L_m due to incomplete treatment or lack of strict compliance in the use of drugs
P_2^α	Probability of treatment success for I_s
$1 - P_2^\alpha$	Proportion of treated I_s moved to L_m due to incomplete treatment or lack of strict compliance in the use of drugs
P_3^α	Probability of treatment success for I_m
$1 - P_3^\alpha$	proportion of treated I_m moved to L_x due to incomplete treatment or lack of strict compliance in the use of drugs
t_{1s}^α	Rate of treatment for L_s
t_{2j}^α	Rate of treatment for I_j. Note that t_{2x} is the rate of successful treatment of I_x, $j \in \{x, m, s\}$

equations (PDEs) with more accuracy than *standard finite difference method* (SFDM). It is considered as a powerful numerical scheme that preserves properties of exact solutions of the differential equation [36].

The main aim of work is to study numerically the solutions of fractional-order model of multistrain TB with time delay memory. The presence of fractional-order and time delays in the model can lead to a notable increase in the complexity of the observed behavior, and the solution continuously depends on all the previous states. An efficient numerical method, NSFDM, is used to numerically solve the fractional-order delay model. The rest of the paper is organized as follows: In Section 2, we present a fractional order model with time delay for multistrain TB. Stability of equilibrium points is presented in Section 3. NSFD for fractional-order delay differential equations is introduced in Section 4. Some numerical simulations are given in Section 5, and conclusion in Section 6. Some definitions on fractional calculus and some properties of nonstandard discretization are given in Appendix.

2. Fractional Multistrain TB Model with Time Delay

In this section, a multistrain TB model of fractional-order and time delay memory is presented. The population of interest is divided into eight compartments depending on their epidemiological stages as follows: susceptible (S); latently infected with drug sensitive TB (L_s); latently infected with MDR TB (L_m); latently infected with XDR TB (L_x); sensitive drug TB infectious (I_s); MDR TB infectious (I_m); XDR TB infectious (I_x); recovered R. One biological meaning of the given parameters is given in Table 1. One of the main assumptions of this model is that the total population $N(t)$, with $N(t) = S(t) + L_s(t) + L_m(t) + L_x(t) + I_s(t) + I_m(t) + I_x(t) + R(t)$, is variable of the time. We introduce a discrete time delay in the state variables I_m and I_x, denoted by τ, that represents the time required for diagnosis and commencement of treatment of active TB infection of two and three strains. The parameters in the modified the model are described in Table 2; see [37]. The modified system of multistrain TB model of fractional-order and time delay is

$$
\begin{aligned}
D_t^\alpha S &= b^\alpha - d^\alpha S - \beta_s^\alpha \frac{SI_s}{N} - \beta_m^\alpha \frac{SI_m}{N} - \beta_x^\alpha \frac{SI_x}{N},\\
D_t^\alpha L_s &= \lambda_s^\alpha \beta_s^\alpha \frac{SI_s}{N} + \sigma_s^\alpha \lambda_s^\alpha \beta_s^\alpha \frac{RI_s}{N} + \gamma_s^\alpha I_s - \alpha_{ss}^\alpha \beta_s^\alpha \frac{L_s I_s}{N}\\
&\quad - \alpha_{sm}^\alpha \beta_m^\alpha \frac{L_s I_m}{N} - \alpha_{sx}^\alpha \beta_x^\alpha \frac{L_s I_x}{N} - \left(d^\alpha + \varepsilon_s^\alpha + t_{1s}^\alpha\right) L_s,\\
D_t^\alpha L_m &= \lambda_m^\alpha \beta_m^\alpha \frac{SI_m}{N} + \sigma_m^\alpha \lambda_m^\alpha \beta_m^\alpha \frac{RI_m}{N} + \gamma_m^\alpha I_m\\
&\quad + \alpha_{sm}^\alpha \beta_m^\alpha \lambda_m^\alpha \frac{L_s I_m}{N} + \left(1 - P_1^\alpha\right) t_{1s}^\alpha L_s + \left(1 - P_2^\alpha\right) t_{2s}^\alpha I_s\\
&\quad - \alpha_{mm}^\alpha \beta_m^\alpha \frac{L_m I_m}{N} - \alpha_{mx}^\alpha \beta_x^\alpha \frac{L_m I_x}{N} - \left(d^\alpha + \varepsilon_m^\alpha\right) L_m,\\
D_t^\alpha L_x &= \lambda_x^\alpha \beta_x^\alpha \frac{SI_x}{N} + \sigma_x^\alpha \lambda_x^\alpha \beta_x^\alpha \frac{RI_x}{N} + \gamma_x^\alpha I_x + \alpha_{sx}^\alpha \beta_x^\alpha \lambda_x^\alpha\\
&\quad \cdot \frac{L_s I_x}{N} + \alpha_{mx}^\alpha \beta_x^\alpha \lambda_x^\alpha \frac{L_m I_x}{N} + \left(1 - P_3^\alpha\right) t_{2m}^\alpha I_m - \alpha_{xx}^\alpha \beta_x^\alpha\\
&\quad \cdot \frac{L_x I_x}{N} - \left(d^\alpha + \varepsilon_x^\alpha\right) L_x,\\
D_t^\alpha I_s &= \alpha_{ss}^\alpha \beta_s^\alpha \frac{L_s I_s}{N} + \left(1 - \lambda_s^\alpha\right) \beta_s^\alpha \left(\frac{SI_s}{N} + \sigma_s^\alpha \frac{RI_s}{N}\right)\\
&\quad + \varepsilon_s^\alpha L_s - \left(d^\alpha + \delta_s^\alpha + t_{2s}^\alpha + \gamma_s^\alpha\right) I_s,\\
D_t^\alpha I_m &= \alpha_{mm}^\alpha \beta_m^\alpha \frac{L_m I_m}{N} + \left(1 - \lambda_m^\alpha\right)\\
&\quad \cdot \beta_m^\alpha \left(\frac{SI_m}{N} + \sigma_m^\alpha \frac{RI_m}{N} + \alpha_{sm}^\alpha \frac{L_s I_m}{N}\right) + \varepsilon_m^\alpha L_m\\
&\quad - \left(d^\alpha + \delta_m^\alpha + \gamma_m^\alpha\right) I_m - t_{2m}^\alpha I_m (t - \tau),\\
D_t^\alpha I_x &= \alpha_{xx}^\alpha \beta_x^\alpha \frac{L_x I_x}{N} + \left(1 - \lambda_x^\alpha\right)\\
&\quad \cdot \beta_x^\alpha \left(\frac{SI_x}{N} + \sigma_x^\alpha \frac{RI_x}{N} + \alpha_{sx}^\alpha \frac{L_s I_x}{N} + \alpha_{mx}^\alpha \frac{L_m I_x}{N}\right) + \varepsilon_x^\alpha L_x\\
&\quad - \left(d^\alpha + \delta_x^\alpha + \gamma_x^\alpha\right) I_x - t_{2x}^\alpha I_x (t - \tau),\\
D_t^\alpha R &= P_1^\alpha t_{1s}^\alpha L_s + P_2^\alpha t_{2s}^\alpha I_s + P_3^\alpha t_{2m}^\alpha I_m + t_{2x}^\alpha I_x (t - \tau)\\
&\quad - \sigma_s^\alpha \beta_s^\alpha \frac{RI_s}{N} - \sigma_m^\alpha \beta_m^\alpha \frac{RI_m}{N} - \sigma_x^\alpha \beta_x^\alpha \frac{RI_x}{N} - d^\alpha R.
\end{aligned}
\tag{1}
$$

The initial conditions for system (1) are $S(\xi) = \theta_1(\xi)$, $L_s(\xi) = \theta_2(\xi)$, $L_m(\xi) = \theta_3(\xi)$, $L_x(\xi) = \theta_4(\xi)$, $I_s(\xi) = \theta_5(\xi)$, $I_m(\xi) = \theta_6(\xi)$, $I_x(\xi) = \theta_7(\xi)$, $R(\xi) = \theta_8(\xi)$, $\xi \in [-\tau, 0]$, where $\theta = (\theta_1, \theta_2, \ldots, \theta_8)^T \in C$, where C is the Banach space $C([0,\tau], \mathbb{R}^8)$. From biological meaning, we further assume that $\theta_i > 0$ for $i = 1, \ldots, 8$. Throughout this paper, we focus on the dynamics of the solutions of (1) in the restricted region, $\Omega = \{(S, L_s, L_m, L_x, I_s, I_m, I_x, R) \in \mathbb{R}^8 \mid S + L_s + L_m + L_x + I_s + I_m + I_x + R \le b^\alpha/d^\alpha\}$. We refer here to [24, 31], for local existence, uniqueness, and continuation results.

The unique solution $(S(t), L_s(t), L_m(t), L_x(t), I_s(t), I_m(t), I_x(t), R(t))$ of (1) with initial condition exists for all time $t \ge 0$. Consider the solutions of (1), for $(S, L_s, L_m, L_x, I_s, I_m, I_x, R) \in \Omega'$, where Ω' is the interior of Ω, for all $\xi \in [-\tau, 0]$. Then the solutions stay in the interior of the region for all time $t \ge 0$; that is, the region is positively invariant with respect to system (1) (see, e.g., [31]). Model (1) has a disease-free equilibrium given by $E_0 = (b^\alpha/d^\alpha, 0, 0, 0, 0, 0, 0, 0)$; see [32].

2.1. Basic Reproduction Number. The basic reproduction number, R_0, is defined as the expected number of secondary cases produced, in a completely susceptible population, by a typical infective individual [32]. Herein, we apply the method in [32] to drive R_0. The order of the infected variables is

$$
\mathfrak{I} := \left(L_s, L_m, L_x, I_s, I_m, I_x\right)'. \tag{2}
$$

The vector representing new infections into the infected classes F is given by

$$
F := \begin{pmatrix}
\lambda_s^\alpha \beta_s^\alpha \frac{SI_s}{N} + \sigma_s^\alpha \lambda_s^\alpha \beta_s^\alpha \frac{RI_s}{N}\\
\lambda_m^\alpha \beta_m^\alpha \frac{SI_m}{N} + \sigma_m^\alpha \lambda_m^\alpha \beta_m^\alpha \frac{RI_m}{N}\\
\lambda_x^\alpha \beta_x^\alpha \frac{SI_x}{N} + \sigma_x^\alpha \lambda_x^\alpha \beta_x^\alpha \frac{RI_x}{N}\\
\left(1 - \lambda_s^\alpha\right) \beta_s^\alpha \left(\frac{SI_s}{N} + \sigma_s^\alpha \frac{RI_s}{N}\right)\\
\left(1 - \lambda_m^\alpha\right) \beta_m^\alpha \left(\frac{SI_m}{N} + \sigma_m^\alpha \frac{RI_m}{N}\right)\\
\left(1 - \lambda_x^\alpha\right) \beta_x^\alpha \left(\frac{SI_x}{N} + \sigma_x^\alpha \frac{RI_x}{N}\right)
\end{pmatrix}. \tag{3}
$$

The vector V representing other flows within and out of the infected classes $\mathfrak{I}$ is given by

$$
V := \begin{pmatrix}
\alpha_{ss}^\alpha \beta_s^\alpha \frac{L_s I_s}{N} - \alpha_{sm}^\alpha \beta_m^\alpha \frac{L_s I_m}{N} - \alpha_{sx}^\alpha \beta_x^\alpha \frac{L_s I_x}{N} + \gamma_s^\alpha I_s - \left(d^\alpha + \varepsilon_s^\alpha + t_{1s}^\alpha\right) L_s,\\
+\gamma_m^\alpha I_m + \alpha_{sm}^\alpha \beta_m^\alpha \lambda_m^\alpha \frac{L_s I_m}{N} + \left(1 - P_1^\alpha\right) t_{1s}^\alpha L_s + \left(1 - P_2^\alpha\right) t_{2s}^\alpha I_s,\\
-\alpha_{mm}^\alpha \beta_m^\alpha \frac{L_m I_m}{N} - \alpha_{mx}^\alpha \beta_x^\alpha \frac{L_m I_x}{N} - \left(d^\alpha + \varepsilon_m^\alpha\right) L_m,\\
+\gamma_x^\alpha I_x + \alpha_{sx}^\alpha \beta_x^\alpha \lambda_x^\alpha \frac{L_s I_x}{N} + \alpha_{mx}^\alpha \beta_x^\alpha \lambda_x^\alpha \frac{L_m I_x}{N} + \left(1 - P_3^\alpha\right) t_{2m}^\alpha I_m - \alpha_{xx}^\alpha \beta_x^\alpha \frac{L_x I_x}{N} - \left(d^\alpha + \varepsilon_x^\alpha\right) L_x,\\
\alpha_{ss}^\alpha \beta_s^\alpha \frac{L_s I_s}{N} + \varepsilon_s^\alpha L_s - \left(d^\alpha + \delta_s^\alpha + t_{2s}^\alpha + \gamma_s^\alpha\right) I_s,\\
\left(\alpha_{mm}^\alpha \beta_m^\alpha \frac{L_m I_m}{N} + \alpha_{sm}^\alpha \frac{L_s I_m}{N}\right) + \varepsilon_m^\alpha L_m - \left(d^\alpha + \delta_m^\alpha + \gamma_m^\alpha + t_{2m}^\alpha\right) I_m,\\
\left(\alpha_{xx}^\alpha \beta_x^\alpha \frac{L_x I_x}{N} + \left(1 - \lambda_x^\alpha\right) \beta_x^\alpha + \alpha_{sx}^\alpha \frac{L_s I_x}{N} + \alpha_{mx}^\alpha \frac{L_m I_x}{N}\right) + \varepsilon_x^\alpha L_x - \left(d^\alpha + \delta_x^\alpha + \gamma_x^\alpha + t_{2x}^\alpha\right) I_x,
\end{pmatrix}. \tag{4}
$$

The matrix of new infections F and the matrix of transfers between compartments V are the Jacobian matrices obtained by differentiating F and V with respect to the infected variables $\mathfrak{I}$ and evaluating at the disease-free equilibrium. They take the form

$$F := \begin{pmatrix} 0 & A \\ 0 & B \end{pmatrix}, \quad V := \begin{pmatrix} C & D \\ E & F_2 \end{pmatrix}, \tag{5}$$

where

$$\begin{aligned}
A &= \begin{pmatrix} \lambda_s^\alpha \beta_s^\alpha & 0 & 0 \\ 0 & \lambda_m^\alpha \beta_m^\alpha & 0 \\ 0 & 0 & \lambda_s^\alpha \beta_s^\alpha \end{pmatrix}, \\
B &= \begin{pmatrix} \left(1-\lambda_s^\alpha\right)\beta_s^\alpha & 0 & 0 \\ 0 & \left(1-\lambda_m^\alpha\right)\beta_m^\alpha & 0 \\ 0 & 0 & \left(1-\lambda_s^\alpha\right)\beta_s^\alpha \end{pmatrix}, \\
C &= \begin{pmatrix} \left(d^\alpha + \varepsilon_s^\alpha + t_{1s}^\alpha\right) & 0 & 0 \\ \left(-1+P_1^\alpha\right) t_{1s}^\alpha & \left(d^\alpha + \varepsilon_m^\alpha\right) & 0 \\ 0 & 0 & \left(d^\alpha + \varepsilon_x^\alpha\right) \end{pmatrix}, \\
D &= \begin{pmatrix} -\gamma_s^\alpha & 0 & 0 \\ \left(-1+P_2^\alpha\right) t_{2s}^\alpha & -\gamma_m^\alpha & 0 \\ 0 & \left(-1+P_3^\alpha\right) t_{2m}^\alpha & -\gamma_x^\alpha \end{pmatrix}, \\
F_2 &= \begin{pmatrix} \left(d^\alpha + \delta_s^\alpha + \gamma_s^\alpha + t_{2s}^\alpha\right) & 0 & 0 \\ 0 & \left(d^\alpha + \delta_m^\alpha + \gamma_m^\alpha + t_{2m}^\alpha\right) & 0 \\ 0 & 0 & \left(d^\alpha + \delta_x^\alpha + \gamma_x^\alpha + t_{2x}^\alpha\right) \end{pmatrix}, \\
E &= \begin{pmatrix} -\varepsilon_s^\alpha & 0 & 0 \\ 0 & -\varepsilon_m^\alpha & 0 \\ 0 & 0 & -\varepsilon_x^\alpha \end{pmatrix}.
\end{aligned} \tag{6}$$

Then the basic reproduction number R_0 for system (1) is the spectral radius of the next generation matrix and is given by

$$R_0 = \rho\left(FV^{-1}\right) = \max\left(R_{0s}, R_{0m}, R_{0x}\right), \tag{7}$$

where

$$\begin{aligned}
R_{0s} &= \frac{\beta_s^\alpha\left(\varepsilon_s^\alpha + \left(1-\lambda_s^\alpha\right)\left(d^\alpha + t_{1s}^\alpha\right)\right)}{\left(\varepsilon_s^\alpha + d^\alpha + t_{1s}^\alpha\right)\left(t_{2s}^\alpha + \delta_s^\alpha + d^\alpha\right) + \gamma_s^\alpha\left(t_{1s}^\alpha + d^\alpha\right)}, \\
R_{0m} &= \frac{\beta_m^\alpha\left(\varepsilon_m^\alpha + \left(1-\lambda_m^\alpha\right) d^\alpha\right)}{\left(\varepsilon_m^\alpha + d^\alpha\right)\left(t_{2m}^\alpha + \delta_m^\alpha + d^\alpha\right) + d^\alpha \gamma_m^\alpha}, \\
R_{0x} &= \frac{\beta_x^\alpha\left(\varepsilon_x^\alpha + \left(1-\lambda_x^\alpha\right) d^\alpha\right)}{\left(\varepsilon_x^\alpha + d^\alpha\right)\left(t_{2x}^\alpha + \delta_x^\alpha + d^\alpha\right) + d^\alpha \gamma_x^\alpha}.
\end{aligned} \tag{8}$$

3. Equilibrium Points and Their Asymptotic Stability

To discuss the local asymptotic stability for evaluating the equilibrium points, let us consider the following [38]:

$$\begin{aligned} D_t^\alpha S &= D_t^\alpha L_s = D_t^\alpha L_m = D_t^\alpha L_x = D_t^\alpha I_s = D_t^\alpha I_m \\ &= D_t^\alpha I_x = D_t^\alpha R = 0. \end{aligned} \tag{9}$$

Then, from (A.1)

$$g_i\left(\overline{S}, \overline{L_s}, \overline{L_m}, \overline{L_x}, \overline{I_s}, \overline{I_m}, \overline{I_x}, \overline{R}\right) = 0, \quad i = 1, 2, 3, \ldots, 8, \tag{10}$$

where $(\overline{S}, \overline{L_s}, \overline{L_m}, \overline{L_x}, \overline{I_s}, \overline{I_m}, \overline{I_x}, \overline{R})$ denotes any equilibrium point.

3.1. Stability of the Disease-Free Equilibrium. If $I_s(t) = I_m(t) = I_x(t) = 0$ then $L_s(t) = L_m(t) = L_x(t) = 0$, $R(t) = 0$, and

$S(t) = b^\alpha/d^\alpha$. Then the disease-free equilibrium (DFE) is $E_0 = \{(b^\alpha/d^\alpha, 0, 0, 0, 0, 0, 0, 0)\}$.

Let us consider the coordinate transformation: $s(t) = S(t) - \overline{S}$, $l_s(t) = L_s(t) - \overline{L_s}$, $l_m(t) = L_m(t) - \overline{L_m}$, $l_x(t) = L_x(t) - \overline{L_x}$, $i_s(t) = I_s(t) - \overline{I_s}$, $i_m(t) = I_m(t) - \overline{I_m}$, $i_x(t) = I_x(t) - \overline{I_x}$, $r(t) = R(t) - \overline{R}$. The corresponding characteristic equation for DFE is given as follows:

$$(J(E_0) - \lambda I) = \begin{pmatrix} \lambda - a & 0 & 0 & 0 & b & c & d_1 & 0 \\ 0 & \lambda - e & 0 & 0 & f & 0 & 0 & 0 \\ 0 & g & \lambda - h & 0 & p & q & 0 & 0 \\ 0 & 0 & 0 & \lambda - r & 0 & s & t & 0 \\ 0 & u & 0 & 0 & \lambda - v & 0 & 0 & 0 \\ 0 & 0 & w & 0 & 0 & \lambda - x + t_{2m}^\alpha e^{(-\lambda\tau)} & 0 & 0 \\ 0 & 0 & 0 & y & 0 & 0 & \lambda - z + t_{2x}^\alpha e^{(-\lambda\tau)} & 0 \\ 0 & m & 0 & 0 & n & j & t_{2x}^\alpha e^{(-\lambda\tau)} & \lambda - a \end{pmatrix}, \quad (11)$$

where $a = -d^\alpha$, $b = -\beta_s^\alpha$, $c = -\beta_m^\alpha$, $d_1 = -\beta_x^\alpha$, $e = -(d^\alpha + \varepsilon_s^\alpha + t_{1s}^\alpha)$, $f = \gamma_s^\alpha + \lambda_s^\alpha\beta_s^\alpha$, $g = (1 - p_1^\alpha)t_{1s}^\alpha$, $h = -(d^\alpha + \varepsilon_m^\alpha)$, $p = (1-p_2^\alpha)t_{2s}^\alpha$, $q = \gamma_m^\alpha + \lambda_m^\alpha\beta_m^\alpha$, $r = -(d^\alpha + \varepsilon_x^\alpha)$, $s = (1-p_3^\alpha)t_{2m}^\alpha$, $t = \gamma_x^\alpha + \lambda_x^\alpha\beta_x^\alpha$, $u = \varepsilon_s^\alpha$, $v = -(d^\alpha + \delta_s^\alpha + t_{2s}^\alpha + \gamma_s^\alpha)$, $w = \varepsilon_m^\alpha$, $x = -(d^\alpha + \delta_m^\alpha + \gamma_m^\alpha)$, $y = \varepsilon_x^\alpha$, $z = -(d^\alpha + \delta_x^\alpha + \gamma_x^\alpha)$, $m = p_1^\alpha t_{1s}^\alpha$, $n = p_2^\alpha t_{2s}^\alpha$, $j = p_3^\alpha t_{2m}^\alpha$.

The characteristic equation associated with above matrix is [38]

$$\begin{aligned} &\Delta(\lambda) = \left|J(E_0) - \lambda I\right| = 0, \\ &(a-\lambda)^2 \left(\lambda^2 - \left(r + z + t_{2x}^\alpha e^{(-\lambda\tau)}\right)\lambda - yt \right. \\ &\quad \left. + \left(z - t_{2x}^\alpha e^{(-\lambda\tau)}\right) r\right) \left(-\lambda^2 + \left(h + x - t_{2m}^\alpha e^{(-\lambda\tau)}\right)\lambda \right. \\ &\quad \left. - \left(x + t_{2m}^\alpha e^{(-\lambda\tau)}\right) h + wq\right) \left(-\lambda^2 + (e+v)\lambda + uf \right. \\ &\quad \left. - ve\right) = 0. \end{aligned} \quad (12)$$

Lemma 1. *If $R_0 < 1$, then the disease-free equilibrium E_0 is locally asymptotically stable for $\tau = 0$.*

Proof. When $\tau = 0$, the associated transcendental characteristic equation $\Delta(\lambda)$ of system (1) at E_0 becomes $\Delta(\lambda) = P(\lambda) = 0$, and then the eigenvalues of the Jacobian matrix are

$$\begin{aligned} &\lambda_{1,2} = -d, \\ &\lambda_{3,4} \\ &= \frac{r + (z - t_{2x}^\alpha) \pm \sqrt{\left(r^2 - 2(z - t_{2x}^\alpha) r + (z - t_{2x}^\alpha)^2 + 4yt\right)}}{2}, \\ &\lambda_{5,6} \\ &= \frac{x - t_{2m}^\alpha + h \pm \sqrt{(x - t_{2m}^\alpha)^2 - 2(x - t_{2m}^\alpha) h + h^2 + 4wq}}{2}, \\ &\lambda_{7,8} = \frac{v + e \pm \sqrt{(v^2 - 2ve + e^2 + 4uf)}}{2}, \end{aligned} \quad (13)$$

and by using Routh Hurwitz Theorem [28], these roots are negative or have negative real parts and all eigenvalues satisfy Matignon's conditions [39], given by ($|\arg\lambda_i| > \alpha\pi/2$) so the disease-free equilibrium E_0 is locally asymptotically stable. □

Lemma 2. *Let $R_0 < 1$, and then the disease-free equilibrium E_0 is locally asymptotically stable for $\tau > 0$.*

Proof. Let us consider $\tau > 0$, and we noted that second and third factor of the characteristic equation (12), which are $(\lambda^2 - (r + z + t_{2x}^\alpha e^{(-\lambda\tau)})\lambda - yt + (z - t_{2x}^\alpha e^{(-\lambda\tau)})r)$ and $(-\lambda^2 + (h + x - t_{2m}^\alpha e^{(-\lambda\tau)})\lambda - (x + t_{2m}^\alpha e^{(-\lambda\tau)})h + wq)$, have no pure imaginary roots for any value of the delay τ, if $R_0 < 1$. Hence all the roots of the characteristic equation have negative real parts and we get that DFE is locally asymptotically stable regardless of the value of the delay and all eigenvalues satisfy Matignon's conditions [39], given by ($|\arg\lambda_i| > \alpha\pi/2$) so the disease-free equilibrium E_0 is locally asymptotically stable. □

3.2. Stability of the Endemic Equilibrium. System (1) has an endemic equilibrium if at least one of the infected variables is not zero. The expression "analytic" is complexity and not useful for our purposes. Consider the values of parameters from Table 3. Then the basic reproduction number is $R_0 > 1$. The endemic equilibrium $S = 338.2$, $L_s = 0$, $L_m = 0$, $L_x = 2233.8$, $I_s = 0$, $I_m = 0$, $I_x = 4820.6$, $R = 62.0$. The matrices

A_1 and A_2 associated with the linearized system at the endemic equilibrium are computed as

$$A_1 = \begin{pmatrix} -9.0226 & 0.4107 & 0.4107 & 0.4107 & -0.2244 & -0.2244 & -0.2244 & 0.4107 \\ 0 & -2.2127 & 0 & 0 & 0.6321 & 0 & 0 & 0 \\ 0 & 0.8800 & -1.3327 & 0 & 0.800 & 0.6321 & 0 & 0 \\ 4.4475 & 0.1472 & 0.1472 & -1.4118 & -0.0791 & -0.0750 & 0.3432 & 1.0525 \\ 0 & 0.5000 & 0 & 0 & -1.2729 & 0 & 0 & 0 \\ 0 & 0.0146 & 0.5 & 0 & 0 & -0.4415 & 0 & 0 \\ 4.1762 & -0.1241 & -0.3181 & 0.6023 & -0.3504 & -0.3504 & -0.5675 & 0.7813 \\ 0.0188 & 0.0188 & 0.0188 & 0.0188 & -0.0103 & 0.0196 & 0.0237 & -2.6245 \end{pmatrix},$$
$$A_2 = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -t_{2m}^{\alpha} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -t_{2x}^{\alpha} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & t_{2x}^{\alpha} & 0 \end{pmatrix}. \tag{14}$$

The transcendental characteristic equation $\Delta\lambda = (\lambda I - A_1 - e^{-\tau\lambda}A_2)$ is given by

$$\begin{aligned} &\lambda^8 + \left(18.8862 - 0.0680e^{-\tau\lambda}\right)\lambda^7 \\ &\quad + \left(1.2702 \times 10^2 - 1.2255e^{-\tau\lambda} + 0.0012e^{-2\tau\lambda}\right)\lambda^6 \\ &\quad + \left(4.2273 \times 10^2 - 7.5306e^{-\tau\lambda} + 0.0198e^{-2\tau\lambda}\right)\lambda^5 \\ &\quad + \left(7.7354 \times 10^2 - 22.1163e^{-\tau\lambda} + 0.10986e^{-2\tau\lambda}\right)\lambda^4 \\ &\quad + \left(7.9327 \times 10^2 - 34.3423e^{-\tau\lambda} + 0.2751e^{-2\tau\lambda}\right)\lambda^3 \\ &\quad + \left(4.3522 \times 10^2 - 28.4367e^{-\tau\lambda} + 0.3354e^{-2\tau\lambda}\right)\lambda^2 \\ &\quad + \left(1.1156 \times 10^2 - 11.6693e^{-\tau\lambda} + 0.18817e^{-2\tau\lambda}\right) \\ &\quad \cdot \lambda\left(9.6913 - 1.8329e^{-\tau\lambda} + 0.0367e^{-2\tau\lambda}\right) = 0, \end{aligned} \tag{15}$$

when $\tau = 0$, and we have the following characteristic equation:

$$\begin{aligned} &\lambda^8 + 18.8182\lambda^7 + 125.7957\lambda^6 + 415.2192\lambda^5 \\ &\quad + 751.5336\lambda^4 + 759.2028\lambda^3 + 407.1187\lambda^2 \\ &\quad + 100.0789\lambda + 7.8951 = 0. \end{aligned} \tag{16}$$

The roots of (16) are −0.14208, −0.41505, −1.57465, −1.40036, −1.01044, −9.15198, $-2.56181 + 0.05148i$, and $-2.56181 + 0.05148i$, and these roots are negative or have negative real parts and all eigenvalues satisfy Matignon's conditions [39], given by ($|\arg\lambda_i| > \alpha\pi/2$) $i = 1, 2, \ldots, 8$ so the endemic equilibrium is locally asymptotically stable.

Consider now the case $\tau > 0$; we noted that the roots of the characteristic equation (15) have no pure imaginary roots for any value of the delay τ, if $R_0 > 1$. Hence all the roots of the characteristic equation have negative real parts and all eigenvalues satisfy Matignon's conditions [39]. Therefore, the endemic equilibrium is locally asymptotically.

4. NSFD for Fractional Delay Differential Equations

In this section, we apply NSFD method with GLFDs to obtain the discretization of the delay fractional multistrain TB model (1), which will yield the following equations:

$$\begin{aligned} \sum_{j=0}^{n+1}\omega_j^{\alpha}S^{n+1-j} &= b^{\alpha} - d^{\alpha}S^{n+1} - \beta_s^{\alpha}\frac{S^{n+1}I_s^n}{N^n} - \beta_m^{\alpha}\frac{S^{n+1}I_m^n}{N^n} \\ &\quad - \beta_x^{\alpha}\frac{S^{n+1}I_x^n}{N^n}, \end{aligned}$$

$$\sum_{j=0}^{n+1}\omega_j^\alpha L_s^{n+1-j} = \lambda_s^\alpha\beta_s^\alpha\frac{S^{n+1}I_s^n}{N^n} + \sigma_s^\alpha\lambda_s^\alpha\beta_s^\alpha\frac{R^{n+1}I_s^n}{N^n} + \gamma_s^\alpha I_s^n - \alpha_{ss}^\alpha\beta_s\frac{L_s^{n+1}I_s^n}{N^n} - \alpha_{sx}^\alpha\beta_x^\alpha\frac{L_s^{n+1}I_x^n}{N^n} - \left(d^\alpha + \varepsilon_s^\alpha + t_{1s}^\alpha\right)\cdot L_s^{n+1} - \alpha_{sm}^\alpha\beta_m^\alpha\frac{L_s^{n+1}I_m^n}{N^n},$$

$$\sum_{j=0}^{n+1}\omega_j^\alpha L_m^{n+1-j} = \lambda_m^\alpha\beta_m^\alpha\frac{S^{n+1}I_m^n}{N^n} + \sigma_m^\alpha\lambda_m^\alpha\beta_m^\alpha\frac{R^{n+1}I_m^n}{N^n} + \lambda_m^\alpha\alpha_{sm}^\alpha\beta_m^\alpha\frac{L_s^{n+1}I_m^n}{N^n} + \gamma_m^\alpha I_m^n + t_{1s}^\alpha L_s^{n+1} - P_1^\alpha t_{1s}^\alpha L_s^{n+1} + t_{2s}^\alpha I_s^n - P_2^\alpha t_{2s}^\alpha I_s^n - \alpha_{mm}^\alpha\beta_m^\alpha\frac{L_m^{n+1}I_m^n}{N^n} - \alpha_{mx}^\alpha\beta_x^\alpha\frac{L_m^{n+1}I_x^n}{N^n} - \left(d^\alpha + \varepsilon_m^\alpha\right)L_m^{n+1},$$

$$\sum_{j=0}^{n+1}\omega_j^\alpha L_x^{n+1-j} = \lambda_x^\alpha\beta_x^\alpha\frac{S^{n+1}I_x^n}{N^n} + \sigma_x^\alpha\lambda_x^\alpha\beta_x^\alpha\frac{R^{n+1}I_x^n}{N^n} + \lambda_x^\alpha\alpha_{sx}^\alpha\beta_x^\alpha\frac{L_s^{n+1}I_x^n}{N^n} + \gamma_x^\alpha I_x^n + \lambda_x^\alpha\alpha_{mx}^\alpha\beta_x^\alpha\frac{L_m^{n+1}I_x^n}{N^n} + t_{2m}^\alpha I_m^n - P_3^\alpha t_{2m}^\alpha I_m^n - \alpha_{xx}^\alpha\beta_x^\alpha\frac{L_x^{n+1}I_x^n}{N^n} - \left(d^\alpha + \varepsilon_x^\alpha\right)\cdot L_x^{n+1},$$

$$\sum_{j=0}^{n+1}\omega_j^\alpha I_s^{n+1-j} = \alpha_{ss}^\alpha\beta_s^\alpha\frac{L_s^{n+1}I_s^n}{N^n} + \left(1-\lambda_s^\alpha\right)\cdot\beta_s^\alpha\left(\frac{S^{n+1}I_s^n}{N^n} + \sigma_s^\alpha\frac{R^{n+1}I_s^n}{N^n}\right) + \varepsilon_s^\alpha L_s^{n+1} - \left(d^\alpha + \delta_s^\alpha\right)\cdot I_s^{n+1} - \left(\gamma_s^\alpha + t_{2s}^\alpha\right)I_s^n,$$

$$\sum_{j=0}^{n+1}\omega_j^\alpha I_m^{n+1-j} = \alpha_{mm}^\alpha\beta_m^\alpha\frac{L_m^{n+1}I_m^n}{N^n} + \left(1-\lambda_m^\alpha\right)\cdot\beta_m^\alpha\left(\frac{S^{n+1}I_m^n}{N^n} + \sigma_m^\alpha\frac{R^{n+1}I_m^n}{N^n} + \alpha_{sm}^\alpha\frac{L_s^{n+1}I_m^n}{N^n}\right) + \varepsilon_m^\alpha L_m^{n+1} - \left(d^\alpha + \delta_m^\alpha\right)I_m^{n+1} - \gamma_m^\alpha I_m - t_{2m}^\alpha I_m^{n-\kappa},$$

$$\sum_{j=0}^{n+1}\omega_j^\alpha I_x^{n+1-j} = \alpha_{xx}^\alpha\beta_x^\alpha\frac{L_x^{n+1}I_x^n}{N^n} + \left(1-\lambda_x^\alpha\right)\cdot\beta_m\left(\frac{S^{n+1}I_x^n}{N^n} + \sigma_x\frac{R^{n+1}I_x^n}{N^n} + \alpha_{mx}\frac{L_x^{n+1}I_m^n}{N^n}\right) + \varepsilon_x^\alpha L_x^{n+1} - \left(d^\alpha + \delta_x^\alpha\right)I_x^{n+1} - \gamma_x^\alpha I_x - t_{2x}^\alpha I_x^{n-\kappa},$$

$$\sum_{j=0}^{n+1}\omega_j^\alpha R^{n+1-j} = P_1^\alpha t_{1s}^\alpha L_s^{n+1} + P_2^\alpha t_{2s}^\alpha I_s^n + P_3^\alpha t_{2m}^\alpha I_m^n + t_{2x}^\alpha I_x^{n-\kappa} - d^\alpha R^{n+1} - \sigma_s^\alpha\beta_s^\alpha\frac{R^{n+1}I_s^n}{N^n} - \sigma_m^\alpha\beta_m^\alpha\frac{R^{n+1}I_m^n}{N^n} - \sigma_x^\alpha\beta_x^\alpha\frac{R^{n+1}I_x^n}{N^n}, \tag{17}$$

where

$$N^n = S^n + L_s^n + L_m^n + L_x^n + I_s^n + I_m^n + I_x^n + R^n, \tag{18}$$

and $\omega_0^\alpha = (\varphi_i(h))^{-\alpha}$, $i = 1, 2, \ldots, 8$, $n = -\kappa, -\kappa+1, \ldots, 0, 1$, where the nonlocal approximations are used for the nonlinear terms and the following functions of denominator:

$$\begin{aligned}
\varphi_1(h) &= \frac{e^{d^\alpha h} - 1}{d^\alpha},\\
\varphi_2(h) &= \frac{e^{(d^\alpha+\varepsilon_s^\alpha+t_{1s}^\alpha)h} - 1}{\left(d^\alpha + \varepsilon_s^\alpha + t_{1s}^\alpha\right)},\\
\varphi_3(h) &= \frac{e^{(d^\alpha+\varepsilon_m^\alpha)h} - 1}{\left(d^\alpha + \varepsilon_m^\alpha\right)},\\
\varphi_4(h) &= \frac{e^{(d^\alpha+\varepsilon_x^\alpha)h} - 1}{\left(d^\alpha + \varepsilon_x^\alpha\right)},\\
\varphi_5(h) &= \frac{1 - e^{-(d^\alpha+\delta_s^\alpha)h}}{\left(\gamma_s^\alpha + t_{2s}^\alpha\right)},\\
\varphi_6(h) &= \frac{1 - e^{-(d^\alpha+\delta_m^\alpha)h}}{\left(\gamma_m^\alpha + t_{2m}^\alpha\right)},\\
\varphi_7(h) &= \frac{1 - e^{-(d^\alpha+\delta_x^\alpha)h}}{\left(\gamma_x^\alpha + t_{2x}^\alpha\right)},\\
\varphi_8(h) &= \frac{e^{d^\alpha h} - 1}{d^\alpha}.
\end{aligned} \tag{19}$$

Then we obtain

$$S^{n+1} = \frac{b^\alpha - \sum_{j=1}^{n+1}\omega_j^\alpha S^{n+1-j}}{\left(\varphi_1(h)\right)^{-\alpha} + d^\alpha + \left(\beta_s^\alpha I_s^n + \beta_m^\alpha I_m^n + \beta_x^\alpha I_x^n\right)/N^n},$$

$$L_s^{n+1} = \frac{\left(\beta_s^\alpha I_s^n/N^n\right)\lambda_s^\alpha\left(S^{n+1} + \sigma_s^\alpha R^{n+1}\right) + \gamma_s^\alpha I_s^n - \sum_{j=1}^{n+1}\omega_j^\alpha L_s^{n+1-j}}{\left(\varphi_2(h)\right)^{-\alpha} + \left(d^\alpha + t_{1s}^\alpha + \varepsilon_s^\alpha\right) + \left(1/N^n\right)\left(\alpha_{ss}^\alpha\beta_s^\alpha I_s^n + \alpha_{sm}^\alpha\beta_m^\alpha I_m^n + \alpha_{sx}^\alpha\beta_x^\alpha I_x^n\right)},$$

$$L_m^{n+1} = \frac{\left(\beta_m^\alpha \lambda_m^\alpha I_m^n / N^n\right)\left(S^{n+1} + \sigma_m^\alpha R^{n+1} + \alpha_{sm}^\alpha L_s^{n+1}\right) + \gamma_m^\alpha I_m^n + t_{1s}^\alpha L_s^{n+1}\left(1 - P_1^\alpha\right)}{\left(\varphi_3(h)\right)^{-\alpha} + \left(d^\alpha + \varepsilon_m^\alpha\right) + \left(1/N^n\right)\left(\alpha_{mm}^\alpha \beta_m^\alpha I_m^n + \alpha_{mx}^\alpha \beta_x^\alpha I_x^n\right)} + \frac{t_{2s}^\alpha I_s^n\left(1 - P_2^\alpha\right) - \sum_{j=1}^{n+1} \omega_j^\alpha L_m^{n+1-j}}{\left(\varphi_3(h)\right)^{-\alpha} + \left(d^\alpha + \varepsilon_m^\alpha\right) + \left(1/N^n\right)\left(\alpha_{mm}^\alpha \beta_m^\alpha I_m^n + \alpha_{mx}^\alpha \beta_x^\alpha I_x^n\right)},$$

$$L_x^{n+1} = \frac{\left(\beta_x^\alpha \lambda_x^\alpha I_x^n / N^n\right)\left(S^{n+1} + \sigma_x^\alpha R^{n+1} + \alpha_{sx}^\alpha L_s^{n+1} + \alpha_{mx}^\alpha L_m^{n+1}\right) + t_{2m}^\alpha I_m^n\left(1 - P_3^\alpha\right)}{\left(\varphi_4(h)\right)^{-\alpha} + \left(d^\alpha + \varepsilon_x^\alpha\right) + \left(1/N^n\right)\left(\alpha_{xx}^\alpha \beta_x^\alpha I_x^n\right)} + \frac{\gamma_x^\alpha I_x^n - \sum_{j=1}^{n+1} \omega_j^\alpha L_x^{n+1-j}}{\left(\varphi_4(h)\right)^{-\alpha} + \left(d^\alpha + \varepsilon_x^\alpha\right) + \left(1/N^n\right)\left(\alpha_{xx}^\alpha \beta_x^\alpha I_x^n\right)},$$

$$I_s^{n+1} = \frac{\varphi_5(h)\,\beta_s^\alpha\left(I_s^n / N^n\right)\left(\alpha_{ss}^\alpha L_s^{n+1} + \left(1 - \lambda_s^\alpha\right)\left(S^{n+1} + \sigma_s^\alpha R^{n+1}\right)\right)}{\left(\varphi_5(h)\right)^{-\alpha} + \left(d^\alpha + \delta_s^\alpha\right)} - \frac{\left(\gamma_s^\alpha + \left(t_{2s}^\alpha\right)\right) I_s^n + \varepsilon_s^\alpha L_s^{n+1} - \sum_{j=1}^{n+1} \omega_j^\alpha I_s^{n+1-j}}{\left(\varphi_5(h)\right)^{-\alpha} + \left(d^\alpha + \delta_s^\alpha\right)},$$

$$I_m^{n+1} = \frac{\beta_m^\alpha\left(I_m^n / N^n\right)\left(\alpha_{mm}^\alpha L_m^{n+1} + \left(1 - \lambda_m^\alpha\right)\left(S^{n+1} + \sigma_m^\alpha R^{n+1} + \alpha_{sm}^\alpha L_s^{n+1}\right)\right)}{\left(\varphi_6(h)\right)^{-\alpha} + \left(d^\alpha + \delta_m^\alpha\right)} - \frac{\gamma_m I_m^n - t_{2m}^\alpha I_m^{n-\kappa} + \varepsilon_m^\alpha L_m^{n+1} - \sum_{j=1}^{n+1} \omega_j^\alpha I_m^{n+1-j}}{\left(\varphi_6(h)\right)^{-\alpha} + \left(d^\alpha + \delta_m^\alpha\right)},$$

$$I_x^{n+1} = \frac{\beta_x^\alpha\left(I_x^n / N^n\right)\left(\alpha_{xx}^\alpha L_x^{n+1} + \left(1 - \lambda_x^\alpha\right)\left(S^{n+1} + \sigma_x^\alpha R^{n+1} + \alpha_{sx}^\alpha L_s^{n+1} + \alpha_{mx}^\alpha L_m^{n+1}\right)\right)}{\left(\varphi_7(h)\right)^{-\alpha} + \left(d^\alpha + \delta_x^\alpha\right)} - \frac{\gamma_x^\alpha I_x^n - t_{2x}^\alpha I_x^{n-\kappa} + \varepsilon_x^\alpha L_x^{n+1} - \sum_{j=1}^{n+1} \omega_j^\alpha I_x^{n+1-j}}{\left(\varphi_7(h)\right)^{-\alpha} + \left(d^\alpha + \delta_x^\alpha\right)},$$

$$R^{n+1} = \frac{t_{1s}^\alpha P_1^\alpha L_s^{n+1} + P_2^\alpha t_{2s}^\alpha I_s^n + t_{2m}^\alpha P_3^\alpha I_m^n + t_{2x}^\alpha I_x^{n-\kappa} - \sum_{j=1}^{n+1} \omega_j^\alpha R^{n+1-j}}{\left(\varphi_8(h)\right)^{-\alpha} + d^\alpha + \left(1/N^n\right)\left(\sigma_s^\alpha \beta_s^\alpha I_s^n + \sigma_m^\alpha \beta_m^\alpha I_m^n + \sigma_x^\alpha \beta_x^\alpha I_x^n\right)}. \tag{20}$$

5. Numerical Results and Simulations

In this section, we show the effectiveness of the numerical technique for delay fractional differential equations. Throughout this section, all simulations are performed with initial conditions $(S(0), L_s(0), L_m(0), L_x(0), I_s(0), I_m(0), I_x(0), R(0)) = (5000, 50, 50, 50, 30, 30, 30, 60)$, with the parameters in Table 3. The approximate solutions of the proposed system are given in Figures 1–12 at different values of τ and α. Figure 1 shows the behavior of the approximate solutions of $R(t)$ in two cases with and without delay using dde23 at $\alpha = 1$ and $\tau = 0.3$. In Figure 2, we use the same data in Figure 1 and use NSFDM; we noted that the number of individuals $R(t)$ increases in the case of nondelay, that is, the delays in diagnosis and commencement of treatment to the individuals of I_m and I_x causing a shortage in the number of individuals of $R(t)$. Figure 3 shows the relationship between $I_m(t)$ and $I_m(t-\tau)$ and chaotic attractors at $\tau = 0.1$ and $\alpha = 1$. Figure 4, shows the relationship between $I_x(t)$ and $I_x(t-\tau)$ at $\tau = 0.1$ in case of integer order. Figures 5 and 6 show the relationship between $I_m(t)$ and $I_m(t-\tau)$ and $I_x(t)$ with $I_x(t-\tau)$, respectively, in case of fraction order where $\alpha = 0.95$. Figures 7 and 8 show the approximate solutions for $I_m(t-\tau)$ and $I_x(t-\tau)$ at $\tau = 2$, $\alpha = 0.98$ by using NSFDM. Figures 9 and 10 show the approximate solutions of different τ in both fraction and integer cases; we noted that increasing the value of τ causes decreasing the values of $R(t)$. Figures 11 and 12 show the behavior of the approximate solutions with different value of α, which are given to demonstrate how the fractional model is a generalization of the integer order model.

6. Conclusion

Fractional models have the potential to describe more complex dynamics than the integer models and can include easily the memory effect present in many real world phenomena. In this paper, multistrain TB model of fractional order derivatives with time delay memory is presented. A nonstandard numerical scheme is introduced to numerically study the approximate solution of proposed model problem. The obtained results show that the delays in diagnosis and commencement of treatment to the individuals of I_m and I_x cause a shortage in the number of individuals of $R(t)$. The approximate solution of proposed model changes when τ and

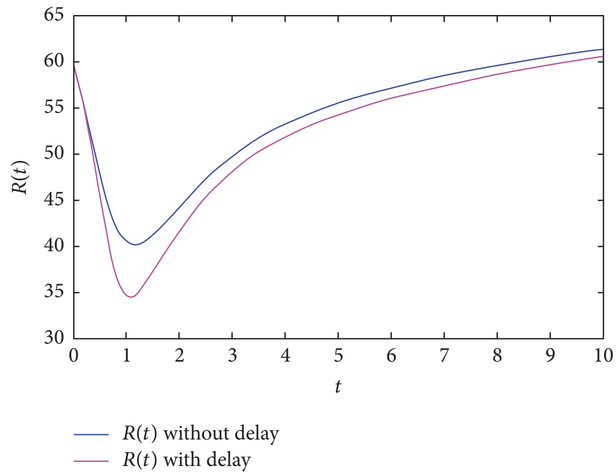

Figure 1: The approximate solution of $R(t)$ with $\tau = 0.3$, using dde23.

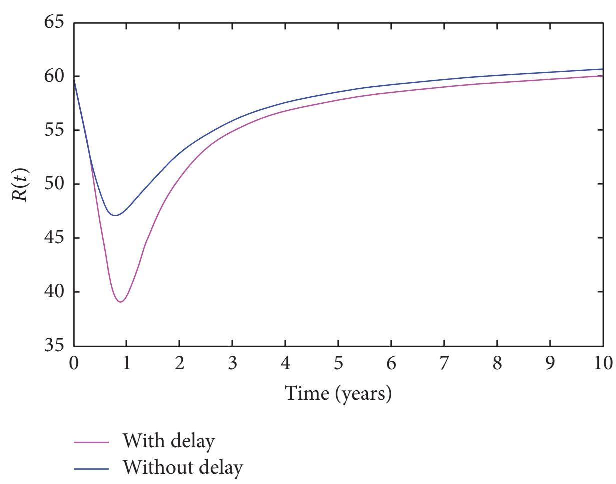

Figure 2: The approximate solution of $R(t)$ with $\tau = 0.3$, using NSFDM, $\alpha = 1$.

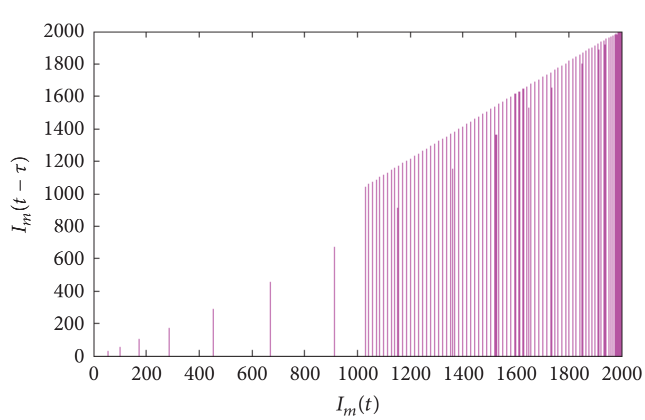

Figure 3: The relationship between $I_m(t)$, $I_m(t-\tau)$ with $\tau = 0.1$, $\alpha = 1$ using NSFDM.

Table 3: Parameter values of system (1).

Parameter	Value
b^α	$3190^\alpha \left(\frac{1}{\text{year}}\right)^\alpha$
d^α	$0.38^\alpha \left(\frac{1}{\text{year}}\right)^\alpha$
$\beta_s^\alpha = \beta_m^\alpha = \beta_x^\alpha$	$14^\alpha \left(\frac{1}{\text{year}}\right)^\alpha$
$\lambda_s^\alpha = \lambda_m^\alpha = \lambda_x^\alpha$	$0.5^\alpha \left(\frac{1}{\text{year}}\right)^\alpha$
$\varepsilon_s^\alpha = \varepsilon_m^\alpha = \varepsilon_x^\alpha$	$0.5^\alpha \left(\frac{1}{\text{year}}\right)^\alpha$
$\alpha_{r1,r2}^\alpha$	$0.05^\alpha \left(\frac{1}{\text{year}}\right)^\alpha$
$\gamma_s^\alpha = \gamma_m^\alpha = \gamma_x^\alpha$	$0.3^\alpha \left(\frac{1}{\text{year}}\right)^\alpha$
t_{1s}^α	$0.88^\alpha \left(\frac{1}{\text{year}}\right)^\alpha$
$t_{2r}^\alpha : r \in (s, m, x)$	$t_{2s}^\alpha = 0.88^\alpha$; $t_{2m}^\alpha = t_{2x}^\alpha = 0.034^\alpha \left(\frac{1}{\text{year}}\right)^\alpha$
σ_r^α	$0.25^\alpha \left(\frac{1}{\text{year}}\right)^\alpha$
P_r^α	$0.88^\alpha \left(\frac{1}{\text{year}}\right)^\alpha$
δ_r^α	$0.045^\alpha \left(\frac{1}{\text{year}}\right)^\alpha$

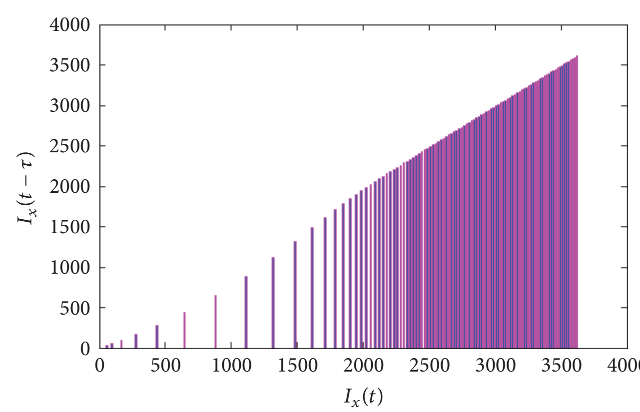

Figure 4: The relationship between $I_x(t)$, $I_x(t-\tau)$ with $\tau = 0.1$, $\alpha = 1$ using NSFDM.

α take different values. Some figures are given to demonstrate how the fractional delay model is a generalization of the integer order model. It is concluded that NSFDM can be applied to solve such fractional delay differential equations simply and effectively. All results are obtained by using MATLAB programming.

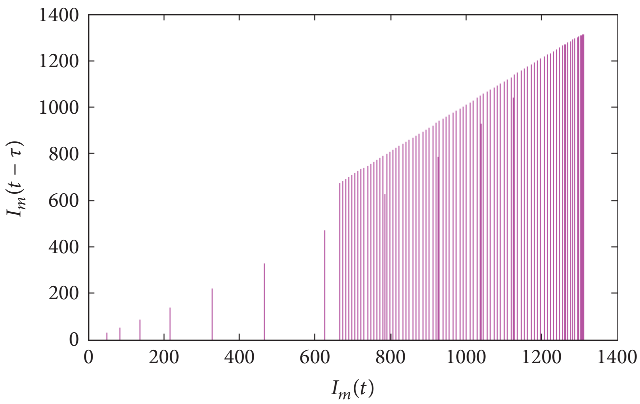

FIGURE 5: The relationship between $I_m(t)$, $I_m(t-\tau)$ with $\tau = 0.1$, $\alpha = 0.95$ using NSFDM.

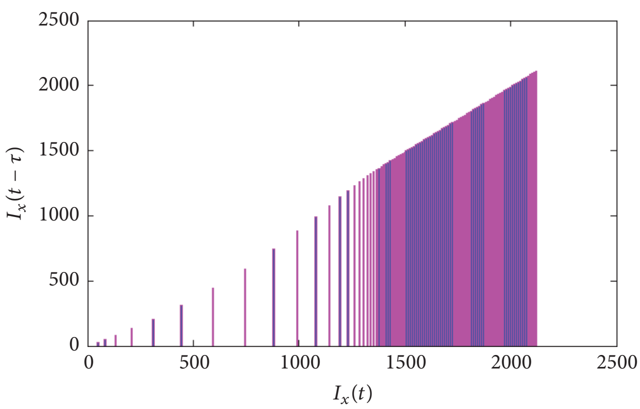

FIGURE 6: The relationship between $I_x(t)$, $I_x(t-\tau)$ with $\tau = 0.1$, $\alpha = 0.95$ using NSFDM.

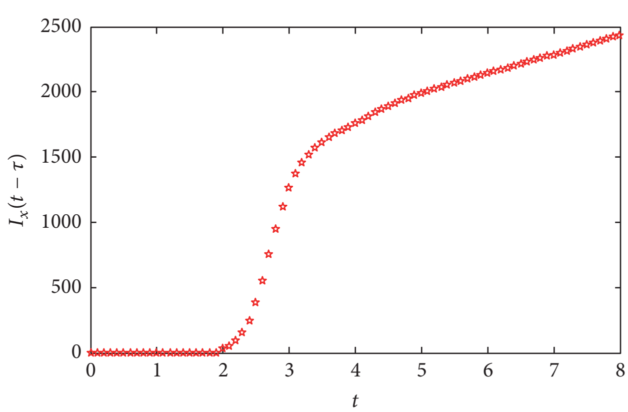

FIGURE 7: The approximate solutions $I_x(t-\tau)$ with $\tau = 2$, $\alpha = 0.98$ using NSFDM.

Appendix

A. Preliminaries and Notations

In this section, some basic definitions and properties in the theory of the fractional calculus are presented. Moreover,

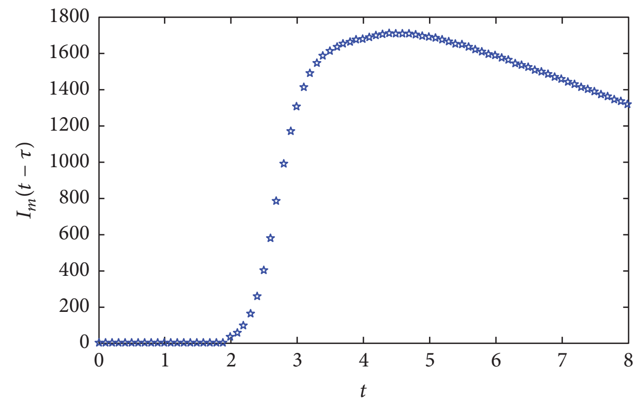

FIGURE 8: The approximate solutions $I_m(t-\tau)$ with $\tau = 2$, $\alpha = 0.98$ using NSFDM.

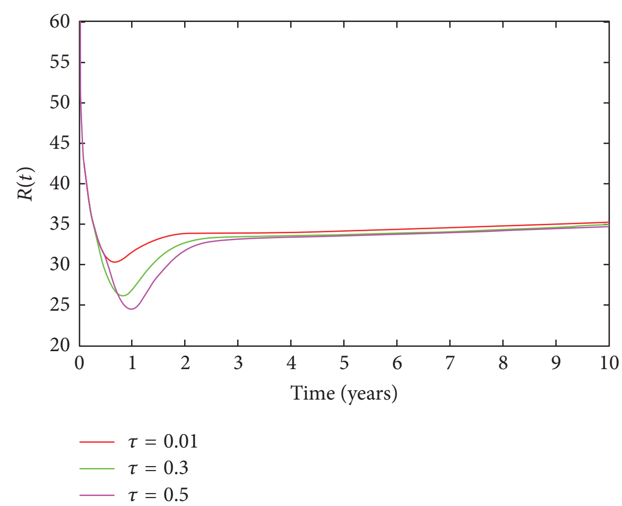

FIGURE 9: The approximate solutions with different τ and $\alpha = 0.9$ using NSFDM.

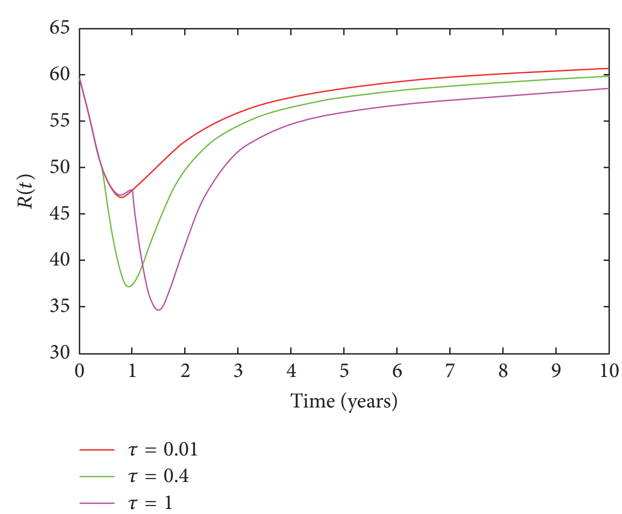

FIGURE 10: The approximate solution of $R(t)$ with different τ, using NSFDM, $\alpha = 1$.

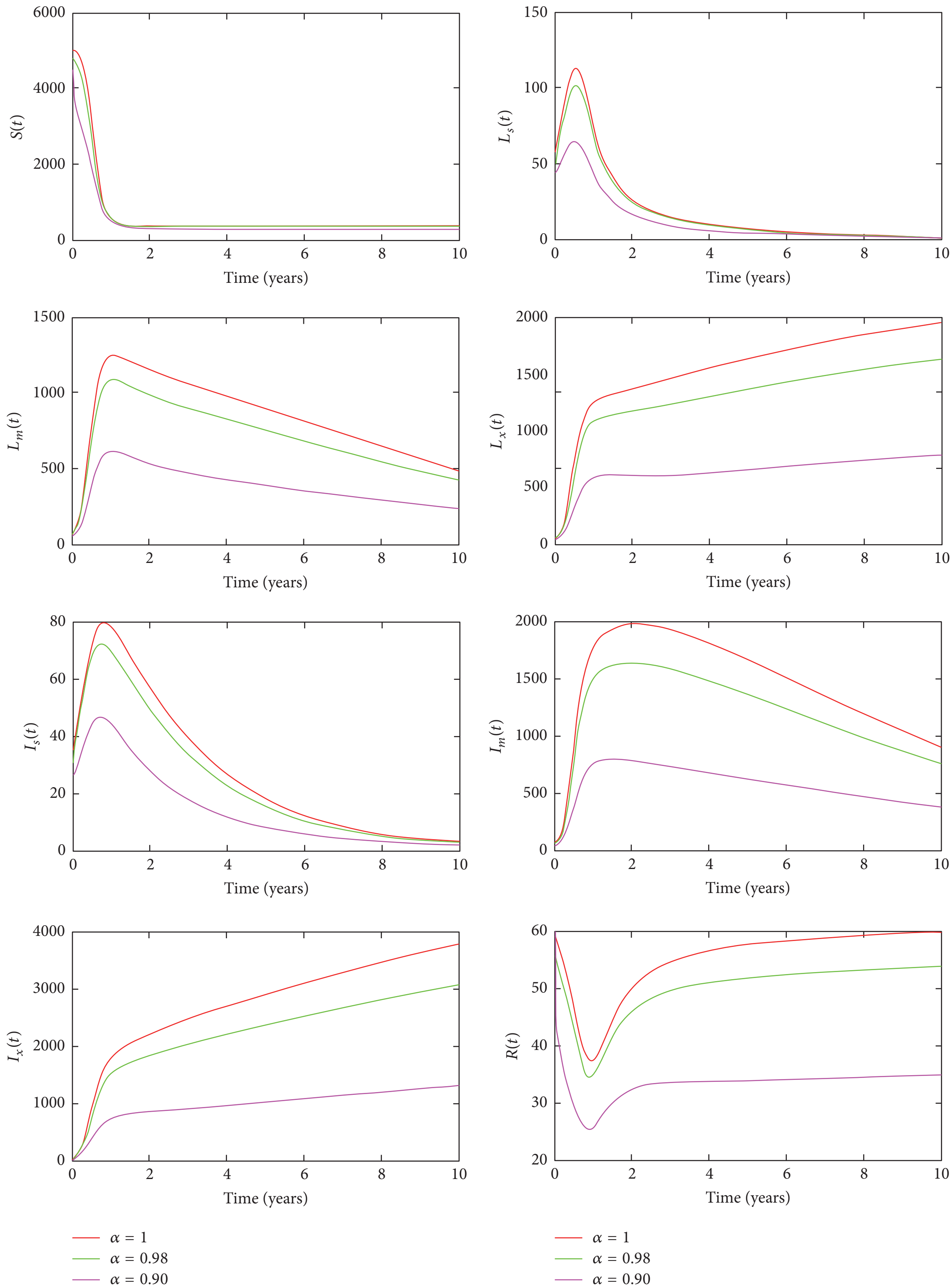

FIGURE 11: The approximate solutions with $\tau = 0.4$ and different α using NSFDM.

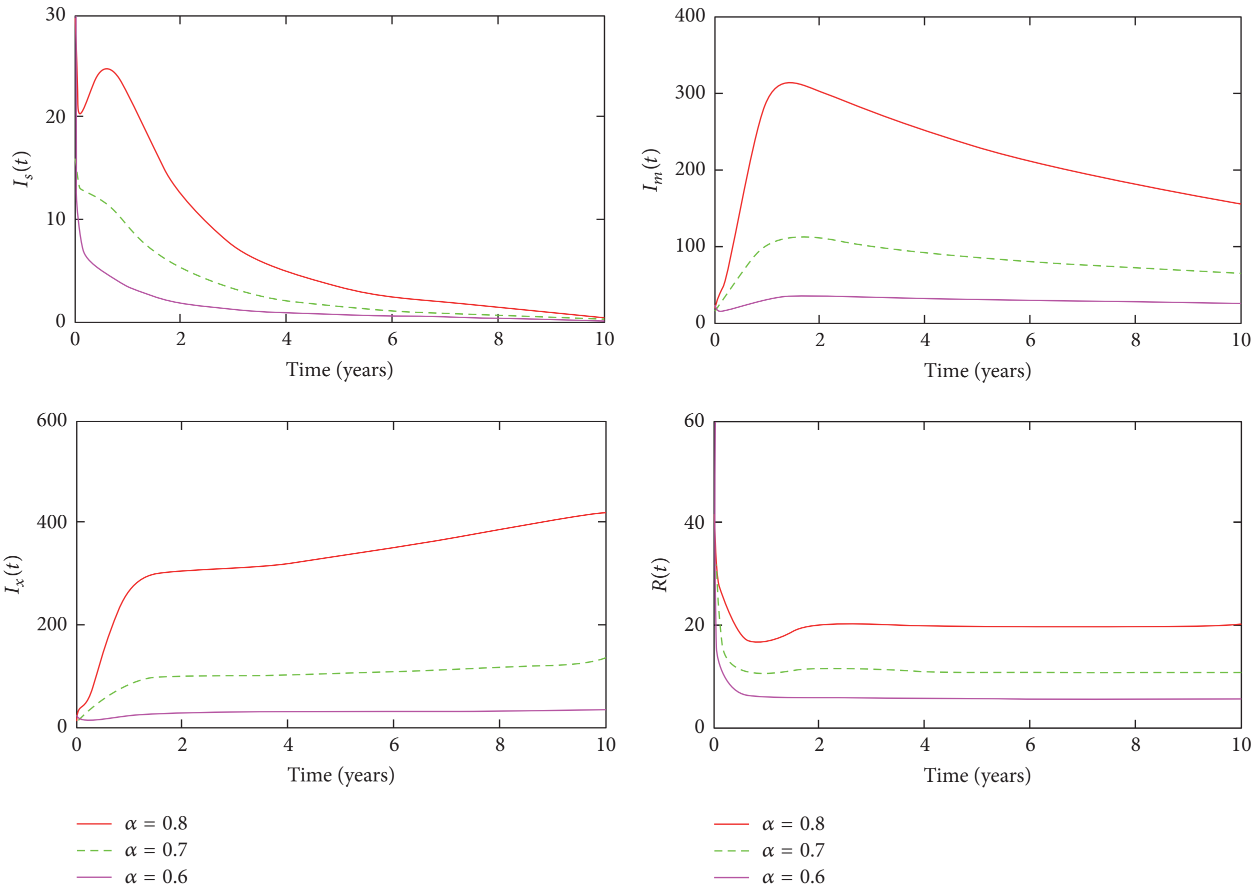

FIGURE 12: The approximate solutions with $\tau = 0.4$ and different α using NSFDM.

we introduce the main aspects concerning nonstandard discretization methods.

A.1. Grünwald–Letinkov Fractional Derivatives (GLFDs). We will begin with the signal fractional differential equation (see [17, 40, 41])

$$\begin{aligned} D_x^{\alpha} z(x) &= g(x, z(x)), \quad T \geq x \geq 0, \\ z(x_0) &= 0, \end{aligned} \tag{A.1}$$

where $\alpha > 0$. T is the final time and D^{α} denotes the fractional derivative, where $n-1 < \alpha < n$, defined by

$$D_x^{\alpha} z(x) = J^{n-\alpha} D_x^{\alpha} z(x), \tag{A.2}$$

$\forall n \in \mathbb{N}$ and J^n is the nth-order Riemann–Liouville integral operator:

$$J^n z(x) = \frac{1}{\Gamma(x)} \int_0^x (x-\tau)^{n-1} z(\tau)\, d\tau, \tag{A.3}$$

with $\Gamma(\cdot)$ being the gamma function,

and $x > 0$. The Grünwald–Letinkov approximation of the fractional derivative is defined as follows [42]:

$$D_x^{\alpha} z(x) = \lim_{h \to 0} h^{-\alpha} \sum_{r=0}^{m} (-1)^r \binom{\alpha}{r} z(x - rh), \tag{A.4}$$

where $m = [x/h]$ denotes the integer part of x/h and h is the step-size. Equation (A.4) can be discretized as follows:

$$\sum_{r=0}^{m} \omega_r^{\alpha} z(x_{n-r}) = g(x_n, z(x_n)) \quad n = 1, 2, 3, \ldots, \tag{A.5}$$

where $x_n = nh$ and ω_r^{α} are the Grünwald–Letinkov coefficients defined as

$$\omega_r^{\alpha} = \left(1 - \frac{1+\alpha}{r}\right) \omega_{r-1}^{\alpha}, \quad \omega_0^{\alpha} = h^{-\alpha}, \ r = 1, 2, 3, \ldots. \tag{A.6}$$

A.2. NSFD Discretization. It is known that the numerical scheme is called nonstandard method if at least one of the following conditions is satisfied [36]:

(1) the discretization of derivatives is not traditional and uses a nonnegative function [35, 43],

(2) nonlocal approximations are used.

To construct the numerical scheme for system (1) using NSFDM, the approximations of temporal derivatives are made based on generalized forward scheme of first order. Hence, if $g(t) \in C^1(\mathbb{R})$, we define its derivative as follows:

$$\frac{dg(t)}{dt} = \frac{g(t+\triangle t) - g(t)}{\varphi(\triangle t)} + O(\varphi(\triangle t)), \quad \text{as } \triangle t \longrightarrow 0, \tag{A.7}$$

where $\varphi(\triangle t)$ is a real-valued function on $\mathbb{R}$ and $\triangle t = h$. In the following, the denominator functions are little complex functions of the step-size of time than the classical one [44].

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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Research Article

Extinction and Persistence in Mean of a Novel Delay Impulsive Stochastic Infected Predator-Prey System with Jumps

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In this paper, we explore an impulsive stochastic infected predator-prey system with Lévy jumps and delays. The main aim of this paper is to investigate the effects of time delays and impulse stochastic interference on dynamics of the predator-prey model. First, we prove some properties of the subsystem of the system. Second, in view of comparison theorem and limit superior theory, we obtain the sufficient conditions for the extinction of this system. Furthermore, persistence in mean of the system is also investigated by using the theory of impulsive stochastic differential equations (ISDE) and delay differential equations (DDE). Finally, we carry out some simulations to verify our main results and explain the biological implications.

1. Introduction

With the development of the economy, environmental pollution is caused by various industries and other activities of human, which has been one of the most important social problems in the world today. Many species have gone extinct due to the toxicant in the environment. Therefore, controlling the environmental pollution has been the important topics around the world. There are many researchers which have investigated the pollution models in recent years [1–3]. In addition, a lot of animal populations suffer from infectious disease, so some scholars investigated the predator-prey systems with diseases [4–8]. For example, a deterministic predator-prey model with infected predator in an impulsive polluted environment is described by the following equation:

$$
\begin{aligned}
&\mathrm{d}X(t) = X(t)\left[r - \delta_1 c_1(t) - a_{11}X(t) - a_{12}S(t)\right]\mathrm{d}t,\\
&\mathrm{d}S(t) = S(t)\\
&\quad\cdot\left[-\mu_1 - \delta_2 c_2(t) + a_{21}X(t) - \beta I(t) - a_{22}S(t)\right]\mathrm{d}t,\\
&\mathrm{d}I(t) = I(t)\left[-\mu_2 - \delta_3 c_3(t) + \beta S(t) - a_{33}I(t)\right]\mathrm{d}t,\\
&\dot{c}_1(t) = k_1 c_e(t) - g_1 c_1(t) - m_1 c_1(t),\\
&\dot{c}_2(t) = k_2 c_e(t) - g_2 c_2(t) - m_2 c_2(t),\\
&\dot{c}_3(t) = k_3 c_e(t) - g_3 c_3(t) - m_3 c_3(t),\\
&\dot{c}_e(t) = -h c_e(t),\\
&\qquad\qquad t \neq nT,\\
&\Delta X(t) = 0,\\
&\Delta S(t) = 0,\\
&\Delta I(t) = 0,\\
&\Delta c_i(t) = 0,\\
&\Delta c_e(t) = u,\\
&\qquad\qquad i = 1,2,3,\ t = nT,\ n \in \mathbb{Z}^+,
\end{aligned}
\tag{1}
$$

where $\Delta X(t) = X(t^+) - X(t)$, $\Delta S(t) = S(t^+) - S(t)$, $\Delta I(t) = I(t^+) - I(t)$, $\Delta c_i(t) = c_i(t^+) - c_i(t)$, $\Delta c_e(t) = c_e(t^+) - c_e(t)$, $X(t)$ is the density of the prey at time t, and $S(t)$ and $I(t)$ represent the density of susceptible predator and infected predator at time t, respectively. $c_i(t)$ $(i = 1,2,3)$ and $c_e(t)$ stand for the concentrations of the toxicant in the organism and the environment at time t, respectively. δ_i $(i = 1,2,3)$ are dose-response parameter to the toxicant. r stands for the intrinsic growth rate of the prey. μ_i $(i = 1,2)$ denote the death rates of $S(t)$ and $I(t)$, respectively. β is the infection rate. a_{ii} $(i = 1,2,3)$ are density-dependent coefficients, and a_{12} and a_{21} represent predation rate and ingestion rate, respectively. k_i $(i = 1,2,3)$ are environmental toxicant uptake rates, m_i $(i = 1,2,3)$ denote organismal net depuration rates, g_i $(i = 1,2,3)$ represent organismal net ingestion rates, h is the loss rate of toxicant from environment, and u denotes the amount of pulsed input concentration of the toxicant at every time. The above parameters are all positive constants. Next, we propose a new mathematical model by taking more factors into account based on model (1).

In the natural world, time delay often occurs in almost every situation. Thus it is significant to take time delay into consideration [9–14]. As we know, deterministic model is not enough to describe the species activities. Sometimes, the species activities may be disturbed by environmental noises. May [15] revealed that the birth rates, death rates, carrying capacities, competition coefficients, and other parameters involved in the system should exhibit random fluctuation to a greater or lesser extent. Hence some parameters should be stochastic [16–26]. First, we assume that the intrinsic growth rate and the death rates of species are disturbed by white noise, then r and μ_i can be replaced by

$$\begin{aligned}
r &\longrightarrow r + \sigma_1 \dot{B}_1(t), \\
-\mu_1 &\longrightarrow -\mu_1 + \sigma_2 \dot{B}_2(t), \\
-\mu_2 &\longrightarrow -\mu_2 + \sigma_3 \dot{B}_3(t),
\end{aligned} \tag{2}$$

where $B_i(t)$ $(i = 1,2,3)$ are standard Brownian motions and σ_i are the intensities of $B_i(t)$. $B_i(t)$ are mutually independent defined on a complete probability space $(\Omega, \mathscr{F}, \{\mathscr{F}\}_{t\ge 0}, \mathscr{P})$.

Furthermore, populations may suffer from sudden environmental fluctuations, such as floods and earthquakes, which cannot be described by Brownian motions. To explain these phenomena, introducing a jump process into the underlying population dynamics is one of the important methods. Thus, there are many scholars introduce Lévy jumps into the population system [27–31]. Taking all above influences into consideration, we focus on the infected stochastic predator-prey system with Lévy jumps and delays in a polluted environment

$$\begin{aligned}
\mathrm{d}X(t) &= X(t^-)\left[r - \delta_1 c_1(t) - a_{11} X(t^-) \right. \\
&\quad \left. - a_{12} e^{-d_1\tau_1} S(t^- - \tau_1)\right] \mathrm{d}t + \sigma_1 X(t)\,\mathrm{d}B_1(t) \\
&\quad + \int_{\mathbb{Y}} X(t^-)\,\gamma_1(u)\,\widetilde{N}(\mathrm{d}t, \mathrm{d}u), \\
\mathrm{d}S(t) &= S(t^-)\left[-\mu_1 - \delta_2 c_2(t) + a_{21} e^{-d_2\tau_2} X(t^- - \tau_2) \right. \\
&\quad \left. - \beta e^{-d_3\tau_3} I(t^- - \tau_3) - a_{22} S(t^-)\right] \mathrm{d}t \\
&\quad + \sigma_2 S(t)\,\mathrm{d}B_2(t) + \int_{\mathbb{Y}} S(t^-)\,\gamma_2(u)\,\widetilde{N}(\mathrm{d}t, \mathrm{d}u), \\
\mathrm{d}I(t) &= I(t^-)\left[-\mu_2 - \delta_3 c_3(t) + \beta e^{-d_4\tau_4} S(t^- - \tau_4) \right. \\
&\quad \left. - a_{33} I(t^-)\right] \mathrm{d}t + \sigma_3 I(t)\,\mathrm{d}B_3(t) \\
&\quad + \int_{\mathbb{Y}} I(t^-)\,\gamma_3(u)\,\widetilde{N}(\mathrm{d}t, \mathrm{d}u), \\
\dot{c}_1(t) &= k_1 c_e(t) - g_1 c_1(t) - m_1 c_1(t), \\
\dot{c}_2(t) &= k_2 c_e(t) - g_2 c_2(t) - m_2 c_2(t), \\
\dot{c}_3(t) &= k_3 c_e(t) - g_3 c_3(t) - m_3 c_3(t), \\
\dot{c}_e(t) &= -h c_e(t), \\
& \qquad\qquad\qquad\qquad t \ne nT, \\
\Delta X(t) &= 0, \\
\Delta S(t) &= 0, \\
\Delta I(t) &= 0, \\
\Delta c_i(t) &= 0, \\
\Delta c_e(t) &= u, \\
& \qquad\qquad i = 1,2,3,\ t = nT,\ n \in \mathbb{Z}^+,
\end{aligned} \tag{3}$$

where $X(t^-)$, $S(t^-)$, and $I(t^-)$ stand for the left limits of $X(t)$, $S(t)$, and $I(t)$, respectively. $N(\mathrm{d}t, \mathrm{d}u)$ denotes a Poisson counting measure with characteristic measure ν which defines a measurable bounded subset $\mathbb{Y}$ of $(0,\infty)$ with $\nu(\mathbb{Y}) < \infty$ and $\widetilde{N}(\mathrm{d}t, \mathrm{d}u) = N(\mathrm{d}t, \mathrm{d}u) - \nu(\mathrm{d}u)\mathrm{d}t$, and γ_i is bounded and continuous with respect to ν and is $\mathfrak{B}(\mathbb{Y}) \times \mathscr{F}_t$-measurable, and $1 + \gamma_i > 0$ $(i = 1,2,3)$ (see [27–30]). Moreover, $B_i(t)$ $(i = 1,2,3)$ are independent of N, d_i are death rates of species, and $\tau_i \ge 0$ $(i = 1,2,3,4)$ represent the time delay. Other parameters are defined as system (1).

The rest of this paper is arranged as follows. Section 2 introduces some lemmas which will be used in our main results. In Section 3, we show the main results. We examine the extinction of system (3) in Section 3.1; in Section 3.2 we also prove the permanence in mean of this system. Finally, we present some simulations and conclusions in Section 4.

2. Preliminary Results

Throughout the paper, we assume that $X(t)$, $S(t)$, $I(t)$, and $c_i(t)$ are continuous at $t = nT$ and $c_e(t)$ is left continuous at $t = nT$ and $c_e(nT^+) = \lim_{t\to nT^+} c_e(t)$. Moreover, let $(\Omega, \mathscr{F}, \{\mathscr{F}\}_{t\ge 0}, \mathscr{P})$ be a complete probability space with a filtration $\{\mathcal{F}_t\}_{t\geq 0}$ satisfying the common conditions (i.e., it is increasing and right continuous while $\mathcal{F}_0$ contains all $\mathcal{P}$-null sets).

For the sake of convenience, we introduce some notions and some lemmas which will be used for the main results. We define

$$\begin{aligned}
\tau &= \max\{\tau_1,\tau_2,\tau_3,\tau_4\},\\
b_1 &= r - \frac{1}{2}\sigma_1^2 - \int_{\mathbb{Y}} (\gamma_1(u) - \ln(1+\gamma_1(u)))\,\nu(\mathrm{d}u),\\
b_2 &= \mu_1 + \frac{1}{2}\sigma_2^2 + \int_{\mathbb{Y}} (\gamma_2(u) - \ln(1+\gamma_2(u)))\,\nu(\mathrm{d}u),\\
b_3 &= \mu_2 + \frac{1}{2}\sigma_3^2 + \int_{\mathbb{Y}} (\gamma_3(u) - \ln(1+\gamma_3(u)))\,\nu(\mathrm{d}u),\\
\Delta_1 &= (b_1 - \delta_1\bar{c}_1)\,a_{21}e^{-d_2\tau_2} - (b_2 + \delta_2\bar{c}_2)\,a_{11},\\
\Delta' &= a_{11}a_{22} + a_{12}a_{21}e^{-d_1\tau_1 - d_2\tau_2},\\
\Delta_2 &= (b_1 - \delta_1\bar{c}_1)\left(a_{22}a_{33} + \beta^2 e^{-d_3\tau_3 - d_4\tau_4}\right) + (b_2 + \delta_2\bar{c}_2)\,a_{33}a_{12}e^{-d_1\tau_1} - (b_3 + \delta_3\bar{c}_3)\,a_{12}\beta e^{-d_1\tau_1 - d_3\tau_3},\\
\Delta_3 &= a_{33}\Delta_1 + (b_3 + \delta_3\bar{c}_3)\,a_{11}\beta e^{-d_3\tau_3},\\
\Delta_4 &= \beta e^{-d_4\tau_4}\Delta_1 - (b_3 + \delta_3\bar{c}_3)\,\Delta',\\
\Delta &= a_{33}\Delta' + a_{11}\beta^2 e^{-(d_3\tau_3 + d_4\tau_4)},\\
\mathcal{R} &= \frac{\beta e^{-d_4\tau_4}\Delta_1}{(b_3 + \delta_3\bar{c}_3)\,a_{11}a_{22}},\\
\langle f(t)\rangle &= \frac{1}{t}\int_0^t f(t)\,\mathrm{d}t,\\
f^* &= \limsup_{t\to+\infty} f(t),\\
f_* &= \liminf_{t\to+\infty} f(t),
\end{aligned} \tag{4}$$

where $f(t)$ is a bounded continuous function on $[0,+\infty)$.

Then we show some basic properties of the subsystem of system (3)

$$\begin{aligned}
\dot{c}_1(t) &= k_1c_e(t) - g_1c_1(t) - m_1c_1(t),\\
\dot{c}_2(t) &= k_2c_e(t) - g_2c_2(t) - m_2c_2(t),\\
\dot{c}_3(t) &= k_3c_e(t) - g_3c_3(t) - m_3c_3(t),\\
\dot{c}_e(t) &= -hc_e(t), \qquad t \neq nT,\ n\in Z^+,\\
\Delta c_i(t) &= 0,\\
\Delta c_e(t) &= u, \qquad i = 1,2,3,\ t = nT,\ n\in Z^+.
\end{aligned} \tag{5}$$

Lemma 1 (see [3]). *System (5) has a unique positive T-periodic solution $(\widetilde{c}_1(t),\widetilde{c}_2(t),\widetilde{c}_3(t),\widetilde{c}_e(t))^T$ which is globally asymptotical stable. Furthermore, if $c_i(0) > \widetilde{c}_i(0)$ and $c_e(0) > \widetilde{c}_e(0)$, then $c_i(t) > \widetilde{c}_i(t)$ and $c_e(t) > \widetilde{c}_e(t)$ for all $t \geq 0$, where*

$$\begin{aligned}
\widetilde{c}_i(t) &= \widetilde{c}_i(0)\,e^{-(g_i+m_i)(t-nT)} + \frac{k_iu\left(e^{-(g_i+m_i)(t-nT)} - e^{-h(t-nT)}\right)}{(h-g_i-m_i)\left(1-e^{-hT}\right)},\\
\widetilde{c}_e(t) &= \frac{ue^{-h(t-nT)}}{1-e^{-hT}},\\
\widetilde{c}_i(0) &= \frac{k_iu\left(e^{-(g_i+m_i)T} - e^{-hT}\right)}{(h-g_i-m_i)\left(1-e^{-(g_i+m_i)T}\right)\left(1-e^{-hT}\right)},\\
\widetilde{c}_e(0) &= \frac{u}{1-e^{-hT}},
\end{aligned} \tag{6}$$

for $t\in(nT,(n+1)T]$, $i = 1,2,3$, and $n\in Z^+$.

It can be obtained from a simple calculation that

$$\int_{nT}^{(n+1)T} \widetilde{c}_i(t)\,\mathrm{d}t = \frac{k_iu}{h(g_i+m_i)}. \tag{7}$$

Since $\widetilde{c}_i(t)$ is a periodic function, then we get

$$\begin{aligned}
\lim_{t\to\infty}\langle c_i(t)\rangle^* &\leq \lim_{n\to\infty}\frac{1}{nT}\int_0^{(n+1)T}\widetilde{c}_i(t)\,\mathrm{d}t = \lim_{n\to\infty}\frac{n+1}{nT}\int_{nT}^{(n+1)T}\widetilde{c}_i(t)\,\mathrm{d}t = \frac{k_iu}{h(g_i+m_i)T},\\
\lim_{t\to\infty}\langle c_i(t)\rangle_* &\geq \lim_{n\to\infty}\frac{1}{(n+1)T}\int_0^{nT}\widetilde{c}_i(t)\,\mathrm{d}t = \lim_{n\to\infty}\frac{n}{(n+1)T}\int_{(n-1)T}^{nT}\widetilde{c}_i(t)\,\mathrm{d}t = \frac{k_iu}{h(g_i+m_i)T}.
\end{aligned} \tag{8}$$

Thus we have

$$\lim_{t\to+\infty}\langle c_i(t)\rangle = \frac{k_iu}{h(g_i+m_i)T} := \bar{c}_i. \tag{9}$$

From Lemma 1, we know that the long time dynamical behaviors of system (3) can be replaced by the dynamical behaviors of the following limiting system:

$$\begin{aligned}
\mathrm{d}X(t) &= X(t^-)\left[r-\delta_1\tilde{c}_1(t)-a_{11}X(t^-)\right.\\
&\quad \left.-a_{12}e^{-d_1\tau_1}S(t^- -\tau_1)\right]\mathrm{d}t+\sigma_1X(t)\,\mathrm{d}B_1(t)\\
&\quad +\int_{\mathbb{Y}}X(t^-)\gamma_1(u)\widetilde{N}(\mathrm{d}t,\mathrm{d}u),\\
\mathrm{d}S(t) &= S(t^-)\left[-\mu_1-\delta_2\tilde{c}_2(t)+a_{21}e^{-d_2\tau_2}X(t^- -\tau_2)\right.\\
&\quad \left.-\beta e^{-d_3\tau_3}I(t^- -\tau_3)-a_{22}S(t^-)\right]\mathrm{d}t\\
&\quad +\sigma_2S(t)\,\mathrm{d}B_2(t)\\
&\quad +\int_{\mathbb{Y}}S(t^-)\gamma_2(u)\widetilde{N}(\mathrm{d}t,\mathrm{d}u),\\
\mathrm{d}I(t) &= I(t^-)\left[-\mu_2-\delta_3\tilde{c}_3(t)+\beta e^{-d_4\tau_4}S(t^- -\tau_4)\right.\\
&\quad \left.-a_{33}I(t^-)\right]\mathrm{d}t+\sigma_3I(t)\,\mathrm{d}B_3(t)\\
&\quad +\int_{\mathbb{Y}}I(t^-)\gamma_3(u)\widetilde{N}(\mathrm{d}t,\mathrm{d}u).
\end{aligned} \tag{10}$$

Now we give an assumption which will be used in the following proof.

Assumption 2. There exist constants C_i such that

$$\int_{\mathbb{Y}}\left[\gamma_i-\ln(1+\gamma_i)\right]\nu(\mathrm{d}u)\le C_i,\quad (i=1,2,3). \tag{11}$$

Lemma 3. *For any given initial value $((\phi_1(t),\phi_2(t),\phi_3(t)):-\tau\le t\le 0,\ \tau=\max\{\tau_1,\tau_2,\tau_3,\tau_4\})\in C([-\tau,0];R_+^3)$, there is a unique solution $(X(t),S(t),I(t))$ of (10) on $t\ge\tau$ and the solution will remain in $\mathbb{R}_+^2$ with probability 1.*

Proof. This proof is the same as Theorem 3.1 in [11] by defining

$$V(X,S,I)=V_1(X,S,I)+V_2(X,S,I), \tag{12}$$

where

$$\begin{aligned}
V_1(X,S,I) &= X(t)-1-\ln X(t)+S(t)-1-\ln S(t)\\
&\quad +I(t)-1-\ln I(t),\\
V_2(X,S,I) &= a_{12}e^{-d_1\tau_1}\int_t^{t+\tau_1}S(s-\tau_1)\,\mathrm{d}s\\
&\quad +\frac{1}{2}\int_t^{t+\tau_2}X^2(s-\tau_2)\,\mathrm{d}s\\
&\quad +\beta e^{-d_3\tau_3}\int_t^{t+\tau_3}I(s-\tau_3)\,\mathrm{d}s\\
&\quad +\frac{1}{2}\int_t^{t+\tau_4}S^2(s-\tau_4)\,\mathrm{d}s.
\end{aligned} \tag{13}$$

Thus, we omit it here. □

The stochastic comparison theorem and limit superior and limit inferior theory are given as follows.

Lemma 4 (see [27]). *Suppose that $Y(t)\in C(\Omega\times[0,\infty),\mathbb{R}_+)$.*

(i) If there exist three positive constants T, λ, and λ_0 such that

$$\begin{aligned}
\ln Y(t) &\le \lambda t-\lambda_0\int_0^t Y(s)\,\mathrm{d}s+\alpha B(t)\\
&\quad +\sum_{i=1}^{n}\eta_i\int_0^t\int_{\mathbb{Y}}\ln(1+\gamma_i(u))\widetilde{N}(\mathrm{d}s,\mathrm{d}u)\quad a.s.
\end{aligned} \tag{14}$$

for all $t\ge T$, where α and η_i are constants, then

$$\begin{aligned}
&\limsup_{t\to\infty}\langle Y(t)\rangle=\langle Y(t)\rangle^*\le\frac{\lambda}{\lambda_0}\quad a.s.,\ \text{if } \lambda\ge 0,\\
&\lim_{t\to\infty}Y(t)=0\quad a.s.,\ \text{if } \lambda<0.
\end{aligned} \tag{15}$$

(ii) If there exist three positive constants T, λ, and λ_0 such that

$$\begin{aligned}
\ln Y(t) &\ge \lambda t-\lambda_0\int_0^t Y(s)\,\mathrm{d}s+\alpha B(t)\\
&\quad +\sum_{i=1}^{n}\eta_i\int_0^t\int_{\mathbb{Y}}\ln(1+\gamma_i(u))\widetilde{N}(\mathrm{d}s,\mathrm{d}u)\quad a.s.
\end{aligned} \tag{16}$$

for all $t\ge T$, then $\liminf_{t\to\infty}\langle Y(t)\rangle=\langle Y(t)\rangle_*\ge\lambda/\lambda_0$ a.s.

First, we explore the following auxiliary system:

$$\begin{aligned}
\mathrm{d}X_1(t) &= X(t^-)\left[r-\delta_1\tilde{c}_1(t)-a_{11}X_1(t^-)\right]\mathrm{d}t\\
&\quad +\sigma_1X_1(t)\,\mathrm{d}B_1(t)\\
&\quad +\int_{\mathbb{Y}}X_1(t^-)\gamma_1(u)\widetilde{N}(\mathrm{d}t,\mathrm{d}u),\\
\mathrm{d}S_1(t) &= S_1(t^-)\left[-\mu_1-\delta_2\tilde{c}_2(t)\right.\\
&\quad \left.+a_{21}e^{-d_2\tau_2}X_1(t^- -\tau_2)-a_{22}S_1(t^-)\right]\mathrm{d}t\\
&\quad +\sigma_2S_1(t)\,\mathrm{d}B_2(t)\\
&\quad +\int_{\mathbb{Y}}S_1(t^-)\gamma_2(u)\widetilde{N}(\mathrm{d}t,\mathrm{d}u),\\
\mathrm{d}I_1(t) &= I_1(t^-)\left[-\mu_2-\delta_3\tilde{c}_3(t)+\beta e^{-d_4\tau_4}S_1(t^- -\tau_4)\right.\\
&\quad \left.-a_{33}I_1(t^-)\right]\mathrm{d}t+\sigma_3I_1(t)\,\mathrm{d}B_3(t)\\
&\quad +\int_{\mathbb{Y}}I_1(t^-)\gamma_3(u)\widetilde{N}(\mathrm{d}t,\mathrm{d}u).
\end{aligned} \tag{17}$$

Lemma 5. *For system (17), let $(X_1(t),S_1(t),I_1(t))$ be the solution of this system with initial value $((\phi_1(t),\phi_2(t),\phi_3(t)):-\tau\le t\le 0)\in C([-\tau,0];R_+^3)$.*

(i) If $b_1 < \delta_1 \bar{c}_1$, then

$$\begin{gathered}\lim_{t\to\infty} X_1(t) = 0,\\ \lim_{t\to\infty} S_1(t) = 0,\\ \lim_{t\to\infty} I_1(t) = 0,\\ a.s.\end{gathered} \tag{18}$$

(ii) If $b_1 > \delta_1 \bar{c}_1$, when $\Delta_1 < 0$, then

$$\begin{gathered}\lim_{t\to\infty} \langle X_1(t)\rangle = \frac{b_1 - \delta_1 \bar{c}_1}{a_{11}},\\ \lim_{t\to\infty} S_1(t) = 0,\\ \lim_{t\to\infty} I_1(t) = 0,\\ \lim_{t\to\infty} \frac{\ln X_1(t)}{t} = 0,\\ a.s.\end{gathered} \tag{19}$$

(iii) If $b_1 > \delta_1 \bar{c}_1$, $\Delta_1 > 0$, when $\mathscr{R} < 1$, then

$$\begin{gathered}\lim_{t\to\infty} \langle X_1(t)\rangle = \frac{b_1 - \delta_1 \bar{c}_1}{a_{11}},\\ \lim_{t\to\infty} \langle S_1(t)\rangle = \frac{\Delta_1}{a_{11}a_{22}},\\ \lim_{t\to\infty} I_1(t) = 0,\\ \lim_{t\to\infty} \frac{\ln S_1(t)}{t} = 0,\\ a.s.\end{gathered} \tag{20}$$

(iv) If $b_1 > \delta_1 \bar{c}_1$, when $\mathscr{R} > 1$, then

$$\begin{gathered}\lim_{t\to\infty} \langle X_1(t)\rangle = \frac{b_1 - \delta_1 \bar{c}_1}{a_{11}},\\ \lim_{t\to\infty} \langle S_1(t)\rangle = \frac{\Delta_1}{a_{11}a_{22}},\\ a.s,\\ \lim_{t\to\infty} \langle I_1(t)\rangle = \frac{\beta e^{-d_4\tau_4}\Delta_1 - (b_3 + \delta_3\bar{c}_3) a_{11}a_{22}}{a_{11}a_{22}a_{33}},\\ \lim_{t\to\infty} \frac{\ln I_1(t)}{t} = 0,\\ a.s.\end{gathered} \tag{21}$$

Proof. Applying Itô's formula to system (17) leads to

$$\begin{aligned}
\mathrm{d}\ln X_1 &= \left[b_1 - \delta_1\tilde{c}_1(t) - a_{11}X_1(t)\right]\mathrm{d}t + \sigma_1 \mathrm{d}B_1(t)\\
&\quad + \int_{\mathbb{Y}} \ln(1+\gamma_1(u))\widetilde{N}(\mathrm{d}t,\mathrm{d}u),\\
\mathrm{d}\ln S_1 &= \left[-b_2 - \delta_2\tilde{c}_2(t) + a_{21}e^{-d_2\tau_2}X_1(t-\tau_2)\right.\\
&\quad \left. - a_{22}S_1(t)\right]\mathrm{d}t + \sigma_2 \mathrm{d}B_2(t)\\
&\quad + \int_{\mathbb{Y}} \ln(1+\gamma_2(u))\widetilde{N}(\mathrm{d}t,\mathrm{d}u),\\
\mathrm{d}\ln I_1 &= \left[-b_3 - \delta_3\tilde{c}_3(t) + \beta e^{-d_4\tau_4}S_1(t-\tau_4)\right.\\
&\quad \left. - a_{33}I_1(t)\right]\mathrm{d}t + \sigma_3 \mathrm{d}B_3(t)\\
&\quad + \int_{\mathbb{Y}} \ln(1+\gamma_3(u))\widetilde{N}(\mathrm{d}t,\mathrm{d}u).
\end{aligned} \tag{22}$$

Integrating both sides of (22), we have

$$\begin{aligned}
\ln X_1(t) - \ln X_1(0) &= b_1 t - \delta_1 \int_0^t \tilde{c}_1(s)\,\mathrm{d}s\\
&\quad - a_{11}\int_0^t X_1(s)\,\mathrm{d}s + \sigma_1 B_1(t)\\
&\quad + \int_0^t\int_{\mathbb{Y}} \ln(1+\gamma_1(u))\widetilde{N}(\mathrm{d}s,\mathrm{d}u),\\
\ln S_1(t) - \ln S_1(0) &= -b_2 t - \delta_2 \int_0^t \tilde{c}_2(s)\,\mathrm{d}s\\
&\quad + a_{21}e^{-d_2\tau_2}\int_0^t X_1(t-\tau_2) - a_{22}\int_0^t S_1(s)\,\mathrm{d}s\\
&\quad + \sigma_2 B_2(t) + \int_0^t\int_{\mathbb{Y}} \ln(1+\gamma_2(u))\widetilde{N}(\mathrm{d}s,\mathrm{d}u)\\
&= -b_2 t - \delta_2\int_0^t \tilde{c}_2(s)\,\mathrm{d}s + a_{21}e^{-d_2\tau_2}\int_0^t X_1(s)\,\mathrm{d}s\\
&\quad - a_{22}\int_0^t S_1(s)\,\mathrm{d}s\\
&\quad - a_{21}e^{-d_2\tau_2}\left(\int_t^{t+\tau_2} X_1(s-\tau_2)\,\mathrm{d}s\right.\\
&\quad \left. - \int_0^{\tau_2} X_1(s-\tau_2)\,\mathrm{d}s\right) + \sigma_2 B_2(t)\\
&\quad + \int_0^t\int_{\mathbb{Y}} \ln(1+\gamma_2(u))\widetilde{N}(\mathrm{d}s,\mathrm{d}u),\\
\ln I_1(t) - \ln I_1(0) &= -b_3 t - \delta_3 \int_0^t \tilde{c}_3(s)\,\mathrm{d}s\\
&\quad + \beta e^{-d_4\tau_4}\int_0^t S_1(s-\tau_4)\,\mathrm{d}s - a_{33}\int_0^t I_1(s)\,\mathrm{d}s\\
&\quad + \sigma_3 B_3(t) + \int_0^t\int_{\mathbb{Y}} \ln(1+\gamma_3(u))\widetilde{N}(\mathrm{d}s,\mathrm{d}u)\\
&= -b_3 t - \delta_3\int_0^t \tilde{c}_3(s)\,\mathrm{d}s + \beta e^{-d_4\tau_4}\int_0^t S_1(s)\,\mathrm{d}s\\
&\quad - a_{33}\int_0^t I_1(s)\,\mathrm{d}s - \beta e^{-d_4\tau_4}\left(\int_t^{t+\tau_4} S_1(s-\tau_4)\,\mathrm{d}s\right.\\
&\quad \left. - \int_0^{\tau_4} S_1(s-\tau_4)\,\mathrm{d}s\right) + \sigma_3 B_3(t)\\
&\quad + \int_0^t\int_{\mathbb{Y}} \ln(1+\gamma_3(u))\widetilde{N}(\mathrm{d}s,\mathrm{d}u).
\end{aligned} \tag{23}$$

Then we can obtain

$$\frac{\ln X_1(t)-\ln X_1(0)}{t}=b_1-\delta_1\langle\widetilde{c}_1(t)\rangle-a_{11}\langle X_1(t)\rangle+\frac{\sigma_1 B_1(t)}{t}+\frac{1}{t}\int_0^t\int_{\mathbb{Y}}\ln(1+\gamma_1(u))\widetilde{N}(\mathrm{d}s,\mathrm{d}u), \tag{24}$$

$$\begin{aligned}\frac{\ln S_1(t)-\ln S_1(0)}{t}&+a_{21}e^{-d_2\tau_2}\cdot\frac{\left(\int_t^{t+\tau_2}X_1(s-\tau_2)\,\mathrm{d}s-\int_0^{\tau_2}X_1(s-\tau_2)\,\mathrm{d}s\right)}{t}=-b_2\\&-\delta_2\langle\widetilde{c}_2(t)\rangle+a_{21}e^{-d_2\tau_2}\langle X_1(t)\rangle-a_{22}\langle S_1(t)\rangle\\&+\frac{\sigma_2 B_2(t)}{t}+\frac{1}{t}\int_0^t\int_{\mathbb{Y}}\ln(1+\gamma_2(u))\widetilde{N}(\mathrm{d}s,\mathrm{d}u),\end{aligned} \tag{25}$$

$$\begin{aligned}\frac{\ln I_1(t)-\ln I_1(0)}{t}&+\beta e^{-d_4\tau_4}\cdot\frac{\left(\int_t^{t+\tau_4}S_1(s-\tau_4)\,\mathrm{d}s-\int_0^{\tau_4}S_1(s-\tau_4)\,\mathrm{d}s\right)}{t}=-b_3\\&-\delta_3\langle\widetilde{c}_3(t)\rangle+\beta e^{-d_4\tau_4}\langle S_1(t)\rangle-a_{33}\langle I_1(t)\rangle\\&+\frac{\sigma_3 B_3(t)}{t}+\frac{1}{t}\int_0^t\int_{\mathbb{Y}}\ln(1+\gamma_3(u))\widetilde{N}(\mathrm{d}s,\mathrm{d}u).\end{aligned} \tag{26}$$

Case (i). From Lemma 4 and (24), if $b_1<\delta_1\bar{c}_1$, then we have

$$\lim_{t\to\infty}X_1(t)=0\quad\text{a.s.} \tag{27}$$

Obviously, we find

$$\lim_{t\to\infty}S_1(t)=0,\qquad\lim_{t\to\infty}I_1(t)=0,\qquad\text{a.s.} \tag{28}$$

Case (ii). By Lemma 4, it is derived from (24) and conditions that

$$\langle X_1(t)\rangle^*\le\frac{b_1-\delta_1\langle\widetilde{c}_1(t)\rangle_*}{a_{11}},\qquad\langle X_1(t)\rangle_*\ge\frac{b_1-\delta_1\langle\widetilde{c}_1(t)\rangle^*}{a_{11}}. \tag{29}$$

Since

$$\lim_{t\to\infty}\langle\widetilde{c}_i(t)\rangle_*=\lim_{t\to\infty}\langle\widetilde{c}_i(t)\rangle^*=\bar{c}_i,\quad i=1,2,3, \tag{30}$$

then we obtain

$$\lim_{t\to\infty}\langle X_1(t)\rangle=\frac{b_1-\delta_1\bar{c}_1}{a_{11}}. \tag{31}$$

Using Assumption 2 and the strong law of large numbers for local martingales, one has

$$\lim_{t\to+\infty}\frac{1}{t}\int_0^t\int_{\mathbb{Y}}\ln(1+\gamma_i(u))\widetilde{N}(\mathrm{d}s,\mathrm{d}u)=0,\qquad\lim_{t\to+\infty}\frac{\sigma_i B_i(t)}{t}=0,\qquad\text{a.s,}\ i=1,2,3. \tag{32}$$

Then, substituting (31) into (24) yields

$$\lim_{t\to\infty}\frac{\ln X_1(t)}{t}=0,\quad\text{a.s.} \tag{33}$$

Since

$$\lim_{t\to\infty}\frac{\int_t^{t+\tau_2}X_1(s-\tau_2)\,\mathrm{d}s}{t}=\lim_{t\to\infty}\frac{1}{t}\int_{t-\tau_2}^{t}X_1(s)\,\mathrm{d}s=0\quad\text{a.s.,} \tag{34}$$

$$\lim_{t\to\infty}\frac{\int_0^{\tau_2}X_1(s-\tau_2)\,\mathrm{d}s}{t}=\lim_{t\to\infty}\frac{\int_{-\tau_2}^{0}X_1(s)\,\mathrm{d}s}{t}=0\quad\text{a.s.,} \tag{35}$$

then we have that, for any $0<\varepsilon_1<\Delta_1$, there exists $T_1>0$ such that

$$-\varepsilon_1<a_{21}e^{-d_2\tau_2}\cdot\frac{\left(\int_t^{t+\tau_2}X_1(s-\tau_2)\,\mathrm{d}s-\int_0^{\tau_2}X_1(s-\tau_2)\,\mathrm{d}s\right)}{t}<\varepsilon_1,\qquad t\ge T_1. \tag{36}$$

Combining (25) with (36) yields

$$\begin{aligned}\frac{\ln S_1(t)-\ln S_1(0)}{t}&\le-b_2-\delta_2\langle\widetilde{c}_2(t)\rangle_*+a_{21}e^{-d_2\tau_2}\langle X_1(t)\rangle^*+\varepsilon_1\\&-a_{22}\langle S_1(t)\rangle+\frac{\sigma_2 B_2(t)}{t}\\&+\frac{1}{t}\int_0^t\int_{\mathbb{Y}}\ln(1+\gamma_2(u))\widetilde{N}(\mathrm{d}s,\mathrm{d}u).\end{aligned} \tag{37}$$

From Lemma 4 and conditions, we have

$$\lim_{t\to\infty}S_1(t)=0\quad\text{a.s.} \tag{38}$$

Obviously, we have

$$\lim_{t\to\infty}I_1(t)=0\quad\text{a.s.} \tag{39}$$

Case (iii). By (25), we obtain

$$\begin{aligned}\frac{\ln S_1(t)-\ln S_1(0)}{t} &\geq -b_2-\delta_2\left\langle\widetilde{c}_2(t)\right\rangle^*+a_{21}e^{-d_2\tau_2}\left\langle X_1(t)\right\rangle_*-\varepsilon_1 \\ &\quad -a_{22}\left\langle S_1(t)\right\rangle+\frac{\sigma_2 B_2(t)}{t} \\ &\quad +\frac{1}{t}\int_0^t\int_{\mathbb{Y}}\ln\left(1+\gamma_2(u)\right)\widetilde{N}(\mathrm{d}s,\mathrm{d}u).\end{aligned} \tag{40}$$

It can infer from (37), (40), and Lemma 4 that

$$\begin{aligned}\left\langle S_1(t)\right\rangle^* &\leq \frac{\Delta_1+\varepsilon_1}{a_{11}a_{22}}, \\ \left\langle S_1(t)\right\rangle_* &\geq \frac{\Delta_1-\varepsilon_1}{a_{11}a_{22}}.\end{aligned} \tag{41}$$

Since ε_1 is an arbitrary number, then we get

$$\lim_{t\to\infty}\left\langle S_1(t)\right\rangle=\frac{\Delta_1}{a_{11}a_{22}} \quad \text{a.s.} \tag{42}$$

Combining this equality with (25) leads to

$$\lim_{t\to\infty}\frac{\ln S_1(t)}{t}=0, \quad \text{a.s.} \tag{43}$$

Similar to (34) and (35), we have that, for any $0<\varepsilon_2<\beta e^{-d_4\tau_4}\Delta_1-(b_3+\delta_3\bar{c}_3)a_{11}a_{22}$, there exists $T_2>0$ such that

$$\begin{aligned}\frac{\ln I_1(t)-\ln I_1(0)}{t} &\leq -b_3-\delta_3\left\langle\widetilde{c}_3(t)\right\rangle_*+\beta e^{-d_4\tau_4}\left\langle S_1(t)\right\rangle^*+\varepsilon_2 \\ &\quad -a_{33}\left\langle I_1(t)\right\rangle+\frac{\sigma_3 B_3(t)}{t} \\ &\quad +\frac{1}{t}\int_0^t\int_{\mathbb{Y}}\ln\left(1+\gamma_3(u)\right)\widetilde{N}(\mathrm{d}s,\mathrm{d}u).\end{aligned} \tag{44}$$

Note that $\mathscr{R}<1$, so we have

$$\lim_{t\to\infty}I_1(t)=0 \quad \text{a.s.} \tag{45}$$

Case (iv). By (26), we get

$$\begin{aligned}\frac{\ln I_1(t)-\ln I_1(0)}{t} &\geq -b_3-\delta_3\left\langle\widetilde{c}_3(t)\right\rangle^*+\beta e^{-d_4\tau_4}\left\langle S_1(t)\right\rangle_*-\varepsilon_2 \\ &\quad -a_{33}\left\langle I_1(t)\right\rangle+\frac{\sigma_3 B_3(t)}{t} \\ &\quad +\frac{1}{t}\int_0^t\int_{\mathbb{Y}}\ln\left(1+\gamma_3(u)\right)\widetilde{N}(\mathrm{d}s,\mathrm{d}u).\end{aligned} \tag{46}$$

When $\mathscr{R}>1$, from (44) and (46), using Lemma 4 results in

$$\begin{aligned}\left\langle I_1(t)\right\rangle^* &\leq \frac{\beta e^{-d_4\tau_4}\Delta_1-\left(b_3+\delta_3\left\langle\widetilde{c}_3(t)\right\rangle_*\right)a_{11}a_{22}+\varepsilon_2}{a_{11}a_{22}a_{33}}, \\ \left\langle I_1(t)\right\rangle_* &\geq \frac{\beta e^{-d_4\tau_4}\Delta_1-\left(b_3+\delta_3\left\langle\widetilde{c}_3(t)\right\rangle^*\right)a_{11}a_{22}-\varepsilon_2}{a_{11}a_{22}a_{33}}.\end{aligned} \tag{47}$$

Since ε_2 is an arbitrary number, then we can obtain

$$\lim_{t\to\infty}\left\langle I_1(t)\right\rangle=\frac{\beta e^{-d_4\tau_4}\Delta_1-\left(b_3+\delta_3\bar{c}_3\right)a_{11}a_{22}}{a_{11}a_{22}a_{33}} \quad \text{a.s.} \tag{48}$$

Combining this equality with (26) leads to

$$\lim_{t\to\infty}\frac{\ln I_1(t)}{t}=0, \quad \text{a.s.} \tag{49}$$

This completes the proof of Lemma 1. □

3. Main Results

3.1. Extinction. Now we are going to show our main results. By Lemma 5, we can get the extinction of system (10).

Theorem 6. *For system (10), let $(X(t),S(t),I(t))$ be the solution of this system with initial value $((\phi_1(t),\phi_2(t),\phi_3(t)):-\tau\leq t\leq 0)\in C([-\tau,0];R_+^3)$.*

(i) If $b_1<\delta_1\bar{c}_1$, then

$$\begin{aligned}&\lim_{t\to\infty}X(t)=0, \\ &\lim_{t\to\infty}S(t)=0, \\ &\lim_{t\to\infty}I(t)=0, \\ &\qquad \textit{a.s.}\end{aligned} \tag{50}$$

(ii) If $b_1>\delta_1\bar{c}_1$, when $\Delta_1<0$, then

$$\begin{aligned}&\lim_{t\to\infty}\left\langle X(t)\right\rangle=\frac{b_1-\delta_1\bar{c}_1}{a_{11}}, \\ &\lim_{t\to\infty}S(t)=0, \\ &\lim_{t\to\infty}I(t)=0, \\ &\qquad \textit{a.s.}\end{aligned} \tag{51}$$

(iii) If $b_1>\delta_1\bar{c}_1$, $\Delta_1>0$, when $\mathscr{R}<1$, then

$$\begin{aligned}&\lim_{t\to\infty}\left\langle X(t)\right\rangle=\frac{\left(b_1-\delta_1\bar{c}_1\right)a_{22}+\left(b_2+\delta_2\bar{c}_2\right)a_{12}e^{-d_1\tau_1}}{\Delta'} \quad \textit{a.s}, \\ &\lim_{t\to\infty}\left\langle S(t)\right\rangle=\frac{\Delta_1}{\Delta'} \quad \textit{a.s}, \\ &\lim_{t\to\infty}I(t)=0 \quad \textit{a.s.}\end{aligned} \tag{52}$$

Proof. By stochastic comparison theorem, we have

$$\begin{aligned} X(t) &\le X_1(t), \\ S(t) &\le S_1(t), \\ I(t) &\le I_1(t). \end{aligned} \tag{53}$$

By (34), we derive

$$\lim_{t\to\infty} \frac{\int_t^{t+\tau_2} X(s-\tau_2)\,\mathrm{d}s}{t} = 0. \tag{54}$$

In the same way, we can verify that

$$\begin{aligned} \lim_{t\to\infty} \frac{\int_t^{t+\tau_2} S(s-\tau_2)\,\mathrm{d}s}{t} &= 0, \\ \lim_{t\to\infty} \frac{\int_t^{t+\tau_2} I(s-\tau_2)\,\mathrm{d}s}{t} &= 0. \end{aligned} \tag{55}$$

It follows from (33), (43), and (49) that

$$\left[\frac{\ln X(t)}{t}\right]^* \le \lim_{t\to\infty} \frac{\ln X_1(t)}{t} = 0, \tag{56}$$

$$\left[\frac{\ln S(t)}{t}\right]^* \le \lim_{t\to\infty} \frac{\ln S_1(t)}{t} = 0, \tag{57}$$

$$\left[\frac{\ln I(t)}{t}\right]^* \le \lim_{t\to\infty} \frac{\ln I_1(t)}{t} = 0. \tag{58}$$

Applying Itô's formula to system (10) leads to

$$\begin{aligned} \mathrm{d}\ln X &= \left[b_1 - \delta_1 \tilde{c}_1(t) - a_{11}X(t) \right. \\ &\quad \left. - a_{12}e^{-d_1\tau_1} S(t-\tau_1)\right] \mathrm{d}t + \sigma_1 \mathrm{d}B_1(t) \\ &\quad + \int_{\mathbb{Y}} \ln(1+\gamma_1(u))\, \widetilde{N}(\mathrm{d}t, \mathrm{d}u), \\ \mathrm{d}\ln S &= \left[-b_2 - \delta_2 \tilde{c}_2(t) + a_{21}e^{-d_2\tau_2} X(t-\tau_2) \right. \\ &\quad \left. - \beta e^{-d_3\tau_3} I(t-\tau_3) - a_{22}S(t)\right] \mathrm{d}t + \sigma_2 \mathrm{d}B_2(t) \\ &\quad + \int_{\mathbb{Y}} \ln(1+\gamma_2(u))\, \widetilde{N}(\mathrm{d}t, \mathrm{d}u), \\ \mathrm{d}\ln I &= \left[-b_3 - \delta_3 \tilde{c}_3(t) + \beta e^{-d_4\tau_4} S(t-\tau_4) \right. \\ &\quad \left. - a_{33}I(t)\right] \mathrm{d}t + \sigma_3 \mathrm{d}B_3(t) \\ &\quad + \int_{\mathbb{Y}} \ln(1+\gamma_3(u))\, \widetilde{N}(\mathrm{d}t, \mathrm{d}u). \end{aligned} \tag{59}$$

Then we can obtain

$$\begin{aligned} \frac{\ln X(t) - \ln X(0)}{t} &= b_1 - \delta_1 \langle \tilde{c}_1(t) \rangle \\ &\quad - a_{12}e^{-d_1\tau_1} \langle S(t) \rangle - a_{11} \langle X(t) \rangle - a_{12}e^{-d_1\tau_1} \\ &\quad \cdot \frac{\left(\int_0^{\tau_1} X(s-\tau_1)\,\mathrm{d}s - \int_t^{t+\tau_1} X(s-\tau_1)\,\mathrm{d}s\right)}{t} \\ &\quad + \frac{\sigma_1 B_1(t)}{t} + \frac{1}{t}\int_0^t \int_{\mathbb{Y}} \ln(1+\gamma_1(u))\, \widetilde{N}(\mathrm{d}s, \mathrm{d}u), \end{aligned} \tag{60}$$

$$\begin{aligned} \frac{\ln S(t) - \ln S(0)}{t} &= -b_2 - \delta_2 \langle \tilde{c}_2(t) \rangle \\ &\quad + a_{21}e^{-d_2\tau_2} \langle X(t) \rangle - \beta e^{-d_3\tau_3} \langle I(t) \rangle - a_{22} \langle S(t) \rangle \\ &\quad - a_{21}e^{-d_2\tau_2} \\ &\quad \cdot \frac{\left(\int_t^{t+\tau_2} X(s-\tau_2)\,\mathrm{d}s - \int_0^{\tau_2} X(s-\tau_2)\,\mathrm{d}s\right)}{t} \\ &\quad + \beta e^{-d_3\tau_3} \frac{\left(\int_t^{t+\tau_2} I(s-\tau_2)\,\mathrm{d}s - \int_0^{\tau_2} I(s-\tau_2)\,\mathrm{d}s\right)}{t} \\ &\quad + \frac{\sigma_2 B_2(t)}{t} + \frac{1}{t}\int_0^t \int_{\mathbb{Y}} \ln(1+\gamma_2(u))\, \widetilde{N}(\mathrm{d}s, \mathrm{d}u), \end{aligned} \tag{61}$$

$$\begin{aligned} \frac{\ln I(t) - \ln I(0)}{t} &= -b_3 - \delta_3 \langle \tilde{c}_3(t) \rangle + \beta e^{-d_4\tau_4} \langle S(t) \rangle \\ &\quad - a_{33} \langle I(t) \rangle - \beta e^{-d_4\tau_4} \\ &\quad \cdot \frac{\left(\int_t^{t+\tau_4} S(s-\tau_4)\,\mathrm{d}s - \int_0^{\tau_4} S(s-\tau_4)\,\mathrm{d}s\right)}{t} \\ &\quad + \frac{\sigma_3 B_3(t)}{t} + \frac{1}{t}\int_0^t \int_{\mathbb{Y}} \ln(1+\gamma_3(u))\, \widetilde{N}(\mathrm{d}s, \mathrm{d}u). \end{aligned} \tag{62}$$

Computing (60) $\times\, a_{21}e^{-d_2\tau_2}$ + (61) $\times\, a_{11}$ leads to

$$\begin{aligned} & a_{21}e^{-d_2\tau_2} \frac{\ln X(t) - \ln X(0)}{t} + a_{11} \frac{\ln S(t) - \ln S(0)}{t} \\ &\quad = \left(b_1 - \delta_1 \langle \tilde{c}_1(t) \rangle\right) a_{21}e^{-d_2\tau_2} \\ &\qquad - \left(b_2 + \delta_2 \langle \tilde{c}_2(t) \rangle\right) a_{11} - \Delta' \langle S(t) \rangle \\ &\qquad - a_{11}\beta e^{-d_3\tau_3} \langle I(t) \rangle + \Gamma_1, \end{aligned} \tag{63}$$

where Γ_1 is given in Appendix.

Case (i). By Lemma 5, we know that $\lim_{t\to\infty} X_1(t) = 0$, if $b_1 < \delta_1 \bar{c}_1$. From (53), we have

$$\lim_{t\to\infty} X(t) = 0 \quad \text{a.s.} \tag{64}$$

Obviously, we get

$$\begin{aligned} \lim_{t\to\infty} S(t) &= 0, \\ \lim_{t\to\infty} I(t) &= 0, \end{aligned} \tag{65}$$

a.s.

Case (ii). By Lemma 5, we know that $\lim_{t\to\infty} S_1(t) = 0$, if $b_1 > \delta_1\bar{c}_1$ and $\Delta_1 < 0$. From (53), we have

$$\lim_{t\to\infty} S(t) = 0 \quad \text{a.s.} \tag{66}$$

Then we obtain

$$\lim_{t\to\infty} I(t) = 0 \quad \text{a.s.} \tag{67}$$

By using (60) and Lemma 4, we can prove

$$\lim_{t\to\infty} \langle X(t)\rangle = \frac{b_1 - \delta_1\bar{c}_1}{a_{11}} \quad \text{a.s.} \tag{68}$$

Case (iii). Similarly, by Lemma 5, we get that $\lim_{t\to\infty} I_1(t) = 0$, if $b_1 > \delta_1\bar{c}_1$, $\Delta_1 > 0$, and $\mathscr{R} < 1$. By (53), we obtain

$$\lim_{t\to\infty} I(t) = 0 \quad \text{a.s.} \tag{69}$$

Combining Lemma 4 with (56) and (63), we get

$$\langle S(t)\rangle_* \geq \frac{\Delta_1}{\Delta'}. \tag{70}$$

From (60), we have

$$\begin{aligned}
&\frac{\ln X(t) - \ln X(0)}{t} \\
&\quad \leq b_1 - \delta_1 \langle \tilde{c}_1(t)\rangle_* - a_{12}e^{-d_1\tau_1}\langle S(t)\rangle_* - a_{11}\langle X(t)\rangle \\
&\quad + \frac{\sigma_1 B_1(t)}{t} + \frac{1}{t}\int_0^t\int_{\mathbb{Y}} \ln(1+\gamma_1(u))\widetilde{N}(ds,du).
\end{aligned} \tag{71}$$

Then we infer from Lemma 4 that

$$\begin{aligned}
&\langle X(t)\rangle^* \\
&\leq \frac{(b_1 - \delta_1\langle \tilde{c}_1(t)\rangle_*)a_{22} + (b_2 + \delta_2\langle\tilde{c}_2(t)\rangle^*)a_{12}e^{-d_1\tau_1}}{\Delta'}.
\end{aligned} \tag{72}$$

By (61), we get

$$\begin{aligned}
&\frac{\ln S(t) - \ln S(0)}{t} \\
&\quad \leq -b_2 - \delta_2\langle\tilde{c}_2(t)\rangle_* + a_{21}e^{-d_2\tau_2}\langle X(t)\rangle^* \\
&\quad - a_{22}\langle S(t)\rangle + \frac{\sigma_2 B_2(t)}{t} \\
&\quad + \frac{1}{t}\int_0^t\int_{\mathbb{Y}} \ln(1+\gamma_2(u))\widetilde{N}(ds,du).
\end{aligned} \tag{73}$$

From Lemma 4, we obtain

$$\langle S(t)\rangle^* \leq \frac{\Delta_1}{\Delta'}. \tag{74}$$

By (60), we have

$$\begin{aligned}
&\frac{\ln X(t) - \ln X(0)}{t} \\
&\quad \geq b_1 - \delta_1\langle\tilde{c}_1(t)\rangle^* - a_{12}e^{-d_1\tau_1}\langle S(t)\rangle^* \\
&\quad - a_{11}\langle X(t)\rangle + \frac{\sigma_1 B_1(t)}{t} \\
&\quad + \frac{1}{t}\int_0^t\int_{\mathbb{Y}} \ln(1+\gamma_1(u))\widetilde{N}(ds,du).
\end{aligned} \tag{75}$$

In view of Lemma 4, we can see that

$$\begin{aligned}
&\langle X(t)\rangle_* \\
&\geq \frac{(b_1 - \delta_1\langle\tilde{c}_1(t)\rangle^*)a_{22} + (b_2 + \delta_2\langle\tilde{c}_2(t)\rangle_*)a_{12}e^{-d_1\tau_1}}{\Delta'}.
\end{aligned} \tag{76}$$

Consequently,

$$\begin{aligned}
&\lim_{t\to\infty}\langle X(t)\rangle = \frac{(b_1 - \delta_1\bar{c}_1)a_{22} + (b_2 + \delta_2\bar{c}_2)a_{12}e^{-d_1\tau_1}}{\Delta'} \\
&\qquad \text{a.s,} \\
&\lim_{t\to\infty}\langle S(t)\rangle = \frac{\Delta_1}{\Delta'} \quad \text{a.s.}
\end{aligned} \tag{77}$$

This completes the proof of Theorem 6. □

3.2. Permanence in Mean. In this section, we prove the permanence in mean of system (10).

Theorem 7. *Let $(X(t), S(t), I(t))$ be the solution of system (10) with initial value $((\phi_1(t), \phi_2(t), \phi_3(t)) : -\tau \leq t \leq 0) \in C([-\tau, 0]; R_+^3)$. If $\Delta_2 > 0$ and $\Delta_3 > 0$, when $\widehat{\mathscr{R}} = (a_{11}a_{22}/\Delta')\mathscr{R} > 1$, then*

$$\begin{aligned}
\lim_{t\to\infty}\langle X(t)\rangle &= \frac{\Delta_2}{\Delta}, \\
\lim_{t\to\infty}\langle S(t)\rangle &= \frac{\Delta_3}{\Delta}, \\
\lim_{t\to\infty}\langle I(t)\rangle &= \frac{\Delta_4}{\Delta}, \\
&\textit{a.s.}
\end{aligned} \tag{78}$$

Proof. Computing $(62) \times \Delta' + (63) \times \beta e^{-d_4\tau_4}$, we obtain

$$\begin{aligned}
&\Delta'\frac{\ln I(t) - \ln I(0)}{t} \\
&\quad + \beta a_{21}e^{-d_2\tau_2 - d_4\tau_4}\frac{\ln X(t) - \ln X(0)}{t} \\
&\quad + a_{11}\beta e^{-d_4\tau_4}\frac{\ln S(t) - \ln S(0)}{t} \\
&= -(b_3 + \delta_3\langle\tilde{c}_3(t)\rangle)\Delta' \\
&\quad + (b_1 - \delta_1\langle\tilde{c}_1(t)\rangle)a_{21}\beta e^{-d_2\tau_2 - d_4\tau_4} \\
&\quad - (b_2 + \delta_2\langle\tilde{c}_2(t)\rangle)a_{11}\beta e^{-d_4\tau_4} \\
&\quad - (a_{33}\Delta' + a_{11}\beta^2 e^{-d_3\tau_3 - d_4\tau_4})\langle I(t)\rangle + \Gamma_2,
\end{aligned} \tag{79}$$

where Γ_2 is given in Appendix.

When $\widehat{\mathscr{R}} = (a_{11}a_{22}/\Delta')\mathscr{R} > 1$, by Lemma 4, we have

$$\langle I(t)\rangle_* \geq \frac{\Delta_4}{\Delta}. \tag{80}$$

So

$$\lim_{t\to\infty}\frac{\ln I(t)}{t}=0 \quad \text{a.s.} \tag{81}$$

Computing (63) × a_{33} − (62) × $a_{11}\beta e^{-d_3\tau_3}$, we have

$$\begin{aligned}
&a_{33}a_{21}e^{-d_2\tau_2}\frac{\ln X(t)-\ln X(0)}{t}\\
&\quad+a_{11}a_{33}\frac{\ln S(t)-\ln S(0)}{t}\\
&\quad-a_{11}\beta e^{-d_3\tau_3}\frac{\ln I(t)-\ln I(0)}{t}\\
&=\left(b_3+\delta_3\left\langle\widetilde{c}_3(t)\right\rangle\right)a_{11}\beta e^{-d_3\tau_3}\\
&\quad+\left(b_1-\delta_1\left\langle\widetilde{c}_1(t)\right\rangle\right)a_{33}a_{21}e^{-d_2\tau_2}\\
&\quad-\left(b_2+\delta_2\left\langle\widetilde{c}_2(t)\right\rangle\right)a_{11}a_{33}\\
&\quad-\left(a_{33}\Delta'+a_{11}\beta^2e^{-d_3\tau_3-d_4\tau_4}\right)\langle S(t)\rangle+\Gamma_3,
\end{aligned} \tag{82}$$

where Γ_3 is given in Appendix.

When $\Delta_3>0$, by Lemma 4, we have

$$\langle S(t)\rangle_*\geq\frac{\Delta_3}{\Delta}. \tag{83}$$

From (71), when $\Delta_2>0$, we obtain

$$\langle X(t)\rangle^*\leq\frac{\Delta_2}{\Delta}. \tag{84}$$

By (61), we get

$$\begin{aligned}
&\frac{\ln S(t)-\ln S(0)}{t}\\
&\quad\leq-b_2-\delta_2\left\langle\widetilde{c}_2(t)\right\rangle_*+a_{21}e^{-d_2\tau_2}\langle X(t)\rangle^*\\
&\quad-\beta e^{-d_3\tau_3}\langle I(t)\rangle_*-a_{22}\langle S(t)\rangle+\frac{\sigma_2B_2(t)}{t}\\
&\quad+\frac{1}{t}\int_0^t\int_{\mathbb{Y}}\ln\left(1+\gamma_2(u)\right)\widetilde{N}(\mathrm{d}s,\mathrm{d}u),
\end{aligned} \tag{85}$$

then from Lemma 4 we prove that

$$\langle S(t)\rangle^*\leq\frac{\Delta_3}{\Delta}. \tag{86}$$

By (60), we have

$$\begin{aligned}
&\frac{\ln X(t)-\ln X(0)}{t}\\
&\quad\geq b_1-\delta_1\left\langle\widetilde{c}_1(t)\right\rangle^*-a_{12}e^{-d_1\tau_1}\langle S(t)\rangle^*\\
&\quad-a_{11}\langle X(t)\rangle+\frac{\sigma_1B_1(t)}{t}\\
&\quad+\frac{1}{t}\int_0^t\int_{\mathbb{Y}}\ln\left(1+\gamma_1(u)\right)\widetilde{N}(\mathrm{d}s,\mathrm{d}u),
\end{aligned} \tag{87}$$

and then from Lemma 4 we get

$$\langle X(t)\rangle_*\geq\frac{\Delta_2}{\Delta}. \tag{88}$$

It can be inferred from (62) that

$$\begin{aligned}
&\frac{\ln I(t)-\ln I(0)}{t}\\
&\quad\leq-b_3-\delta_3\left\langle\widetilde{c}_3(t)\right\rangle_*+\beta e^{-d_4\tau_4}\langle S(t)\rangle^*-a_{33}\langle I(t)\rangle\\
&\quad-\beta e^{-d_4\tau_4}\frac{\left(\int_t^{t+\tau_4}S(s-\tau_4)\,\mathrm{d}s-\int_0^{\tau_4}S(s-\tau_4)\,\mathrm{d}s\right)}{t}\\
&\quad+\frac{\sigma_3B_3(t)}{t}+\frac{1}{t}\int_0^t\int_{\mathbb{Y}}\ln\left(1+\gamma_3(u)\right)\widetilde{N}(\mathrm{d}s,\mathrm{d}u),
\end{aligned} \tag{89}$$

and then from Lemma 4 we have

$$\langle I(t)\rangle^*\leq\frac{\Delta_4}{\Delta}. \tag{90}$$

Consequently,

$$\begin{aligned}
\lim_{t\to\infty}\langle X(t)\rangle&=\frac{\Delta_2}{\Delta},\\
\lim_{t\to\infty}\langle S(t)\rangle&=\frac{\Delta_3}{\Delta},\\
\lim_{t\to\infty}\langle I(t)\rangle&=\frac{\Delta_4}{\Delta},\\
&\text{a.s.}
\end{aligned} \tag{91}$$

This completes the proof of Theorem 7. □

4. Conclusion and Simulations

This paper explores the dynamics of a stochastic predator-prey model with time delays in the polluted environment. We show some properties of the subsystem of the predator-prey system. Then by using comparison theorem and limit superior theory, we obtain the sufficient conditions for the extinction of this system. From Theorem 6, we know that if environmental noises are large enough, the species will be extinct (see Figure 1) and if the amount of pulsed input concentration of the toxicant is large enough or the pulse period is small enough, the species will also be extinct (see Figures 2 and 3). In addition, Theorem 7 indicates that the permanence of populations has high correlation with the intensity of environmental noises (see Figure 2(a)). The main results show that time delays can lead to extinction of this system. Therefore, we realize that the environmental noises, the toxicant input, and delays are harmful to the permanence of the populations. Now we show some simulations to verify our main results.

Choose some parameters as follows $r=1.6$, $\mu_1=0.1$, $\mu_2=0.1$, $\delta_1=0.3$, $\delta_2=0.1$, $\delta_3=0.1$, $a_{11}=0.3$, $a_{12}=0.3$, $a_{21}=0.3$, $a_{22}=0.3$, $a_{33}=0.1$, $d_1=0.1$, $d_2=0.1$, $d_3=0.1$,

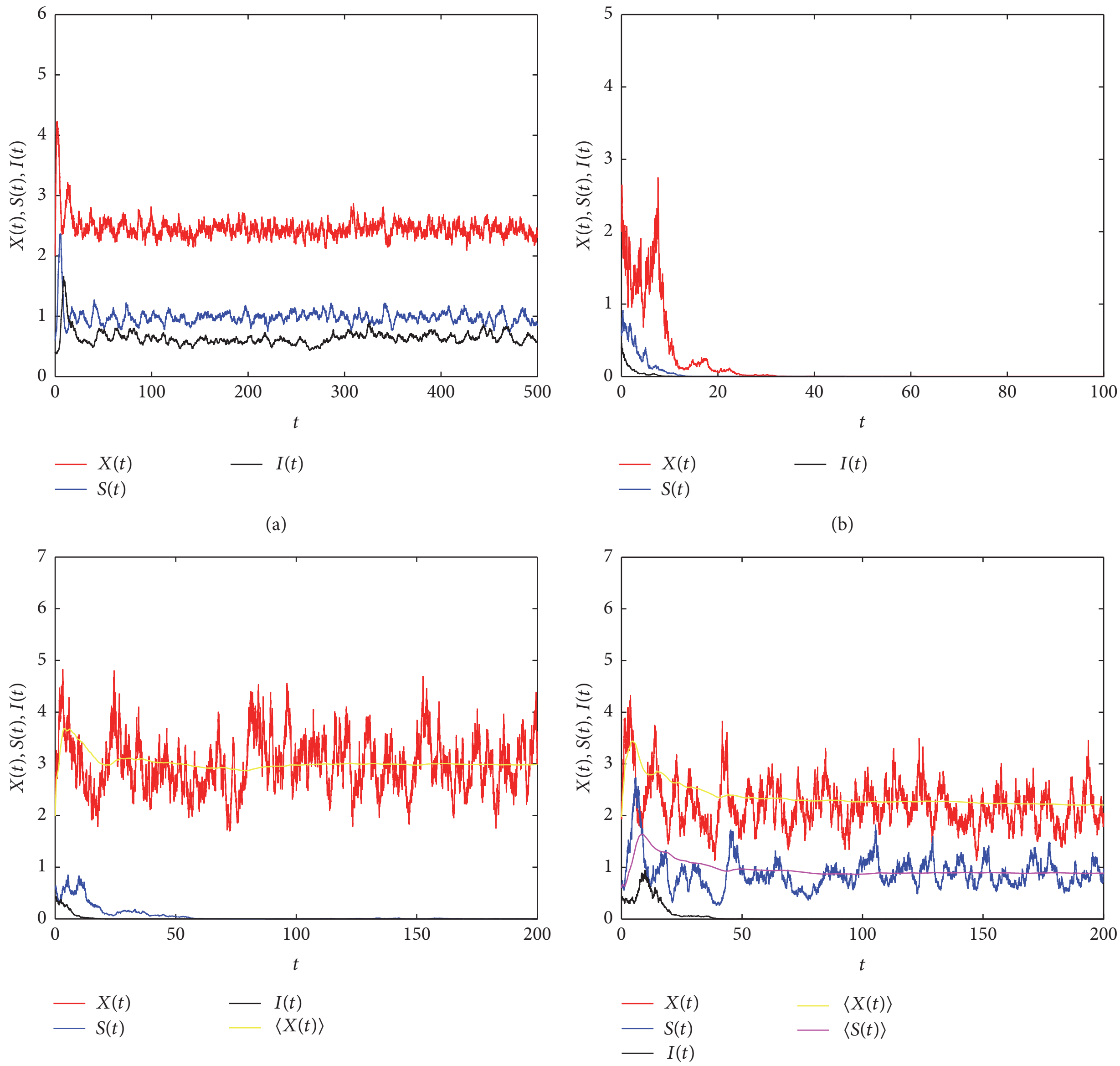

Figure 1: In (a), $\gamma_1 = 0$, $\gamma_2 = 0$, $\gamma_3 = 0$, and the species are permanent; in (b), $\gamma_1 = 2.2$, $\gamma_2 = 1.5$, $\gamma_3 = 1.2$, and then the species are extinct; in (c), $\gamma_1 = 0.5$, $\gamma_2 = 1.5$, $\gamma_3 = 1.2$, $X(t)$ is permanent, $S(t)$ and $I(t)$ are extinct, and $\lim_{t\to\infty}\langle X(t)\rangle = 2.953$; in (d), $\gamma_1 = 0.5$, $\gamma_2 = 0.5$, $\gamma_3 = 1.2$, $X(t)$ and $S(t)$ are permanent, $I(t)$ is extinct, $\lim_{t\to\infty}\langle X(t)\rangle = 2.144$, and $\lim_{t\to\infty}\langle S(t)\rangle = 0.892$.

$d_4 = 0.1$, $\tau_1 = 1$, $\tau_2 = 1$, $\tau_3 = 1$, $\tau_4 = 1$, $h = 0.3$, $\sigma_1 = 0.2$, $\sigma_2 = 0.2$, $\sigma_3 = 0.1$, $k_1 = 0.3$, $g_1 = 0.1$, $m_1 = 0.1$, $k_2 = 0.3$, $g_2 = 0.2$, $m_2 = 0.2$, $k_3 = 0.3$, $g_3 = 0.2$, and $m_3 = 0.2$. Based on the above parameters, we give simulations to explain the biological implications.

In Figure 1, we keep $u = 0.4$ and $T = 1$. In Figure 1(a), choose $\gamma_1 = 0$, $\gamma_2 = 0$, and $\gamma_3 = 0$, there is no Lévy noises, and we can see that the species are permanent. In Figure 1(b), if $\gamma_1 = 2.2$, $\gamma_2 = 1.5$, and $\gamma_3 = 1.2$, the intensities of Lévy noises are large and then we get $b_1 = 0.543 < \delta_1\bar{c}_1 = 0.600$, which means that the productiveness of the prey is less than its death loss rate; from Theorem 6, the species go extinction. In Figure 1(c), if $\gamma_1 = 0.5$, $\gamma_2 = 1.5$, and $\gamma_3 = 1.2$, then $b_1 = 0.886 > \delta_1\bar{c}_1 = 0.600$ and $\Delta_1 = -0.009 < 0$, from Theorem 6 we have that $X(t)$ is permanent and $S(t)$ and $I(t)$ are extinct; furthermore, we have $\lim_{t\to\infty}\langle X(t)\rangle = 2.953$. In Figure 1(d), if $\gamma_1 = 0.5$, $\gamma_2 = 0.5$, and $\gamma_3 = 1.2$, then $b_1 = 0.886 > \delta_1\bar{c}_1 = 0.600$, $\Delta_1 = 0.146 > 0$, and $\mathscr{R} = 0.946 < 1$; from Theorem 6 we obtain that $X(t)$ and $S(t)$ are permanent and $I(t)$ is extinct and we get $\lim_{t\to\infty}\langle X(t)\rangle = 2.144$ and $\lim_{t\to\infty}\langle S(t)\rangle = 0.892$.

In Figure 2, we keep $\gamma_1 = 0.5$, $\gamma_2 = 0.5$, $\gamma_3 = 0.1$, and $T = 1$. In Figure 2(a), we choose $u = 0.4$, and then $\Delta_2 = 0.114 > 0$, $\Delta_3 = 0.037 > 0$, and $\mathscr{R} = 2.809 > (a_{11}a_{22}/\Delta')\mathscr{R} = 1.559 > 1$. From Theorem 7, we have that $X(t)$, $S(t)$, and $I(t)$ are permanent and we obtain that $\lim_{t\to\infty}\langle X(t)\rangle = 2.072$, $\lim_{t\to\infty}\langle S(t)\rangle = 0.680$ and $\lim_{t\to\infty}\langle I(t)\rangle = 0.345$. In

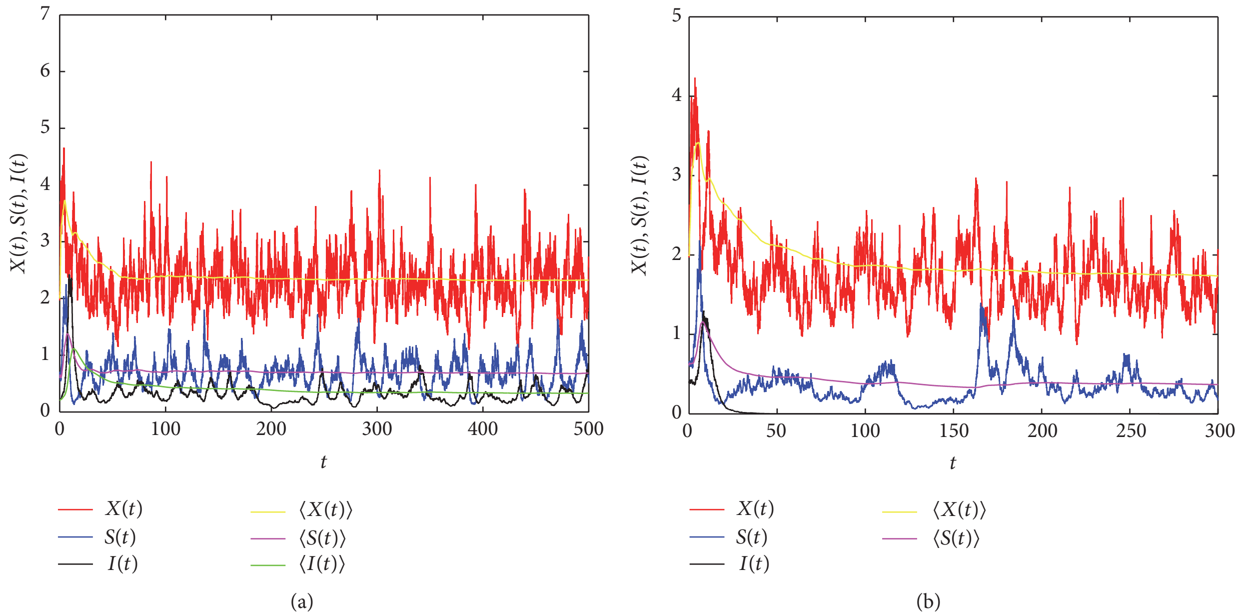

FIGURE 2: Keep $\gamma_1 = 0.5$, $\gamma_2 = 0.5$, $\gamma_3 = 0.1$, and $T = 1$. In (a), $u = 0.4$, $X(t)$, $S(t)$, and $I(t)$ are permanent, $\lim_{t\to\infty}\langle X(t)\rangle = 2.072$, $\lim_{t\to\infty}\langle S(t)\rangle = 0.680$, and $\lim_{t\to\infty}\langle I(t)\rangle = 0.345$; in (b), $u = 0.6$, $X(t)$ and $S(t)$ are permanent, $I(t)$ is extinct, $\lim_{t\to\infty}\langle X(t)\rangle = 1.719$, and $\lim_{t\to\infty}\langle S(t)\rangle = 0.313$; in (c), $u = 0.8$, $X(t)$ is permanent, $S(t)$ and $I(t)$ are extinct, and $\lim_{t\to\infty}\langle X(t)\rangle = 0.952$; in (d), $u = 1$ and then the species are extinct.

Figure 2(b), if $u = 0.6$, then $\Delta_1 = 0.050 > 0$ and $\mathscr{R} = 0.768 < 1$, and from Theorem 6, we get that $X(t)$ and $S(t)$ are permanent and $I(t)$ is extinct and $\lim_{t\to\infty}\langle X(t)\rangle = 1.719$ and $\lim_{t\to\infty}\langle S(t)\rangle = 0.313$. In Figure 2(c), if $u = 0.8$, then $\Delta_1 = -0.047 < 0$, $X(t)$ is permanent, $S(t)$ and $I(t)$ are extinct by Theorem 6, and $\lim_{t\to\infty}\langle X(t)\rangle = 0.952$. In Figure 2(d), we choose $u = 1$, and then $b_1 = 1.4855 < \delta_1\bar{c}_1 = 1.5$; from Theorem 6 the species are extinct.

In Figure 3, we keep $\gamma_1 = 0.5$, $\gamma_2 = 0.5$, $\gamma_3 = 0.1$, and $u = 0.4$. In Figure 3(a), we choose $T = 1$ and then $\Delta_2 = 0.114 > 0$, $\Delta_3 = 0.037 > 0$, and $\mathscr{R} = 2.809 > (a_{11}a_{22}/\Delta')\mathscr{R} = 1.559 > 1$. From Theorem 7, we have that $X(t)$, $S(t)$, and $I(t)$ are permanent and we obtain that $\lim_{t\to\infty}\langle X(t)\rangle = 2.072$, $\lim_{t\to\infty}\langle S(t)\rangle = 0.680$, and $\lim_{t\to\infty}\langle I(t)\rangle = 0.345$. In Figure 3(b), if $T = 0.7$, then $\Delta_1 = 0.063 > 0$ and $\mathscr{R} = 0.710 < 1$, and from Theorem 6, we get that $X(t)$ and $S(t)$ are permanent and $I(t)$ is extinct and $\lim_{t\to\infty}\langle X(t)\rangle = 1.743$ and $\lim_{t\to\infty}\langle S(t)\rangle = 0.386$. In Figure 3(c), if $T = 0.5$, then $\Delta_1 = -0.047 < 0$, $X(t)$ is permanent, $S(t)$ and $I(t)$ are extinct by Theorem 6, and $\lim_{t\to\infty}\langle X(t)\rangle = 0.952$. In Figure 3(d), we choose $T = 0.4$ and then $b_1 = 1.4855 < \delta_1\bar{c}_1 = 1.5$; from Theorem 6 the species are extinct.

From Figures 1–3, we can obtain the following conclusions:

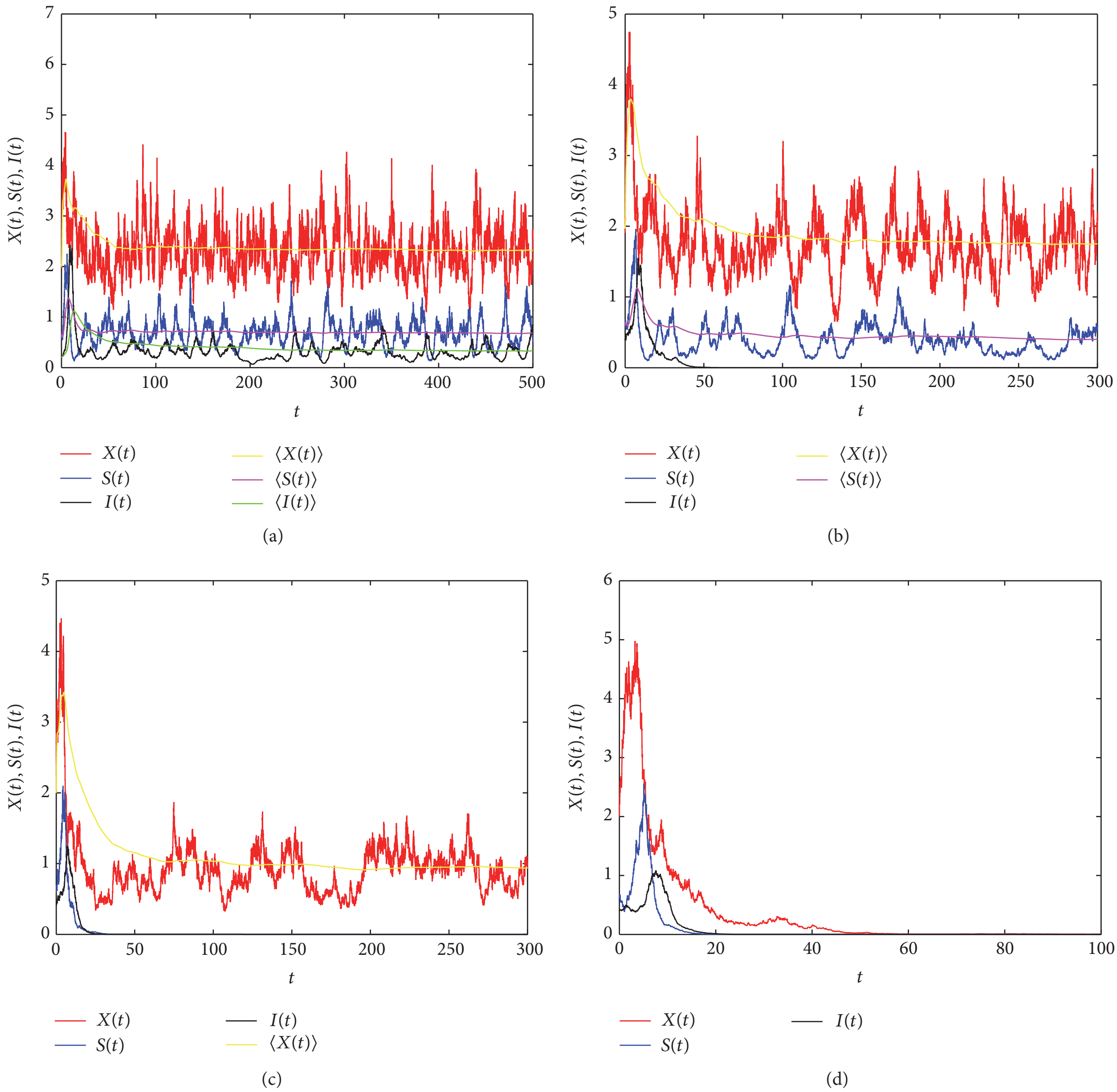

FIGURE 3: Keep $\gamma_1 = 0.5$, $\gamma_2 = 0.5$, $\gamma_3 = 0.1$, and $u = 0.4$. In (a), $T = 1$, $X(t)$, $S(t)$ and $I(t)$ are permanent, $\lim_{t\to\infty}\langle X(t)\rangle = 2.072$, $\lim_{t\to\infty}\langle S(t)\rangle = 0.680$, and $\lim_{t\to\infty}\langle I(t)\rangle = 0.345$; in (b), $T = 0.7$, $X(t)$ and $S(t)$ are permanent, $I(t)$ is extinct, $\lim_{t\to\infty}\langle X(t)\rangle = 1.743$, and $\lim_{t\to\infty}\langle S(t)\rangle = 0.386$; in (c), $T = 0.5$, $X(t)$ is permanent, $S(t)$ and $I(t)$ are extinct, and $\lim_{t\to\infty}\langle X(t)\rangle = 0.952$; in (d), $u = 0.4$ and then the species are extinct.

(1) Large stochastic disturbance can cause the populations to go to extinction; that is, the persistent population of a deterministic system can become extinct due to the white noise stochastic disturbance.

(2) Large impulsive input concentration of the toxicant or small impulsive period of the exogenous input of toxicant can cause the populations to go to extinction.

Therefore, the above numerical simulations illustrate the performance of the theoretical results, and the biological results show that the white noise stochastic disturbance and impulsive toxicant input are disadvantage for the permanence of system.

Appendix

For the sake of convenience, we define

$$\Gamma_1 = -a_{12}a_{21}e^{-d_1\tau_1-d_2\tau_2} \cdot \frac{\left(\int_0^{\tau_1} X(s-\tau_1)\,ds - \int_t^{t+\tau_1} X(s-\tau_1)\,ds\right)}{t}$$

$$
\begin{aligned}
& - a_{11} a_{21} e^{-d_2 \tau_2} \\
& \cdot \frac{\left(\int_t^{t+\tau_2} X(s-\tau_2)\, \mathrm{d}s - \int_0^{\tau_2} X(s-\tau_2)\, \mathrm{d}s \right)}{t} \\
& + a_{11} \beta e^{-d_3 \tau_3} \\
& \cdot \frac{\left(\int_t^{t+\tau_3} I(s-\tau_3)\, \mathrm{d}s - \int_0^{\tau_3} I(s-\tau_3)\, \mathrm{d}s \right)}{t} \\
& + a_{21} e^{-d_2 \tau_2} \left(\frac{\sigma_1 B_1(t)}{t} \right. \\
& \left. + \frac{1}{t} \int_0^t \int_{\mathbb{Y}} \ln\left(1 + \gamma_1(u)\right) \widetilde{N}(\mathrm{d}s, \mathrm{d}u) \right) \\
& + a_{11} \left(\frac{\sigma_2 B_2(t)}{t} \right. \\
& \left. + \frac{1}{t} \int_0^t \int_{\mathbb{Y}} \ln\left(1 + \gamma_2(u)\right) \widetilde{N}(\mathrm{d}s, \mathrm{d}u) \right),
\end{aligned}
$$

$$
\begin{aligned}
\Gamma_2 = & -\beta a_{12} a_{21} e^{-d_1 \tau_1 - d_2 \tau_2 - d_4 \tau_4} \\
& \cdot \frac{\left(\int_0^{\tau_1} X(s-\tau_1)\, \mathrm{d}s - \int_t^{t+\tau_1} X(s-\tau_1)\, \mathrm{d}s \right)}{t} \\
& - a_{11} a_{21} \beta e^{-d_2 \tau_2 - d_4 \tau_4} \\
& \cdot \frac{\left(\int_t^{t+\tau_2} X(s-\tau_2)\, \mathrm{d}s - \int_0^{\tau_2} X(s-\tau_2)\, \mathrm{d}s \right)}{t} \\
& + a_{11} \beta^2 e^{-d_3 \tau_3 - d_4 \tau_4} \\
& \cdot \frac{\left(\int_t^{t+\tau_3} I(s-\tau_3)\, \mathrm{d}s - \int_0^{\tau_3} I(s-\tau_3)\, \mathrm{d}s \right)}{t} \\
& - \Delta' \beta e^{-d_4 \tau_4} \\
& \cdot \frac{\left(\int_t^{t+\tau_4} S(s-\tau_4)\, \mathrm{d}s - \int_0^{\tau_4} S(s-\tau_4)\, \mathrm{d}s \right)}{t} \\
& + a_{21} \beta e^{-d_2 \tau_2 - d_4 \tau_4} \left(\frac{\sigma_1 B_1(t)}{t} \right. \\
& \left. + \frac{1}{t} \int_0^t \int_{\mathbb{Y}} \ln\left(1 + \gamma_1(u)\right) \widetilde{N}(\mathrm{d}s, \mathrm{d}u) \right) \\
& + a_{11} \beta e^{-d_4 \tau_4} \left(\frac{\sigma_2 B_2(t)}{t} \right. \\
& \left. + \frac{1}{t} \int_0^t \int_{\mathbb{Y}} \ln\left(1 + \gamma_2(u)\right) \widetilde{N}(\mathrm{d}s, \mathrm{d}u) \right) \\
& + \Delta' \left(\frac{\sigma_3 B_3(t)}{t} \right. \\
& \left. + \frac{1}{t} \int_0^t \int_{\mathbb{Y}} \ln\left(1 + \gamma_3(u)\right) \widetilde{N}(\mathrm{d}s, \mathrm{d}u) \right),
\end{aligned}
$$

$$
\begin{aligned}
\Gamma_3 = & -a_{33} a_{12} a_{21} e^{-d_1 \tau_1 - d_2 \tau_2 - d_4 \tau_4} \\
& \cdot \frac{\left(\int_0^{\tau_1} X(s-\tau_1)\, \mathrm{d}s - \int_t^{t+\tau_1} X(s-\tau_1)\, \mathrm{d}s \right)}{t} \\
& - a_{11} a_{33} a_{21} e^{-d_2 \tau_2} \\
& \cdot \frac{\left(\int_t^{t+\tau_2} X(s-\tau_2)\, \mathrm{d}s - \int_0^{\tau_2} X(s-\tau_2)\, \mathrm{d}s \right)}{t} \\
& + a_{11} a_{33} \beta e^{-d_3 \tau_3} \\
& \cdot \frac{\left(\int_t^{t+\tau_3} I(s-\tau_3)\, \mathrm{d}s - \int_0^{\tau_3} I(s-\tau_3)\, \mathrm{d}s \right)}{t} \\
& + a_{11} \beta^2 e^{-d_3 \tau_3 - d_4 \tau_4} \\
& \cdot \frac{\left(\int_t^{t+\tau_4} S(s-\tau_4)\, \mathrm{d}s - \int_0^{\tau_4} S(s-\tau_4)\, \mathrm{d}s \right)}{t} \\
& + a_{33} a_{21} \beta e^{-d_2 \tau_2} \left(\frac{\sigma_1 B_1(t)}{t} \right. \\
& \left. + \frac{1}{t} \int_0^t \int_{\mathbb{Y}} \ln\left(1 + \gamma_1(u)\right) \widetilde{N}(\mathrm{d}s, \mathrm{d}u) \right) \\
& + a_{11} a_{33} \left(\frac{\sigma_2 B_2(t)}{t} \right. \\
& \left. + \frac{1}{t} \int_0^t \int_{\mathbb{Y}} \ln\left(1 + \gamma_2(u)\right) \widetilde{N}(\mathrm{d}s, \mathrm{d}u) \right) \\
& - a_{11} \beta e^{-d_3 \tau_3} \left(\frac{\sigma_3 B_3(t)}{t} \right. \\
& \left. + \frac{1}{t} \int_0^t \int_{\mathbb{Y}} \ln\left(1 + \gamma_3(u)\right) \widetilde{N}(\mathrm{d}s, \mathrm{d}u) \right).
\end{aligned}
\tag{A.1}
$$

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Acknowledgments

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