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Fokas transform method for a brain tumor invasion model with heterogeneous diffusion in 1 + 1 dimensions ☆

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ABSTRACT

Gliomas are among the most aggressive forms of brain tumors. Over the last years mathematical models have been well developed to study gliomas growth. We consider a simple and well established mathematical model focused on proliferation and diffusion. Due to the heterogeneity of the brain tissue (white and grey matter) the diffusion coefficient is considered to be discontinuous. Fokas transform approach for the solution of linear PDE problems, apart from the fact that it avoids solving intermediate ODE problems, yields novel integral representations of the solution in the complex plane that decay exponentially fast and converge uniformly at the boundaries. To take advantage of these properties for the solution of the model problem at hand, we have successfully implemented Fokas transform method in the multi-domain environment induced by the interface discontinuities of our problem's domain. The fact that the integral representation of the solution at any time–space point of our problem's domain is independent on any other points of the domain, except of course on initial data, coupled with a simple composite trapezoidal rule, implemented on appropriately chosen integration contours, yields a fast and efficient analytical–numerical technique capable of producing directly high-order approximations of the solution at any point of the domain requiring no prior knowledge of the solution at any other time instances or space information.

1. Introduction

Gliomas, the most common primary brain tumors, are well known to be highly invasive. Recent mathematical models [7,1,2,15,18] formulated the problem of glioma growth where the basic parameters of the models were estimated by CT scan data. These models focus on two parameters: the spread D of glioma cells to tissues and the net proliferation rate ρ of glioma cells. Swanson [11,13,14,12] developed a model based on the differential motility of gliomas cells in white and grey matter suggesting that the diffusion coefficient in white matter is greater than in grey matter. Key role in the mathematical formulation of the problem plays the differential equation:

$$\frac{\partial \bar{c}}{\partial \bar{t}} = \nabla \cdot \left(\bar{D}(\bar{\mathbf{x}})\nabla \bar{c}\right) + \rho \bar{c}, \tag{1}$$

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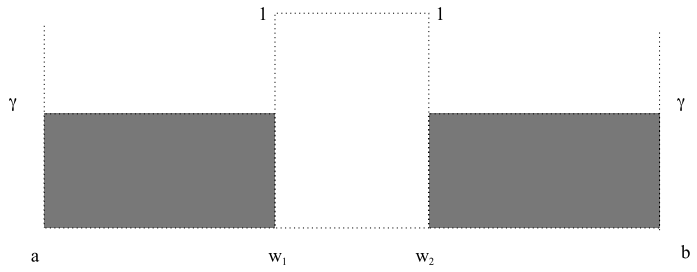

Fig. 1. Diffusion coefficient.

where $\bar{c}(\bar{\mathbf{x}}, \bar{t})$ denotes the tumor cell density at location $\bar{x}$ and time $\bar{t}$, ρ denotes the net proliferation rate, and $\bar{D}(\bar{\mathbf{x}})$ is the diffusion coefficient representing the active motility of malignant cells satisfying

$$\bar{D}(\bar{\mathbf{x}}) = \begin{cases} D_g, & \bar{\mathbf{x}} \text{ in grey matter} \\ D_w, & \bar{\mathbf{x}} \text{ in white matter} \end{cases}, \tag{2}$$

with D_g and D_w scalars and $D_w > D_g$. The model formulation is completed by zero flux boundary conditions which impose no migration of cells beyond the brain boundaries and an initial condition $\bar{c}(\bar{\mathbf{x}}, 0) = \bar{f}(\bar{\mathbf{x}})$, where $\bar{f}(\bar{x})$ is the initial spatial distribution of malignant cells.

In this work, we consider the dimensionless form of the previous model in one dimension and on a finite domain (grey matter – white matter – grey matter). By making use [11] the dimensionless variables:

$$x = \sqrt{\frac{\rho}{D_w}}\bar{x}, \tag{3}$$

$$t = \rho \bar{t}, \tag{4}$$

$$c(x,t) = \bar{c}\left(\sqrt{\frac{\rho}{D_w}}\bar{x}\rho\bar{t}\right)\frac{D_w}{\rho N_0}, \tag{5}$$

$$f(x) = \bar{f}\left(\sqrt{\frac{\rho}{D_w}}\bar{x}\right) \tag{6}$$

with $N_0 = \int \bar{f}(\bar{x})d\bar{x}$ to denote the initial number of tumor cells in the brain at $\bar{t} = 0$, we arrive at the dimensionless system:

$$\begin{cases} c_t = (Dc_x)_x + c, \quad x \in [a,b],\ t \geq 0 \\ c_x(a,t) = 0 \quad \text{and} \quad c_x(b,t) = 0 \\ c(x,0) = f(x) \end{cases} \tag{7}$$

and by substituting

$$c(x,t) = e^t u(x,t) \tag{8}$$

we obtain

$$\begin{cases} u_t = (Du_x)_x, \quad x \in [a,b],\ t \geq 0 \\ u_x(a,t) = 0 \quad \text{and} \quad u_x(b,t) = 0\,. \\ u(x,0) = f(x) \end{cases} \tag{9}$$

Note that the initial source of tumor cells $f(x)$ is defined through out of this paper to be:

$$f(x) := \delta(x - \xi), \quad \xi \in (a,b) \tag{10}$$

where $\delta(x)$ denotes the Dirac's delta function. Furthermore, the dimensionless parameter D is considered to be constant defined by:

$$D(x) = \begin{cases} \gamma, & a \leq x < w_1 \\ 1, & w_1 \leq x < w_2 \\ \gamma, & w_2 \leq x \leq b \end{cases}, \tag{11}$$

where $\gamma := D_g/D_w < 1$ is the dimensionless diffusion coefficient in grey matter and the dimensionless diffusion coefficient in white matter is to considered to be unity (see Fig. 1). Estimates of the values of the physiological parameters for a high grade tumor are included in Table 1 (cf. [11] and the references therein).