NUMERICAL METHODS FOR DRUG APPLICATION IN TUMOR TREATMENT

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The mathematical model of drug delivery to brain tumors is not new. There are various configurations of different complexity, for example, in [1] authors consider the full momentum equation instead of Darcy's law, but a few terms in the drug concentration equation are neglected. Walker et. all [3] take up Darcy's law instead of full momentum equation.

In the present work, the governing system of equations was taken from [1] and consists of:

- the mass conservation equation

$$\nabla \cdot \vec{V} = \begin{cases} F_v - F_l, & \text{in wafers and cavity} \\ 0, & \text{elsewhere} \end{cases}$$

- the momentum equation

$$\frac{\partial(\rho\vec{V})}{\partial t} + \nabla \cdot (\rho\vec{V}\vec{V}) = \rho\vec{g} - \nabla P_i + [\nabla \cdot \Gamma] + \theta\mu\vec{V} + \frac{1}{2}\rho\Psi\left|\vec{V}\right|\vec{V}$$

- the drug concentration into the brain tumor

$$\frac{\partial C}{\partial t} + \nabla(C \cdot \vec{V}) = D\Delta C - R + F_s - F_{ls},$$

where F_v and F_l are the net gain of fluid from blood vessels and the net fluid loss to the lymphatic per unit volume of tissues, correspondingly. The fluid sources F_v are described by Starling's law:

$$F_v = \frac{K_v S}{V}(P_v - P_i - \sigma_T(\pi_v - \pi_i)),$$

where P_v and P_i are the interstitial and the vascular pressures, π_v and π_i are the osmotic pressures of plasma and interstitial fluid, $K_v S/V$ is the hydraulic conductivity of the microvascular wall multiplied by the exchange area of blood vessels per unit volume of tissues, σ_T is the osmotic reflection coefficient for the plasma proteins, ρ and μ are the fluid density and viscosity, g and Γ are the stress tensor and gravity acceleration, θ and Ψ are prescribed matrices for the inertial and the viscous loss term, respectively [1].

The domains include such areas as:

- wafers, where $F_s = S_0 \exp(-t/\tau)$, $R = 0$;
- cavity after surgery, where $F_s = 0$, $R = k_c C$;
- remnant tumor tissues and surrounding normal tissues, where

$$F_s = F_v(1-\sigma)C_v + \frac{\delta S}{V}(C_v - C)\cdot\frac{Pe_v}{\exp(Pe_v) - 1},$$

$$R = \frac{V_{\max} C}{K_m + C} + k_e C$$

The system describes the penetration of drugs into the brain tumor. The anti-cancer drug fills the cavity up after surgery. In this work, full mass conservation and momentum equations were considered and they are coupled with the concentration equation depending on the velocity.

The techniques of computational fluid dynamics (CFD) were used to get a solution of the derived partial differential equations (Navier-Stokes equation with the additional equation and terms). Firstly, the governing equations were non-dimensionalized. Then were descritized in space and in time (using Backward Euler method). The following system of equations was obtained:

$$\begin{bmatrix} A(V) & B & 0 \\ B^T & -\mu \cdot I & -\kappa \cdot I \\ 0 & 0 & E(V) \end{bmatrix} \begin{bmatrix} V \\ p \\ C \end{bmatrix} = \begin{bmatrix} f \\ g \\ q \end{bmatrix}$$

The given problem is similar to a saddle point problem. It is a well know problem for CFD, which requests special techniques [4]. The modern CFD tool like FEATFLOW was used to get numerical solutions of this problem. Depending on the part, where the solution of the system should be obtained, different values of constant μ and κ were used.

Table 1: Test results for the Stokes Problem (NLI-number of non-linear iterations and LI-number of linear iterations).

Number of the test	Coef.value	$\|u - reference\|_{L2}$	$\|p - reference\|_{L2}$	$\|C - reference\|_{L2}$
♯ 1(NLI=4,LI=11)	$\mu=0$, $\kappa=0$, $r=0$	3.753784E-16	5.023719E-14	1.243867E-14
♯ 2(NLI=6,LI=21)	$\mu=0$, $\kappa=1$, $r=0$	8.535401E-15	5.615831E-13	6.851949E-14
♯ 3(NLI=4,LI=11)	$\mu=0$, $\kappa=0$, $r=1$	3.753784E-16	5.023719E-14	1.637723E-14
♯ 4(NLI=6,LI=21)	$\mu=0$, $\kappa=1$, $r=1$	6.711526E-15	4.546867E-13	5.952960E-14
♯ 5(NLI=2,LI=2)	$\mu=1$, $\kappa=0$, $r=0$	3.512095E-15	1.252401E-14	5.966827E-15
♯ 6(NLI=5,LI=5)	$\mu=1$, $\kappa=1$, $r=0$	4.126838E-14	7.951236E-13	9.241469E-13
♯ 7(NLI=2,LI=2)	$\mu=1$, $\kappa=0$, $r=1$	3.512095E-15	1.252401E-14	1.181159E-14
♯ 8(NLI=5,LI=5)	$\mu=1$, $\kappa=1$, $r=1$	3.423239E-14	6.492284E-13	7.563755E-13

Table 2: Test results for the Navier-Stokes Problem (NLI-number of non-linear iterations and LI-number of linear iterations).

Number of the test	Coef.value	$\|u - reference\|_{L2}$	$\|p - reference\|_{L2}$	$\|C - reference\|_{L2}$
♯ 1(NLI=5,LI=14)	$\mu=0$, $\kappa=0$, $r=0$	6.439795E-14	3.037016E-13	8.395213E-14
♯ 2(NLI=6,LI=21)	$\mu=0$, $\kappa=1$, $r=0$	8.125284E-14	1.718677E-12	62.305856E-13
♯ 3(NLI=5,LI=14)	$\mu=0$, $\kappa=0$, $r=1$	6.439795E-14	3.037016E-13	8.412142E-14
♯ 4(NLI=6,LI=21)	$\mu=0$, $\kappa=1$, $r=1$	8.316850E-14	1.593549E-12	2.231409E-13
♯ 5(NLI=9,LI=9)	$\mu=1$, $\kappa=0$, $r=0$	6.524818E-14	2.006768E-13	1.374437E-13
♯ 6(NLI=9,LI=9)	$\mu=1$, $\kappa=1$, $r=0$	6.636437E-14	2.294126E-13	1.377964E-13
♯ 7(NLI=9,LI=9)	$\mu=1$, $\kappa=0$, $r=1$	6.524818E-14	2.006768E-13	1.267686E-13
♯ 8(NLI=9,LI=9)	$\mu=1$, $\kappa=1$, $r=1$	6.702731E-14	2.274583E-13	1.279417E-13

The result of the tests of the Stokes problem and of the Navier-Stokes problem on the unit square with the given right hand side are presented in tables 1 and 2. The results were compared with the analytical solution for the velocity, pressure and concentration. These tests helped to evaluate the code based on FEATFLOW program and show a very good accuracy of the results.

LITERATURE:

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