Title: Phase-field model for cellular monolayers : a cancer cell migration studyauthors : Benoit Palmieri and Martin Grant

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Abstract: Recent experimental work [1] suggests that the increased motility of cancer cells observed in a confluent monolayer of normal cells is due to the mechanical mismatch between the two cell types. The soft cancer cell undergoes large deformations and can squeeze between small channels defined by the space between the normal cells. We developed a phase-field model description of cellular monolayers to study such a process. The system is setup as a free-boundary problem where each cell is a highly deformable soft body [2]. The motion of each cell is described by a persistent random walk where the velocities and persistent times can be obtained from experimental observations. Our model is used to test the hypothesis that the mechanical mismatch alone increases the motility of softer cells when all other parameters are the same.[1] Lee et al. Biophys. J. vol. 102 p. 2731 (2012).[2] Najem et al. Europhys. Lett. vol. 102 p. 16001 (2013).

Phase-field model for cellular monolayers : a cancer cell migration study

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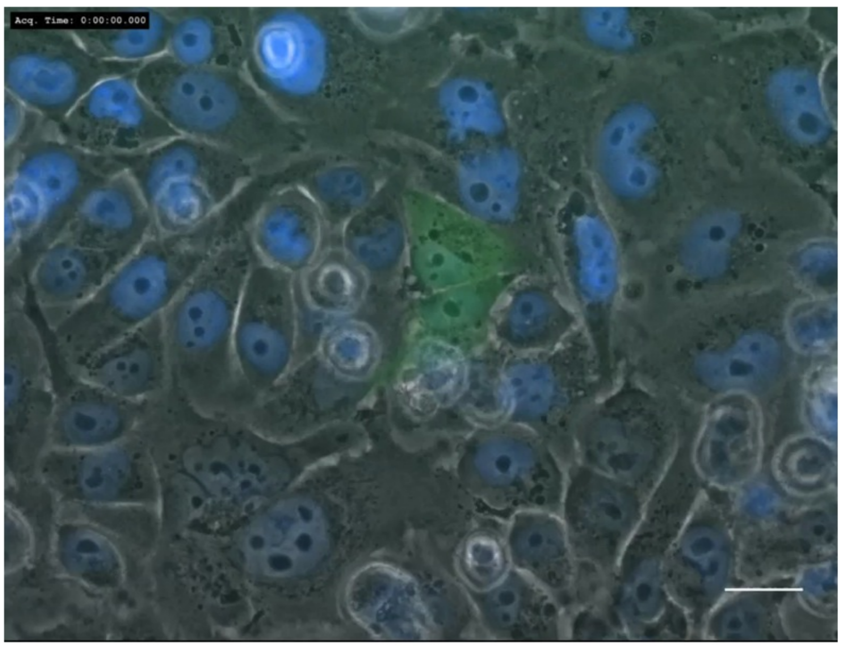
Experiments : Motile Cancer Cells in a monolayer of Normal or other Cancer cells

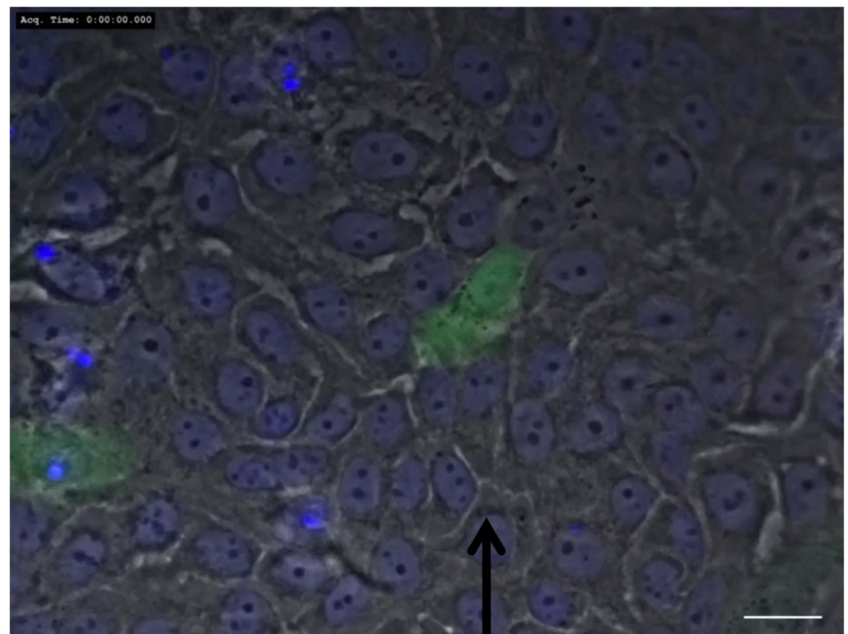
Lee et al., Biophys. J., **102**, 2732 (2012)

Cancer cell monolayer

Cancer cell in a monolayer of normal cells

Acquisition time - hours





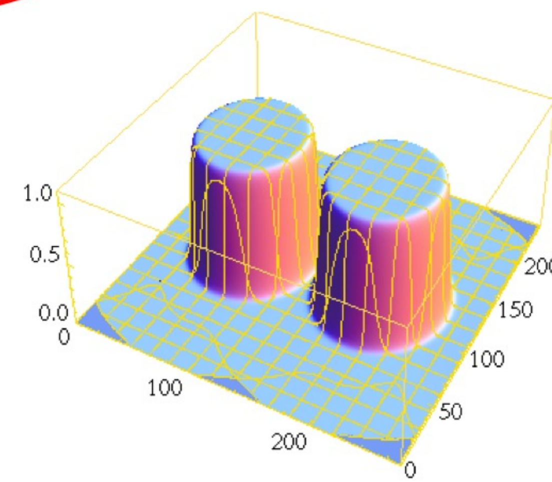
Increased Motility

Cancer cells are 3-4 times softer ➡ Watermelon seed mechanism?

Phase-field model for Cells: Highly deformable elastic bodies

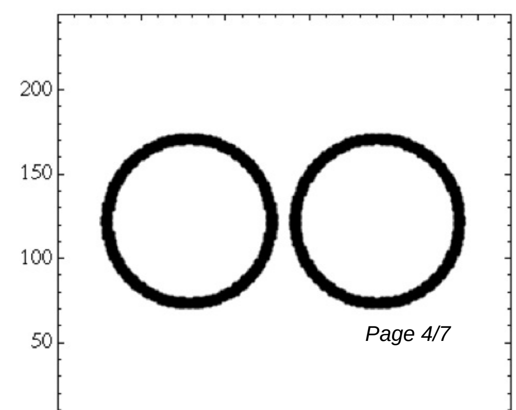
$$\mathcal{F}_n = \int dx \int dy \left[\sum_n \left\{ \gamma_n (\nabla \phi_n)^2 + a_n \phi_n^2 (\phi_n - 1)^2 \right\} + \sum_{n,m \neq n} \kappa \phi_n^2 \phi_m^2 \right]$$

Energy cost for overlapping cells



For each cell	ϕ_n	$=$	1	inside the cell
		$=$	0	outside the cell

Cell Interface width: $\lambda_n = \left(\frac{30\gamma_n}{a_n} \right)^{1/2}$



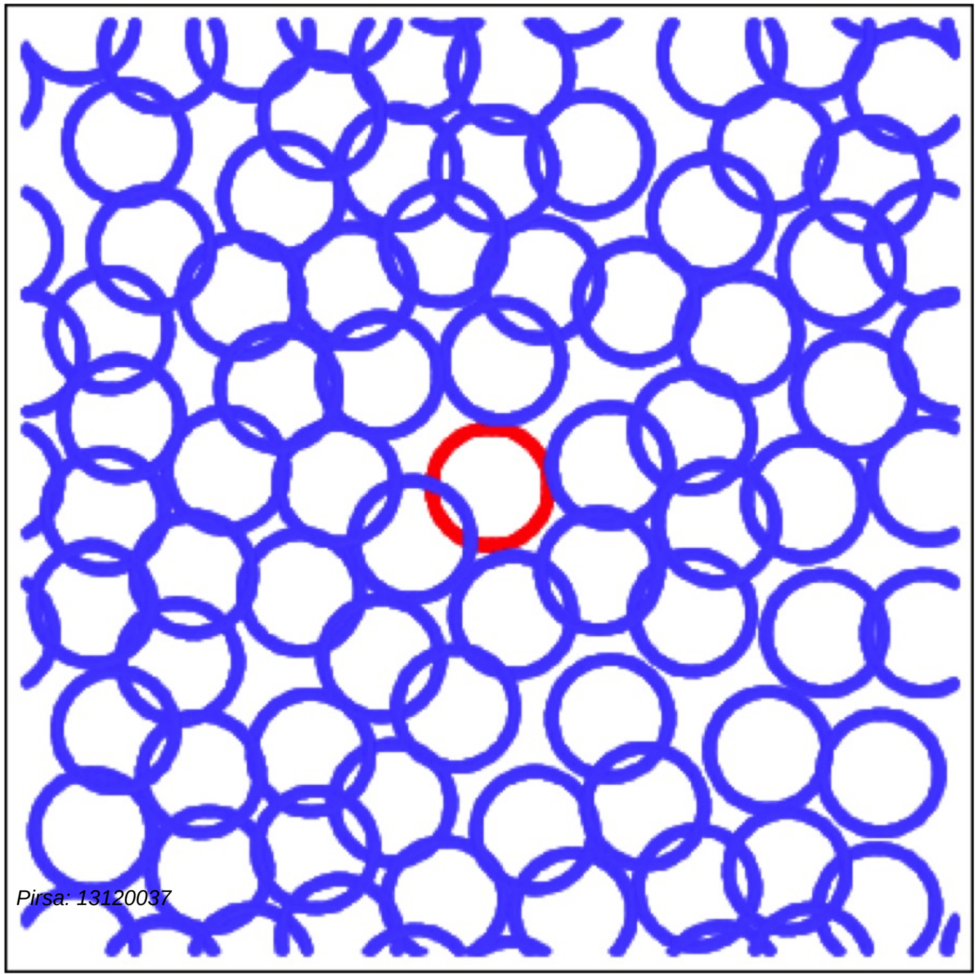
Deformation of cell boundary: $R'_n = R_n + \epsilon \cos k\theta$

$$\Delta \mathcal{F}_{def} = \frac{\epsilon^2 (k^2 - 1/2)\pi}{R_n} \left(\frac{\gamma_n a_n}{30} \right)^{1/2}$$

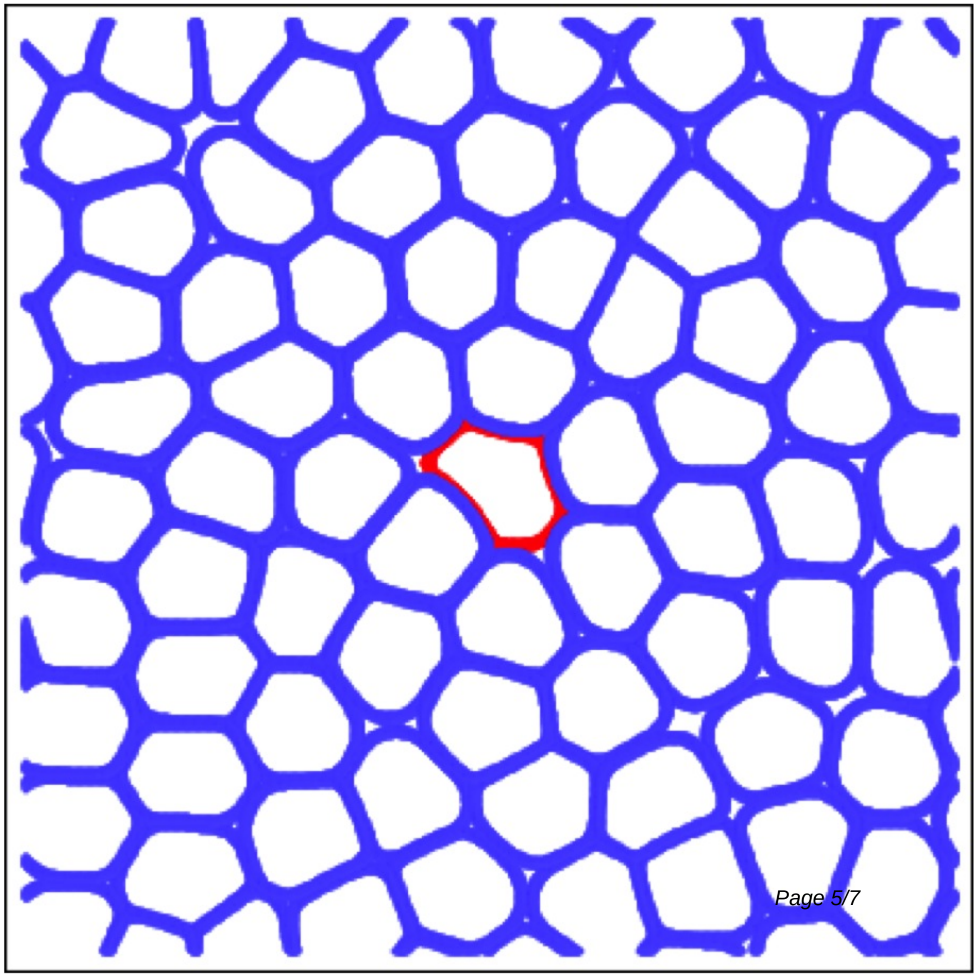
Numerical Simulations : all model parameters can be measured/estimated by experiments

Red cell (cancer cell) is 3 times softer than the others

Aging – no velocity



Persistent Random walk for each cell



Conclusions

Future avenues:

- 1 soft cell vs all normal cells.
- Follow cell deformation as it migrates.
- Cell internal degrees of freedom.
- Cell-Cell adhesion
- Other applications
    1. Soft glasses[1].
    2. Confluent monolayers response to external stresses and forces[2].
    3. …

Talk to me

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ISRAEL SCIENCE FOUNDATION

Fonds de recherche sur la nature et les technologies Québec

NSERC CRSNG

The Azrieli Foundation

Posdoctoral fellowship opportunities for Canadians!

1. Kajiya et al. Soft Matter (2013).
2. Pietuch et al. Soft Matter (2013).

Phase-field model for Cells: Elastic bodies with a free-boundary

Dynamics:
(Conserved Field)[1,2]

$$\frac{\partial \phi_n}{\partial t} + \mathbf{v}_n \cdot \nabla \phi_n = D_n \nabla^2 \frac{\delta \mathcal{F}}{\delta \phi_n}$$

→ Cell Shape rearrangement

Cell translation : Persistent Random Walk[3]

Force due to the other cells

$$\gamma \mathbf{v}_n = \gamma \mathbf{v}_0^{\dagger} + \int dx \int dy \; 4\phi_n \left(\nabla \phi_n\right) \sum_{m \neq n} \kappa \phi_m^2$$

$\mathbf{v}_0^{\dagger}$ has a constant amplitude v_0.
Random time between reorientation events:
(exponential distribution)

$$P(t_r)dt_r = \frac{1}{\tau} e^{-t_r/\tau} dt_r$$

1. Hohenberg and Halperin, Rev. Mod. Phys (1997).
2. Wise et al. J. Theor. Biol. (2008).