Solving the 3-D ‘Sphoisson’ Equation

David Gross

MATH 164

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An Overview

Motivation

- Research from Summers '05, '06 and '07
- Supported by the National Science Foundation under 3-year grant NSF-DMS-041-4011
- Optimal control theory published in *EJDE*, Vol. 2007, No. 171
- Paper pending minor revisions in *Journal of Computation and Mathematical Methods in Medicine*
- Looking for paper to discuss spatial modeling attempts and techniques, for both spherically symmetric and spherically asymmetric case

ODE Variables

M_B: Chemotherapy drug concentration in the blood, [IU/L]

D_B: Dendritic cell concentration in the blood [cells/L]

L_B: Antigen-specific activated CD8+ T lymphocytes, [cells/L]

ODE Equations

$$
\begin{aligned}
\frac{dM_B}{dt} &= -\omega_{M_B} M_B \\
\frac{dD_B}{dt} &= \alpha_{D_B} \frac{\langle T \rangle}{\langle T \rangle + k_{D_B}} - \omega_{D_B} D_B - K_{D_B}(1 - e^{-\delta_{D_B} M_B}) D_B \\
\frac{dL_B}{dt} &= \alpha_{L_B} \frac{D_B}{\zeta_{L_B} + D_B} \frac{L_B}{k_{L_B} + L_B} L_B - u_{L_B} e^{\epsilon_{L_B} D_B} \frac{L_B}{k_{L_B} + L_B} L_B^2 \\
&\quad - K_{L_B}(1 - e^{-\delta_{L_B} M_B}) L_B - \omega_{L_B} L_B
\end{aligned}
$$

where

$$\langle T \rangle = \int_0^R \int_0^\pi \int_0^{2\pi} T(r, \phi, \theta) \; d\theta d\phi dr$$

is the integral of tumor density, i.e. the volume of the tumor

PDE Variables

- T: Tumor cell density, [cells/mm^3]
- $\vec{v}$: Tumor cell velocity, [mm/s]
- N: Nutrient density, [mol/mm^3]
- M: Chemotherapy drug density, [mg/mm^3]
- S: Chemical signal responsible for inducing CD8+ T cells to move towards the center of the tumor by chemotaxis, [mol/mm^3]
- L: Antigen specific CD8+ T lymphocytes, [cells/mm^3]

PDE Equations

$$
\begin{aligned}
T_t - \nabla \cdot (\vec{v} T) &= D_T \Delta T + \alpha_T \frac{N}{N+\zeta} T - \omega_T T \\
&\quad - \frac{(L/T)^\sigma}{s + (L/T)^\sigma} - K_T(1 - e^{-\delta_T M}) T \\
N_t &= D_N \Delta N - \Gamma \frac{N}{N+\zeta} T \\
M_t &= D_M \Delta M - (\bar{\omega}_M + \gamma T) M \\
S_t &= D_S \Delta S + \alpha_S - \omega_S S \\
L_t &= -\mu \Delta S + \Delta L - \omega_L T L - K_L (1 - e^{-\delta_L M}) L
\end{aligned}
$$

Intratumoral Pressure via Darcy's Law

We assume that there exists an intratumoral pressure $p(r, \theta, \phi, t)$ following Darcy's Law. That is, for some proportionality constant ν,

$$\vec{v} = -\nu \nabla p$$

Furthermore, we stipulate that the tumor has constant density, i.e. $T = 1$. This reduces equation the T PDE to

$$\nu \Delta p = \alpha_T \frac{N}{N + \zeta} - \omega_T - \frac{L^\sigma}{s + L^\sigma} - K_T(1 - e^{-\delta_T M})$$

and we solve for p instead of both T and $\vec{v}$.

Tumor Boundary Evolution

We let the boundary be given by $R = R(\theta, \phi, t)$. To define the time evolution of R, we introduce the moving boundary condition as follows:

$$\left(\frac{\partial \mathrm{R}}{\partial \mathrm{t}}\vec{\mathrm{u}}\right) \cdot \vec{\mathrm{n}_\mathrm{R}} = \vec{\mathrm{n}_\mathrm{R}} \cdot \Big(-\nu \nabla \mathrm{p} \,\Big|_{\mathrm{r}=\mathrm{R}}$$

where novel terms in this equation are defined by

$$\begin{aligned} \vec{u}(\theta, \phi) &= (\cos\theta \sin\phi, \sin\theta\sin\phi, \cos\phi) \\ \vec{F} &= R\vec{u} \\ \vec{n_R} &= \frac{\vec{F}_\theta \times \vec{F}_\phi}{\|\vec{F}_\theta \times \vec{F}_\phi\|} \end{aligned}$$

Boundary Conditions

$$N(R) = N_B \quad L(R) = L_B(t) \quad M(R) = M_B(t) \quad S(R) = 0 \tag{1}$$

$$p(R) = \alpha_\kappa \kappa = \alpha_\kappa \left(\frac{1}{R} - \frac{\mathcal{L}(R)}{2R^2} \right) \tag{2}$$

Note here N_B is constant, but L_B and M_B are functions of time. We assume that pressure is proportional to mean curvature $\kappa = \kappa(r, \theta, \phi)$ of the boundary. Here $\mathcal{L}$ is used to denote the angular component of the spherical Laplacian.

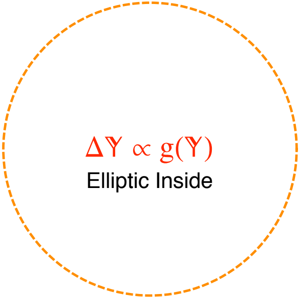
PDE Types

Hyperbolic Boundary

$$\frac{\partial \mathbb{Z}}{\partial t} \propto \nabla \mathbb{X}$$

Parabolic from Boundary to Interior

$$\mathbb{X}_t \propto \Delta \mathbb{X} + f(\mathbb{X})$$



Order of Solution

- Update ODE (Body)
- Update Parabolic Equations (Chemicals)
- Solve Elliptic Equation (Pressure)
- Update Hyperbolic Equations (Boundary)

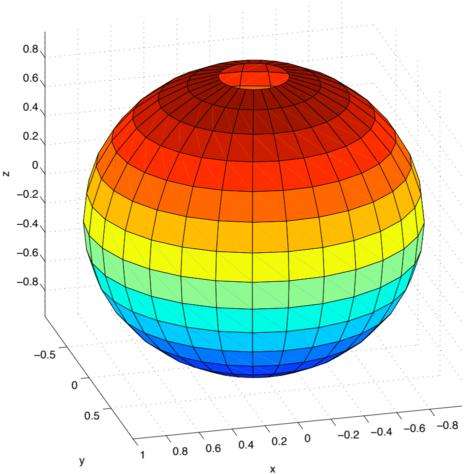
How to Solve

- Body - Finite Difference
- Chemicals - ?
- Pressure - ?
- Boundary - ?

Naive (and Not Naive) Methods

- Finite differences on the sphere - Parousia
- Finite Element Methods
- Finite Volume Methods

Truncated Spherical Coordinates



Spherical Harmonics

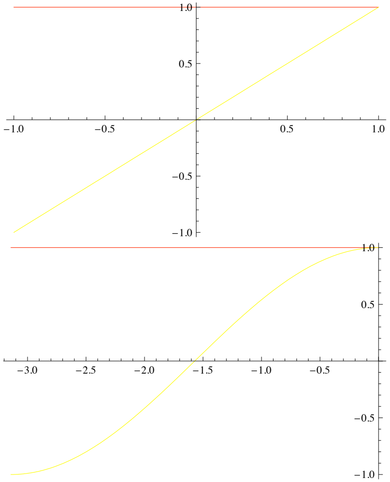
- Atomic electron configurations
- Representation of the gravitational field,
- Magnetic field of planetary bodies
- Cosmic microwave background radiation
- Indirect lighting

$$Y_\ell^m(\theta, \phi) = P_\ell^m(\cos(\theta))e^{-im\phi}$$

Chebyshev Polynomials

- Your friendly neighborhood family—of orthogonal polynomials
- Solutions to a DE
- Solutions of a recurrence relation
- Family friends with Cosine.

$$T_n(x) = \cos(n \cos^{-1}(x))$$



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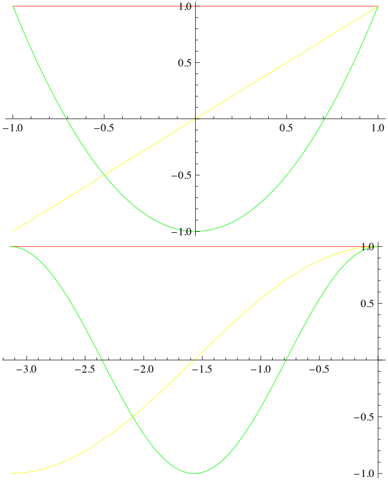

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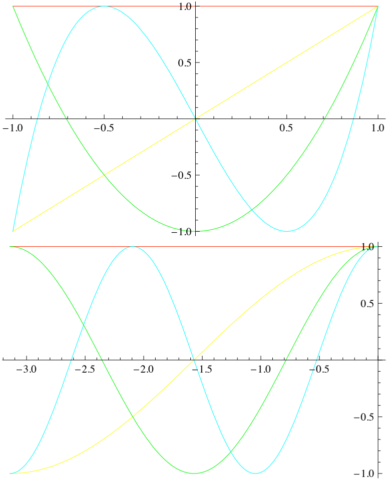

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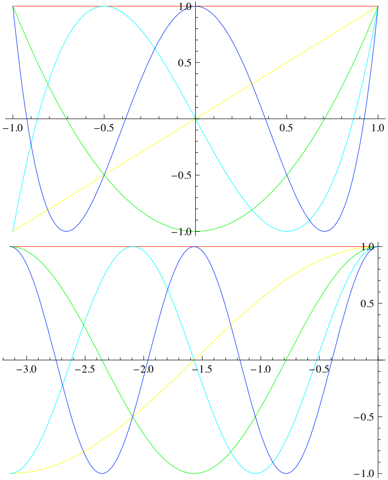

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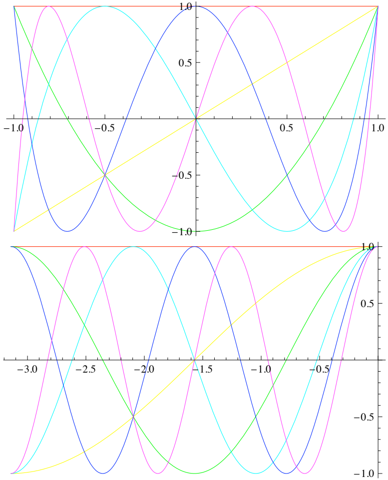

Two Spectrums

We start with a function throughout the sphere,

$$Y = y(r, \theta, \phi),$$

project onto spherical harmonics by

$$Y = \sum_{\ell=0}^{\infty} \sum_{m=-\ell}^{\ell} y_{\ell m}(r) Y_{\ell}^{m}(\theta, \phi),$$

and then project onto Chebyshev Polynomials

$$Y = \sum_{\ell=0}^{\infty} \sum_{m=-\ell}^{\ell} \left(\sum_{n=0}^{\infty} y_{lm}^{n} T_n(x) \right) Y_{\ell}^{m}(\theta, \phi).$$

Multi-Domain Approach

Computing Solutions

- Problem is MATLAB oriented
- Use MexS2Kit for Spherical Harmonic Transform Package S2Kit
- Use FFT (cleverly) for Chebyshev Transform
- Solve Linear system for y^n_{lm}
- Reverse both transforms, and voila!

Solution Stitching

Results

- Affirmative on spherically symmetric case
- Negatory on the assymetric case
- Negatory on the multiple shell case

Issues

- Matrices are Badly Badly Conditioned
- bicgstab works only so well, and if the matrix is sparse and banded
- Bookkeeping is difficult

Future Work

- Complete implementation of multi-domain spectral method
- Extend implementation to include moving spherical boundary and internally diffusing molecules
- Extend even further to include moving asymmetric boundary

Questions