An agent-based model for cell collective dynamics

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May 24th 2024

Introduction

Context: ANR MAPEFLU project in collaboration with biophysicists (IGBMC, Strasbourg) and biologists (Institut Pasteur).

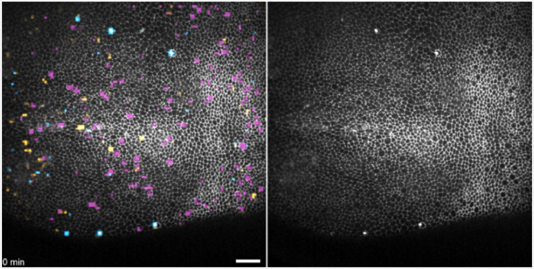


Figure: Villars et Letort et al., 2023, BiorXiv

Objectif: Design a mathematical and computational model to study the role of apoptosis (*i.e.* programmed cell death) on collective cells dynamics.

Summary

I. Mathematical model

- Positions and velocity dynamics
- Polarity dynamics
- Well-posedness
- Apoptosis in the model

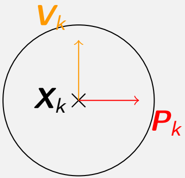
II. Numerical discretization

III. Numerical experiment

Model

There are N cells that evolve in a $2D$ space Ω. Each cell has a position $\boldsymbol{X}_k \in \mathbb{R}^2$, a velocity $\boldsymbol{V}_k \in \mathbb{R}^2$, a polarity $\boldsymbol{P}_k \in \mathbb{S}^1$, which described the preferred direction, and a radius $\boldsymbol{R}_k(t) \in [0, R_{\max}]$.

- positions: $\boldsymbol{X} = (\boldsymbol{X}_k)_k \in \mathbb{R}^{2N}$
- velocities: $\boldsymbol{V} = (\boldsymbol{V}_k)_k \in \mathbb{R}^{2N}$
- polarities: $\boldsymbol{P} = (\boldsymbol{P}_k)_k \in (\mathbb{S}^1)^N$
- radii of the cells: $\boldsymbol{R} = (\boldsymbol{R}_k)_k \in [0, R_{\max}]^N$
- apoptosis states: $\boldsymbol{\alpha} = (\boldsymbol{\alpha}_k)_k \in \{0, 1\}^N$



Model ingredient

The following model includes three ingredients

- Vicsek-type interaction[1]
- contact forces[2]
- soft attraction-repulsion forces[3]

Adapted from a model validated against experimental data[4].

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[1] T. Vicsek, A. Czirók, E. Ben-Jacob, *et al.*, "Novel type of phase transition in a system of self-driven particles," *Phys. Rev. Lett.*, vol. 75, no. 6, p. 1226, 1995.

[2] B. Maury and J. Venel, "A discrete contact model for crowd motion," *ESAIM Math. Model. Numer. Anal.*, vol. 45, no. 1, pp. 145–168, 2011.

[3] C. Beatrici, C. Kirch, S. Henkes, *et al.*, "Comparing individual-based models of collective cell motion in a benchmark flow geometry," *Soft Matter*, vol. 19, no. 29, pp. 5583–5601, 2023.

[4] S. L. Vecchio, O. Pertz, M. Szopos, *et al.*, "Spontaneous rotations in epithelia as an interplay between cell polarity and boundaries," *Nature Physics*, 2024.

Equations on $\boldsymbol{X}$, $\boldsymbol{V}$ and $\boldsymbol{P}$

Positions dynamics

$$\frac{d\boldsymbol{X}_k(t)}{dt} = \boldsymbol{V}_k(t).$$

Velocities dynamics:

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

Polarity dynamics:

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

Equation on $\boldsymbol{V}$: soft attraction-repulsion force

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

$\boldsymbol{F} = (\boldsymbol{F}_k)_{k=1,\dots,N}$ is described by:

$$\boldsymbol{F}_k(\boldsymbol{X}) = \sum_{j, \|\boldsymbol{X}_k - \boldsymbol{X}_j\| \leqslant R_{\text{int}}^{\text{ar}}} \nabla_{\boldsymbol{X}_k} W(\|\boldsymbol{X}_k - \boldsymbol{X}_j\|)$$

We consider the following interaction potential [3]:

$$W(r) = -\kappa \left(\frac{r^2}{2} - \frac{r^3}{3D_c} \right)$$

γ is the inverse friction coefficient
κ is the rigidity constant
R_{int}^{ar} is the radius of cells polarity interaction
D_c is the diameter of cells comfort zone.

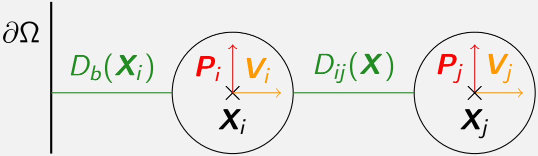
Equation on $\boldsymbol{V}$: contact interactions

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

Set of admissible velocities :

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

- $D_{i,j}(\boldsymbol{X}) = \|\boldsymbol{X}_i - \boldsymbol{X}_j\| - \boldsymbol{R}_i - \boldsymbol{R}_j$ the distance between the i-th and j-th cells.
- $D_b(\boldsymbol{X}_i) = \inf_{\boldsymbol{y} \in \partial\Omega} \|\boldsymbol{y} - \boldsymbol{X}_i\| - \boldsymbol{R}_i$ the distance between the i-th cell and the boundary.



Equation on $\boldsymbol{P}$: Vicsek-like model

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

- Alignment of the polarity (Vicsek-type interactions [1]):
  $$\overline{\boldsymbol{P}}_k = \frac{\sum_{j, \|x_j - x_k\| \leqslant R_{\text{int}}^{\text{po}}} \boldsymbol{P}_j}{\left\| \sum_{j, \|x_j - x_k\| \leqslant R_{\text{int}}^{\text{po}}} \boldsymbol{P}_j \right\|}$$
- Relaxation to the velocity direction: $\frac{\boldsymbol{V}_k}{\|\boldsymbol{V}_k\|}$
- Gaussian white random noise: dB_t
- Projection on $\boldsymbol{P}_k^\perp$ so that the polarity remains of norm 1

$R_{\text{int}}^{\text{po}}$ is the radius of polarity
μ and δ are relaxation parameters
D is the angular diffusion

Well-posedness: reformulation of the systems

- Polar formula for the polarity: $\boldsymbol{P}_k = (\cos(\theta_k), \sin(\theta_k))^T$
- The equation on $\boldsymbol{P}$ becomes:

$$\frac{d\theta_k}{dt}\begin{pmatrix} -\sin(\theta_k) \\ \cos(\theta_k) \end{pmatrix} = \left[\begin{pmatrix} -\sin(\theta_k) \\ \cos(\theta_k) \end{pmatrix} \cdot \left(\mu \bar{\boldsymbol{P}}_k + \delta \frac{\boldsymbol{V}_k}{\|\boldsymbol{V}_k\|}\right)\right]\begin{pmatrix} -\sin(\theta_k) \\ \cos(\theta_k) \end{pmatrix}$$

- denoting $\bar{\theta}_k$ and ψ_k the angles of the vectors $\bar{\boldsymbol{P}}_k$ and $\boldsymbol{V}_k / \|\boldsymbol{V}_k\|$

$$\frac{d\theta_k}{dt} = \mu \sin(\bar{\theta}_k - \theta_k) + \delta \sin(\psi_k - \theta_k).$$

- The system becomes: $\boxed{\frac{d}{dt}(\boldsymbol{X}, \theta) = \mathrm{Proj}_{\mathcal{C}_{\boldsymbol{X}} \times \mathbb{R}^N} \boldsymbol{U}(\boldsymbol{X}, \theta)}$

$$\boldsymbol{U}(\boldsymbol{X}, \theta)_j = \begin{cases} c\,(\cos\theta_j, \sin\theta_j)^T + \gamma \mathrm{F}_j(\boldsymbol{X}), & \text{if } 1 \leqslant j \leqslant N, \\ \mu\, \sin(\bar{\theta}_{j-N} - \theta_{j-N}) + \delta\, \sin(\psi_{j-N} - \theta_{j-N}), & \text{if } N+1 \leqslant j \leqslant 2N \end{cases}$$

Differential inclusion

$$\frac{d}{dt}(\boldsymbol{X}, \theta) = \mathrm{Proj}_{\mathcal{C}_{\boldsymbol{X}} \times \mathbb{R}^N} \boldsymbol{U}(\boldsymbol{X}, \theta)$$

- The polar cone of $C_{\boldsymbol{X}} \times \mathbb{R}^N$ is $\mathcal{N}_{\boldsymbol{X}} \times \{0\}$ and

$$\mathrm{Proj}_{\mathcal{C}_{\boldsymbol{X}} \times \mathbb{R}^N} + \mathrm{Proj}_{\mathcal{N}_{\boldsymbol{X}} \times \{0\}} = \mathrm{Id}$$

- We obtain: $\frac{d}{dt}(\boldsymbol{X}, \theta) = \boldsymbol{U}(\boldsymbol{X}, \theta) - \mathrm{Proj}_{\mathcal{N}_{\boldsymbol{X}} \times \{0\}} \boldsymbol{U}(\boldsymbol{X}, \theta)$
- Differential inclusion:

$$\boxed{\frac{d(\boldsymbol{X}, \theta)}{dt} + \mathcal{N}_{\boldsymbol{X}} \times \{0\} \ni \boldsymbol{U}(\boldsymbol{X}, \theta)}$$

Well-posedness result

Proposition

Let $Q = \{\boldsymbol{X} \in \mathbb{R}^{2N} \mid \forall i < j,\ D_{ij}(\boldsymbol{X}) \geqslant 0\}$ *be the set of admissible configurations. We suppose that* U *is Lipschitz and bounded. Then, for any initial data* $(\boldsymbol{X}_0, \theta_0) \in Q \times \mathbb{R}^N$ *and any time* $T > 0$*, there exists a unique absolutely continuous solutionon the interval* $(0, T)$ *to the system*

$$\begin{cases} \dfrac{d(\boldsymbol{X}, \theta)}{dt} + \mathcal{N}_{\boldsymbol{X}} \times \{0\} \ni \mathrm{U}(\boldsymbol{X}, \theta), \\ (\boldsymbol{X}, \theta)(0) = (\boldsymbol{X}_0, \theta_0). \end{cases}$$

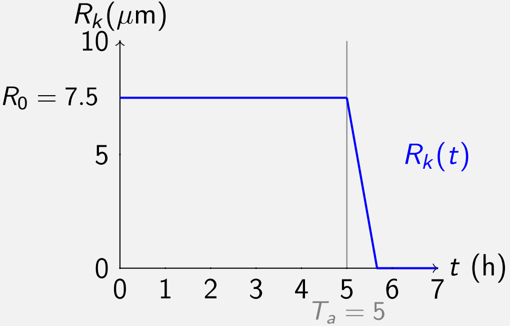
Generalization of results from J. Venel's thesis[5]

[5] J. Venel, "Modélisation mathématique et numérique de mouvements de foule," Ph.D. dissertation, Université Paris Sud-Paris XI, 2008.

Apoptosis

Apoptosis occurs at time T_a, the apoptotic state becomes $\alpha_k = 1$, the cell radius decreases

$$R_k(t) = \left(R_0 + \mathbb{1}_{[T_a,+\infty[}\beta[T_a - t]\right)_+$$



Modification of the interactions

- additional polarity relaxation towards the apoptotic cells:

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

with $$\boldsymbol{M}_k = \sum_{j, \|X_j - X_k\| \leqslant R_{\text{int}}^{\text{po}}} \alpha_j \frac{(X_j - X_k)}{\|(X_j - X_k)\|}$$

- apoptotic cells exert stronger attraction-repulsion force:

$$\boldsymbol{F}_k(\boldsymbol{X}) = \sum_{j, \|\boldsymbol{X}_k - \boldsymbol{X}_j\| \leqslant R_{\text{int}}^{\text{ar}}} \nabla_{\boldsymbol{X}_k} W_j(\|\boldsymbol{X}_k - \boldsymbol{X}_j\|)$$

with $$W_j(r) = -\boxed{((1-\alpha_j)\,\kappa + \alpha_j \kappa_{apop})} \left(\frac{r^2}{2} - \frac{r^3}{3D_c} \right)$$

I. Mathematical model

II. Numerical discretization
- Discretization of the position and velocity
- Discretization of the polarity
- Apoptosis part in the discretization

III. Numerical experiment

Discretization

Let $\Delta t > 0$ be the time step and denote by $(\boldsymbol{X}_k^n)$, $(\boldsymbol{V}_k^n)$ and $(\boldsymbol{P}_k^n)$ the approximate positions, velocities and polarities at time $t^n = n\Delta t$, $n \in \mathrm{N}$, respectively.
The update of $\boldsymbol{X}^n$ is:

$$X_k^{n+1} = X_k^n + V_k^{n+1}\Delta t.$$

Following the method proposed in[6]:

$$\boldsymbol{V}^{n+1} = \mathrm{Proj}_{\mathcal{C}^{\Delta t}_{X^n}}(c\boldsymbol{P}^{n+1} + \gamma \boldsymbol{F}(\boldsymbol{X}^n)),$$

$$\begin{aligned}\mathcal{C}^{\Delta t}_{\boldsymbol{X}^n} = \{\boldsymbol{V} \in (\mathbb{R}^2)^N \mid \forall i < j,\ & D_{i,j}(\boldsymbol{X}^n) + \Delta t\, \nabla D_{i,j}(\boldsymbol{X}^n) \cdot \boldsymbol{V} \geqslant 0,\\ \forall i,\ \ & D_b(\boldsymbol{X}^n_i) + \Delta t\, \nabla D_b(\boldsymbol{X}^n_i) \cdot \boldsymbol{V}_i \geqslant 0\}.\end{aligned}$$

Difficulty: deal with the projection

$$\mathcal{C}^{\Delta t}_{\boldsymbol{X}^n} = \{\boldsymbol{V} \in (\mathbb{R}^2)^N \mid \widetilde{B}\boldsymbol{V} - \widetilde{\boldsymbol{D}} \leqslant 0\},$$

$$\widetilde{\boldsymbol{D}} = \begin{bmatrix} \boldsymbol{D} \\ \boldsymbol{D}_b \end{bmatrix} \in \mathbb{R}^{\frac{N(N-1)}{2}+N}, \quad \widetilde{B} = \begin{bmatrix} B \\ B_b \end{bmatrix} \in \mathcal{M}_{\frac{N(N-1)}{2}+N,2N},$$

[6] B. Maury and J. Venel, "A discrete contact model for crowd motion," *ESAIM Math. Model. Numer. Anal.*, vol. 45, no. 1, pp. 145–168, 2011.

Optimization: Uzawa

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

The associated Lagrangian functional:

$$\mathcal{L}(\boldsymbol{V}, \boldsymbol{\lambda}) = \frac{1}{2} \left\| \boldsymbol{V} - c\boldsymbol{P}^{n+1} - \gamma \mathrm{F}(\boldsymbol{X}^n) \right\|^2 + \boldsymbol{\lambda} \cdot \left(\widetilde{B} \boldsymbol{V} - \widetilde{\boldsymbol{D}} \right),$$

Constructing the sequences $(\boldsymbol{V}^{(j)})_j$ and $(\boldsymbol{\lambda}^{(j)})_j$ as follows:

1. $\boldsymbol{V}^{(0)} = \boldsymbol{V}^n, \boldsymbol{\lambda}^{(0)} = 0,$
2. $\boldsymbol{V}^{(j+1)} = \min\limits_{\boldsymbol{V} \in \mathbb{R}^{2N}} \mathcal{L}(\boldsymbol{V}, \boldsymbol{\lambda}^j) = c\boldsymbol{P}^{n+1} + \gamma \mathrm{F}(\boldsymbol{X}^n) - \widetilde{B}^T \boldsymbol{\lambda}^{(j)},$
3. $\boldsymbol{\lambda}^{(j+1)} = \max \left(0, \boldsymbol{\lambda}^{(j)} + \rho \left(\widetilde{B} \boldsymbol{V}^{(j)} - \widetilde{\boldsymbol{D}} \right) \right),$

$\rho > 0$ is the the gradient-descent step of the method.

Semi-implicit scheme[7] that ensures $\|\boldsymbol{P}_k\| = 1$:

$$\boldsymbol{P}_k^{n+1} = \boldsymbol{P}_k^n + \mathrm{Proj}_{(\boldsymbol{P}_k^{n+1/2})^\perp} \left(\mu\,\Delta t \left(\overline{\boldsymbol{P}}_k^n - \boldsymbol{P}_k^n \right) + \delta\,\Delta t \left(\frac{\boldsymbol{V}_k^n}{\|\boldsymbol{V}_k^n\|} - \boldsymbol{P}_k^n \right) + \sqrt{2D\Delta t}\,\xi_k^n \right),$$

- $\boldsymbol{P}_k^{n+1/2} = (\boldsymbol{P}_k^n + \boldsymbol{P}_k^{n+1})/2$
- ξ_k^n: random number following a standard Normal distribution

[7] S. Motsch and L. Navoret, "Numerical simulations of a nonconservative hyperbolic system with geometric constraints describing swarming behavior," *Multiscale Model. Simul.*, vol. 9, no. 3, pp. 1253–1275, 2011.

Explicit implementation

Polar formulation: $\theta_k^n \in [0, 2\pi)$, such that $\boldsymbol{P}_k^n = \left(\cos\left(\theta_k^n\right), \sin\left(\theta_k^n\right)\right)^T$. The semi-implicit scheme become:

$$\theta_k^{n+1} = \theta_k^n + 2\left(\hat{\boldsymbol{Q}}_k^n - \theta_k^n\right) + \sqrt{2D\Delta t}\,\xi_k^n$$

- $\boldsymbol{Q}_k^n = \boldsymbol{P}_k^n + \frac{\Delta t}{2}\left(\mu\left(\overline{\boldsymbol{P}}_k^n - \boldsymbol{P}_k^n\right) + \delta\left(\frac{\boldsymbol{V}_k^n}{\left\|\boldsymbol{V}_k^n\right\|} - \boldsymbol{P}_k^n\right)\right)$
- $\hat{\boldsymbol{Q}}_k^n$ is the polar angle of the vector $\boldsymbol{Q}_k^n$

Apoptosis part in the discretization

- Decreasing radius: $\boldsymbol{R}_k^n = \left[R_0 + \mathbb{1}_{[T_a,+\infty[}(n\Delta t)\beta[T_a - n\Delta t]\right]_+$
- Center polarity on the dying cell:

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

- Stronger attraction-repulsion force: change κ to $((1-\boldsymbol{\alpha}_j)\,\kappa + \boldsymbol{\alpha}_j\kappa_{apop})$ in the potential.

I. Mathematical model

II. Numerical discretization

III. Numerical experiment

- Influence of the shape of the domain
- Influence of the smooth attraction-repulsion
- Apoptosis

Parameters

Taken from [4][8], IGBMC, calibrated numerically

Cells radius	R_0	7.5	μm
Cells comfort radius	R_c	9.5	μm
Cells attraction-repulsion interaction radius	$R_{\text{int}}^{\text{ar}}$	19	μm
Cells polarity interaction radius	$R_{\text{int}}^{\text{po}}$	60	μm
Cell speed	c	21.6	$\mu\text{m h}^{-1}$
Angular diffusion	D	0.96	$\text{rad}^2\,\text{h}^{-1}$
Relaxation parameter: polarity to mean polarity	μ	6.2	rad h^{-1}
Relaxation parameter: polarity to velocity	δ	6.2	rad h^{-1}
Rigidity constant	κ	10^4	$\text{pN}\,\mu\text{m}^{-1}$
Inverse friction coefficient	γ	10^{-5}	$\text{pN}^{-1}\text{h}^{-1}\mu\text{m}$
Apoptosis on P	ν	10	rad h^{-1}
Apoptosis spring force (on V)	κ_{apop}	5.10^4	$\text{pN}\mu\text{m}^{-1}$
Speed of decreasing for radius	β	11.25	$\mu\text{m h}^{-1}$

[8] S. L. Vecchio, O. Pertz, M. Szopos, *et al.*, "Spontaneous rotations in epithelia as an interplay between cell polarity and boundaries," *Nature Physics*, 2024.

Indicators of the emergence of collective movement

- The normalized global mean speed:

$$\bar{v}(t) = \frac{1}{c}\frac{1}{N}\sum_{k=1}^{N} \|\boldsymbol{V}_k(t)\|,$$

- The rotation order parameter:

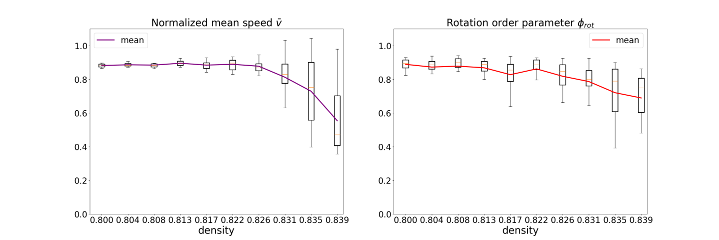
$$\phi_{\text{rot}}(t) = \frac{1}{N}\sum_{k=1}^{N} \boldsymbol{P}_k(t)\cdot \boldsymbol{e}_k(t),$$

where $\boldsymbol{e}_k = (\boldsymbol{X}_k - \boldsymbol{X}_c)^{\perp}/\|\boldsymbol{X}_k - \boldsymbol{X}_c\|$ is the unit tangential vector with respect to the domain center $\boldsymbol{X}_c$.

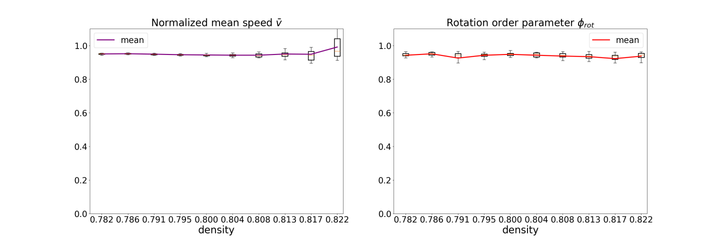
Influence of the shape of the domain

Compare cells collective dynamics in a square and in a disk

- Dense regime (density larger than 0.8)
- Domains with same area
- Final time: $T = 20\,\mathrm{h}$, time step $\Delta t = 10^{-2}\,\mathrm{h}$
- Indicators averaged over the last $T/8 = 2.5\mathrm{h}$
- 20 different numerical simulations for each density.

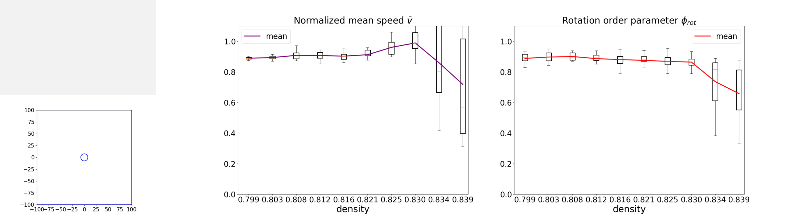


Square domain of length 200 μm: **jamming** effect at higher density, **rotational** movement elsewhere.

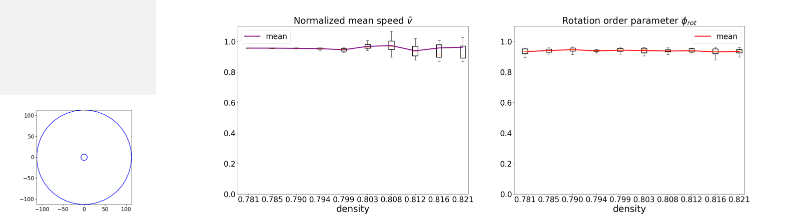


Disk domain of radius $200/\sqrt{\pi}\,\mu$m: **rotational** movement independent of the density.

With an obstacle



Helps the movement but still jamming effect in the largest densites.



Rotational movement.

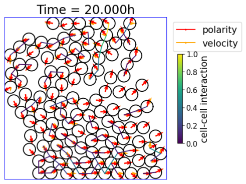
Influence of the attraction-repulsion force

Default parameters:

$R_c = 9.5\mu m$

$\kappa = 10^4 pN\,\mu m^{-1}$

$\gamma = 10^{-5} pN^{-1} h^{-1} \mu m$



Observation:

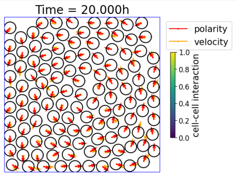
- Rotating movement
- Lot of contacts

Strong attraction-repulsion:

$R_c = 9.5\mu m$

$\boxed{\kappa = 16.10^4 pN\,\mu m^{-1}}$

$\boxed{\gamma = 10^{-4} pN^{-1} h^{-1} \mu m}$



Observation:

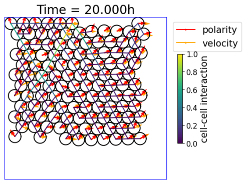
- Better rotating movement
- Few contact

Strong attraction:

$\boxed{R_c = 7.5\mu m (= R_0)}$

$\boxed{\kappa = 16.10^4 pN\,\mu m^{-1}}$

$\boxed{\gamma = 10^{-4} pN^{-1} h^{-1} \mu m}$



Observation:

- Movement up-down
- Cells glued together

Apoptosis

Apoptosis starts at $T_a = 5$h for 2 randomly chosen cells. It takes 40min for a cell to die. Apoptotic cells are in green.

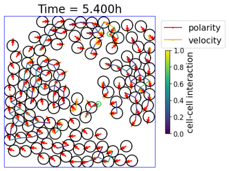
Default parameters:

$R_c = 9.5\mu$m

$\kappa = 10^4$pN μm^{-1}

$\gamma = 10^{-5}$pN^{-1}h$^{-1}\mu$m

$\kappa_{apop} = 5.10^4$pN μm^{-1}



- Change in the direction of the neighbour
- Some change in the global movement

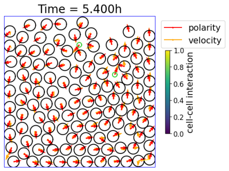
Strong attraction-repulsion:

$R_c = 9.5\mu$m

$\kappa = 16.10^4$pN μm^{-1}

$\gamma = 10^{-4}$pN^{-1}h$^{-1}\mu$m

$\kappa_{apop} = 5.16.10^4$pN μm^{-1}



- Change of direction less important
- Less change in the global movement

Conclusion & perspectives

- Construction of a mathematical and computational model for cells collective dynamics
- Include the phenomena of apoptosis
- Observation of different behaviors depending of the shape of the domain and the intensity of the attraction-repulsion force
- Macroscopic model
- Calibration of last parameters
- Design a fluidity indicator

Biblio I

[1] T. Vicsek, A. Czirók, E. Ben-Jacob, I. Cohen, and O. Shochet, "Novel type of phase transition in a system of self-driven particles," *Phys. Rev. Lett.*, vol. 75, no. 6, p. 1226, 1995.

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[4] S. L. Vecchio, O. Pertz, M. Szopos, L. Navoret, and D. Riveline, "Spontaneous rotations in epithelia as an interplay between cell polarity and boundaries," *Nature Physics*, 2024.

Biblio II

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