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Research Article

Three-Dimensional Visualization with Large Data Sets: A Simulation of Spreading Cortical Depression in Human Brain

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We developed 3D simulation software of human organs/tissues; we developed a database to store the related data, a data management system to manage the created data, and a metadata system for the management of data. This approach provides two benefits: first of all the developed system does not require to keep the patient's/subject's medical images on the system, providing less memory usage. Besides the system also provides 3D simulation and modification options, which will help clinicians to use necessary tools for visualization and modification operations. The developed system is tested in a case study, in which a 3D human brain model is created and simulated from 2D MRI images of a human brain, and we extended the 3D model to include the spreading cortical depression (SCD) wave front, which is an electrical phoneme that is believed to cause the migraine.

1. Introduction

3-D visualization is both a part of all of the computerized environments, and it provides a new method for the presentation of results. Besides 3-D visualizations can be used for esthetic purposes and providing a correct visual communication. 3-D visualizations affect the users more than 2D counterparts and provide a way of simulation that reflects the reality as much as possible. For those purposes 2-D visualizations are insufficient, and 3-D visualizations provide more information than 2-D ones. 3-D visualizations provide more details of the products and projects, and by the help of texture, color, and lightening effects they provide realistic images of all the details. Besides 3-D visualizations are capable of rotating the scene, providing effective interaction. Due to these advantages 3-D visualizations are commonly used in prototype production phase or presenting the results after completing the projects.

An important application area of 3-D simulations will be the healthcare applications, in which 3-D models of human organs can be modeled and that can help the clinicians to diagnose the illnesses. Recent developments in electronics lead to new medical imaging devices; those are capable of providing anatomical properties of human body. These imaging techniques include magnetic resonance imaging (MRI), computerized tomography (CT), ultrasound, nuclear medicine, and Positron emission tomography (PET). The fundamental features used in medical imaging techniques include physical properties such as difference in tissue intensity, electrical conductivities, and elasticity. Those imaging techniques provide high resolution 2D images of the body tissues and/or organs. Besides by using new simulation methods it is also possible to develop 3-D simulations of those tissues/organs. It is believed that 3D simulations will also help the clinicians to diagnose the illnesses more effectively, and it will increase the correctness of the diagnosis, and by comparing the 3D models of the same organs created in different times it will be also possible to track the changes in those organs. For example, it is possible to detect a tumor in human brain by this way. Besides it is also possible to append some simulations on the 3-D model that can help the clinicians to perform their work. For example, creating a 3D model of a human brain and adding a tumor on it by simulations will allow the surgeons to plan a surgery operation depending on the 3D model already developed.

Creating a 3D model of the organs requires segmentation of the organs in 2D images, creating a mesh (usually triangles), simulating the models. All of the aforementioned methods will produce huge amount of data sets, and they need to be appropriately managed, and those simulations also need metadata information for each organ/tissue. Under the light of those needs, in this study we developed 3-D simulation software of human organs/tissues; we developed a database to store the related data, a data management system to manage the created data, and a metadata system for the management of data. Some of the healthcare applications may require modifications on the 3D model as an engineering approach. In order to meet those requirements we added the modification examples. The developed system is tested in a case study, in which a 3-D human brain model is created and simulated from 2-D MRI images of a human brain, and we extended the 3D model to include the spreading cortical depression (SCD) wave front, which is an electrical phoneme that is believed to cause the migraine. The organization of the paper is as follows: in the remaining parts of the Introduction section the electrical activities of the brain and the details of the SCD are presented. In Materials and Methods section the segmentation process and mesh generation algorithms are presented. The details of the application software are presented, and database system and metadata information are provided. In the results section the developed application software is given. In Discussion section general comments about the process and new suggestions are provided.

1.1. Human Brain, Its Electrical Activities, and SCD. Brain and heart perform the most important activities for human life. Brain controls the vital activities of human life such as motion and breathing and it also controls the feelings. During these processes the brain intakes electrical signals coming from the other part of the body, and it processes and interprets these electrical signals. A human brain is composed of 100 billion of nerve cells, called neurons. Human brain and heart perform their activities by means of electrical activities. These electrical activities also introduce a biomagnetic field as well. The measurements of electrical and magnetic field generated by the electrical activities of the human body have been possible by the technical developments achieved in the last decade. The electrical activities are measured by the surface electrodes, and biomagnetic fields are measured by the biomagnetometers. The SQUIDs (superconducting quantum iInterference devices) are the most known biomagnetometer. The electrical activities of the human heart are measured by the ECG (electrocardiography), and brain's electrical activity is measured by the EEG (electroencephalography).

EEG is a technique that measures the electrical activities of the human brain by using measurement electrodes located on the scalp. The first measurements were made at 1870s on the animals; the human measurements were performed in 1929 by Hans Berger [1]. When the measurements performed in patients suffering epilepsy, migrne, Parkinson's, Schizophrenia, Alzheimer's, depression and so on are examined, it is found that EEG activities are different than the normal subjects.

The electrical activities of the human brain can be modeled by different methods such as monopole, dipole, line, surface or volume currents [2]. The commonly used method is the dipole in human activities [3]. The measurements performed in the surface electrodes can be explained as results of electrically active dipoles in the brain. A dipole represents a small electrical activity on the cortex of the brain. There are two approaches commonly assumed in electrical activity modeling: parametric and imaging-based methods. In parametric methods it is assumed that electrical activities can be modeled by a few current dipoles. On the other hand in imaging methods electrical activities are modeled by the intracellular currents of the cortical pyramidal neurons [4]. In these assumption tens of thousands of dipoles are used, which are aligned normally to the cortical surface. In this study an imaging based method is assumed.

It is known that the abnormalities in electrical activities of human brain cause epilepsy, Parkinson, Alzheimer, schizophrenia, and depression. For example, extreme electrical activities of human brain cause the epilepsy crisis. On the other hand, the electrical activities can be suppressed for a temporary period of time, due to some reasons. This suppression of the electrical activities is known as spreading cortical depression (it is abbreviated as SCD, and sometimes it is called as cortical spreading depression). The SCD is first discovered by Leao in rabbit brain in 1944 [5, 6]. In this study we developed simulation software of SCD in human brain.

SCD concept is first discovered by Leao in 1944, and there have been studies about the reasons, spreading mechanisms and results of it since then. Recent studies showed that the SCD causes the migraine headache. The initiation mechanism of SCD is still unknown, but it is assumed that the SCD can be initiated by the electrical or chemical stimulus of the brain. After initiation SCD propagates as wave front on the brain surface. Its propagation velocity is about 3–5 mm/min, and during the propagation the electrical activities of the brain are temporarily suppressed. Due to this suppression the electroencephalography of the suppressed neurons cannot be measured. Since it was first discovered in 1944 by Leao, there have been many laboratory experiments about the initiation mechanism of the SCD. Recent studies showed that there is a strong relation between the spreading cortical depression and migraine [7–18]. But on the other hand the initiation mechanism of the SCD is still unknown. There have been only two simulation studies dealing with the electrical activities occurring during the SCD: in the first one, the propagation mechanism of the SCD is simulated on the rabbit brain by Baysal and Haueisen in 2002 [19]. In the second study, simulation is performed in human brain, and only the propagation boundaries are calculated by Baysal et. al. in 2007 [20]. In that study it is assumed that the SCD is initiated on a point on the brain surface and propagates with a constant velocity. They calculated the propagation boundaries of the SCD and showed them on the brain surface. Unlike the study performed by the Baysal et al., our simulations include the determination of electrically active/inactive dipoles of the brain during the SCD propagation.

The purpose of the SCD simulation is neither to investigate the initiation process of the SCD nor to show the relationship between the migraine and SCD. In this study the electrical activity changes of the human brain during the SCD are determined as a case study; besides the propagation mechanism of the SCD is determined depending on the initiation point, and then the suppressed region of the brain due to the SCD is calculated and visualized. And affected electrical dipoles on the brain cortex are determined.

2. Materials and Methods

2.1. Obtaining Realistic Head Models. Recent developments in electronics lead to new medical imaging devices; those are capable of providing anatomical properties of human body. These imaging techniques include magnetic resonance imaging (MRI), computerized tomography (CT), ultrasound, nuclear medicine, positron emission tomography (PET). In order to obtain realistic head model used in this study, MR images of a subject are used. The fundamental features used in medical imaging techniques include physical properties such as difference in tissue intensity, electrical conductivities, and elasticity. In magnetic resonance imaging first the body is located in magnetic fields, and then radio signals are sent to the body. By this way inside image of the body is obtained. MRI is commonly used in imaging of soft tissues. Besides nervous system, heart and vein investigations are also possible by MRI. In computerized tomography X-rays are used for imaging.

For brain research studies such as EEG/MEG source localization, SCD simulation, or other anatomical investigations it is necessary to obtain realistic head models of the subject/patients. These realistic head models are obtained by segmentation of MRI or CT images. Image segmentation can be defined as determining the edges or boundaries of the tissues in high-resolution images. Image segmentation also includes classification of objects depending on the object/image properties [21]. Before segmentation each image is first filtered in order to reduce the noise levels. These filtering techniques include median filtering, gray-level transformation, and local filtering. [22]. The realistic head model used in this study is obtained by segmentation of MRI images. The MRI images are composed of 256 parallel axial T1 weighted 256 $\times$ 256 MRI slices separated by 1 mm. The cortical surface has been triangulated by a commercial automatic mesh generator routine. The cortical surface triangulars have an average of 3 mm size length. Each triangular element has been numbered in order to differentiate each of them.

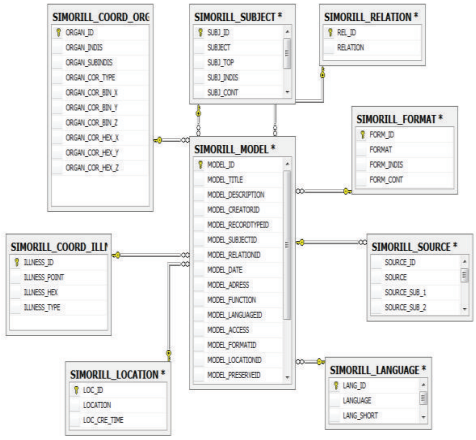
The medical images obtained from the patients are usually kept using DICOM standard. DICOM (Digital Imaging and Communications in Medicine) is a primary standard for the transmission and exchange of medical images in different modalities (CT, MRI, etc.) and it allows sharing medical images across a wide set of users and applications easier. DICOM differs from other image formats in that it groups information into data sets. A DICOM file consists of a header and image data sets, all packed into a single file. Although DICOM images have found wide acceptance in medical practice, they have two disadvantages: file sizes are large and special software is required for viewing them on personal computers [23, 24]. Due to these disadvantages, we developed a system that stores the boundaries of the organs/tissues first and then extracts the metadata related to the images and stores those data in VRA and Dublin Core standards which are commonly used to define the information and documentation sources of electronic systems, instead of storing the all images in DICOM format [25, 26].

2.2. Generating the Application Software to Visualize Human Brain. In order to perform the simulation, a realistic head model obtained from the MRI images of a real subject is visualized. First of all T-1 weighted, with a 1 mm separation 256 $\times$ 256 MRI images of a real subject is are obtained. The MRI images of the subject are segmented with commercial source localization software. The segmented tissue boundaries are stored on a database instead of preserving the original images. Besides all the metadata related to original MR images separated and stored as VRA elements on database. This allows us to store the tissue/organ boundaries and related metadata in a database. So the simulation elements are stored in the memory with a decreased memory usage and they are managed easily with faster accessibility.

In order to visualize the brain surface, a simulation program is written in C# programming language and XNA framework. The database system is developed by using Microsoft SQL Server 2008, which allows easy management of the data and high security. The implemented database named as SIMORILL_DAT, which is working synchronously with the simulation software model (SIMORILL), is developed in Microsoft SQL Server 2008. The developed image metadata is composed of 16 elements; 6 of them are optional. 9 tables are designed on the database, and metadata elements named SIMORILL_METDAT are indexed on the database conformant to UTF-8 language structure. The following figure (Figure 1) provides table elements and an example of metadata. The output of the brain visualization software is also given in Figure 2.

2.3. Simulating the SCD on the Human Brain. After visualizing the human brain, the SCD mechanism is also simulated, depending on the initiation point and velocity of the SCD. In the first simulations the propagation velocity of the SCD is assumed to be 3 mm/minute, and with the initiation point assumption the SCD propagation is also simulated. It is also assumed that the electrical activities of the neurons in the depressed regions are also suppressed; that is, their activities can not be measured by the EEG. Assuming that human brain is visualized with the triangles, the propagation is calculated on the triangular surfaces, with the help of the surface data. A sample output of the SCD propagation is shown in Figure 3.

Figure 3 shows a sample output of the simulation software developed in this study. In this simulation we assumed that the SCD is initiated on a fixed point on the cortex. The initiation mechanism is not taken into consideration, and it is assumed that the SCD propagates with a velocity of 3 mm/min. In the figure the central point shows the initiation



Metadata element	Value	Obligation
Identifier	57893454	Mandatory
Title	SCD in human brain	Mandatory
Subject	Bioinformatics	Mandatory
Description	3D visu. of SCD with circles	Optional
Creator	Brain	Mandatory
Date	2 February 2012	Mandatory
Address	XNUR_4563244	Optional
Record type	XNA 3D	Mandatory
Relation	SCD	Mandatory
Function	ASP.NET and C#	Optional
Language	En	Optional
Location	Server KLE	Mandatory
Access	Public	Mandatory
Format	Image	Optional
Preservation	Endless	Optional

Figure 1: SIMORILL_DAT database table elements and a model SIMORILL_METDAT metadata.

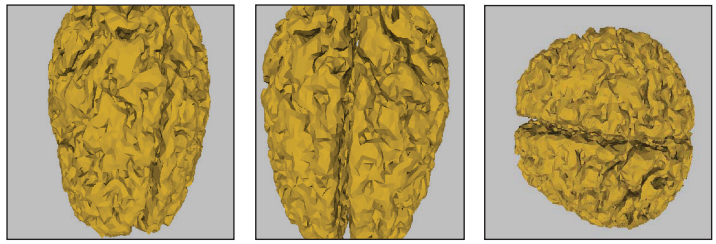


Figure 2: 3D views of the brain used in this study.

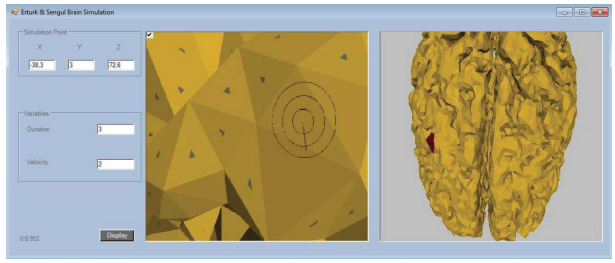
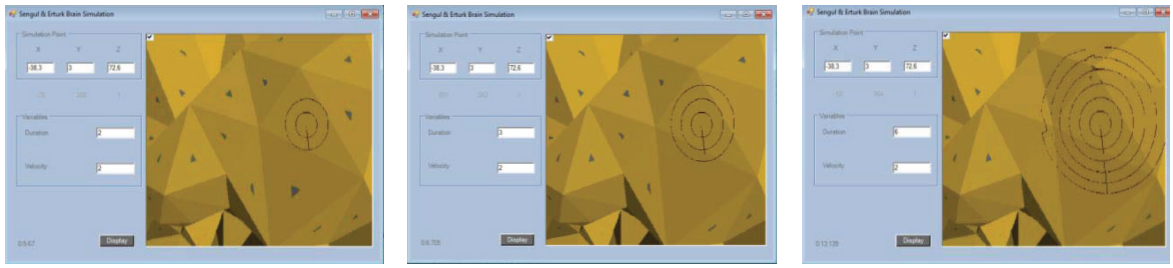


Figure 3: The simulation work that shows the propagation mechanism of the SCD. The central point shows the initiation point of the SCD, which is located on the occipital lobe of the brain. The gray small triangles show the electrical dipoles, and the brown lines show the propagated points of the SCD after 10 seconds, each.

point of the SCD, which is located on the occipital lobe of the brain. The brown lines in the figure show the propagated points of the SCD after 10 seconds, each. The region inside the circle is the brain part which is electrically inactive due to the SCD.

We performed another simulation in order to relate the electrical activities of the brain and SCD. In this simulation we followed the imaging-based approach for the modeling of the electrical sources. In this model we placed artificial current dipoles (with orientation perpendicular to cortex



(a) (b) (c)

Figure 4: Electrically active and inactive dipoles after the initiation of SCD. The brown lines show the SCD boundaries, and gray triangles show the electrically active dipoles. The electrical dipoles inside the SCD are suppressed and disabled in the figures. The figure on the left shows the SCD boundaries and electrically active dipoles after the 10 seconds of the initiation of SCD, the middle one shows the SCD boundaries and electrically active dipoles after the 20 seconds of the initiation of SCD, and the last one (on the right) shows the SCD boundaries and electrically active dipoles after 60 seconds of the initiation of SCD.

and with unit magnitudes) to the center of each triangle used in the simulations. Those dipoles are shown in Figure 4. In the next step we assumed that SCD begins from the point (−38.3 mm, −3.0 mm, 72.6 mm) and spreads with a velocity of 3 mm/min. After 10 seconds we determined the electrically inactive regions, and we suppressed the electrical activities of the artificial current dipoles inside the propagation region, as in the case of the real SCD mechanism. The aforementioned simulations are repeated with the assumption that the SCD propagates 10 seconds (Figure 4(a)), 20 seconds (Figure 4(b)), and 60 seconds (Figure 4(c)). The results are presented in Figure 4.

3. Discussion

The new technological developments allow development of high-resolution medical imaging systems, and this will lead to new 3D modeling environments in the near future. Due to this new trend the hospitals and other healthcare organizations will begin to store 3D models of the patient's organs/tissues for future use. This will lead to new database requirements, metadata generation, and visualization environments. In this study we developed a pilot model for those requirements.

In classical simulations the original images are kept in classical DICOM format. As a new approach we developed a software and database system which stores the boundaries of organ/tissues in a database, with the related metadata. Besides we also developed a 3-D simulation software that visualizes the organs/tissues, and it allows us to make necessary modifications on it. This approach provides two benefits: first of all the developed system does not require to store the patients/subjects medical images on the system, providing less memory usage. Besides the system also provides 3D simulation and modification options, which will help clinicians to use necessary tools for visualization and modification operations. The developed system is tested in a case study, in which a 3-D human brain model is created and simulated from 2-D MRI images of a human brain, and we extended the 3D model to include the spreading cortical depression (SCD) wave front, which is an electrical phoneme that is believed to cause the migraine.

Development of 3D models of the human organs/tissues requires processing of large amount of data, such as the triangles used in this study. On the other hand, the volume, size, and shape of the organs/tissues differ from patients to patients, and for a specific patient they can change during the time. In order to develop effective models, it is necessary to create patient-specific models. By doing this, there will be very large amount of data sets, which needs to be managed. In this study a database system to manage those data are developed. Besides it is necessary to generate a metadata for each organ. To overcome this problem a metadata system is also suggested.

All the aforementioned requirements are tested on a case study, including 3D simulation of a real patient's brain. Although the developed software is only tested in human brain simulations, the software can be used for other organs such as heart and rivers. Besides the modeling, we also showed that the 3D model can also be extended to include some simulations. For this case we chose to simulate the spreading cortical depression in the brain.

Besides the organizational needs of storing the personal 3D data, it will be necessary to interchange those data between hospitals/health-care organizations. This will lead to decrease the time and effort of imaging of organs and developing already present 3D models as well. In order to provide this interchangeability, it is necessary to develop data interchange standards, as well as 3D visualization software. Besides it will require a database system to be operated on the same manner. In a next study we will focus on this topic.

In the case study example we developed simulation software that first visualizess the human brain and then shows the propagation mechanism of the SCD. Besides the simulation of SCD, we extended the software to determine the electrically active dipoles during the SCD propagation. This is a new approach and relates the SCD and electrical activities at the same time. We believe that the developed software will be useful for medical clinicians and neurologists, as well. Besides we believe that the developed software will be useful to understand the electrical activity changes

during the SCD, and it can be used as a training tool for neurologists and students of the faculty of medicine. As a new study we will focus on determining the presence of SCD by using the EEG measurements.

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