Numerical methods and CFD techniques for drug application in tumor treatment

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Content

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Introduction

- Motivation
- Schematic view

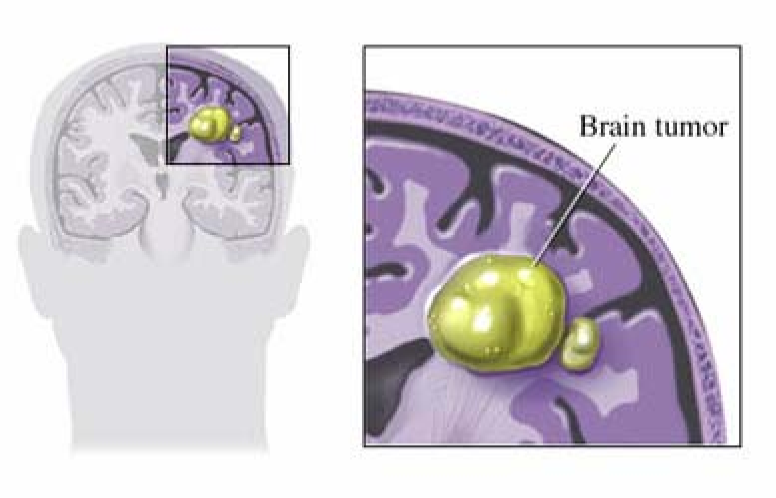
Mathematical model

- Equations
- 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)

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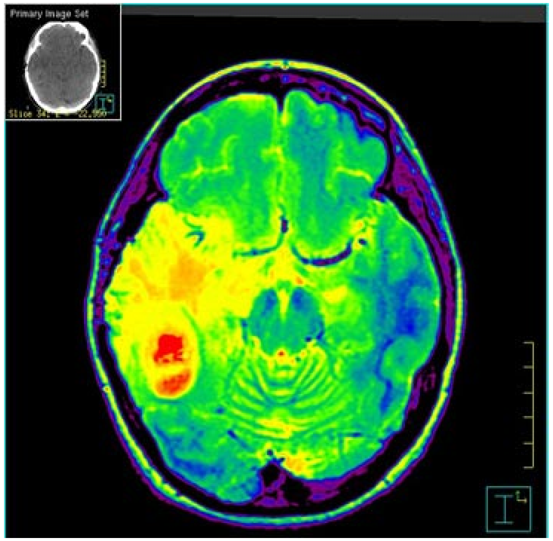
There are two principal physiological barriers:



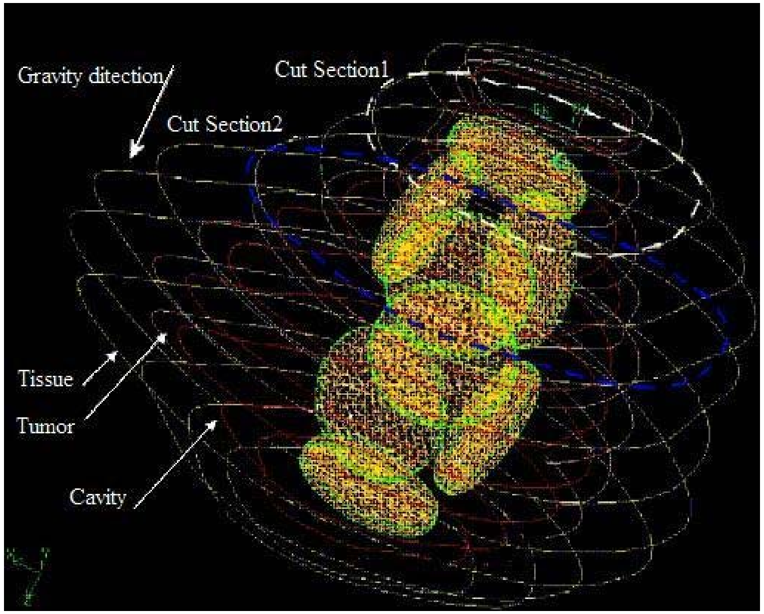
the blood-brain barrier (BBB)

- The BBB hinders the delivery of many potentially important diagnostic and therapeutic agents to the brain

the interstitial fluid pressure

- The interstitial fluid pressure is present within the tumor and reduces the driving force for fluid and solute to be extravasated into the brain tissues

Schematic view



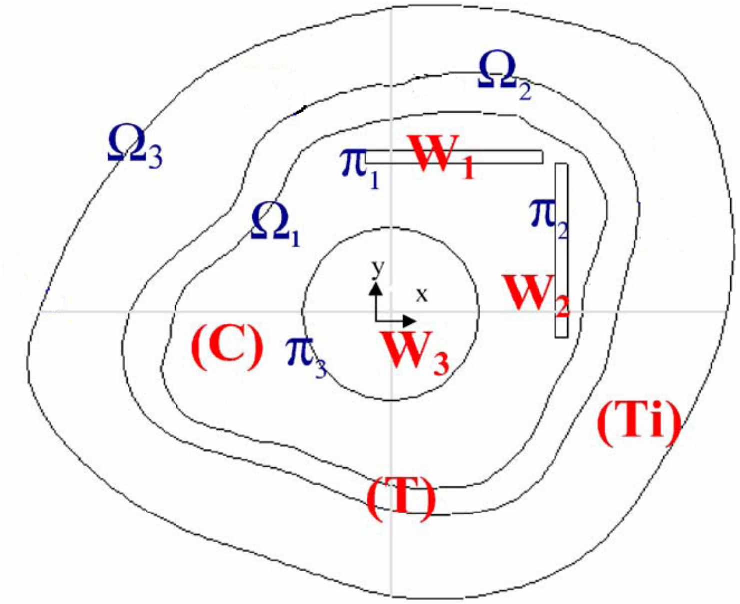


Fig.1: $W_{1,2,3}$ - wafers 1-3, (C) - the resection cavity after the surgery, (T) - the remnant tumor that are not removed in the surgery,(Ti) - the normal tissues surrounding the tumor, Ω_1 - boundary between cavity and tumor, Ω_2 - boundary between tumor and tissues, Ω_3 - external boundary, $\pi_{1,2,3}$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

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

Equations

Abstract view of the dimensionless equations

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

Discretized equations

$$\begin{bmatrix} A & B \\ B^T & -k\cdot I \end{bmatrix} \begin{bmatrix} \tilde{V} \\ P \end{bmatrix} = \begin{bmatrix} f \\ g \end{bmatrix}$$

, where $\tilde{V} = (V, C)$

Discretization

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

Results

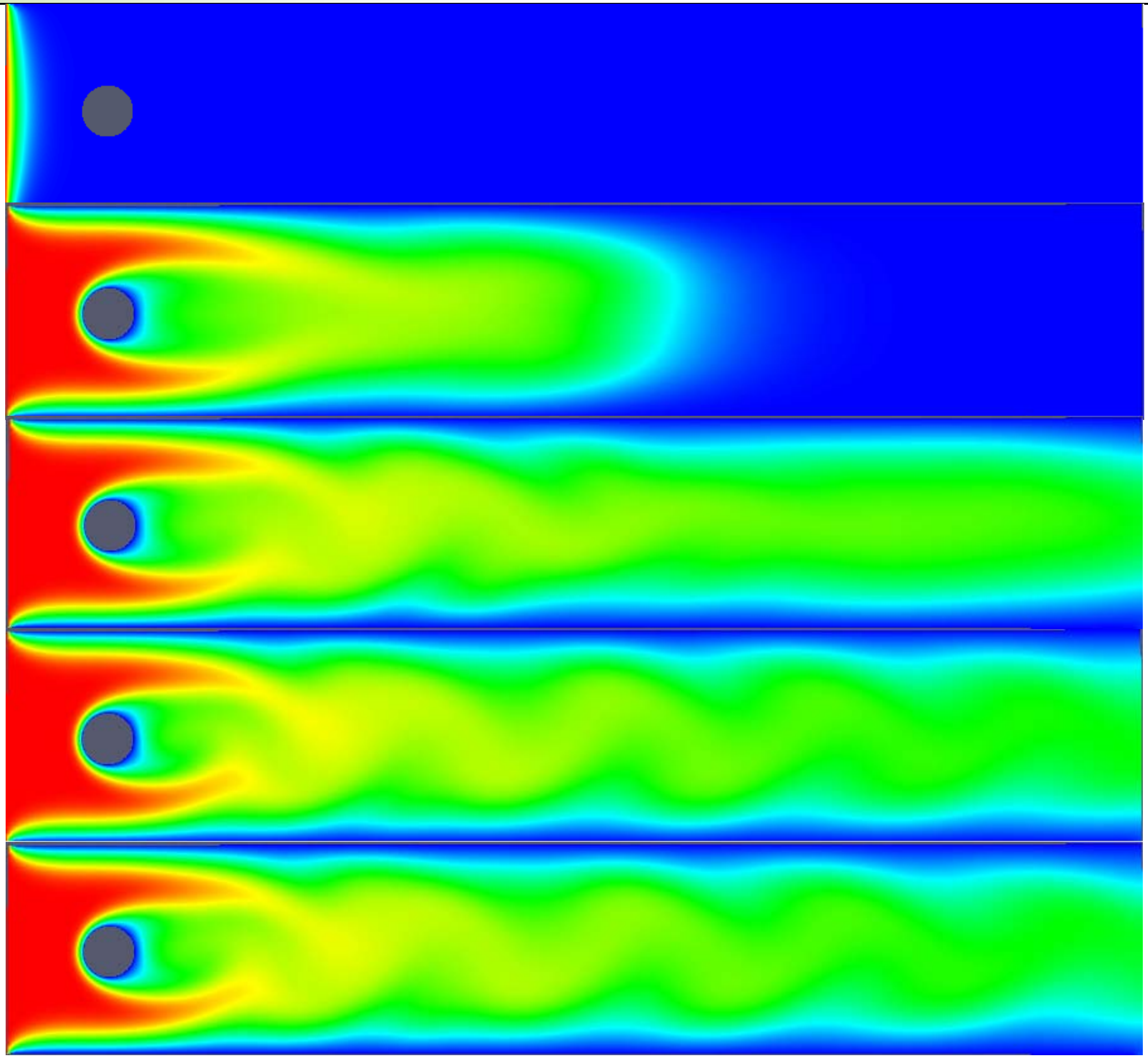
Time step = 001

Time step = 050

Time step = 100

Time step = 150

Time step = 200



Summary

- 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

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Thank you for your attention!!!

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Basic notation

μ	-interstitial fluid viscosity	R	-reaction in the cavity
ρ	-interstitial fluid density	Pe_v	-transcapillar Peclet number
Θ	-matrix for viscous term	F_s	-drug gain from the blood capillaries
Γ	-stress tensor	F_{ls}	-drug loss to the lymphatic vessels
Ψ	-matrix for inertial term	C	-drug concentration
F_l	-net gain fluid	$N_{1,2,3}$	-outward normal vectors of $\Omega_{1,2,3}$
F_v	-net fluid loss	K_v	-hydraulic conductivity
P_v	-interstitial pressure	S/V	-exchange area
P_i	-vascular pressure	π_i	-osmotic pressure of interstitial fluid
π_v	-osmotic pressure of plasma	σ_T	-osmotic reflection coefficient