Modeling Tumor Growth Using a Morphoelastic Biomechanical Model

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Contents

Tumor Growth Model

Mechanical Model
- Morphoelasticity
- Poroelasticity

Biochemical Model

Current Work

Tumor Growth Model

Mechanical Model

- Morphoelasticity
- Poroelasticity

Biochemical Model

Current Work

Tumor Growth

- Combining mechanical & biochemical models
- Morphoelasticity
- Poroelasticity
- Nutrient transport
- Tumor cell growth

- Mechanical equations

$$\rho\left(\frac{D\boldsymbol{v}}{Dt} + (\nabla\cdot\boldsymbol{v})\boldsymbol{v}\right) - \nabla\cdot\boldsymbol{\sigma} + \nabla p + \gamma\nabla\Phi = \boldsymbol{g},$$

$$\frac{D\boldsymbol{\varepsilon}}{Dt} + \boldsymbol{\varepsilon}\,\mathsf{skw}(\nabla\boldsymbol{v}) - \mathsf{skw}(\nabla\boldsymbol{v})\boldsymbol{\varepsilon} + (\mathsf{tr}(\boldsymbol{\varepsilon}) - 1)\,\mathsf{sym}(\nabla\boldsymbol{v}) = -\boldsymbol{G},$$

$$\nabla\cdot\boldsymbol{v} - \nabla\cdot(k\nabla p) = f.$$

- Biochemical equations

$$\frac{Dc}{Dt} + (\nabla\cdot\boldsymbol{v})c - \nabla\cdot(kc\nabla p + \lambda_N\nabla c) = -\Phi N(c),$$

$$\frac{D\Phi}{Dt} + (\nabla\cdot\boldsymbol{v})\Phi - F(\overline{\sigma})\Phi(1-\Phi)M(c) + r_{\mathsf{d}}\Phi = 0.$$

- Unknowns:

$$\boldsymbol{v},\ \boldsymbol{\varepsilon},\ p,\ c,\ \Phi$$

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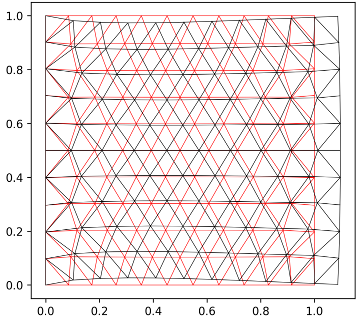
Current Work

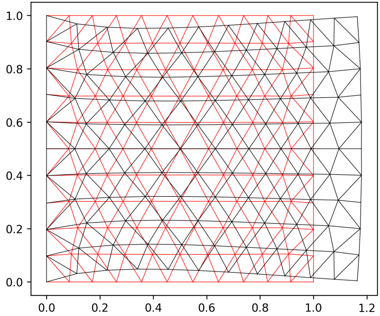
Morphoelasticity - Permanent Deformations

- Strain tensor evolution

$$\frac{D\boldsymbol{\varepsilon}}{Dt} + \boldsymbol{\varepsilon}\,\mathsf{skw}(\nabla \boldsymbol{v}) - \mathsf{skw}(\nabla \boldsymbol{v})\boldsymbol{\varepsilon} + (\mathsf{tr}(\boldsymbol{\varepsilon}) - 1)\,\mathsf{sym}(\nabla \boldsymbol{v}) = -\boldsymbol{G}$$

- $\boldsymbol{G} = \alpha\boldsymbol{\varepsilon}$.





Poroelasticity - Oscillations

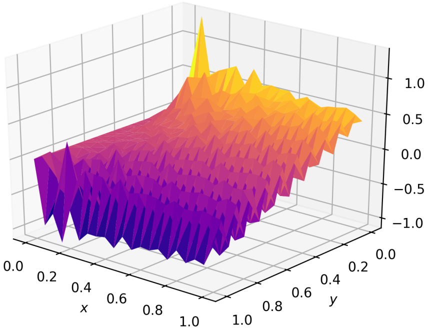
- Problematic equation

$$\nabla \cdot \boldsymbol{v} - \nabla \cdot (k \nabla p) = f$$

- Discretization

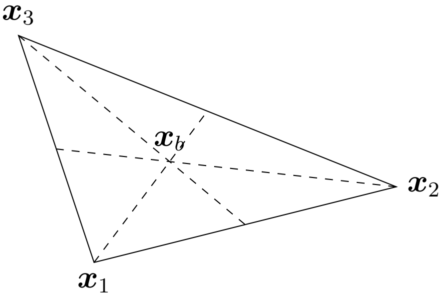
$$D\boldsymbol{v} + kL\boldsymbol{p} = \boldsymbol{f}$$

- Stabilization

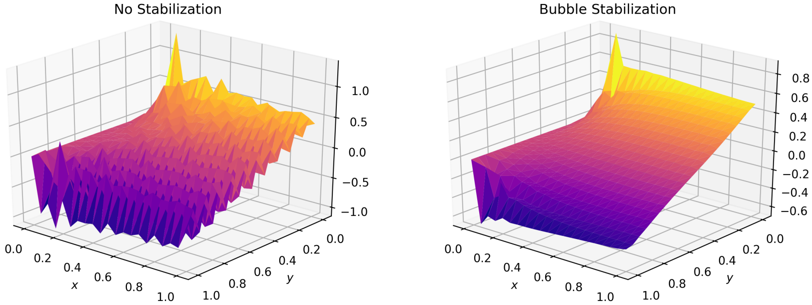


Stabilization - Bubble Functions

- Add bubble functions to test space
- $\varphi_b = 27\varphi_1\varphi_2\varphi_3$



Stabilization - Bubble Functions



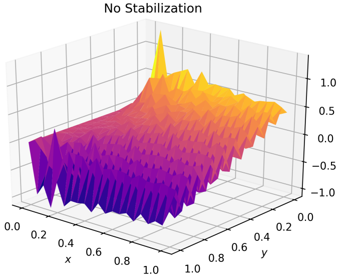
Stabilization - Diffusive

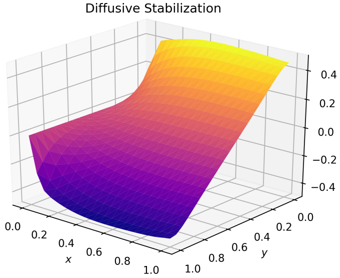
- Recall discretization

$$D\boldsymbol{v} + kL\boldsymbol{p} = \boldsymbol{f}$$

- Artifically increase diffusion

$$D\boldsymbol{v} + (k+\beta)L\boldsymbol{p} = \boldsymbol{f}^*$$





Stabilization - Determine Optimal β

- How to choose β?
- Simple case

$$\rho\left(\frac{D\boldsymbol{v}}{Dt}+(\nabla\cdot\boldsymbol{v})\boldsymbol{v}\right)-\nabla\cdot\boldsymbol{\sigma}+\nabla p=\boldsymbol{g},$$
$$\nabla\cdot\boldsymbol{v}-\nabla\cdot(k\nabla p)=f.$$

- 1D, uniform grid
- Discretization

$$\begin{pmatrix}\rho M+\theta S & -\Delta t D^{\top}\\ D & kL\end{pmatrix}\begin{pmatrix}\boldsymbol{v}\\ \boldsymbol{p}\end{pmatrix}=\cdots$$

- Decouple

$$(kL+\Delta t D(\rho M+\theta S)^{-1}D^{\top})\boldsymbol{p}=\cdots$$

Stabilization - Determine Optimal β

- Approximate $(\rho M + \theta S)^{-1}$
- Solve
$$\rho u - \theta u'' = \delta(x - x_i)$$
- Solution vector close to i'th column
- Obtain
$$\beta = \frac{h^2 \Delta t}{4\theta}$$

Tumor Growth Model

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- Poroelasticity

Biochemical Model

Current Work

Biochemical Model

- Paper by Roose
- Oxygen only nutrient
- Convection diffusion equation:

$$\frac{Dc}{Dt} + (\nabla \cdot \boldsymbol{v})c - \nabla \cdot (kc\nabla p + \lambda_N \nabla c) = -\Phi N(c)$$

- Nutrient absorption:

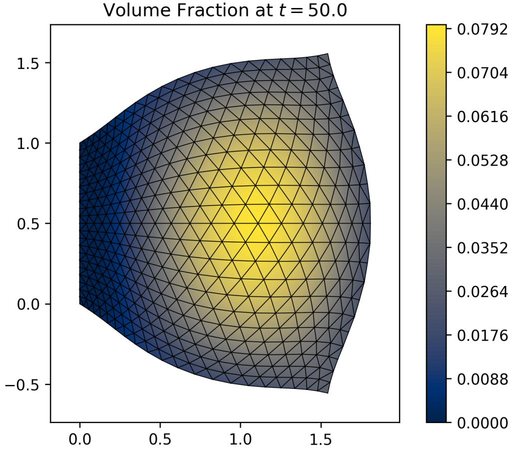
$$N(c) = \frac{N_{\mathsf{max}} c}{c_N + c}.$$

- Source function for Φ:

$$S = F(\overline{\sigma})\Phi(1-\Phi)M(c) - r_{\mathsf{d}}\Phi$$

Biochemical Model - Example

- Start with constant $\Phi = 0.01$
- Initial domain is the unit square



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Morphoelasticity

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Current Work

Current Work

- Quantifying total strain
- Different boundary conditions
- Collaboration with Spain

Sources

- T. Roose, P. A. Netti, L. L. Munn, Y. Boucher, and R. K. Jain, Solid stress generated by spheroid growth estimated using a linear poroelasticity model, Microvascular research, 66 (2003), pp. 204-212.
- G. Aguilar, F. Gaspar, F. Lisbona, and C. Rodrigo, Numerical stabilization of biot's consolidation model by a perturbation on the flow equation, International journal for numerical methods in engineering, 75 (2008), pp. 1282-1300.
- C. Vuik, F. Vermolen, M. van Gijzen, and M. Vuik, Numerical Methods for Ordinary Differential Equations, Delft Academic Press, 2 ed., 2016.

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