A finite element approach to solving a mathematical model for tumour evolution.

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Overview

Abstract

This talk considers a model for in vitro tumour evolution, in which the tumour is large and has been unable to grow blood vessels. Three formulations of the model will be presented, along with three finite element schemes. These include both fitted and unfitted sharp interface schemes, and a diffuse interface scheme. Some analytical results will be introduced. The results of a number of simulations will also be presented.

The model

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$$\begin{aligned} \Delta u &= 1 && \text{on } \Omega(t), \\ u &= \alpha V && \text{on } \Gamma(t), \\ V &= Q - \nabla u \cdot \boldsymbol{n} && \text{on } \Gamma(t). \end{aligned}$$

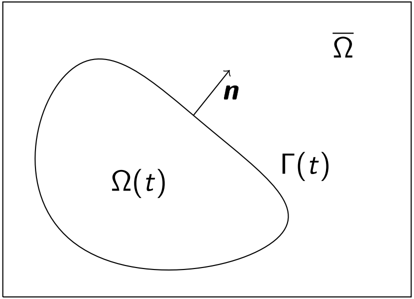


Figure: Curve $\Gamma(t)$, with interior Ω, both in $\overline{\Omega}$.

Formulations

The model

$$\begin{aligned} \Delta u &= 1 && \text{on } \Omega(t), \\ u &= \alpha V && \text{on } \Gamma(t), \\ V &= Q - \nabla u \cdot \boldsymbol{n} && \text{on } \Gamma(t). \end{aligned}$$

Formulation 1

$$\begin{aligned} \Delta u &= 1 && \text{on } \Omega(t) \\ \gamma \nabla u \cdot \boldsymbol{n} + u &= \alpha V && \text{on } \Gamma(t) \\ V = Q - \nabla u \cdot \boldsymbol{n} &+ \beta\kappa && \text{on } \Gamma(t) \end{aligned}$$

Formulation 2

$$\begin{aligned} \Delta u &= 1 && \text{on } \Omega(t) \\ \nabla u \cdot \boldsymbol{n} + \frac{u}{\alpha} &= Q && \text{on } \Gamma(t) \\ V = \frac{u}{\alpha} &+ \beta\kappa && \text{on } \Gamma(t) \end{aligned}$$

Formulation 3

$$\begin{aligned} \Delta u &= 1 && \text{on } \Omega(t) \\ \nabla u \cdot \boldsymbol{n} + \frac{u}{\alpha} &= Q && \text{on } \Gamma(t) \\ V = Q - \nabla u \cdot \boldsymbol{n} &+ \beta\kappa && \text{on } \Gamma(t) \end{aligned}$$

All formulations in one

$$g := \frac{\alpha V}{\gamma} \quad \text{or} \quad g := Q$$

$$\mu := \frac{1}{\alpha} \quad \text{or} \quad \mu := \frac{1}{\gamma}$$

$$f := Q - \nabla u \cdot \boldsymbol{n} \quad \text{or} \quad f := \frac{u}{\alpha}$$

The model

$$\begin{aligned} \Delta u &= 1 && \text{on } \Omega(t) \\ \nabla u \cdot \boldsymbol{n} + \mu u &= g && \text{on } \Gamma(t) \\ V &= f + \beta\kappa && \text{on } \Gamma(t) \end{aligned}$$

Parametric approach

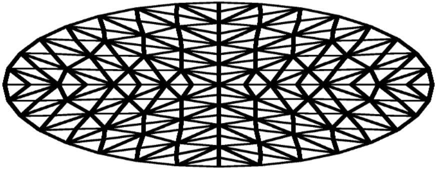
Parametric FEM form

$$\forall \phi_h \in \{\, \phi \in C(\Omega_h^n, \mathbb{R}) : \phi \text{ is linear on each element} \,\}$$

$$\int_{\Omega_h^n} \nabla u_h \cdot \nabla \phi_h \,\mathrm{d}v + \mu \int_{\Gamma_h^n} u_h \phi_h \,\mathrm{d}s + \int_{\Omega_h^n} \phi_h \,\mathrm{d}v - \int_{\Gamma_h^n} g_h \phi_h \,\mathrm{d}s = 0$$

$$\forall \boldsymbol{\rho}_h \in \{\, \boldsymbol{\rho} \in C(\Gamma_h^n, \mathbb{R}^3) : \boldsymbol{\rho} \text{ is linear on each element} \,\}$$

$$\int_{\Gamma_h^n} \frac{\boldsymbol{X}_h^{n+1} - \boldsymbol{X}_h^n}{dt} \cdot \boldsymbol{\rho}_h \,\mathrm{d}s + \beta \int_{\Gamma_h^n} \nabla_\Gamma \boldsymbol{X}_h^{n+1} \cdot \nabla_\Gamma \boldsymbol{\rho}_h \,\mathrm{d}s - \int_{\Gamma_h^n} \boldsymbol{f}_h \cdot \boldsymbol{\rho}_h \,\mathrm{d}s = 0$$



Details found in, among others, [Dziuk, 1990] and [Deckelnick et al, 2005].

Parametric numerical analysis results

$$\max_{\Omega\cup\Gamma} u \leq \max_{\Gamma} u \leq \frac{g}{\mu}$$

$$||\Delta u||^2_{L^2(\Omega)} + ||\nabla u||^2_{L^2(\Omega)} + ||u||^2_{L^2(\Omega)} \leq C$$

$$||\nabla u||^2_{L^2(\Gamma)} \leq C$$

$$||\nabla u \cdot n||^2_{L^\infty(\Gamma)} \leq C$$

$$||u - u_h||^2_{H^1(\Omega)} \leq Ch$$

$$\int_0^T ||\frac{\boldsymbol{X}^{n+1} - \boldsymbol{X}^n}{dt}||^2_{L^2(\Gamma)} \,\mathrm{d}t \quad + \quad \frac{\beta}{2} \sup_{0\leq n\leq N} ||(\nabla_\Gamma \boldsymbol{X}^n)||^2_{L^2(\Gamma)}$$
$$\leq C \int_0^T ||\boldsymbol{f}||^2_{L^2(\Gamma)} \,\mathrm{d}t + \frac{\beta}{2}||(\nabla_\Gamma \boldsymbol{X}^0)||$$

More results to come...

Parametric mesh properties

Volume (harmonic extension)

$$\begin{cases} \Delta \boldsymbol{u} = 0, & \text{on } \Omega \\ \boldsymbol{u} = V\boldsymbol{n}, & \text{on } \Gamma \end{cases}$$

Surface (tangential ω) [Elliott et al 1, 2016]

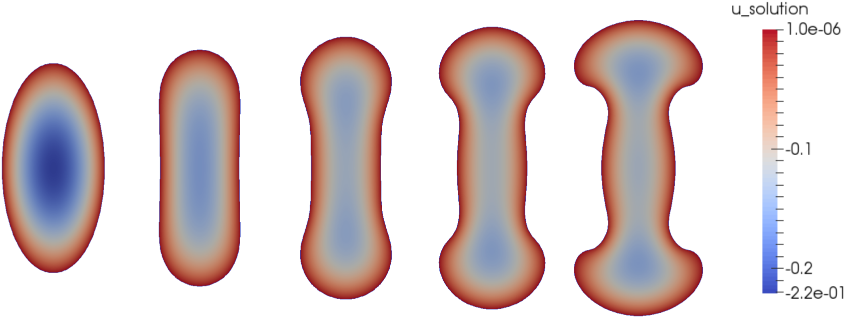
$$M' := M(\omega I + (1-\omega)NN^T)$$

for $\omega \in (0, 1]$.

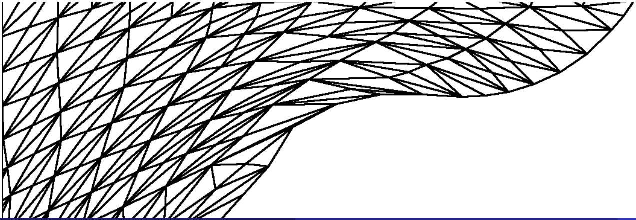
[Elliott et al 2, 2016]

Uses the DeTurck trick and harmonic map heat flow on a reference mesh to achieve good mesh properties, given an initial mesh velocity.

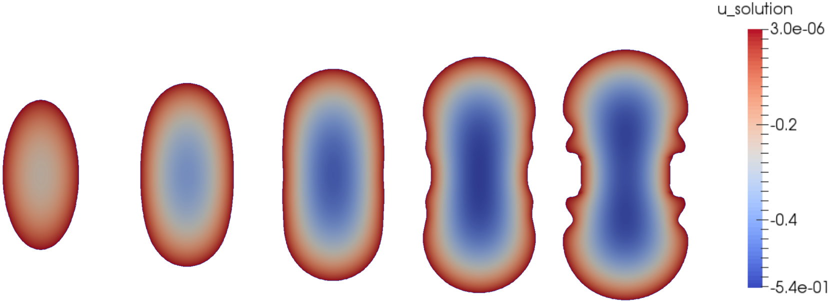
Parametric simulations



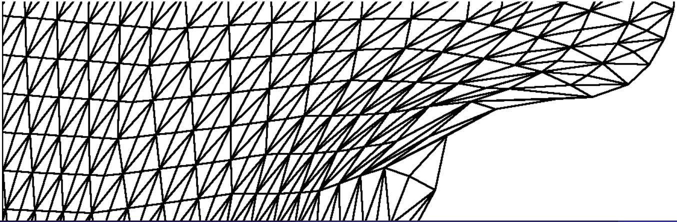
$Q = 0.5$, $\beta = 0.05$ and $\alpha = 10^{-6}$. At $t = 0, 2, 4, 6,$ and 8.



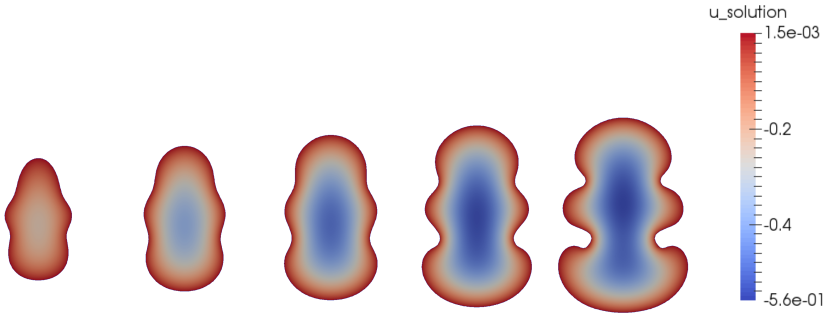
Parametric simulations



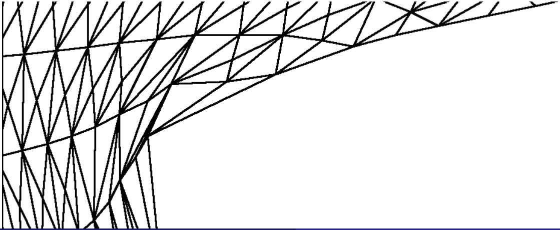
$Q = 1.0$, $\beta = 0.05$ and $\alpha = 10^{-6}$. At $t = 0, 0.7, 1.4, 2.1$, and 2.8.



Parametric simulations

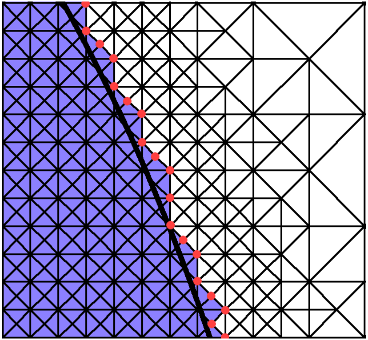


$Q = 1.0$, $\beta = 0.1$ and $\alpha = 10^{-3}$. At $t = 0, 0.7, 1.4, 2.1$, and 2.8.



Unfitted approach

Introduction



■ Boundary nodes.

■ Interior simplices.

$$\mathcal{T}_h := \{\, \mu \in \overline{\Omega}_h \mid \mu \text{ is inside or intersects } \Gamma_h \,\}$$

$$\mathcal{N}_h := \{\, \boldsymbol{p} \in \{\text{nodes}\} \mid \boldsymbol{p} \in \mu \text{ for some } \mu \in \mathcal{T}_h \text{ , and } \boldsymbol{p} \text{ is outside } \Gamma_h \,\}$$

More info in [Barrett et al, 1987] and [Dziuk et al, 2013].

Unfitted FEM form

$$\forall \boldsymbol{\rho}_h \in \{\, \boldsymbol{\rho} \in C(\Gamma_h^n, \mathbb{R}^2) \mid \boldsymbol{\rho} \text{ is linear on each element } \}$$

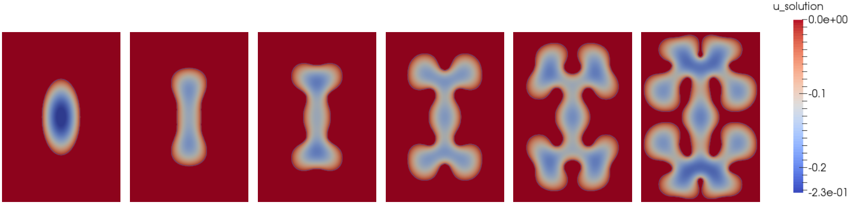
$$\int_{\Gamma_h^n} \frac{\boldsymbol{X}_h^{n+1} - \boldsymbol{X}_h^n}{dt} \boldsymbol{\rho}_h \,\mathrm{d}s \quad + \quad \beta \int_{\Gamma_h^n} \left(\nabla_\Gamma \boldsymbol{X}_h^{n+1} \cdot \nabla_\Gamma \boldsymbol{\rho_h} \right) \mathrm{d}s$$

$$= \quad \int_{\Gamma_h^n} \left(Q - \nabla u_h \cdot \boldsymbol{n}_h \right) \boldsymbol{\rho}_h \,\mathrm{d}s$$

$$\forall \phi \in \mathcal{W}_h := \{\, \phi \in C(\overline{\Omega}_h, \mathbb{R}) \mid \phi \text{ is linear on each element} \,\}$$

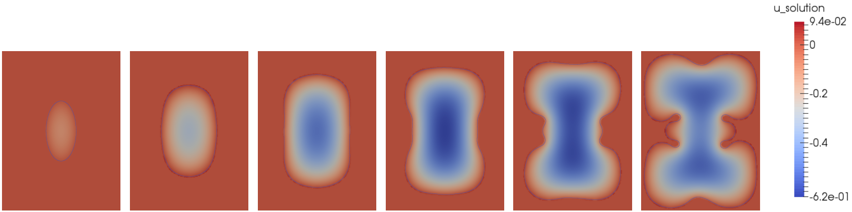
$$\int_{\mathcal{T}_h} \nabla u_h \nabla \phi_h \,\mathrm{dx} + \frac{1}{\gamma} \int_{\mathcal{N}_h} u_h \phi_h \,\mathrm{dx} = \int_{\mathcal{T}_h} \phi_h \,\mathrm{dx} + \frac{1}{\gamma} \int_{\mathcal{N}_h} \alpha V_h \phi_h \,\mathrm{dx}$$

Unfitted simulations



$Q = 0.5$, $\beta = 0.05$ and $\alpha = 10^{-6}$. At $t = 0, 6, 12, 18, 24$ and 30.

Unfitted simulations



$Q = 1.0$, $\beta = 0.05$ and $\alpha = 0.1$. At $t = 0, 1, 2, 3, 4$ and 5.

Phase field approach

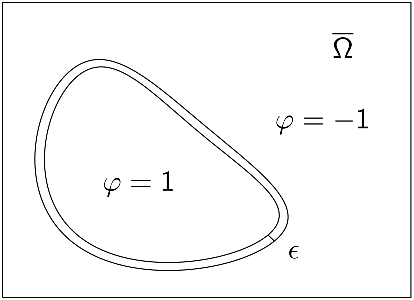


Figure: The phase field $\overline{\Omega}$. Here $\overline{\Omega}$ is a fixed domain that contains $\Gamma(t)$.

$$\zeta := \frac{1+\varphi}{2} \quad \delta := |\nabla \varphi|$$

Phase field FEM form

Only possible for $f = \frac{u}{\alpha}$, $\mu = \frac{1}{\alpha}$ and $g = Q$.

$\forall \rho_h \in \{\, \rho \in C(\overline{\Omega}_h, \mathbb{R}) : |\,\rho| \leq 1$ and ρ is linear on each element $\}$

$$\int_{\overline{\Omega}_h} \frac{\varphi_h^{n+1} - \varphi_h^n}{dt}(\rho_h - \varphi_h^{n+1})dx - \beta \int_{\overline{\Omega}_h} \nabla\varphi_h^{n+1} \cdot \nabla(\rho_h - \varphi_h^{n+1})dx$$
$$- \frac{\beta}{\epsilon^2} \int_{\overline{\Omega}_h} \varphi_h^{n+1}(\rho_h - \varphi_h^{n+1})dx + \frac{\pi}{4\epsilon} \int_{\overline{\Omega}_h} \frac{\overline{u}_h}{\alpha}(\rho_h - \varphi_h^{n+1})dx \geq 0$$

$\forall \phi_h \in \{\, \rho \in C(\overline{\Omega}_h, \mathbb{R}) : \rho$ is linear on each element $\}$

$$\int_{\overline{\Omega}_h} \zeta \nabla \overline{u}_h \nabla \phi_h \,\mathrm{d}\boldsymbol{x} + \int_{\overline{\Omega}_h} \delta \frac{\overline{u}_h}{\alpha} \phi_h \,\mathrm{d}\boldsymbol{x} = \int_{\overline{\Omega}_h} \delta Q \phi_h \,\mathrm{d}\boldsymbol{x} - \int_{\overline{\Omega}_h} \zeta \phi_h \,\mathrm{d}\boldsymbol{x}$$

Phase field numerical analysis results

$$\int_0^T ||\frac{\varphi_h^{n+1} - \varphi_h^n}{dt}||_{L^2}^2 \,\mathrm{d}t + \sup_t ||\nabla \varphi_h||_{L^2}^2 \leq C$$

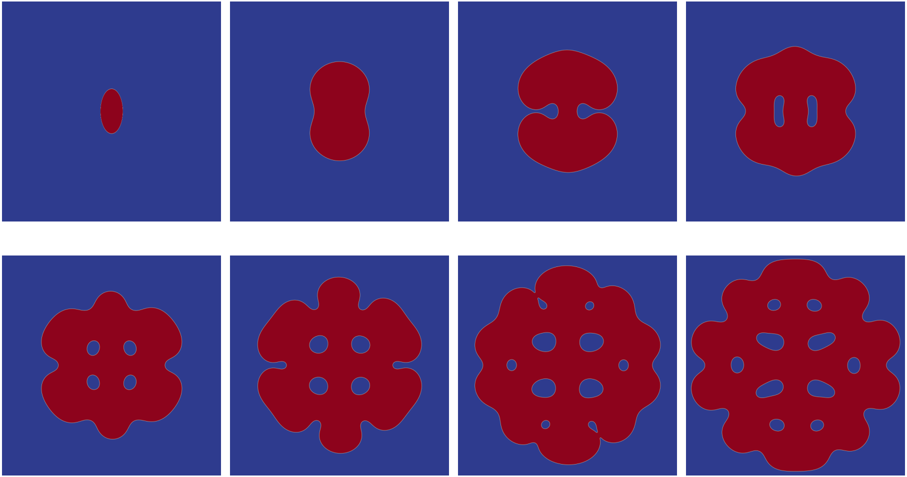
$$\int_0^T ||\nabla(\varphi_h^{n+1} - \varphi_h^n)||_{L^2}^2 \,\mathrm{d}t \leq C\Delta t$$

$$||u - u_h||_{W^1_{2,\zeta}}^2 + ||u - u_h||_{L^2_\delta(\overline{\Omega})}^2 \leq ch^2$$

- $\max_{\Omega \cup \Gamma} u \leq \max_\Gamma u \leq \alpha Q$,
- $\max_i u_i \leq C$

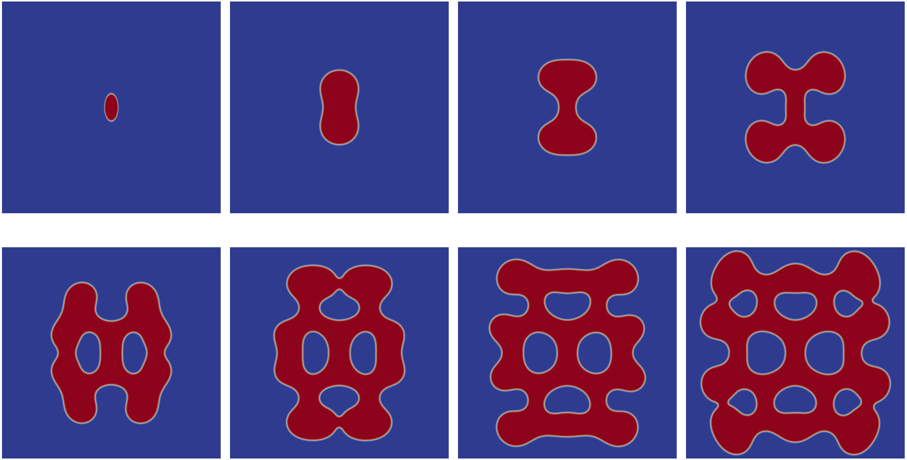
More results to come...

Phase field simulations



$Q = 1.0$, $\beta = 0.1$ and $\alpha = 0.1$. At $t = 0, 4, 8, 10, 12, 14, 16$ and 18.

Phase field simulations



$Q = 1.0$, $\beta = 0.1$ and $\alpha = 1.0$. At $t = 0, 12, 24, 36, 48, 60, 72$ and 84.

Summary

- A simple model for tissue growth
- Methods to preserve parametric mesh properties during the evolution of Ω
- An explanation of a simple unfitted method and the problem relating to self intersection of Γ
- A brief introduction to the phase field, including the limitations imposed upon the model

References

Elliott, Charles M and Fritz, Hans

On Approximations of the Curve Shortening Flow and of the Mean Curvature Flow based on the DeTurck trick

Dziuk, G

Numerische Mathematik An algorithm for evolutionary surfaces Subject classifications

Deckelnick, G and Elliott, Cm and Dziuk, K

Computation of geometric partial differential equations and mean curvature flow

Elliott, Charles M and Fritz, Hans

On algorithms with good mesh properties for problems with moving boundaries based on the Harmonic Map Heat Flow and the DeTurck trick

John W Barrett and Charles M Elliot

Fitted and Unfitted Finite-Element Methods for Elliptic Equations with Smooth Interfaces. IMA Journal of Numerical Analysis (1987) 7, pages 283–300.

Gerhard Dziuk and Charles M. Elliott

Finite element methods for surface PDEs. Acta Numerica, 22(April):289–396, 2013.

Questions?

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