Numerical methods for drug application in tumor treatment

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Introduction

- Motivation
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Mathematical model

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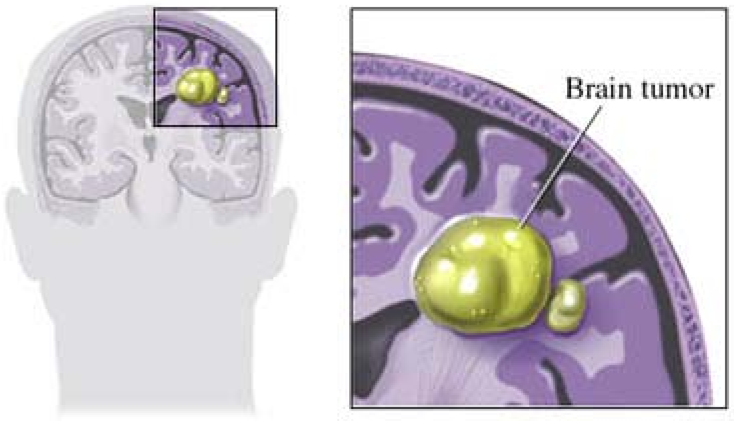
- Discretization
- Results

Summary

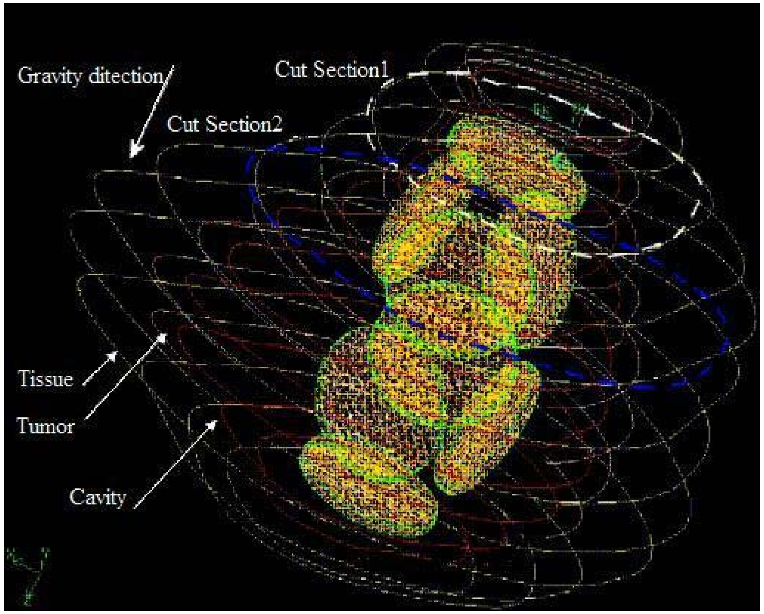
Motivation

- Each year a lot of people in the world are diagnosed with a primary or metastatic tumor
- There are over 120 different types of brain tumors



- application to drug delivery in brain tumors
- solution of derived partial differential equations (PDE's)
- use modern computational fluid dynamics (CFD) tools (Featflow)

Schematic view



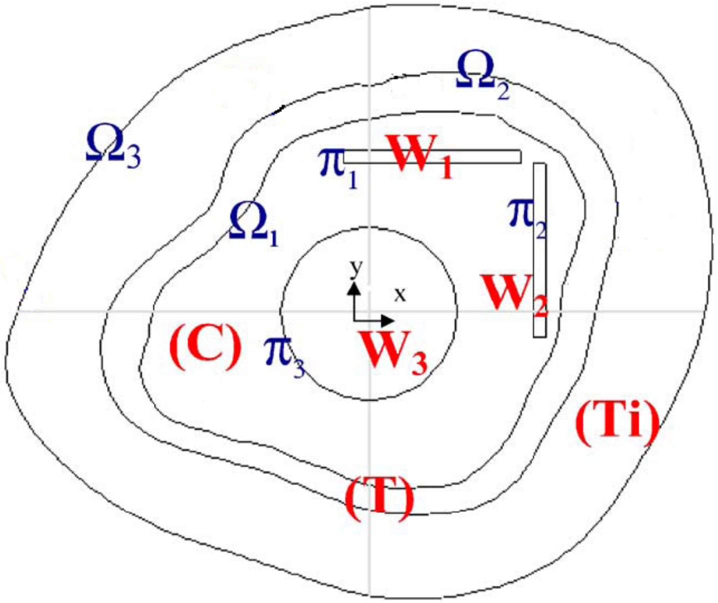


Fig.1: $W_{1,2,3}$ - wafers 1-3, (C) - the resection cavity after the surgery, (T) - the remnant tumor that are not removed in the surgery,(Ti) - the normal tissues surrounding the tumor, Ω_1 - boundary between cavity and tumor, Ω_2 - boundary between tumor and tissues, Ω_3 - external boundary, $\pi_{1,2,3}$ - boundaries cavity and wafers

(T.Lee, W. Tan, C.-H. Wang, 2004)

Governing equations

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The mass conservation equation

$$\nabla\cdot\vec{V} = \begin{cases} F_v - F_l + q & \text{in tumor (T) and normal tissues (Ti)} \\ 0 & \text{in cavity (C) and wafers } (W_{1,2,3}) \end{cases}$$

The momentum equation

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

The drug concentration

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

(T.Lee, W. Tan, C.-H. Wang, 2004)

Formulas

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

$$F_s = \begin{cases} S_0 e^{-t/\tau} & \text{in wafers } (W_{1,2,3}) \\ F_v(1-\sigma)C_v + \frac{\pm S}{V}(C_v - C)\cdot\frac{Pe_v}{e^{Pe_v}-1} & \text{in tumor (T) and tissues (Ti)} \\ 0 & \text{in cavity (C)} \end{cases}$$

$$R = \begin{cases} k_c C & \text{in cavity (C)} \\ \frac{V_{max} C}{K_m + C} + k_e C & \text{in tumor (T) and normal tissues (Ti)} \\ 0 & \text{elsewhere} \end{cases}$$

$$Pe_v = \frac{F_v(1-\sigma)}{\pm S/V}$$ Peclet number

$$\pi_{i,v} = R \cdot T \cdot C_{i,v}$$ Van Hoff /s law

(T.Lee, W. Tan, C.-H. Wang, 2004)

Abstract view of the dimensionless equations

$$\begin{cases} \nabla\cdot\vec{V} - \tilde{k}\cdot P = 0 \\ \frac{\partial\vec{V}}{\partial t} + \nabla\cdot(\vec{V}\vec{V}) = \vec{g} - \nabla P_i + [\nabla\cdot\mathbf{\Gamma}] + \mathbf{\Theta}\nu\vec{V} + \frac{1}{2}\mathbf{\Psi}|\vec{V}|\vec{V} \\ \tilde{q}\cdot\frac{\partial C}{\partial T} + \tilde{d}\vec{V}\cdot\nabla C = \triangle C - \tilde{f}\cdot C \end{cases}$$

Discretized equations

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

Discretization

	Velocity/Pressure	Concentration
element	$\tilde{Q}_1/Q_0$	Q_1
solver	Multigrid	Umfpack
grid	unstuctured	unstuctured

Analytical solution to compare with

$$V_x = x^2$$
$$V_y = y^2$$
$$p = x + y$$
$$C = x^2 + y^2$$

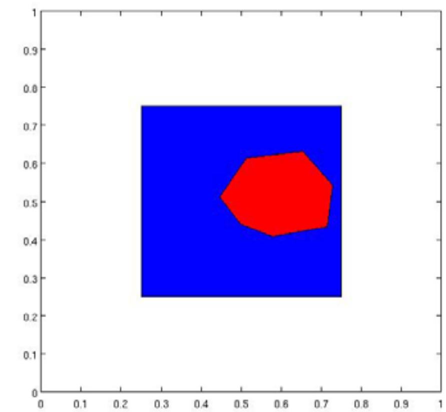

Fig 2: Test domain

The RHS for the Navier-Stokes test case

$$f_1 = 1 - 2 \cdot Re + 2x^3$$
$$f_2 = 1 - 2 \cdot Re + 2y^3$$
$$g = (x + y)(2 + \mu) + \kappa(x^2 + y^2)$$
$$q = 2(x^3 + y^3) + r(x^2 + y^2) - 4D$$

The RHS for the Stokes test case

$$f_1 = 1 - 2 \cdot Re$$
$$f_2 = 1 - 2 \cdot Re$$
$$g = (x + y)(2 + \mu) + \kappa(x^2 + y^2)$$
$$q = 2(x^3 + y^3) + r(x^2 + y^2) - 4D$$

Results

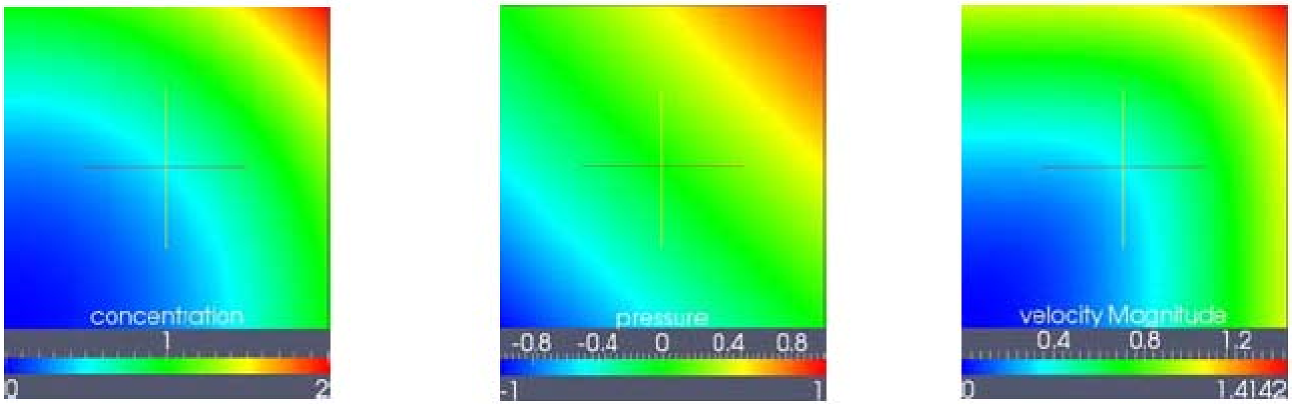

Fig. 3: The results for the concentration , pressure and velocity magnitude for the Stokes and Navier-Stokes case

	Stokes	Navier-Stokes
$\|\|u - reference\|\|_{L2}$	1.784159E-15	3.412009E-12
$\|\|p - reference\|\|_{L2}$	1.134399E-15	2.478050E-12
$\|\|C - reference\|\|_{L2}$	4.833782E-14	1.177962E-13
$\sharp linear iterations$	12	56
$\sharp non - linear iterations$	5	18
$Final\ defect$	7.7820003474E-17	8.0724677392E-14
$NLMAX$	5	5

Summary

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- closed system of PDE's for the velocity, pressure and drug concentration
- saddle-point problem requires techniques for incompressible flow problems
- the fully coupled problem
- numerics for CFD

References

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