Unraveling cell migration using image analysis and mathematical models

Dr Feng Wei Yang

University of Sussex

The Leverhulme Trust

F.W.Yang@sussex.ac.uk

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Outline

1. Cell tracking in a general sense
    - Segmentations
    - Cell (particle) tracking
    - Data analysis
2. Shape analysis for nuclear deformation
3. Experimental-driven modelling
    - Cell morphology reconstruction
    - Prediction on forcing
    - Detection on morphological changes
    - Advanced numerical techniques
    - Phase-field 8-point rule of thumb

About Ibidi

Dr Z. von Guttenberg

Dr E. Horn

Objectives

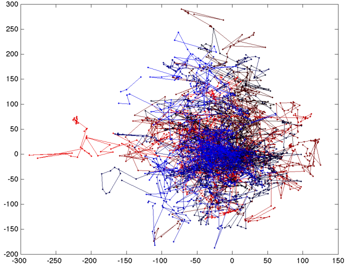
The human fibrosarcoma cell line HT-1080 obtained from DSMZ, Germany

Techniques based upon background removal

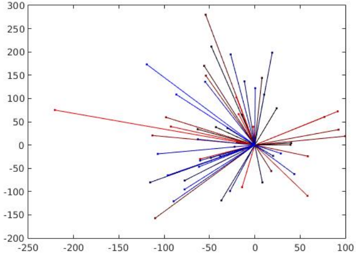
Techniques based upon active contour

Directions of migration

Spider plot



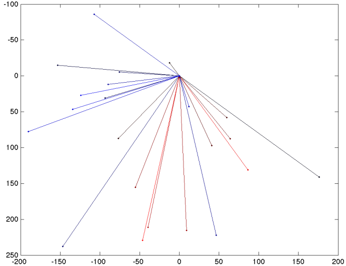
Star plot



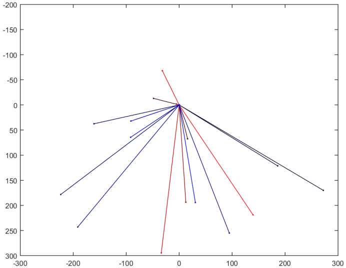
Directional migration

Directions of migration (part 2)

Background reconstruction



Active contour



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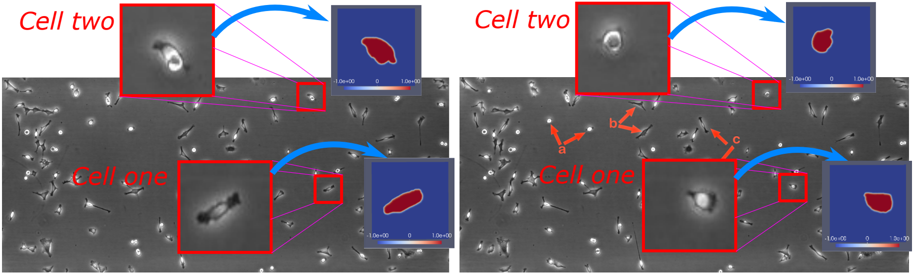
Optimal control for whole cell tracking

Prof A. Madzvamuse

Dr V. Styles

Dr C. Venkataraman

Individual cells



Our optimal control model

The mass constrained mean curvature flow with forcing:

$$\begin{cases} \boldsymbol{V}(\boldsymbol{x},t) & = (-\sigma H(\boldsymbol{x},t) + \eta(\boldsymbol{x},t) + \lambda_V(t))\,\boldsymbol{v}(\boldsymbol{x},t) \ \text{ on } \ \Gamma(t), t \in (0,T], \\ \Gamma(0) = \Gamma^0. \end{cases}$$

The phase-field approximation of the above equation - Allen-Cahn:

$$\begin{cases} \partial_t \phi(\boldsymbol{x},t) & = \triangle \phi(\boldsymbol{x},t) - \frac{1}{\epsilon^2} G'(\phi(\boldsymbol{x},t)) - \frac{1}{\epsilon}(\eta(\boldsymbol{x},t) - \lambda(t)) \ \text{ in } \ \Omega \times (0,T], \\ \nabla \phi \cdot \boldsymbol{\nu}_\Omega & = 0 \ \text{ on } \ \partial\Omega \times (0,T], \\ \phi(\cdot,0) & = \phi^0 \ \text{ in } \ \Omega. \end{cases}$$

Our optimal control model cont.

The objective functional:

$$J(\phi, \eta) = \frac{1}{2} \int_{\Omega} \left(\phi(\boldsymbol{x}, T) - \phi_{obs}(\boldsymbol{x})\right)^2 d\boldsymbol{x} + \frac{\theta}{2} \int_0^T \int_{\Omega} \eta(\boldsymbol{x}, t)^2 d\boldsymbol{x} dt,$$

and now we solve the minimisation problem:

$$min_{\eta} J(\phi, \eta), \text{ with } J \text{ given above.}$$

Our optimal control model cont.

The adjoint equation to help computing the derivative of the objective functional:

$$\begin{cases} \partial_t p(\boldsymbol{x}, t) = -\triangle p(\boldsymbol{x}, t) + \epsilon^{-2} G''(\phi(\boldsymbol{x}, t)) p(\boldsymbol{x}, t) & \text{in } \Omega \times [0, T), \\ p(\boldsymbol{x}, T) = \phi(\boldsymbol{x}, T) - \phi_{obs}(\boldsymbol{x}) & \text{in } \Omega, \end{cases}$$

and we update the control as

$$\eta^{\ell+1} = \eta^{\ell} - \alpha \left(\theta \eta^{\ell} + \frac{1}{\epsilon} p^{\ell} \right).$$

Numerical challenges

- Number of time steps
- Memory requirement (let's consider double precision and 100 time steps)
  - 2-D: 512^2 requires 0.4 gigabytes
  - 3-D: 512^3 requires 215 gigabytes

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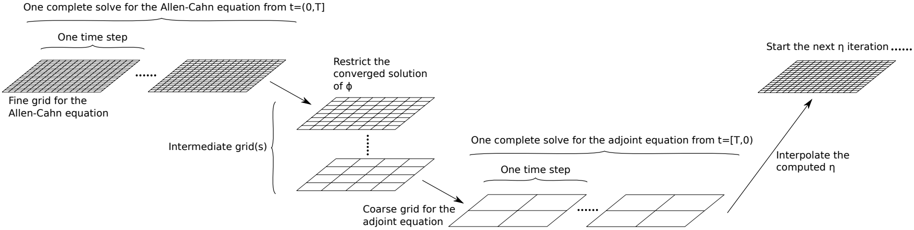
Two-grid solution strategy



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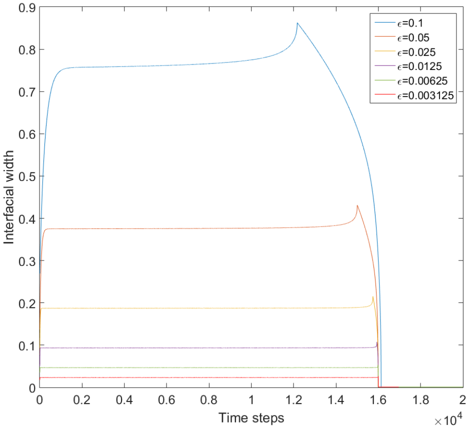
Compact scheme



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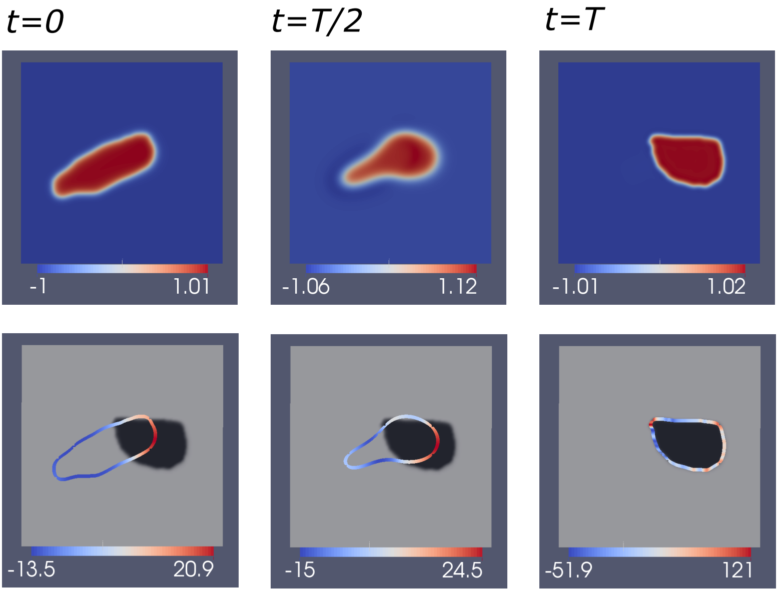
Cell one

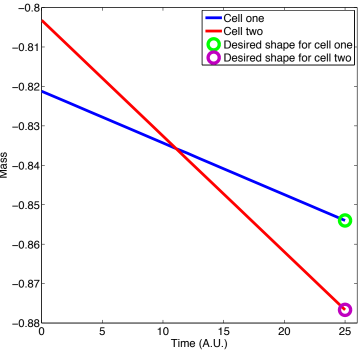


Cell one video

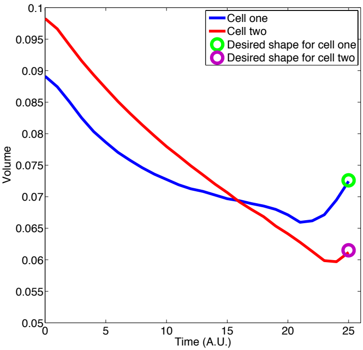
Cell two video

Analysis through tracking morphological changes

$\int_\Omega \phi d\boldsymbol{x}$



$\int_{\{\phi>0\}} 1 d\boldsymbol{x}$



Real world example (2)

Euler number for topological changes

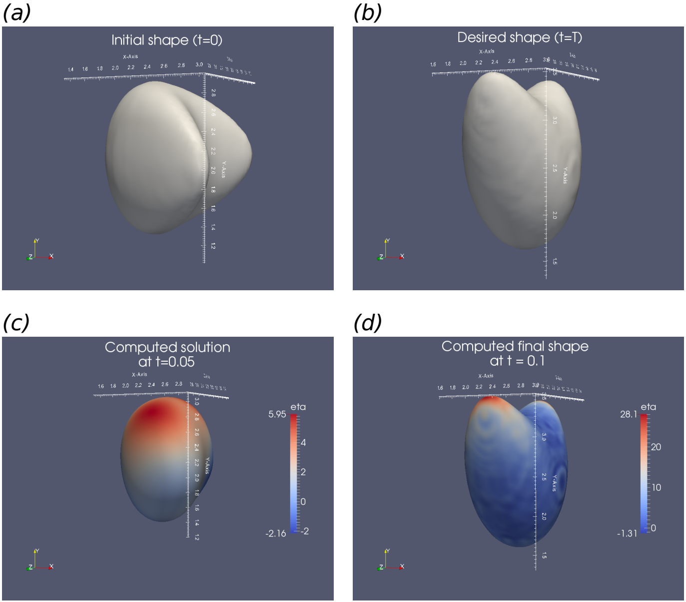
We compute this Euler number for these time steps with an "optimized" control η:

$$\mathcal{X} = \frac{1}{2\pi(a-b)} \int_{\Omega(a,b)} \left(-\triangle\phi + \frac{\nabla|\nabla\phi|^2 \cdot \nabla\phi}{2|\nabla\phi|^2} \right) dx.$$

Q. Du et al. *J. Appl. Math.*, 2005

Real world example (2)

A 3-D example


(a)
Initial shape (t=0)
(b)
Desired shape (t=T)
(c)
Computed solution
at t=0.05
eta
5.95
4
2
0
-2
-2.16
(d)
Computed final shape
at t = 0.1
eta
28.1
20
10
0
-1.31

A 3-D example video

The end

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Journal of Computational Physics, 2016