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Research Article

On Solutions to a Class of Functional Differential Equations with Time-Dependent Coefficients

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In this paper, we study initial boundary value problems that involve functional (nonlocal) partial differential equations with variable coefficients. These problems arise in cell growth models with symmetric and asymmetric modes of division. We determine the general solution to the symmetric cell division problem for a certain class of coefficients and establish the convergence of solutions to a large time asymptotic solution. The existence of a steady size distribution (SSD) solution for an asymmetric cell division problem is established and is shown to be the large time-attracting solution for a certain class of coefficients. The rate of convergence of solutions towards the SSD solution is affected by the choice of coefficients and remains unaffected by the asymmetry in cell division. The uniqueness of solutions to the initial boundary value problem is also established.

1. Introduction

Functional partial differential equations, subject to appropriate initial and boundary conditions, arise in various population models. A population model for animals reproduced by fission was given by Sinko and Streifer [1, 2]. Their model was used in the context of cell growth and division, among others, by Hall and Wake [3]. A size structured model, where the size is the DNA content or mass, entails a pantograph-type first-order partial differential equation (PDE)

$$\frac{\partial}{\partial t}\vartheta(x,t)+\frac{\partial}{\partial x}(\gamma(x,t)\vartheta(x,t))=\alpha^2\sigma(\alpha x,t)\vartheta(\alpha x,t)-\sigma(x,t)\vartheta(x,t), \quad (1)$$

subject to an initial distribution

$$\vartheta(x,0)=\vartheta_0(x) \quad (2)$$

and the boundary condition

$$\lim_{x\longrightarrow 0^+}(\gamma(x,t)\vartheta(x,t))=0 \quad (3)$$

for $t>0$. Here, $\vartheta(x,t)$ is the number density of the cells of size x at time t, $\sigma(x,t)$ is the frequency of division of the cells, and $\gamma(x,t)$ is the growth rate of the cells. The functional term in the PDE (1) is a consequence of symmetric cell division in which $\alpha>1$ daughter cells of equal size x are produced when a the cell of size αx divides. The asymmetric cell division, in which a cell divides into two different sizes of daughter cells, say sizes α and β, yields an initial value problem that involves a PDE, with two functional terms, of the form

$$\frac{\partial}{\partial t}\vartheta(x,t)+\frac{\partial}{\partial x}(\gamma(x,t)\vartheta(x,t))=\alpha\sigma(\alpha x,t)\vartheta(\alpha x,t)+\beta\sigma(\beta x,t)\vartheta(\beta x,t)-\sigma(x,t)\vartheta(x,t), \quad (4)$$

along with conditions (2) and (3). The assumption that division does not cause any loss of DNA content or mass leads to

$$\frac{1}{\alpha}+\frac{1}{\beta}=1, \quad (5)$$

so that $\alpha > 2 > \beta > 1$. These cell growth and division models are thus initial boundary value problems that involve a functional PDE.

The nonlocal terms imply a dearth of analytical techniques for solving such problems, even for a restricted choice of σ and γ. The cell growth model (1) and (2) has been studied for specific choices of division and growth rates. A separable solution to the problem was found for constant σ and γ [3]. Perthame and Ryzhik [4] showed that this separable solution is the long time asymptotic solution towards which solutions to the PDE converge exponentially in time. The separable solutions were called "steady size distributions (SSDs)" by Hall and Wake. The full problem was then solved by Zaidi et al. [5]. Hall and Wake [6] also studied the case of linear growth rates $\gamma(x, t) = gx$ and $\sigma(x, t) = bx^r$, where $r > 0$, $b > 0$, and $g > 0$, and found separable solutions to the initial boundary value problem. The separable solution in this case, however, is not the long time asymptotic solution since the long time asymptotic solution involves time-dependent oscillations [7]. The full problem was solved recently [8]. The division function $\sigma(x, t) = bH(x - c)$, where b and c are positive numbers and H is the Heaviside function, was considered by van-Brunt et al. [9] for constant growth rate. They showed the existence of a steady size distribution solution. For a certain class of functions $\sigma(x)$, the existence of a long time asymptotic solution for $\gamma(x, t) = g$, where $g > 0$, was established in the context of growth-fragmentation equation [4, 10–12].

For asymmetric binary cell division, the PDE (4), together with conditions (2) and (3), was studied for coefficient coefficients ([13, 14]) and for $\gamma(x, t) = gx$ and $\sigma(x, t) = bx^r$, where $r > 0$, $b > 0$, and $g > 0$ [15], and separable solutions were determined. The full problem, even for constant coefficients, has not been solved hitherto. Recently, the existence of a unique solution to the problem for constant coefficients has been established [16].

The major focus, hitherto, has been on the cell growth PDEs where σ and γ are either constant or functions of x alone. This makes the separation of variables possible, and the separable solution in most cases corresponds to the long time asymptotic solution. However, time-dependent coefficients classically appear in biology. Michel et al. [11] studied time-varying coefficients in the context of renewal equation with T-periodic death and birth rates. In this paper, we investigate time-dependent growth and division rates. In the next section, we obtain the general solution to PDE (1), subject to conditions (2) and (3), for the case where the growth and division rates have same time dependence, i.e., $\sigma(x, t) = br(t)$ and $\gamma(x, t) = gr(t)$, where b, g, and $r > 0$. We also find the general solution to PDE (1) for different time dependence of growth and division rates. Specifically, we consider $\sigma(x, t) = bt^{\nu}$ and $\gamma(x, t) = gt^{\mathfrak{u}}$, where $\mathfrak{u} \geq 0$ and $\nu \geq 0$. We then study the large time asymptotics of solutions for $\nu = 0$ and $\mathfrak{u} \geq 0$.

In Section 3, we determine a probability density function eigenvalue and a separable solution to the PDE (4), subject to conditions (2) and (3) for a certain class of division and growth rates. We show that this separable solution is the long time asymptotic solution. We also show that if the problem has a solution, then it is unique.

2. General Solution for Symmetric Division

In this section, we find solutions to PDE (1), subject to conditions (2) and (3), for $\gamma(x, t) = gr(t)$ and $\sigma(x, t) = br(t)$, where $g > 0$, $b > 0$, and $r > 0$ for all $t > 0$. This converts PDE (1) to

$$\frac{\partial}{\partial t}\vartheta(x, t) + gr(t)\frac{\partial}{\partial x}\vartheta(x, t) + br(t)\vartheta(x, t) = b\alpha^2 r(t)\vartheta(\alpha x, t), \tag{6}$$

where $\alpha > 1$. Let

$$R(t) = \int r(t)dt. \tag{7}$$

Using transformations

$$\vartheta(x, t) = \exp(-bR(t))\tilde{\vartheta}(x, t), \quad x = g\hat{x}, \tag{8}$$

equation (6) reduces to

$$\frac{\partial}{\partial t}\vartheta(x, t) + r(t)\frac{\partial}{\partial x}\vartheta(x, t) = b\alpha^2 r(t)\vartheta(\alpha x, t). \tag{9}$$

The above equation was solved for $r(t) \equiv 1$ by Zaidi et al. [5]. Motivated by their analysis, we first find solutions in the region $x \geq R(t)$ and then extend the solution to $0 < x < R(t)$. Let

$$N_0(x, t) = \vartheta_0(x - R(t)), \tag{10}$$

and for $k \geq 1$,

$$\frac{\partial}{\partial t}N_k + r(t)\frac{\partial}{\partial x}N_k = b\alpha^2 r(t)N_{k-1}(\alpha x, t), \tag{11}$$

where N_k satisfy

$$N_k(x, 0) = 0. \tag{12}$$

This can be solved using method of characteristics with characteristic coordinates $\xi = t$ and $\eta = x - R(t)$. For $k \geq 1$, we have

$$N_k = \sum_{j=0}^{k} d_{k,j} T_k\left(w_{k,j}(x, t)\right). \tag{13}$$

Here,

$$d_{0,0} = 1,$$
$$d_{k,j} = \frac{b\alpha^2 d_{k-1,j-1}}{\alpha^{k-j}(\alpha^j - 1)},$$
$$d_{k,0} = -\sum_{j=1}^{k} d_{k,j}, \tag{14}$$
$$w_{k,j}(x,t) = \alpha^{k-j}\left(\alpha^j x - R(t)\right),$$

for $k = 1, 2, \cdots$, and $j = 1, \cdots k$. Moreover, T_k is an antiderivative of T_{k-1}. It can be verified that the series defining $Q(x, t) = \sum_{k=0}^{\infty} N_k(x,t)$ is the solution to (9) and converges uniformly in any set of the form $\{(x,t) \in W_0 : t \le B\}$, where B is any fixed number lying in the region $0 < x < R(t)$. Let $m(x,t) = \int_x^{\infty} \vartheta(\xi, t)d\xi$. Then, PDE (9) reduces to

$$\frac{\partial}{\partial t} m(x,t) + r(t)\frac{\partial}{\partial x} m(x,t) = \mathrm{b}\alpha r(t) m(\alpha x, t). \tag{15}$$

Using a similar approach, the solution to (15) can be gleaned in the region $x \ge R(t)$.

We extend the solutions of (9) in the region $0 < x < R(t)$ by constructing a sequence of wedges in such a ways that if a point (x,t) lies in a given region, the $(\alpha x, t)$ is in a region we already know the solutions (see Figures 1 and 2). This makes the functional PDE local and thus able to be solved by using standard methods.

Let

$$W_n = \left\{(x,t) \colon \frac{R(t)}{\alpha^n} \le x \le \frac{R(t)}{\alpha^{n-1}}\right\}, \tag{16}$$

and let solution to differential equation in the wedge W_n be denoted by h_n for $n \ge 1$. Also, let

$$P_n = \sum_{k=n}^{\infty}\sum_{j=n}^{k} c_{k,j} M_k\left(w_{k,j}\right), \tag{17}$$

for $n \ge 0$, where

$$c_{0,0} = 1,$$
$$c_{k,j} = \frac{b\alpha c_{k-1,j-1}}{\alpha^{k-j}(\alpha^j - 1)}, \tag{18}$$
$$c_{k,0} = -\sum_{j=1}^{k} c_{k,j},$$

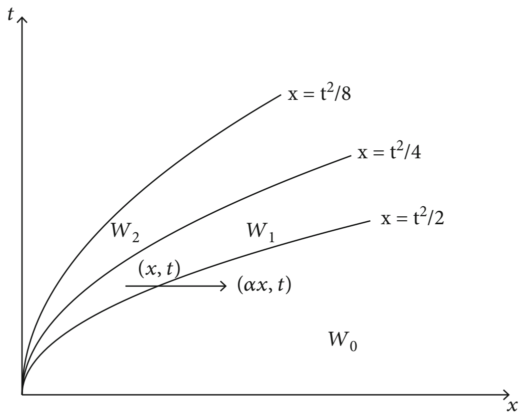

Figure 1: The construction of wedges for the case $r(t) = t$ and $\alpha = 2$.

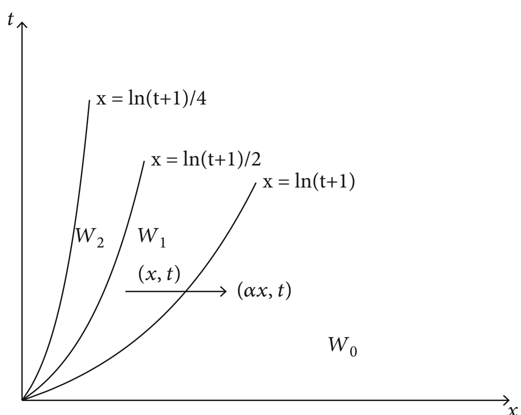

Figure 2: The construction of wedges for the case $r(t) = 1/1 + t$ and $\alpha = 2$.

for $k = 1, 2, \cdots$, and $j = 1, \cdots, k$. We can mimic the analysis in [5]. This yields the solution

$$m(x,t) = \begin{cases} h_0 = P_0 \text{ if}(\mathrm{x},\mathrm{t}) \in \mathrm{W}_0, \\ h_1 = P_1 + G_0 \text{ if}(\mathrm{x},\mathrm{t}) \in \mathrm{W}_1, \\ \vdots \\ h_n = P_n + G_0(w_{0,0}) + \sum_{k=1}^{n-1} \frac{(b\alpha)^k}{\prod_{m=1}^{k}(\alpha^m - 1)} G_k(w_{k,k}) \text{if}(\mathrm{x},\mathrm{t}) \in \mathrm{W}_\mathrm{n}, \\ \vdots \end{cases} \tag{19}$$

where G_0 is an arbitrary function that can be determined from the boundary condition (3).

The analysis of Zaidi et al. [5] can also be mimicked to determine the large time asymptotic of (19). It can be shown that solution to (9) converges to separable solution as $t \longrightarrow \infty$. That is,

$$n(x,t) = e^{-b\alpha R(t)} \sum_{k=0}^{\infty} a_k e^{-b\alpha^k x}, \tag{20}$$

where a_k are determined as in [5].

Even if the growth and division rates have different time dependence, (19) still remains the solution to the PDE (9). For instance, if $\gamma(x,t)=gt^{\mathbf{u}}$ and $\sigma(x,t)=bt^{v}$, where b, g, $\mathbf{u}$, and v are positive constants, (19) solves the PDE

$$\frac{\partial}{\partial t}m(x,t)+t^{\mathbf{u}}\frac{\partial}{\partial x}m(x,t)=b\alpha t^{v}m(\alpha x,t), \tag{21}$$

along with

$$m(0,t)=\exp\left(\frac{b\alpha t^{v}}{v+1}\right), \tag{22}$$

$$m(x,0)=m_0(x)=\int_x^{\infty}\vartheta_0(\sigma)d\sigma. \tag{23}$$

The large time dynamics, however, differ markedly from the same time dependence case. This is because separable solutions do not exist if the growth and division rates have a different time dependence.

We study the long time dynamics when $u>0$ and $v=0$.

The convergence of P_n implies $P_n\longrightarrow 0$ as $n\longrightarrow\infty$. Consequently, the solutions (19) and (22) yield

$$e^{b\alpha t}=h(0,t)=G_0\left(-\frac{t^{\mathbf{u}+1}}{\mathbf{u}+1}\right)+\sum_{k=1}^{\infty}\frac{(b\alpha)^k}{\prod_{m=1}^{k}(\alpha^m-1)}G_k\left(-\frac{t^{\mathbf{u}+1}}{\mathbf{u}+1}\right), \tag{24}$$

so that

$$e^{b\alpha(-\sigma(\mathbf{u}+1))^{1/\mathbf{u}+1}}=G_0(\sigma)+\sum_{k=1}^{\infty}\frac{(b\alpha)^k}{\prod_{m=1}^{k}(\alpha^m-1)}G_k(\sigma), \tag{25}$$

where $\sigma=-(t^{\mathbf{u}+1})/(\mathbf{u}+1)$. Since $e^{b\alpha(-\sigma(\mathbf{u}+1))^{1/(\mathbf{u}+1)}}=\sum_{k=0}^{\infty}((-1)^k(b\alpha)^k/k!)(u+1)^{k/(u+1)}\sigma^{k/(u+1)}$, the Laplace transform yields

$$h(s):=\sum_{k=0}^{\infty}\frac{(-1)^k(b\alpha)^k(\mathbf{u}+1)^{k/(u+1)}}{k!s^{(k+\mathbf{u}+1)/(\mathbf{u}+1)}}\Gamma\left(\frac{k+\mathbf{u}+1}{\mathbf{u}+1}\right), \tag{26}$$

for $s>0$.

Consequently, the Laplace transform of (24) gives $h(s)=g(s)(1+\sum_{k=1}^{\infty}((b\alpha/s)^k/(\prod_{m=1}^{k}(1-q^m))))$, so that the Euler's identity [5] yields

$$h(s)=g(s)\prod_{k=0}^{\infty}\left(1+\frac{b}{\alpha^k s}\right), \tag{27}$$

where $g(s)$ is Laplace transform of $G_0(\sigma)$.

Thus,

$$g(s)=h(s)\cdot\frac{1}{(1+(b/s))(1+(b/\alpha s))(1+(b/\alpha^2 s))\cdots}. \tag{28}$$

Let

$$J(s):=\frac{1}{(1+(b/s))(1+(b/\alpha s))(1+(b/\alpha^2 s))\cdots}. \tag{29}$$

Then, $J(s)$ has simple poles at $s=-b/\alpha^n$ for $n=0,1,2,\cdots$, and consequently, Mittag-Leffer theorem implies

$$J(s)=\frac{a_0}{s+b}+\frac{a_1}{s+(b/\alpha)}+\cdots+Z(s), \tag{30}$$

where $Z(s)$ is the entire function. The inverse transform of $J(s)$ is

$$\widehat{J}(\sigma)=\sum_{n=0}^{\infty}a_n e^{-b\alpha^{-n}\sigma}, \tag{31}$$

where $a_n=\operatorname{Re}s_{s=-b/\alpha^n}J(s)$.

Now,

$$a_0=\operatorname{Re}s_{s=-b}J(s),=\lim_{s\longrightarrow -b}(s+b)J(s),=\frac{-b}{\prod_{k=1}^{\infty}(1-(1/\alpha^k))}=\tilde{R}(b,\alpha). \tag{32}$$

Consequently, for $k\geq 1$,

$$a_k=\frac{(-1)^k}{\prod_{m=1}^{k}}\tilde{R}(b,\alpha). \tag{33}$$

Hence,

$$\widehat{J}(\sigma)=\tilde{R}(b,\alpha)\left\{e^{-b\sigma}+\sum_{k=1}^{\infty}\frac{(-1)^{k+1}}{\prod_{m=1}^{k}(\alpha^m-1)}e^{(-b/\alpha^k)\sigma}\right\}. \tag{34}$$

Equations (27) and (30) imply that

$$G_0(\sigma)=e^{b\alpha(-\sigma(u+1))^{1/u+1}}*\widehat{J}(\sigma), \tag{35}$$

where $*$ represents convolution. This gives

$$G_0(\sigma)=\tilde{R}(b,\alpha)\{M_1(\sigma)+N_1(\sigma)\}, \tag{36}$$

where

$$M_1(\sigma):=\int_0^{\sigma}e^{b\alpha(-\theta(\mathbf{u}+1))^{1/\mathbf{u}+1}}\cdot e^{-b(\sigma-\theta)}d\theta,$$
$$N_1(\sigma)=\sum_{k=1}^{\infty}\frac{(-1)^{k+1}}{\prod_{m=1}^{k}(\alpha^m-1)}\int_0^{\sigma}e^{-b/\alpha^k(\sigma-\theta)}\cdot e^{b\alpha(-\theta(\mathbf{u}+1))^{1/(\mathbf{u}+1)}}d\theta, \tag{37}$$

so that, for $n\geq 1$,

$$G_n(\sigma)=\tilde{R}(b,\alpha)\{M_n(\sigma)+N_n(\sigma)\}, \tag{38}$$

where $M_n(\sigma)$ is an anti-derivative of $M_{n-1}(\sigma)$ and $N_n(\sigma)$ is an anti-derivative of $N_{n-1}(\sigma)$.

3. Steady Size Distribution Solutions and Large Time Asymptotics for Asymmetric Division

Separable solutions are of central interest since these usually correspond to the steady size distribution solutions which attract solutions to the PDE for large time. We show that if σ and γ are separable with same time dependence, i.e., $\sigma(x, t) = br(t)m(x)$ and $\gamma(x, t) = gr(t)h(x)$, where b and g are positive numbers and r, h, and k are positive functions for all $t > 0$ and $x > 0$, then variables can be separated in principle. Consequently, we consider the PDE

$$\frac{\partial}{\partial t}\vartheta(x,t) + gr(t)\frac{\partial}{\partial x}(h(x)\vartheta(x,t)) = \alpha br(t)m(\alpha x)\vartheta(\alpha x,t) + \beta br(t)m(\beta x)\vartheta(\beta x,t) - br(t)m(x)\vartheta(x,t) \tag{39}$$

and solutions of the form

$$\vartheta(x,t) = \omega(t)\rho(x), \tag{40}$$

where ϱ is required to be a probability density function with $\int_0^\infty \varrho(x)dx = 1$ and $\omega(t)$ represents the total population of cells of all sizes at a given time t. The separable form (40) and PDE (39) give

$$\omega'(t)\varrho(x) + gr(t)h'(x)\omega(t)\varrho'(x) + gr(t)h(x)\omega(t)\varrho'(x) + br(t)m(x)\omega(t)\varrho(x) = \alpha br(t)m(\alpha x)\omega(t)\varrho(\alpha x) + \beta br(t)m(\beta x)\omega(t)\varrho(\beta x), \tag{41}$$

which, dividing by $r(t)\omega(t)\varrho(x)$, yields

$$\omega(t) = ce^{-\Lambda R(t)}, \tag{42}$$

for some constant $c > 0$, separation constant Λ (to be determined), and

$$R(t) = \int r(t)dt. \tag{43}$$

The function $\varrho(x)$ satisfies

$$gh(x)\varrho'(x) + \left(gh'(x) + bm(x) - \Lambda\right)\varrho(x) = \alpha bm(\alpha x)\varrho(\alpha x) + \beta bm(\beta x)\varrho(\beta x), \tag{44}$$

along with the conditions

$$\lim_{x\longrightarrow 0^+} gh(x)\varrho(x) = 0, \quad \lim_{x\longrightarrow\infty} gh(x)\varrho(x) = 0. \tag{45}$$

Equation (44) is a pantograph-type equation with two nonlocal terms. It appears in various applications including the absorption of light in the Milky Way [17] and internet protocols [18]. Although there are no general methods of solving (44), solutions have been obtained for constant coefficients [14] and for $h(x) = x$ and $m(x) = x^r$, where $r > 0$ [15]. In both instances, the solution entails a positive Dirichlet series of the form

$$\sum_{\mathrm{u}=0}^{\infty}\sum_{\nu=0}^{\infty} d_{\mathrm{u},\nu} \exp\left(-\alpha^{s\mathrm{u}}\beta^{s\nu}rf(x)\right), \tag{46}$$

where c_k are coefficients, s and r are constants, and f satisfies

$$f(\alpha x) = \alpha^s f(x). \tag{47}$$

Zaidi and van-Brunt [15] showed that for any positive solution to (27), $\Lambda < 0$.

We show that if h is not constant or h is not a linear monomial, then (44) does not possess a Dirichlet series solution of the form (46). To establish this, we suppose on the contrary that a Dirichlet series solution of the form (46) to the PDE (44) exists. Equations (44) and (46) give

$$\begin{aligned}
&\sum_{\mathrm{u}=0}^{\infty}\sum_{\nu=0}^{\infty} d_{\mathrm{u},\nu}\exp\left(-\alpha^{s\mathrm{u}}\beta^{s\nu}rf(x)\right)gh'(x) \\
&+\sum_{\mathrm{u}=0}^{\infty}\sum_{\nu=0}^{\infty}\left(-\alpha^{s\mathrm{u}}\beta^{s\nu}r\right)d_{\mathrm{u},\nu}\exp\left(-\alpha^{s\mathrm{u}}\beta^{s\nu}rf(x)\right)gh(x)f'(x) \\
&+\sum_{\mathrm{u}=0}^{\infty}\sum_{\nu=0}^{\infty} d_{\mathrm{u},\nu}\exp\left(-\alpha^{s\mathrm{u}}\beta^{s\nu}rf(x)\right)m(x) \\
&-\Lambda\sum_{\mathrm{u}=0}^{\infty}\sum_{\nu=0}^{\infty} d_{\mathrm{u},\nu}\exp\left(-\alpha^{s\mathrm{u}}\beta^{s\nu}rf(x)\right) \\
&\quad=\alpha\sum_{\mathrm{u}=0}^{\infty}\sum_{\nu=0}^{\infty} d_{\mathrm{u},\nu}\exp\left(-\alpha^{s(\mathrm{u}+1)}\beta^{s\nu}rf(x)\right)m(\alpha x) \\
&+\beta\sum_{\mathrm{u}=0}^{\infty}\sum_{\nu=0}^{\infty} d_{\mathrm{u},\nu}\exp\left(-\alpha^{s\mathrm{u}}\beta^{s(\nu+1)}rf(x)\right)m(\beta x).
\end{aligned} \tag{48}$$

Balancing the coefficients yields

$$gh'(x) - rh(x)f'(x) + m(x) - \Lambda = 0, \tag{49}$$

so that

$$f(x) = \frac{1}{r}\left(g\int\frac{h'(x)}{h(x)}dx + \int\frac{m(x)}{h(x)}dx - \Lambda\int\frac{1}{h(x)}dx\right). \tag{50}$$

For constant h and m [13], $f(x) = a_1 x$, for some constant a_1, so that f satisfies (47). Also, for $h(x) = x$ and $m(x) = x^s$, $s > 0$ [15]; the eigenvalue $\Lambda = -g$, so that $f(x) = a_2(x^s/s)$ for some constant a_2. Consequently, f satisfies (47). It may be possible that $m(x) \sim -h'(x)$, but since $\Lambda < 0$, balancing coefficients in (48) requires $m(x)$ and $h'(x)$ to be constants. Consequently, if h is not constant or a linear monomial, the first of these integral yields a logarithmic function which is not a homogeneous function in general. Hence, $f(\alpha x) \neq \alpha^s f(x)$ for any $s \in \mathbb{Z}$, and equation (44) does not possess a Dirichlet series solution of the form (46).

For $h \equiv 1$ and $m \equiv 1$, the eigenvalue Λ and the corresponding solution to (44) have been determined [13]. The eigenvalue is

$$\Lambda = 2b, \tag{51}$$

and solution ρ to the corresponding eigenvalue is

$$\rho(x) = \sum_{u=0}^{\infty} \sum_{v=0}^{\infty} d_{u,v} e^{-2b/g\alpha^u \beta^v x}, \tag{52}$$

where $d_{u,v}$'s are determined as in [13].

We now show that the separable solution to ((39)) (((2)) and ((3)) obtained in Section 3 for$\sigma(x,t) = br(t)$ and$\gamma(x,t) = gr(t)$) is the large time-attracting solution for a certain class of$r(t)$. For this choice of coefficients, PDE (39) reduces to

$$\begin{aligned} \frac{\partial}{\partial t}\vartheta(x,t) + gr(t)\frac{\partial}{\partial x}\vartheta(x,t) &= \alpha br(t)\vartheta(\alpha x,t) \\ &+ \beta br(t)\vartheta(\beta x,t) - br(t)\vartheta(x,t). \end{aligned} \tag{53}$$

For constant coefficients and symmetric cell division, Zaidi et al. [5] derived the large time-attracting solution from solutions to the PDE (1). The solution turned out to be the separable solution.

Since the full problem ((53)) (((2)) and ((3))) has not been solved for any choice of coefficients, we employ the tools developed by Perthame and Ryzhik [4] to study the long time dynamics. The analysis in [4], however, is valid for one nonlocal term and for constant coefficients, and certain arguments break down because of the t dependence of coefficients. We can, nonetheless, extend their analysis to a certain class of time-dependent coefficients and asymmetric cell division.

Theorem 1. *Let ϑ be a solution to (53) that satisfies (2) and (3) and $R(t)$ and ρ be defined by (43) and (52), respectively. If $r(t)$ is monotonically decreasing and $R(t)$ is bounded at $t = 0$ and $R(t)$ goes to infinity as t tends to infinity, then*

$$\lim_{t\to\infty}\int_0^\infty \left|\vartheta(x,t)e^{-bR(t)} - k\rho(x)\right| = 0, \tag{54}$$

where $k = e^{-bR(0)}\int_0^\infty \vartheta_0(x)dx$.

Proof. Let

$$u(x,t) = \vartheta(x,t)e^{-bR(t)} - k\rho(x). \tag{55}$$

Then, u satisfies the PDE

$$\begin{aligned} \frac{\partial}{\partial t}u(x,t) + gr(t)\frac{\partial}{\partial x}u(x,t) + 2br(t)u(x,t) &= \alpha br(t)u(\alpha x,t) \\ &+ \beta br(t)u(\beta x,t) \end{aligned} \tag{56}$$

and the conditions

$$\begin{aligned} u(0,t) &= 0, \\ \lim_{x\to\infty} u(x,t) &= 0. \end{aligned} \tag{57}$$

□

Also, the integration of (56) with respect to x from 0 to ∞, along with condition (2), yields

$$\int_0^\infty u(x,t)dx = 0. \tag{58}$$

The transformation

$$\tilde{\zeta}(x,t) = \int_0^x u(s,t)ds \tag{59}$$

yields

$$\begin{aligned} \frac{\partial}{\partial t}\tilde{\zeta}(x,t) + gr(t)\frac{\partial}{\partial x}\tilde{\zeta}(x,t) + 2br(t)\tilde{\zeta}(x,t) &= br(t)\tilde{\zeta}(\alpha x,t) \\ &+ br(t)\tilde{\zeta}(\beta x,t), \end{aligned} \tag{60}$$

along with the conditions

$$\tilde{\zeta}(0,t) = 0, \tag{61}$$

$$\lim_{x\to\infty}\tilde{\zeta}(x,t) = 0. \tag{62}$$

Equation (60) gives

$$\begin{aligned} \frac{\partial}{\partial t}\left[\tilde{\zeta}(x,t)e^{bR(t)}\right] + gr(t)\frac{\partial}{\partial x}\left[\tilde{\zeta}(x,t)e^{bR(t)}\right] \\ + br(t)\left[\tilde{\zeta}(x,t)e^{bR(t)}\right] = br(t)\left[\tilde{\zeta}(\alpha x,t)e^{bR(t)}\right] \\ + br(t)\left[\tilde{\zeta}(\beta x,t)e^{bR(t)}\right], \end{aligned} \tag{63}$$

which, multiplication by sgn $(\tilde{\zeta})$, yields

$$\begin{aligned} \frac{\partial}{\partial t}\left|\tilde{\zeta}(x,t)e^{bR(t)}\right| + gr(t)\frac{\partial}{\partial x}\left|\tilde{\zeta}(x,t)e^{bR(t)}\right| \\ + br(t)\left|\tilde{\zeta}(x,t)e^{bR(t)}\right| \leq br(t)\left|\tilde{\zeta}(\alpha x,t)e^{bR(t)}\right| \\ + br(t)\left|\tilde{\zeta}(\beta x,t)e^{bR(t)}\right|. \end{aligned} \tag{64}$$

Integrating (64) from 0 to ∞ with respect to x and using conditions (61), (62), and (5) yields

$$\frac{d}{dt}\int_0^\infty \left|\tilde{\zeta}e^{bR(t)}\right|dx \le 0, \tag{65}$$

which shows that $\int_0^\infty |\tilde{\zeta}e^{bR(t)}|dx$ is a decreasing function in time, so that

$$\int_0^\infty \left|\tilde{\zeta}e^{bR(t)}\right|dx \le e^{bR_0}\int_0^\infty \left|\tilde{\zeta}_0(x)\right|dx, \tag{66}$$

where $\tilde{\zeta}_0(x) = \tilde{\zeta}(x,0)$ and $R_0 = R(0)$.

$$\bar{P}(x,t) = \tilde{\zeta}(x,t)e^{bR(t)}. \tag{67}$$

Then, (63) becomes

$$\begin{aligned}\frac{\partial}{\partial t}\bar{P}(x,t) + gr(t)\frac{\partial}{\partial x}\bar{P}(x,t) + br(t)\bar{P}(x,t) &= br(t)\bar{P}(\alpha x,t)\\ &+ br(t)P(\beta x,t),\end{aligned} \tag{68}$$

which, differentiating with respect to t, gives

$$\begin{aligned}&\frac{\partial}{\partial t}\kappa(x,t) + gr'(t)\frac{\partial}{\partial x}\bar{P}(x,t) + gr(t)\frac{\partial}{\partial t}\left(\frac{\partial \bar{P}}{\partial x}\right)\\ &\quad + br'(t)\bar{P}(x,t) + br(t)\kappa(x,t) = br'(t)\bar{P}(\alpha x,t)\\ &\quad + br'(t)\bar{P}(\beta x,t) + br(t)\kappa(\alpha x,t) + br(t)\kappa(\beta x,t),\end{aligned} \tag{69}$$

where

$$\kappa = \frac{\partial \bar{P}}{\partial t}. \tag{70}$$

Equations (69) and (68) give

$$\begin{aligned}&\frac{\partial}{\partial t}\kappa(x,t) + gr(t)\frac{\partial}{\partial x}\kappa(x,t) - \frac{r'(t)}{r(t)}\kappa(x,t)\\ &\quad + br(t)\kappa(x,t) = br(t)\kappa(\alpha x,t) + br(t)\kappa(\beta x,t).\end{aligned} \tag{71}$$

Equation (71) can be multiplied with $sgn(\kappa)$. This gives

$$\begin{aligned}&\frac{\partial}{\partial t}|\kappa(x,t)| + gr(t)\frac{\partial}{\partial x}|\kappa(x,t)| - \frac{r'(t)}{r(t)}|\kappa(x,t)|\\ &\quad + br(t)|\kappa(x,t)| \le br(t)|\kappa(\alpha x,t)| + br(t)|\kappa(\beta x,t)|,\end{aligned} \tag{72}$$

which, integrating with respect to x from 0 to ∞ and using (5) and the fact that $\kappa(0,t) = 0 = \kappa(\infty,t)$, yields

$$\frac{d}{dt}\int_0^\infty |\kappa|dx \le 0, \tag{73}$$

which shows that $\int_0^\infty |\kappa|dx \le 0$ is decreasing in t, so that

$$\int_0^\infty |\kappa|dx \le \int_0^\infty |\kappa_0(x)|dx, \tag{74}$$

where

$$\kappa_0(x) = \kappa(x,0) = \left.\frac{\partial \bar{P}}{\partial t}\right|_{t=0}. \tag{75}$$

Since $\bar{P} = \tilde{\zeta}e^{bR(t)}$, we have

$$\kappa_0(x) = \frac{\partial}{\partial t}\left[\tilde{\zeta}e^{bR(t)}\right]\Big|_{t=0} = \tilde{\zeta}_0(x)br_0e^{bR_0} + e^{bR_0}\left.\frac{\partial\tilde{\zeta}}{\partial t}\right|_{t=0}, \tag{76}$$

where $r_0 = r(0)$ and $R_0 = R(0)$. Equations (60) and (59) imply

$$\left.\frac{\partial\tilde{\zeta}}{\partial t}\right|_{t=0} = r_0\left[-gu_0(x) - 2b\tilde{\zeta}_0(x) + b\zeta_0(\alpha x) + b\tilde{\zeta}_0(\beta x)\right], \tag{77}$$

so that

$$\kappa_0(x) = e^{bR_0}r_0\left[-gu_0(x) - 2b\tilde{\zeta}_0(x) + b\tilde{\zeta}_0(\alpha x) + b\tilde{\zeta}_0(\beta x) + b\tilde{\zeta}_0(x)\right]. \tag{78}$$

Equations (74), (78), and (5) give

$$\begin{aligned}\int_0^\infty |\kappa|dx &= \int_0^\infty \left|\frac{\partial}{\partial t}\left[\tilde{\zeta}e^{bR(t)}\right]\right|dx \le e^{bR_0}r_0\int_0^\infty\\ &\cdot\left[|gu_0(x)| + \left|2b\tilde{\zeta}_0(x)\right| + b\left|\tilde{\zeta}_0(\alpha x)\right| + b\left|\tilde{\zeta}_0(\beta x)\right|\right.\\ &\left.+ \left|b\tilde{\zeta}_0(x)\right|\right]dx = e^{bR_0}r_0\left[\int_0^\infty |gu_0(x)| + 4b\int_0^\infty \left|\tilde{\zeta}_0(x)\right|dx\right].\end{aligned} \tag{79}$$

Equations (59) and (63) give

$$\begin{aligned}u(x,t) &= \frac{\partial}{\partial x}\tilde{\zeta}(x,t) = \frac{e^{-bR(t)}}{gr(t)}\left\{-\frac{\partial}{\partial t}\left[\tilde{\zeta}(x,t)e^{bR(t)}\right]\right.\\ &- br(t)\left[\tilde{\zeta}(x,t)e^{bR(t)}\right] + br(t)\left[\tilde{\zeta}(\alpha x,t)e^{bR(t)}\right]\\ &\left.+ br(t)\left[\tilde{\zeta}(\beta x,t)e^{bR(t)}\right]\right\},\end{aligned} \tag{80}$$

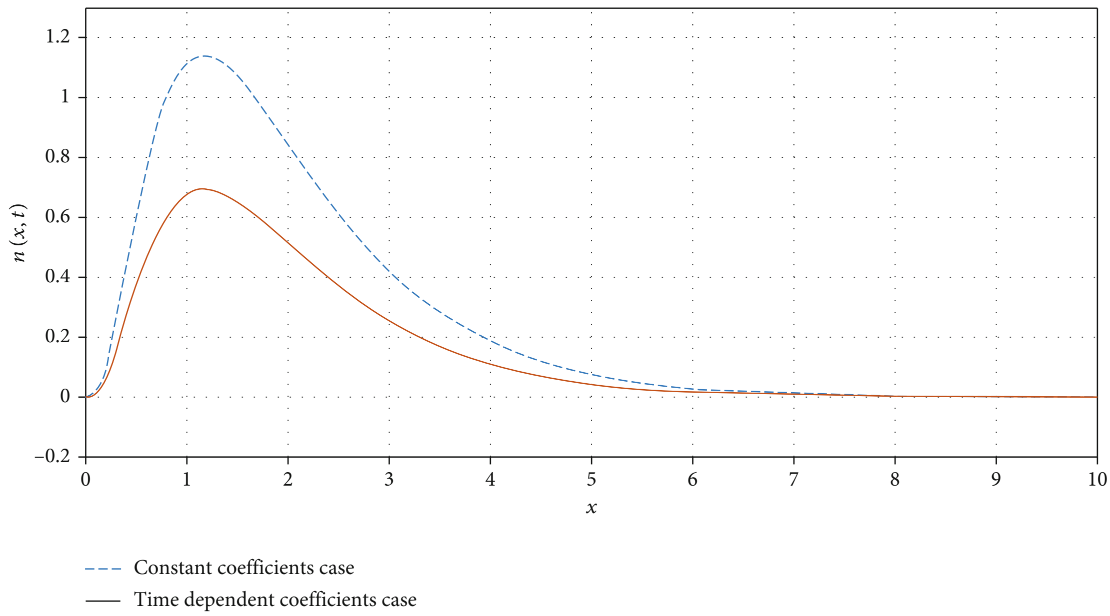

Figure 3: The SSD solution obtained by Zaidi et al. [13] for the constant coefficient case and the SSD solution given by the (40) for $t = 1$, $\alpha = 3$, $\beta = 3/2$, $b = 1$, and $g = 2$ units.

so that

$$\int_0^\infty |u(x,t)|dx \le \frac{e^{-bR(t)}}{gr(t)} \left\{ \int_0^\infty \left| \frac{\partial}{\partial t} \left[\tilde{\zeta}(x,t) e^{bR(t)} \right] \right| dx + br(t) \int_0^\infty \left| \tilde{\zeta}(x,t) e^{bR(t)} \right| dx + br(t) \int_0^\infty \left| \tilde{\zeta}(\alpha x,t) e^{bR(t)} \right| dx + br(t) \int_0^\infty \left| \tilde{\zeta}(\beta x,t) e^{bR(t)} \right| dx \right\}, \tag{81}$$

which, using (5), gives

$$\int_0^\infty |u(x,t)|dx \le \frac{e^{-bR(t)}}{gr(t)} \left\{ \int_0^\infty \left| \frac{\partial}{\partial t} \left[\tilde{\zeta}(x,t) e^{bR(t)} \right] \right| dx + 2br(t) \int_0^\infty \left| \tilde{\zeta}(x,t) e^{bR(t)} \right| dx \right\}. \tag{82}$$

Inequalities (82), (79), and (66) give

$$\int_0^\infty |u(x,t)|dx \le \frac{e^{-bR(t)}}{gr(t)} \left\{ e^{bR_0} r_0 \left[\int_0^\infty |gu_0(x)| dx + 4b \int_0^\infty \left| \tilde{\zeta}_0(x) \right| dx \right] + 2br(t) e^{bR_0} \int_0^\infty \left| \tilde{\zeta}_0(x) \right| dx \right\}, \tag{83}$$

which goes to zero as t goes to infinity.

As seen from the above equation, the rate of convergence to separable solution is not affected by the asymmetry in cell division. An example of the class of functions r discussed in Theorem 1 is $r(t) = 1/(t+k)$, where $k \ge 1$. Also, the analysis in Theorem 1 for $r(t) = 1$ for all $t > 0$ and $\alpha = \beta = 2$ recovers the result of Perthame and Ryzhik [4].

We now show that if there exists a solution to the problem ((53)) (((2)) and ((3))), then it is unique. The uniqueness of solutions to (1) for constant coefficients was established by Zaidi et al. [5]. Their analysis, however, breaks down for time-dependent coefficients and asymmetric cell division equation. To prove uniqueness, we simplify (53) by applying the transformation

$$\tilde{h}(x,t) = \int_x^\infty \vartheta(\varepsilon,t) d\varepsilon. \tag{84}$$

This yields

$$\frac{\partial}{\partial t}\tilde{h}(x,t) + gr(t)\frac{\partial}{\partial x}\tilde{h}(x,t) + br(t)\tilde{h}(x,t) = br(t)\tilde{h}(\alpha x,t) + br(t)\tilde{h}(\beta x,t). \tag{85}$$

Integrating (34) from 0 to ∞ with respect to x, and using (5) and (3), yields

$$\frac{\partial}{\partial t}\tilde{h}(0,t) = br(t)\tilde{h}(0,t), \tag{86}$$

so that

$$\tilde{h}(0,t) = ce^{bR(t)}, \tag{87}$$

for some constant c. Also, equations (2) and (84) give

$$\tilde{h}(x,0) = \tilde{h}_0(x) = \int_x^\infty \vartheta_0(\varepsilon) d\varepsilon. \tag{88}$$

Suppose that $\tilde{h}_1$ and $\tilde{h}_2$ are two distinct solutions to (85) that satisfy (87) and (88). Let $\bar{m}(x,t)=\tilde{h}_1(x,t)-\tilde{h}_2(x,t)$. Then, m satisfies

$$\frac{\partial}{\partial t}\bar{m}(x,t)+gr(t)\frac{\partial}{\partial x}\bar{m}(x,t)+br(t)\bar{m}(x,t)=br(t)\bar{m}(\alpha x,t)+br(t)\bar{m}(\beta x,t) \tag{89}$$

and the conditions

$$\bar{m}(0,t)=0, \tag{90}$$

$$\bar{m}(x,0)=0. \tag{91}$$

The PDE (89) can be multiplied with sgn (m). This gives

$$\frac{\partial}{\partial t}|\bar{m}(x,t)|+gr(t)\frac{\partial}{\partial x}|\bar{m}(x,t)|+br(t)|\bar{m}(x,t)| \le br(t)|\bar{m}(\alpha x,t)|+br(t)|\bar{m}(\beta x,t)|, \tag{92}$$

which, integrating with respect to x from 0 to ∞ and using (5), (90), and (91), yields

$$\frac{d}{dt}\int_0^\infty |\bar{m}(x,t)|dx \le 0, \tag{93}$$

which shows that $\int_0^\infty |\bar{m}(x,t)|dx$ is a decreasing function in t, so that

$$\int_0^\infty |\bar{m}(x,t)|dx \le \int_0^\infty |\bar{m}(x,0)|dx = 0, \tag{94}$$

and consequently, $\tilde{h}_1(x,t)=\tilde{h}_2(x,t)$.

We note that if $r(t)=1$ for all $t>0$, the above analysis establishes the uniqueness of solutions to (4) subject to conditions (2) and (3) for constant coefficients. It also endorses the result of Zaidi et al. [5] for $r(t)\equiv 1$ and $\alpha=\beta=2$.

4. Conclusions

In this paper, we have determined the separable solution to the asymmetric cell division equation (53) subject to conditions (2) and (3) and have shown that solutions to the PDE converge to this separable solution for large time, at least for a certain class of time-dependent coefficients. This longtime behavior is not certain other cases [8].

The asymmetry in cell division does not affect the rate of convergence of solutions towards the SSD solution. We have also established the uniqueness of solutions to the problem ((53)) (((2)) and ((3))).

The shape of the SSD obtained for time-dependent coefficients is a scaling, in time, of the shape of the SSD solution of the constant coefficients case (see Figure 3).

We have also determined unique solutions to the symmetric cell division problems (6) and (15) subject to conditions (2) and (3). The large time dynamics of (6) are markedly different from (15). The same time dependence of the growth and division rates plays a crucial role in the convergence of solutions of (6) to the separable solution (2) for large time.

Data Availability

There is no data in the manuscript.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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