Fokas method for a multi-domain linear reaction-diffusion equation with discontinuous diffusivity

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Abstract. Motivated by proliferation-diffusion mathematical models for studying highly diffusive brain tumors, that also take into account the heterogeneity of the brain tissue, in the present work we consider a multi-domain linear reaction-diffusion equation with a discontinuous diffusion coefficient. For the solution of the problem at hand we implement Fokas transform method by directly following, and extending in this way, our recent work for a white-gray-white matter brain model pertaining to high grade gliomas. Fokas's novel approach for the solution of linear PDE problems, yields novel integral representations of the solution in the complex plane that, for appropriately chosen integration contours, decay exponentially fast and converge uniformly at the boundaries. Combining these method-inherent advantages with simple numerical quadrature rules, we produce an efficient method, with fast decaying error properties, for the solution of the discontinuous reaction-diffusion problem.

1. Introduction

Reaction-diffusion linear PDEs have been the core biomathematical model for studying highly invasive and aggressive forms of brain tumors for many years now (e.g. [1] and the references therein). The incorporation (cf. [2], [3]) of brain's tissue heterogeneity (white-gray matter) into the basic model led to the differential equation:

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

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

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

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

Using the classical transformation $c(x, t) = e^t u(x, t)$, the dimensionless initial-boundary value problem (cf. [2], [4]), in $1D$, may be written as

$$\begin{cases} u_t = (D u_x)_x, & x \in [a, b], \quad t \geq 0 \\ u_x(a, t) = 0 \quad \text{and} \quad u_x(b, t) = 0 \\ u(x, 0) = f(x) := \sum \delta(x - \xi_i), \quad \xi_i \in (a, b) \end{cases}, \tag{3}$$

where $\delta(x)$ denotes Dirac delta function.

Due to brain tissue heterogeneity, the domain $[a, b]$ is considered partitioned into $n+1$ regions $R_j := (w_{j-1}, w_j)$, with $a \equiv w_0 < w_1 < w_2 < \ldots < w_n < w_{n+1} \equiv b$, and if, for some j, R_j is white matter region, then R_{j-1} and R_{j+1} are grey matter regions. Thus, the dimensionless diffusion coefficient $D(x)$ is defined to be:

$$D(x) = \gamma_j \ , \ x \in R_j \ , \ j = 1, \ldots, n+1 \ \text{ with } \ \gamma_j := \begin{cases} D_g/D_w, & \text{when } R_j \text{ is grey matter} \\ 1, & \text{when } R_j \text{ is white matter} \end{cases} . \quad (4)$$

Furthermore, notice that the parabolic nature of the problem directly implies continuity of both u and Du_x across each interface point w_j. Hence:

$$u(w_j, t) \quad := \quad \lim_{x \to w_j^+} u(x,t) = \lim_{x \to w_j^-} u(x,t), \quad \forall j = 1, 2, \ldots, n \quad (5)$$

$$Du_x(w_j, t) \quad := \quad \lim_{x \to w_j^+} D(x)u_x(x,t) = \lim_{x \to w_j^-} D(x)u_x(x,t), \quad \forall j = 1, 2, \ldots, n. \quad (6)$$
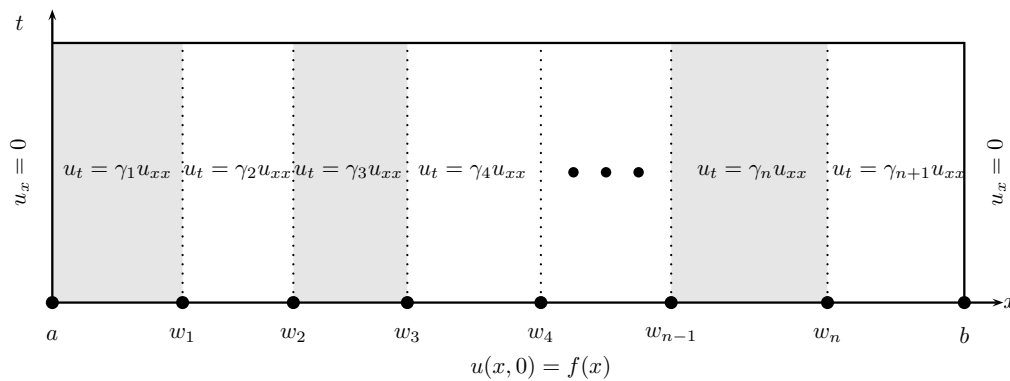
Figure 1. The multi-domain initial-boundary value problem

With the multi-domain problem depicted in Figure 1 above, we proceed, in Section 2, with the development of Fokas method (cf. [5], [6]) for its solution and the numerical investigation of its behaviour in Section 3.

2. Fokas Method

Let $u^{(j)}(x,t)$ denote the solution of the multi-domain problem defined over $\overline{R_j} := [w_{j-1}, w_j]$. Namely,

$$u^{(j)}(x,t) := \begin{cases} u(x,t), & x \in R_j \\ \lim_{x \to w_{j-1}^+} u(x,t), & x = w_{j-1} \\ \lim_{x \to w_j^-} u(x,t), & x = w_j \end{cases} , \quad j = 1, \ldots, n+1, \quad (7)$$

and, naturally,

$$u_x^{(j)}(w_{j-1}, t) := \lim_{x \to w_{j-1}^+} u_x(x,t) \quad \text{and} \quad u_x^{(j)}(w_j, t) := \lim_{x \to w_j^-} u_x(x,t) . \quad (8)$$

Apparently then,

$$u_t^{(j)} = (\gamma_j u_x^{(j)})_x = \gamma_j u_{xx}^{(j)} , \quad (9)$$

while, recalling the constrains (5)-(6), there also holds:

$$u^{(j)}(w_j, t) = u^{(j+1)}(w_j, t) \quad \text{and} \quad \gamma_j u_x^{(j)}(w_j, t) = \gamma_{j+1} u_x^{(j+1)}(w_j, t) . \quad (10)$$

Working similarly as in [4], we write equation (9) in divergence form

$$(e^{-ikx+\gamma_j k^2 t} u^{(j)})_t - (e^{-ikx+\gamma_j k^2 t}\gamma_j(u_x^{(j)} + iku^{(j)}))_x = 0 \ , \ k \in \mathbb{C} \text{ arbitrary,} \tag{11}$$

and by integrating over $A_j := \{(x,t) : x \in \overline{R_j}, \ 0 \le t \le T\}$, using Green's Theorem and Fourier transforms we obtain the "global relation" in the form:

$$
\begin{aligned}
e^{\gamma_j k^2 t}\widehat{u}^{(j)}(k,t) \ = \ \widehat{f}^{(j)}(k) \ &- \ \gamma_j e^{-ikw_{j-1}}\big[\widetilde{u}_x^{(j)}(w_{j-1},\gamma_j k^2) \ + \ ik\widetilde{u}^{(j)}(w_{j-1},\gamma_j k^2)\big] \\
&+ \ \gamma_j e^{-ikw_j}\big[\widetilde{u}_x^{(j)}(w_j,\gamma_j k^2) \ + \ ik\widetilde{u}^{(j)}(w_j,\gamma_j k^2)\big],
\end{aligned}
\tag{12}
$$

where

$$\widehat{f}^{(j)}(k) = \int_{w_{j-1}}^{w_j} e^{-ikx}f^{(j)}(x)dx, \quad \widehat{u}^{(j)}(k,t) = \int_{w_{j-1}}^{w_j} e^{-ikx}u^{(j)}(x,t)dx, \tag{13}$$

and

$$\widetilde{u}^{(j)}(x,\gamma_j k^2) := \int_0^T e^{\gamma_j k^2 t}u^{(j)}(x,t)dt, \quad \widetilde{u}_x^{(j)}(x,\gamma_j k^2) := \int_0^T e^{\gamma_j k^2 t}u_x^{(j)}(x,t)dt. \tag{14}$$

Inverting the windowed Fourier transform $\widehat{u}^{(j)}(k,t)$, setting $k^2 \leftarrow \gamma_j k^2$, $c_j \leftarrow \gamma_j^{-1/2}$, applying conditions (10), and after some algebraic manipulations we find that the solution, for all $j = 1, 2, \ldots, n$, is given by

$$
\begin{aligned}
u^{(j)}(x,t) = \ &\frac{c_j}{2\pi}\int_{-\infty}^{+\infty} e^{ic_j kx - k^2 t}\widehat{f}^{(j)}(c_j k)dk \\
&- \frac{1}{2\pi c_j}\int_{-\infty}^{+\infty} e^{ic_j k(x-w_{j-1})-k^2 t}\big[\frac{\gamma_{j-1}}{\gamma_j}\widetilde{u}_x^{(j-1)}(w_{j-1},k^2) + ic_j k\widetilde{u}^{(j-1)}(w_{j-1},k^2)\big]dk \\
&+ \frac{1}{2\pi c_j}\int_{-\infty}^{+\infty} e^{ic_j k(x-w_j)-k^2 t}\big[\widetilde{u}_x^{(j)}(w_j,k^2) + ic_j k\widetilde{u}^{(j)}(w_j,k^2)\big]dk \ ,
\end{aligned}
\tag{15}
$$

where $\widetilde{u}_x^{(j)}(w_j,k^2)$ and $\widetilde{u}^{(j)}(w_j,k^2)$ are given by the following $2(n+1) \times 2(n+1)$ linear system:

$$G\widetilde{\mathbf{u}} = \widehat{\mathbf{f}}, \tag{16}$$

where:

$$
G = \begin{bmatrix}
A_1^{(1)} & A_3^{(1)} & A_4^{(1)} & 0 & 0 & \cdots & 0 & 0 & 0 & 0 & 0 \\
A_5^{(1)} & A_7^{(1)} & A_8^{(1)} & 0 & 0 & \cdots & 0 & 0 & 0 & 0 & 0 \\
0 & A_1^{(2)} & A_2^{(2)} & A_3^{(2)} & A_4^{(2)} & \cdots & 0 & 0 & 0 & 0 & 0 \\
0 & A_5^{(2)} & A_6^{(2)} & A_7^{(2)} & A_8^{(2)} & \cdots & 0 & 0 & 0 & 0 & 0 \\
\vdots & \vdots & \vdots & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots & \vdots & \vdots \\
0 & 0 & 0 & 0 & 0 & \cdots & A_1^{(n)} & A_2^{(n)} & A_3^{(n)} & A_4^{(n)} & 0 \\
0 & 0 & 0 & 0 & 0 & \cdots & A_5^{(n)} & A_6^{(n)} & A_7^{(n)} & A_8^{(n)} & 0 \\
0 & 0 & 0 & 0 & 0 & \cdots & 0 & 0 & A_1^{(n+1)} & A_2^{(n+1)} & A_3^{(n+1)} \\
0 & 0 & 0 & 0 & 0 & \cdots & 0 & 0 & A_5^{(n+1)} & A_6^{(n+1)} & A_7^{(n+1)}
\end{bmatrix},
$$

i	$A_i^{(j)}$
1	$ic_j\gamma_j ke^{-ic_j kw_{j-1}}$
2	$\gamma_{j-1}e^{-ic_j kw_{j-1}}$
3	$-ic_j\gamma_j ke^{-ic_j kw_j}$
4	$-\gamma_j e^{-ic_j kw_j}$
5	$-ic_j\gamma_j ke^{ic_j kw_{j-1}}$
6	$\gamma_{j-1}e^{ic_j kw_{j-1}}$
7	$ic_j\gamma_j ke^{ic_j kw_j}$
8	$-\gamma_j e^{ic_j kw_j}$

$$
\widetilde{\mathbf{u}} = \begin{bmatrix}
\widetilde{u}^{(1)}(w_0,k^2) \\
\widetilde{u}^{(1)}(w_1,k^2) \\
\widetilde{u}_x^{(1)}(w_1,k^2) \\
\vdots \\
\widetilde{u}^{(n)}(w_n,k^2) \\
\widetilde{u}_x^{(n)}(w_n,k^2) \\
\widetilde{u}^{(n+1)}(w_{n+1},k^2)
\end{bmatrix}
\quad \text{and} \quad
\widehat{\mathbf{f}} = \begin{bmatrix}
\widehat{f}^{(1)}(c_1 k) \\
\widehat{f}^{(1)}(-c_1 k) \\
\widehat{f}^{(2)}(c_2 k) \\
\widehat{f}^{(2)}(-c_2 k) \\
\vdots \\
\widehat{f}^{(n)}(c_n k) \\
\widehat{f}^{(n)}(-c_n k) \\
\widehat{f}^{(n+1)}(c_{n+1}k) \\
\widehat{f}^{(n+1)}(-c_{n+1}k)
\end{bmatrix}.
$$

Finally we point out that the analytic nature of the integrand functions in relation (15) above allows the determination of appropriate integration contours in the complex plane (cf. [7], [4]) to achieve fast decay of the integrands hence stability of the whole calculation.
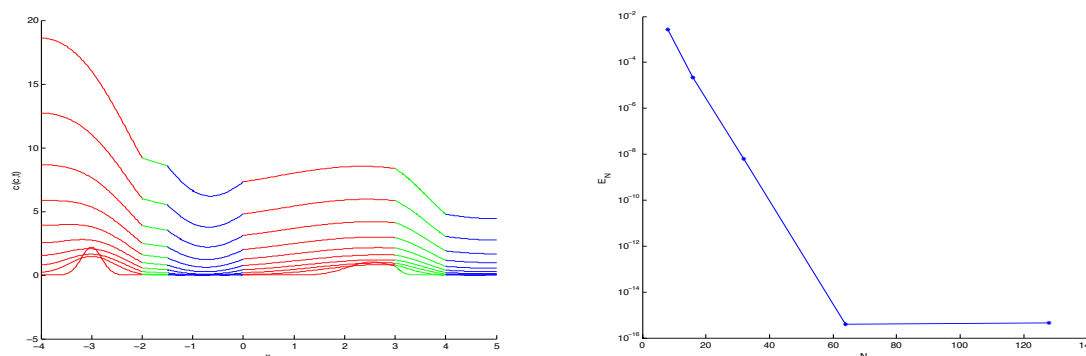
3. Numerical Solution

Following our work in [4], to numerically evaluate the integrals in relation (15) above, we apply the trapezoid rule on appropriate hyperbolic contours (cf. [8]) defined by mapping the points θ on the real line to the points $\pm k(\theta)$ of the complex plane, where $k_\theta \equiv k(\theta) := i\sin(\beta - i\theta)$.

The numerical model used in our experiments is described by:

$$[a, w_1, w_2, w_3, w_4, w_5, b] = [-4, -2, -1.5, 0, 3, 4, 5], \quad \gamma_1 = D_g/D_w = 0.2, \xi_1 = -3 \ .\xi_2 = 2.5 \quad (17)$$

The relative error used in our calculations is given by $E_N := \|u_{N_{i+1}} - u_{N_i}\|_\infty / \|u_{N_{i+1}}\|_\infty$, where N denotes the number of quadrature points, and is depicted in Figure 2 that follows.

Figure 2. Time evolution of cell density $c(x, t)$ and the corresponding relative error E_N

4. Conclusion

The Fokas transform method, combined with numerical integration on hyperbolic contours, is applied to the solution of a multi-domain brain tumor invasion model. The analytical solution is produced in integral form at any space-time point and evaluated by a fast convergent quadrature.

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