An agent-based model for cell collective dynamics

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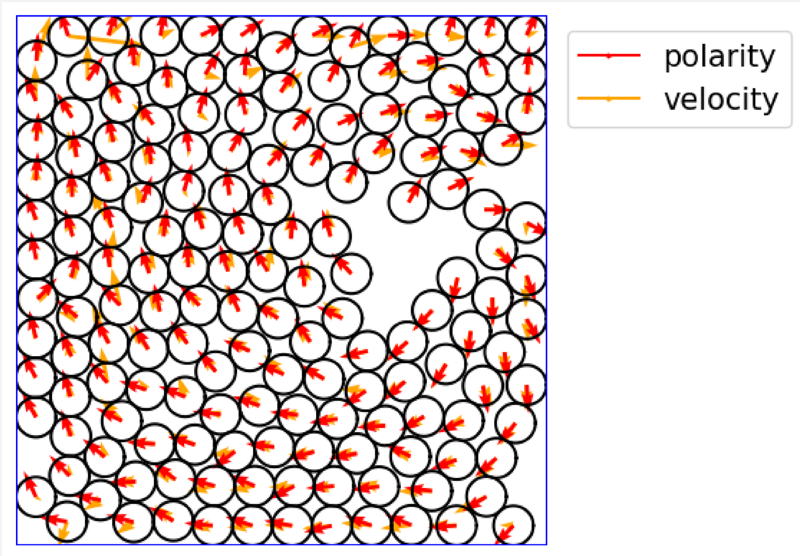
1. Introduction

Collective cell movements are observed during different important phases of epithelial tissue remodelling. The aim of this study is to proposed a mathematical and computational agent-based model that describes cells dynamics in a fixed domain with wall border.

Specifically, the goal is to represent cell collective dynamics over time, and the intensity of cell-cell contact.

2. Geometrical description of the system



We consider N cells, moving in a fixed two-dimensional square domain Ω. Each cell is represented as a hard-sphere of radius $R_0 > 0$ and has a position $\boldsymbol{X}_k(t) \in \mathbb{R}^2$, a velocity $\boldsymbol{V}_k(t) \in \mathbb{R}^2$, and a polarity $\boldsymbol{P}_k(t) \in \mathbb{S}^1$. We denote the vectors of all positions, all velocities and all polarities by:

- $\boldsymbol{X} = (\boldsymbol{X}_k)_k \in \mathbb{R}^{2N}$
- $\boldsymbol{V} = (\boldsymbol{V}_k)_k \in \mathbb{R}^{2N}$
- $\boldsymbol{P} = (\boldsymbol{P}_k)_k \in (\mathbb{S}^1)^N$

3. Mathematical model

Dynamics of the positions:

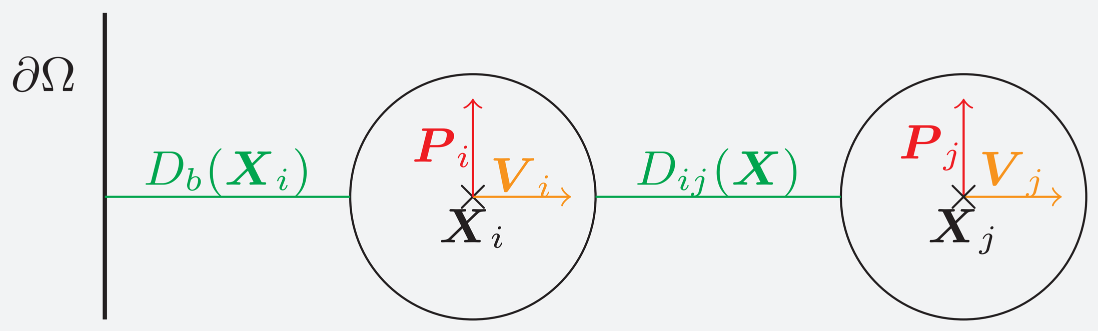
$$\boxed{\frac{d\boldsymbol{X}}{dt} = \boldsymbol{V}}$$

Dynamics of the velocities:

$$\boxed{\boldsymbol{V} = \mathrm{Proj}_{\mathcal{C}_{\boldsymbol{X}}}(c\boldsymbol{P} + \gamma \boldsymbol{F}(\boldsymbol{X}))}$$

- Active force driven by the polarity
- Hard repulsion: projection onto the set of admissible velocities $\mathcal{C}_{\boldsymbol{X}}$:

$$\mathcal{C}_{\boldsymbol{X}} = \{\boldsymbol{V} \in \mathbb{R}^{2N} \,|\, \forall i < j,\ D_{i,j}(\boldsymbol{X}) = 0 \implies \nabla D_{i,j}(\boldsymbol{X}) \cdot \boldsymbol{V} \geqslant 0,$$
$$\forall i,\ D_b(\boldsymbol{X}_i) = 0 \implies \nabla D_b(\boldsymbol{X}_i) \cdot \boldsymbol{V}_i \geqslant 0\}$$



- Soft attraction-repulsion force $\boldsymbol{F} = (\boldsymbol{F}_k)_{k=1,\dots,N}$ derived from a potential W[1]:

$$\mathbf{F}_k(\boldsymbol{X}) = \sum_{j=1}^{N} \nabla_{\boldsymbol{X}_k} W(\|\boldsymbol{X}_k - \boldsymbol{X}_j\|) \mathbb{1}_{\{\|\boldsymbol{X}_k - \boldsymbol{X}_j\| \leqslant R_{\mathrm{int}}^{\mathrm{ar}}\}}, \quad W(r) = -\kappa \left(\frac{r^2}{2} - \frac{r^3}{3D_c}\right)$$

Dynamics of the polarities:

$$\boxed{d\boldsymbol{P}_k = \mathrm{Proj}_{\boldsymbol{P}_k^{\perp}} \circ \left(\mu\,(\overline{\boldsymbol{P}}_k - \boldsymbol{P}_k)\,dt + \delta \left(\frac{\boldsymbol{V}_k}{\|\boldsymbol{V}_k\|} - \boldsymbol{P}_k\right) dt + \sqrt{2D}\,(d\mathbf{B}_t)_k\right)}$$

- Alignment to the local averaged polarity $\overline{\boldsymbol{P}}_k$ (Viscek-type interaction [2])

$$\overline{\boldsymbol{P}}_k = \frac{\sum_{j, \|\boldsymbol{X}_j - \boldsymbol{X}_k\| \leqslant R_{\mathrm{int}}^{\mathrm{po}}} \boldsymbol{P}_j}{\left\| \sum_{j, \|\boldsymbol{X}_j - \boldsymbol{X}_k\| \leqslant R_{\mathrm{int}}^{\mathrm{po}}} \boldsymbol{P}_j \right\|}$$

- Relaxation to the velocity direction $\frac{\boldsymbol{V}_k}{\|\boldsymbol{V}_k\|}$
- Gaussian white noise: $(d\mathbf{B}_t)_k$
- Projection to keep the polarity of norm 1

4. Discretization

Position:

$$\boldsymbol{X}^{n+1} = \boldsymbol{X}^n + \Delta t \boldsymbol{V}^{n+1}$$

Velocity [3]:

We transform the projection problem into the following optimization one, solved using the Uzawa algorithm:

$$\boldsymbol{V}^{n+1} = \underset{\boldsymbol{V} \in \mathcal{C}_{\boldsymbol{X}^n}^{\Delta t}}{\mathrm{argmin}} \frac{1}{2} \left\| \boldsymbol{V} - c\boldsymbol{P}^{n+1} - \gamma \mathbf{F}(\boldsymbol{X}^n) \right\|^2.$$

Polarity [4]:

Denoting $\boldsymbol{P}_k^n = (\cos(\theta_k^n), \sin(\theta_k^n))^T$, the polarity angle θ_k^n is obtained by the semi-implicit scheme:

$$\theta_k^{n+1} = \theta_k^n + 2\,(\theta[\boldsymbol{Q}_k^n] - \theta_k^n) + \sqrt{2D\Delta t}\,\boldsymbol{\xi}_k^n$$

with $\boldsymbol{Q}_k^n$ defined by:

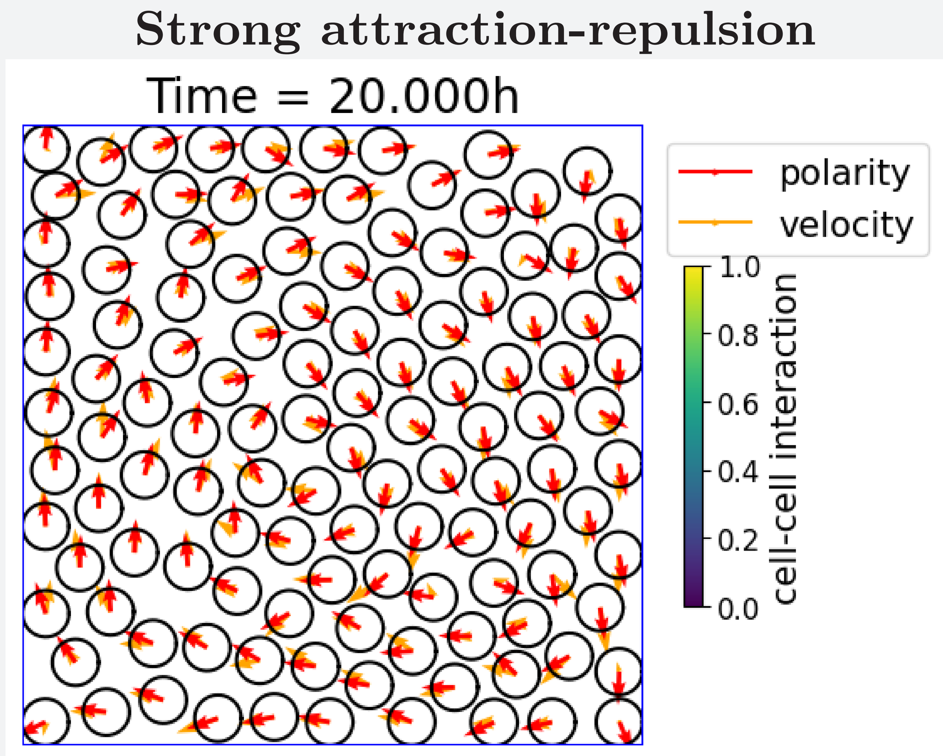
$$\boldsymbol{Q}_k^n = \boldsymbol{P}_k^n + \frac{\Delta t}{2} \left(\mu\,(\overline{\boldsymbol{P}}_k^n - \boldsymbol{P}_k^n) + \delta \left(\frac{\boldsymbol{V}_k^n}{\|\boldsymbol{V}_k^n\|} - \boldsymbol{P}_k^n\right)\right)$$

5. Parameters

Cells radius	R_0	7.5	μm	[5]
Cells comfort radius	R_c	9.5	μm	Numerical calibration
Cells attraction-repulsion interaction radius	$R_{\mathrm{int}}^{\mathrm{ar}}$	19	μm	Numerical calibration
Cells polarity interaction radius	$R_{\mathrm{int}}^{\mathrm{po}}$	60	μm	[5]
Cell speed	c	21.6	$\mu\mathrm{m\,h^{-1}}$	[5]
Angular diffusion	D	0.96	$\mathrm{rad^2\,h^{-1}}$	[5]
Relaxation parameter: polarity to mean polarity	μ	6.2	$\mathrm{rad\,h^{-1}}$	[5]
Relaxation parameter: polarity to velocity	δ	6.2	$\mathrm{rad\,h^{-1}}$	[5]
Rigidity constant	κ	16.10^4	$\mathrm{pN}\,\mu\mathrm{m}^{-1}$	Numerical calibration
Inverse friction coefficient	γ	10^{-4}	$\mathrm{pN^{-1}h^{-1}}\mu\mathrm{m}$	Numerical calibration

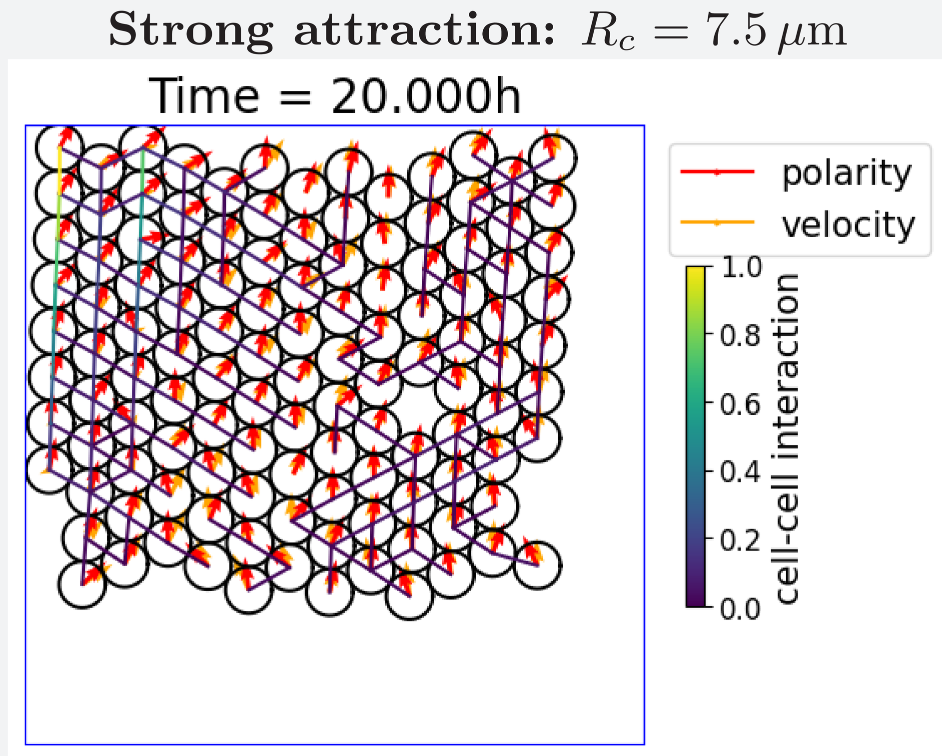
6. Numerical results

Strong attraction-repulsion



- Rotating movement
- Low number of contacts
- Compressibility

Strong attraction: $R_c = 7.5\,\mu m$



- Up-down flocking motion
- Cells glued together
- Incompressibility

7. Conclusion & Perspective

Conclusion:

We proposed a new framework to describe and simulate collective cell movement, combining a Viscek-type description of the cell dynamics and a hard contact model. The model is capable to recover the order-disorder phase transition of the flock, as well as the jamming effect in high density regimes.

Perspectives:

- Derive a macroscopic model
- Incorporate other cellular events (e.g. apoptosis, cell division)

8. Acknowledgements

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9. References

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