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Mathematical Model of Active Migration Glioma Growth on Parallel Computer System

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Abstract: This paper presents the mathematical model for visualizing the active migration glioma growth implemented on distributed parallel computer system. Glioma is the most common type of brain tumor well known as extensively invasive lesions with genetic metabolic abnormalities that contribute to their uncontrolled proliferation and invasion, often leading to death. Apart from obtaining the potential for increased speed on an existing problem, the use of multiple computers or processors offer more accurate and high speed solution for large sparse problem since parallel computers have more distributed memory than a single computer; enabling problems that require larger amounts of main memory to be tackled. The model considered in the research is in partial differential equation describing an active migration tumor cell by considering diffusion, convection and haptotaxis terms. The model equation is discretized using finite difference methods. The discretization will generates the large sparse matrix system of Ax=b, that is solved by Gauss Seidel Red Black method. The paper ends with a concluding remark on the graphical visualization of the active glioma growth with the parallel performance analysis in terms of execution time, speed up, efficiency and effectiveness.

Key words: Mathematical model . active migration glioma . disributed parallel computer system . haptotaxis

INTRODUCTION

Glioma is the most common type of primary brain tumor arises from the glial cells. They are well known as extensively invasive lesions with genetic metabolic abnormalities that contribute to their uncontrolled proliferation and invasion, often leading to death. Serial medical imaging detects only the part of the tumor involving a high concentration of tumor cells, but the undetectable portion of each lesion remains a problem. The limitation of medical imaging is supported by current open problem of image segmentations obtained from Magnetic Resonance Imaging (MRI) which became a difficult task due to the inherent noise and inhomogeneity [1, 2]. Mathematical models are being proposed to be a powerful tool to predict the behaviour and visualize the insight properties of the tumor [3-6]. The models are developed based on a solid knowledge of physical and biological behavior of tumor growth process which leads to the well known mathematical formulation, the reaction-diffusion function [3, 7].

In this paper, the glioma cell migration characterized by a diffusion coefficient, convection and haptotaxis factors. Rates of cell proliferation are coupled with the model to visualize the glioma growth in terms of number of cells. The objectives of this paper are to incorporate haptotaxis term into the models that have been discussed in previous work [8] and investigate its effect to the model and the glioma growth. The models in partial differential equations are descretized and solved using the numerical methods. We use parameters obtained from [5] to simulate the model describing the glioma growth and migration. The results are then compared to the previous work [8] and the data [5]. We discussed some observations for future research to utilize the implementation of the problem to the parallel computer system environment.

Active migration glioma: Glioma migration is believed to involve the passive and active cell movement through the degraded Extracellular Matrix (ECM) in the brain [3]. The passive glioma migration in this paper is referred to the diffusion and convection factor. Diffusion is the process in which the tumor cells spread out evenly in an available space through the undirected random motion usually assumed to follow the Fick's second law [9-11]. In our case, cells are assumed to diffuse from regions of higher concentration to the regions with lower concentration,

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which give the negative sign to the term. The movement of the molecules within the fluids known as convection considered in the model is due to the displacement of ECM substratum in which the cells move with local growth velocity [3]. The active migration term involve haptotaxis that is the directional motility or outgrowth of cells usually up the gradient of cellular adhesion sites or substrate. Haptotaxis is naturally present in ECM of the body during the process such as angiogenesis, which is the process of the new blood vessels development.

MATHEMATICAL MODEL

The mathematical model for the glioma growth considered in this paper is basically based on the model in [3, 9]. Generally, the model equation includes the migration and growth components which are the two key characteristics of the glioma [6,9]. The migration term describes the invasion of the glioma cell consists of J_d, J_k and J_h represents the diffusion, convection and haptotaxis fluxs respectively. The proliferation term, f(c) defines the growth of the glioma cell following the exponential growth [9, 12] and the logistic growth or Verhulst law [13, 14]. The model equation can be written as

$$\frac{\partial c}{\partial t} = -\nabla \cdot \left[J_d + J_k + J_h \right] + f(c) \tag{1}$$

with

$$J_d = -D\nabla c \qquad J_k = c\vec{v} \qquad J_h = hc\nabla w \tag{2}$$

where c(x, t) defines the number of malignant cells at location x and time t, ∇ is the spatial gradient operator, D is the diffusion coefficient for the glioma cells, $\vec{v}$ is the local growth velocity, h is haptotaxis constant and w is extracellular matrix density.

The mathematical formulation of the model is completed by boundary conditions imposing zero flux boundaries

$$(\eta \cdot \nabla) u = 0 \tag{3}$$

which is applied at the brain boundary and ventricles with normal directions η, formulating the fact that glioma cells do not diffuse towards these structures. The initial condition defining the initial distribution of glioma cells is considered

$$u(x,0) = f(x) \tag{4}$$

where f(x) defined the initial spatial distribution of malignant cells, presumably a point source at the center of tumorigenesis.

Dimensionless model equation: Through the governing and nondimensionalization process of Eq. (1) and (2), we have six dimensionless equations representing six models with different combination of migration and proliferation terms. The six equations as in Eq. (6)-(11) referred as Model 1-Model 6 respectively,

$$\frac{\partial c}{\partial t} = \frac{\partial^2 c}{\partial x^2} + c \tag{6}$$

$$\frac{\partial c}{\partial t} = \frac{\partial^2 c}{\partial x^2} - \vec{v}\frac{\partial c}{\partial x} + c \tag{7}$$

$$\frac{\partial c}{\partial t} = \frac{\partial^2 c}{\partial x^2} - \vec{v}\frac{\partial c}{\partial x} - Hc\frac{\partial^2 w}{\partial x^2} + c \tag{8}$$

$$\frac{\partial c}{\partial t} = \frac{\partial^2 c}{\partial x^2} + c - \alpha\left(\frac{c^2}{c_{max}}\right) \tag{9}$$

$$\frac{\partial c}{\partial t} = \frac{\partial^2 c}{\partial x^2} - \vec{v}\frac{\partial c}{\partial x} + c - \alpha\left(\frac{c^2}{c_{max}}\right) \tag{10}$$

$$\frac{\partial c}{\partial t} = \frac{\partial^2 c}{\partial x^2} - \vec{v}\frac{\partial c}{\partial x} - Hc\frac{\partial^2 w}{\partial x^2} + c - \alpha\left(\frac{c^2}{c_{max}}\right) \tag{11}$$

with

$$H = \frac{h\hat{w}}{D} \tag{12}$$

where Model 1consider diffusion flux and exponential growth, Model 2 consider diffusion, convection and exponential growth, Model 3 consider diffusion, convection, haptotaxis and exponential growth, Model 4 consider diffusion and logistic growth, Model 5 consider diffusion, convection and logistic growth and Model 6 consider diffusion, convection, haptotaxis and logistic growth.

We discretized the model equations using the forward approximation for time mesh and Crank Nicolson method for the space. The discretization generates the large sparse matrix system of **Ax = b**[15]. Gauss Seidel Red Black (GSRB) method is implemented for solving the linear system of equation. The computations of sequential algorithm of the methods are supported by Matlab R2009a software.

PARALLEL COMPUTER SYSTEM

Parallel Computer System (PCS) is a form of computation involving multiple autonomous processors (cluster) connected through network and running simultaneously in parallel environment. The system offer high speed, accuracy and memory space than a single computer which will benefit to the researchers in various field especially the one dealing with complex computational problems such as in [16-18]. In this study, we used a set of eight processors each with Intel (R) Pentium (R) and 2.80 GHz processors using standard Ethernet network, called ARS2 cluster. Our PCS is a green computing system since the processors consist of used personal computers that we recycled and transformed into a low-cost computing system.Our approach is in contrast to the massive parallel computer [19] especially in terms of the development cost of the system, however aim the same objective that is to reduce the processing time and computation cost. Open Source LINUX Fedora 7 is used as the operating system and Matlab Distributed Computer Server (MDCS) as the computation and communication platform. We use ARS2 to utilize the memory space of the system to solve our model equation for large size of sparse matrix.

RESULT AND DISCUSSION

The glioma growth in terms of cell numbers for each model according to four different levels of glioma growth; spheroid, detected lesion, diagnosis and death level are visualized in form of graphs shown in Fig. 1. The simulation results are compared to the data from [5] as listed in the Table 1. Generally, the number of cells for each model is slightly different but the growth pattern is the same. However, the simulation results are still lower than the clinical data. Therefore, we conclude that the models are best described the glioma growth at the spheroid and detected lesion level. This might be related to the growth laws that we used for the proliferation term which are well describing the early stage of the tumor growth [12].

Figure 2 shows the number of glioma for each level of glioma growth. In Fig. 2 (a), we found that all the models are following the same growth pattern except for Model 3 and Model 6 due to the presence of haptotaxis term in the equations. Haptotaxis is known to be an active migration factor that naturally present in ECM during the process of angiogenesis which describing the higher stage of tumor growth. Therefore, Model 3 and 6 are not suitable for visualization of the glioma growth at spheroid level.

Parallel performance analysis in terms of time execution, speed up, efficiency and effectiveness is shown in Fig. 3. In this preliminary result, the size of matrix used is 20 000 and eight number of processors running the sequential algorithm. As showed in the figure, by using more number of processors, we reduced the time cost, get higher speed and effectiveness. The graph of efficiency is decreasing because of the processors are not fully utilized since our main objective is to take advantage of the large memory space of the system only. However, this can be improved by embarking the load balancing approach.

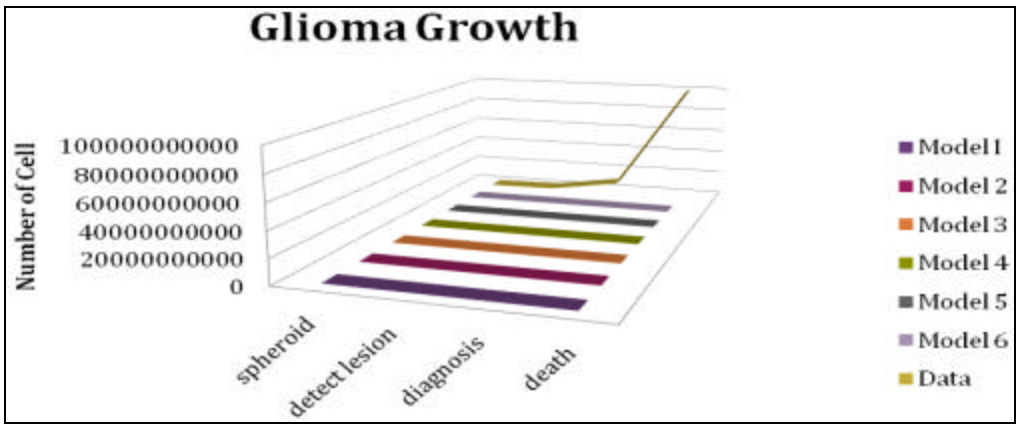

Fig. 1: Graph visualization of glioma growth

Table 1: Comparison of the simulation result with the data from Kansal, 2000 in terms of cell numbers

Model	Spheroid	Detect. Lesion	Diagnosis	Death
1	3.E+06	5.E+07	7.E+07	1.E+08
2	3.E+06	5.E+07	7.E+07	1.E+08
3	1.E+07	5.E+07	7.E+07	1.E+08
4	3.E+06	5.E+07	7.E+07	1.E+08
5	2.E+06	5.E+07	7.E+07	1.E+08
6	9.E+06	5.E+07	7.E+07	1.E+08
DATA	1.E+06	1.E+09	1.E+10	1.E+11

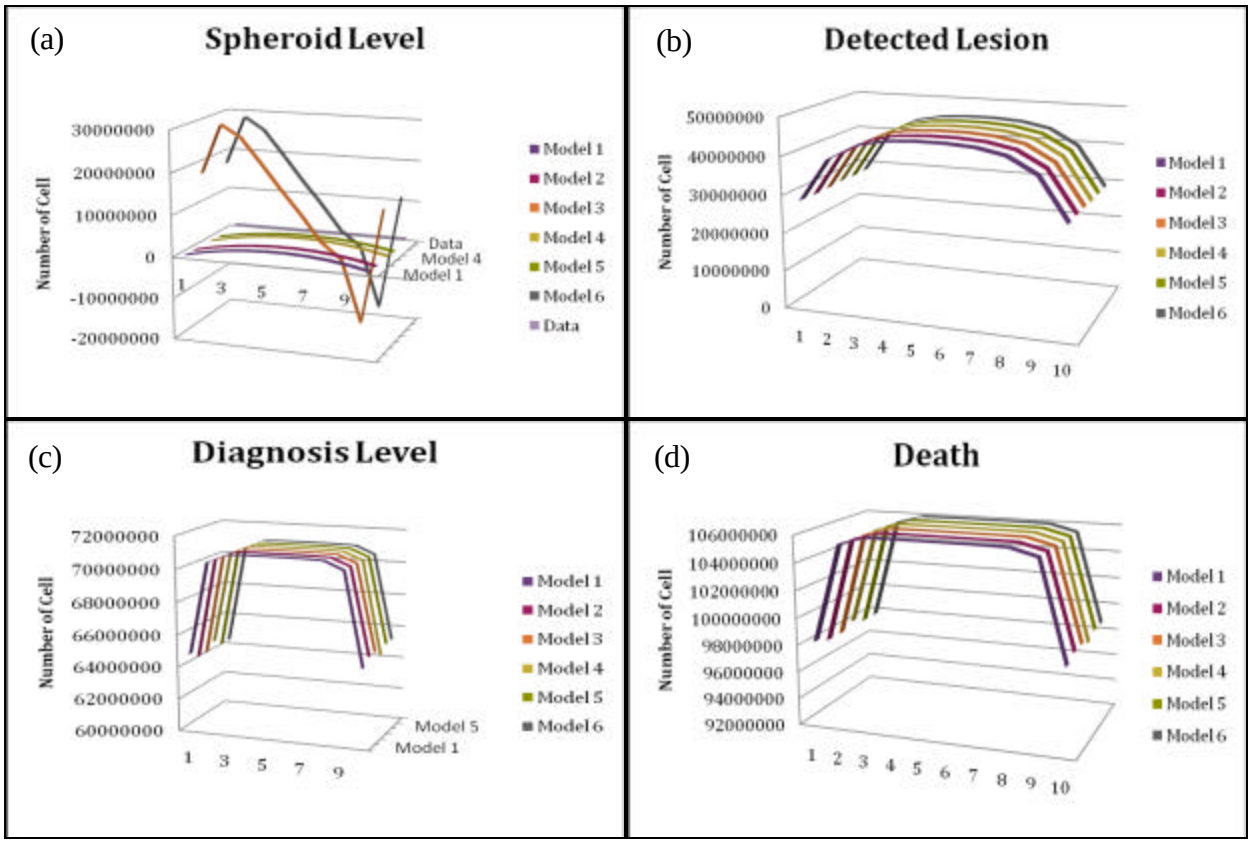

Fig. 2: Visualization of glioma growth for four level of glioma growth

FUTURE WORK

Our future work will be to utilize the ARS2 parallel computer system in visualizing the glioma growth in more proper and detail form. This can be done by using larger matrix size and more complex algorithm that can be applied in parallel environment.

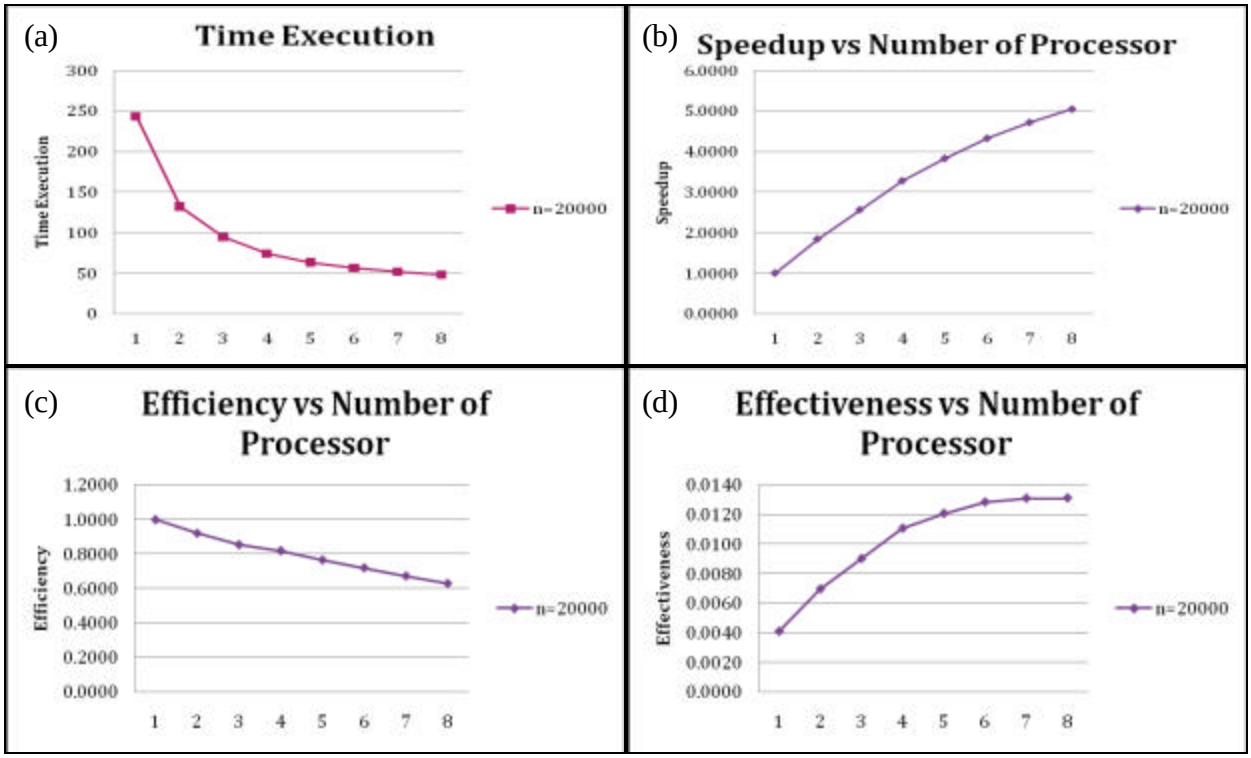

Fig. 3: Parallel performance analysis

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