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Stochastic model of cell migration over curved substrate

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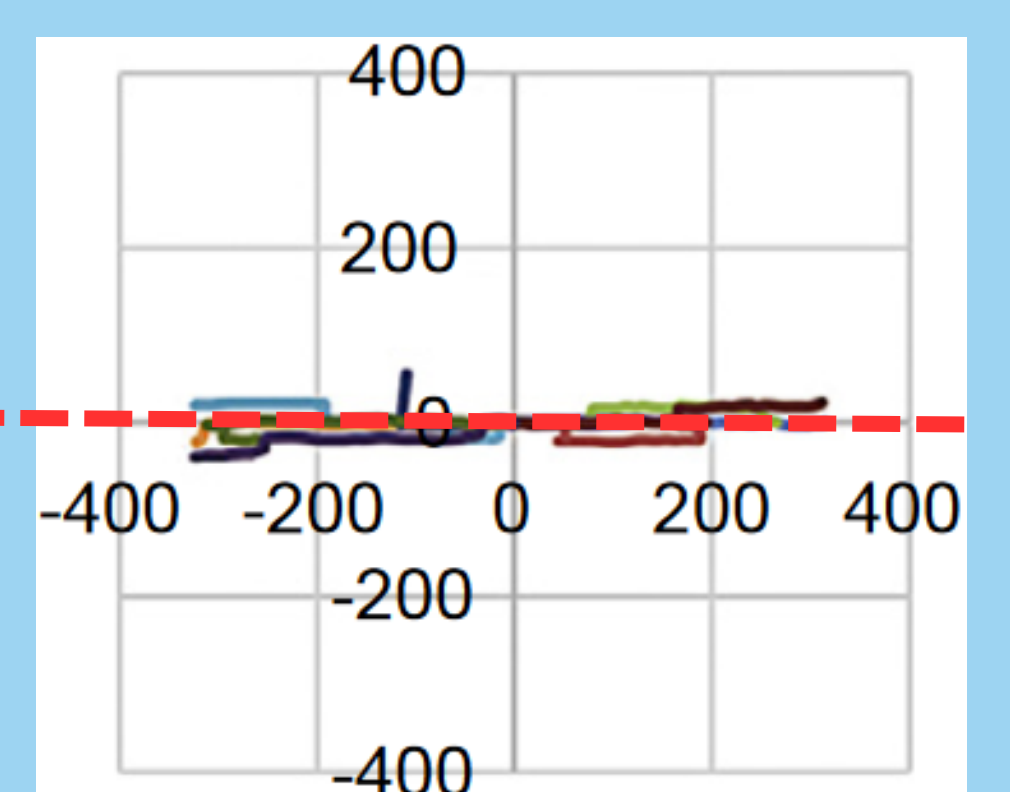
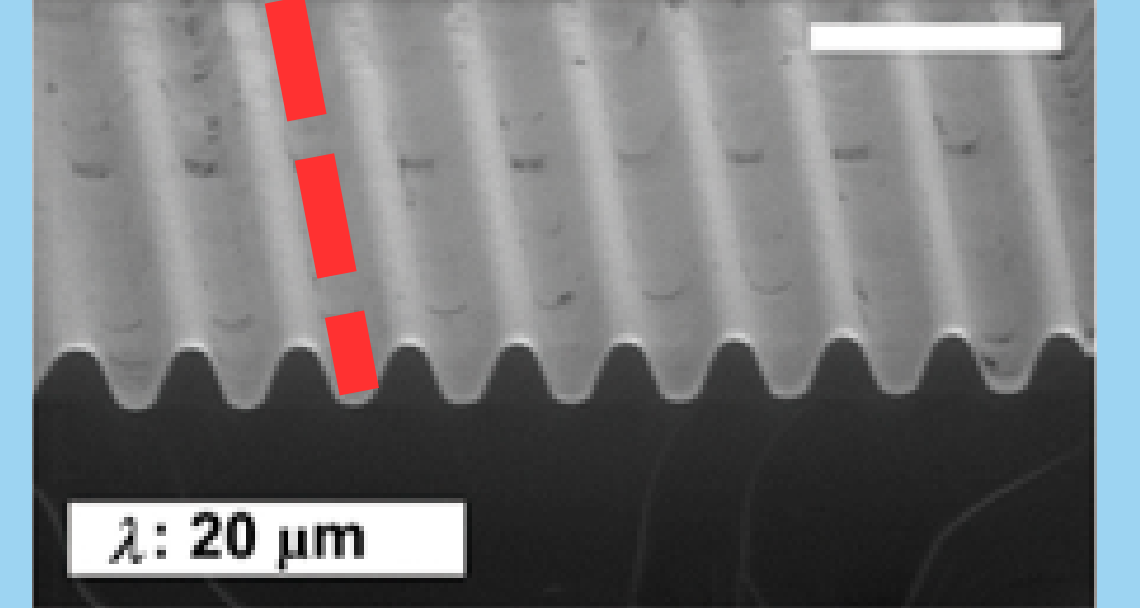
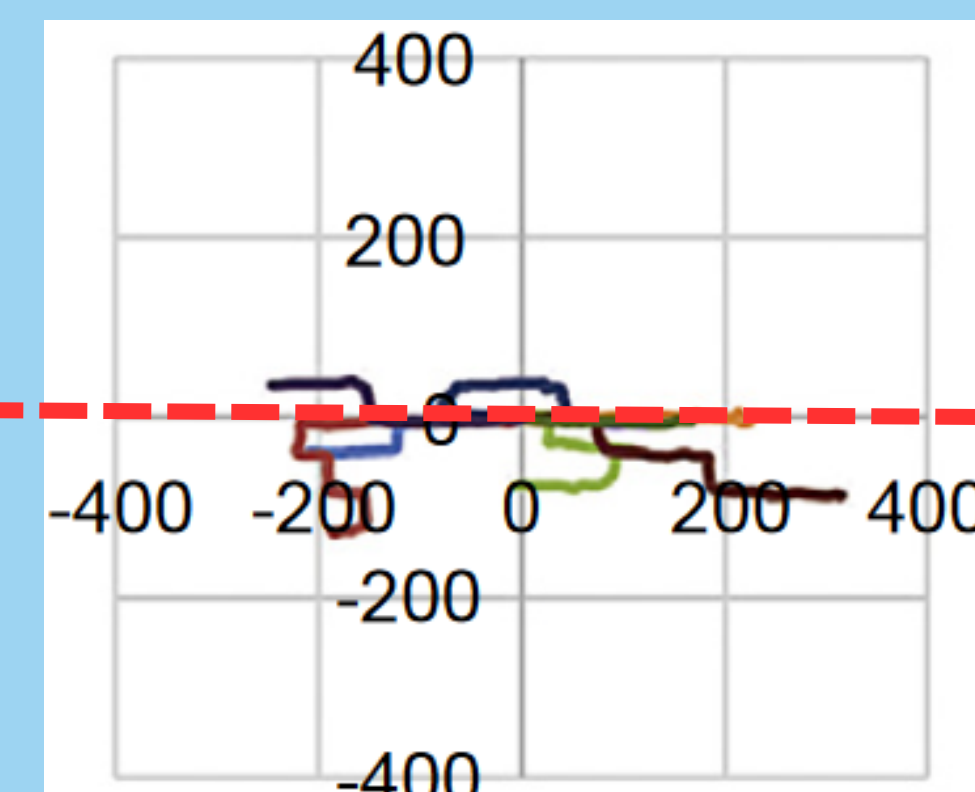
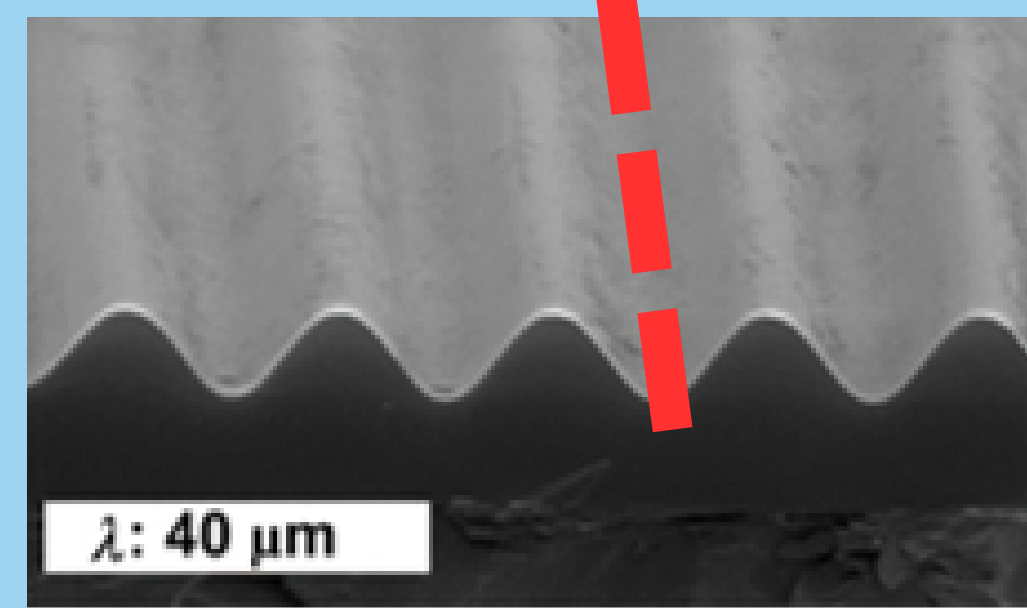
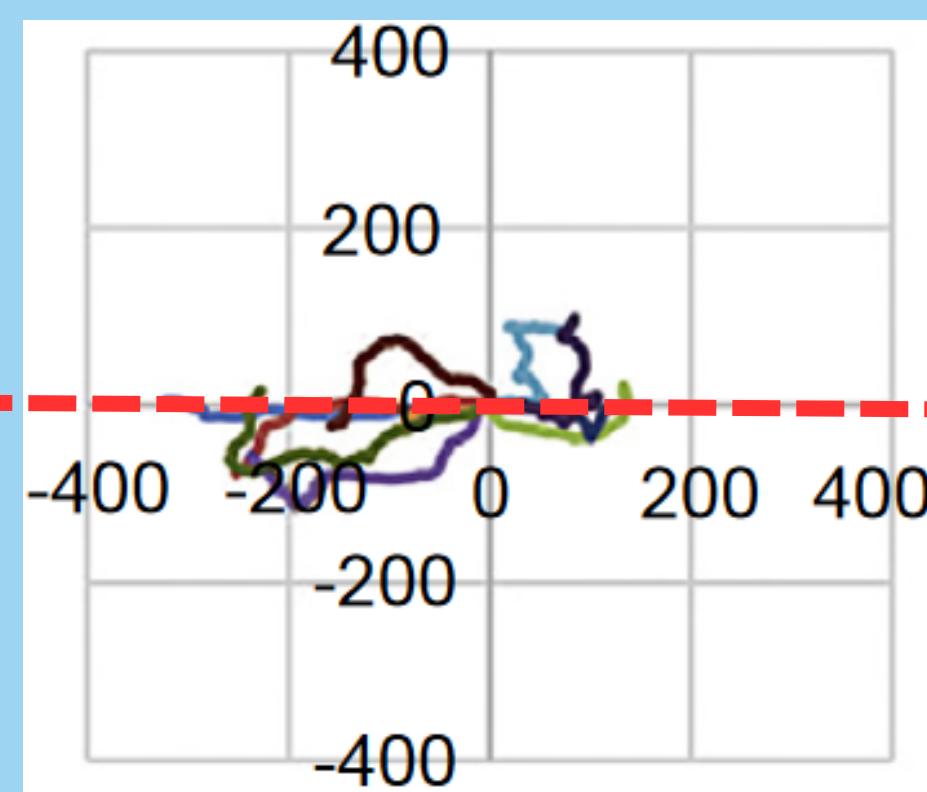
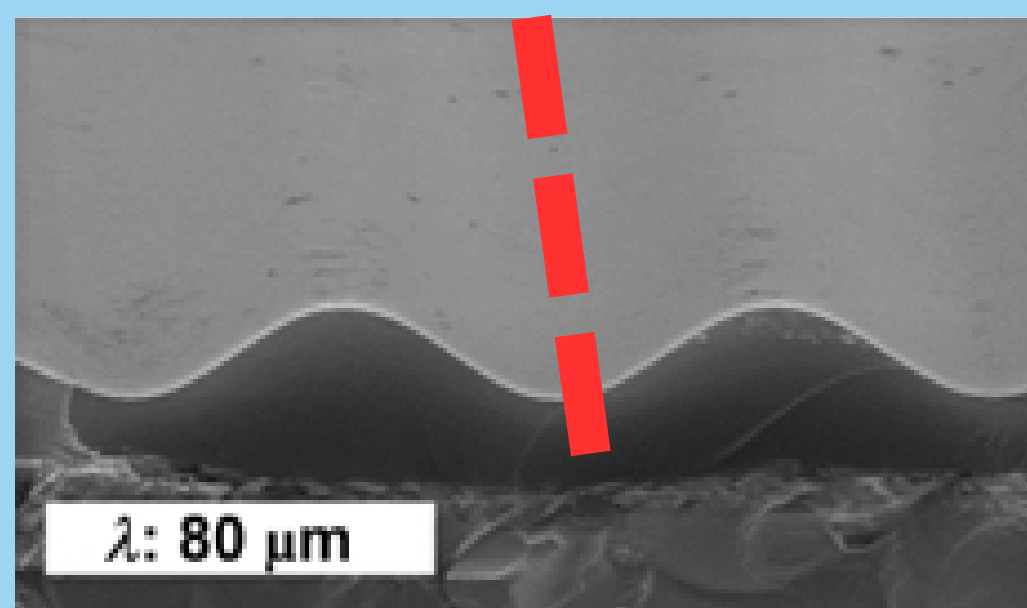
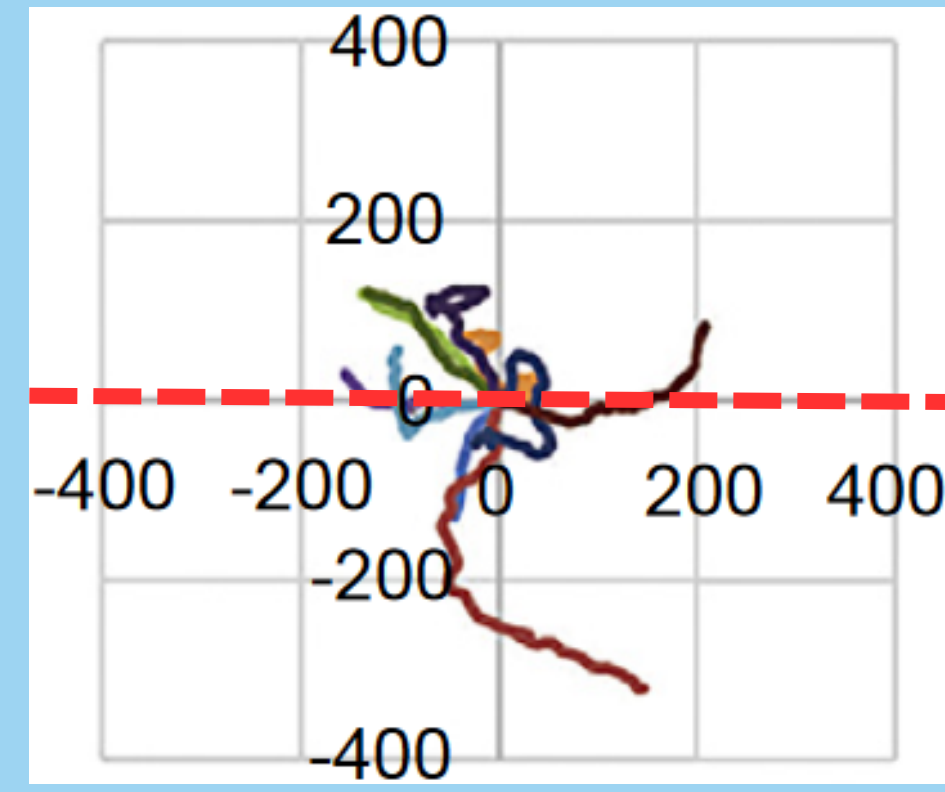
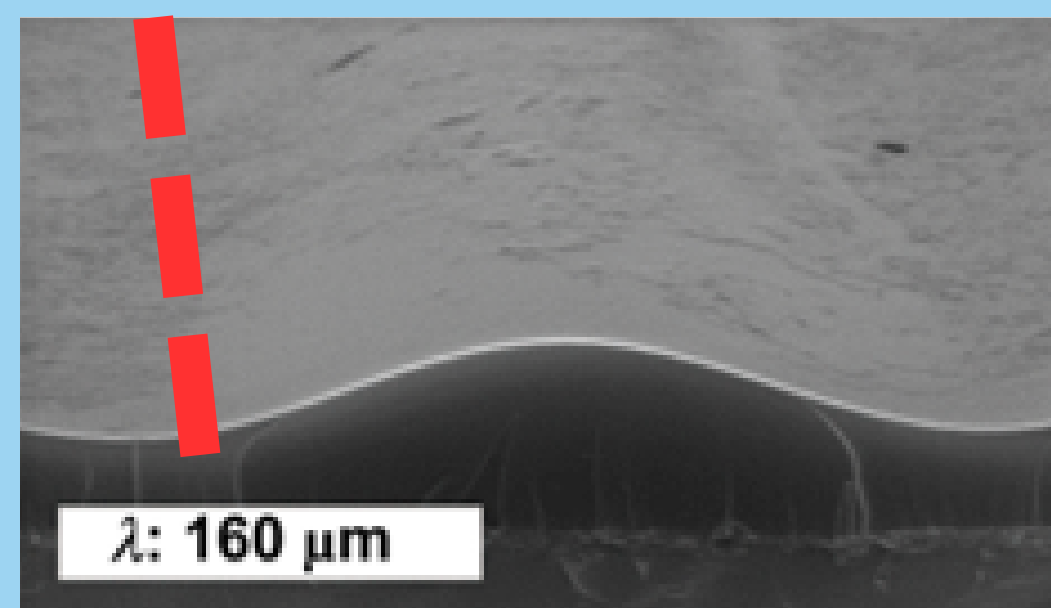
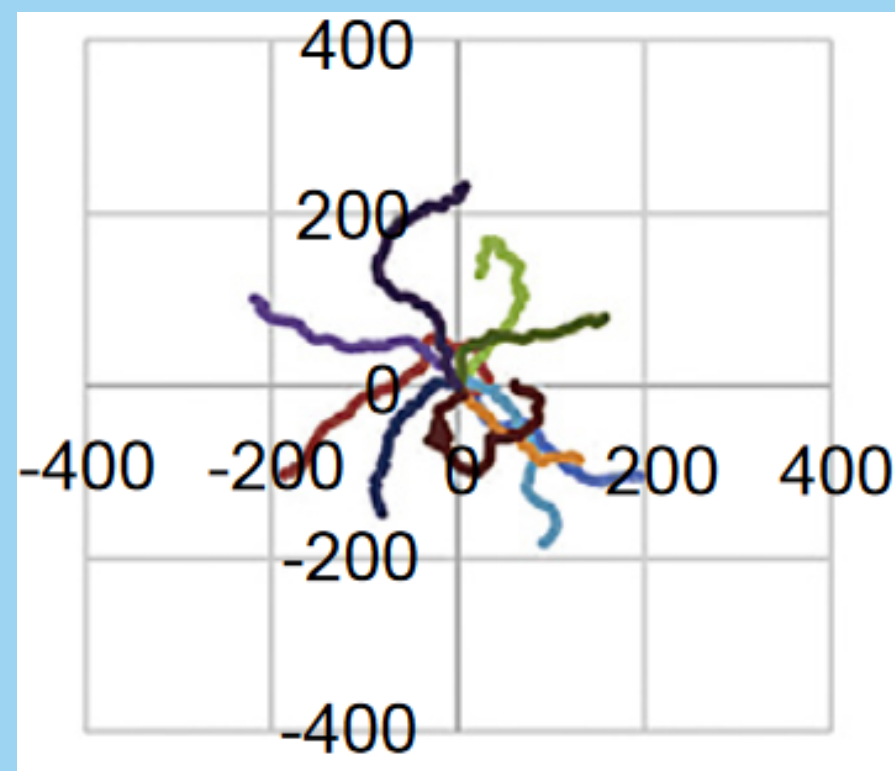


HAL Authorization

Trajectories of T-cells on sinusoidal substrate

$$h(x, y) = A \cos\left(\frac{2\pi}{\lambda} x\right)$$

Flat substrate (control)



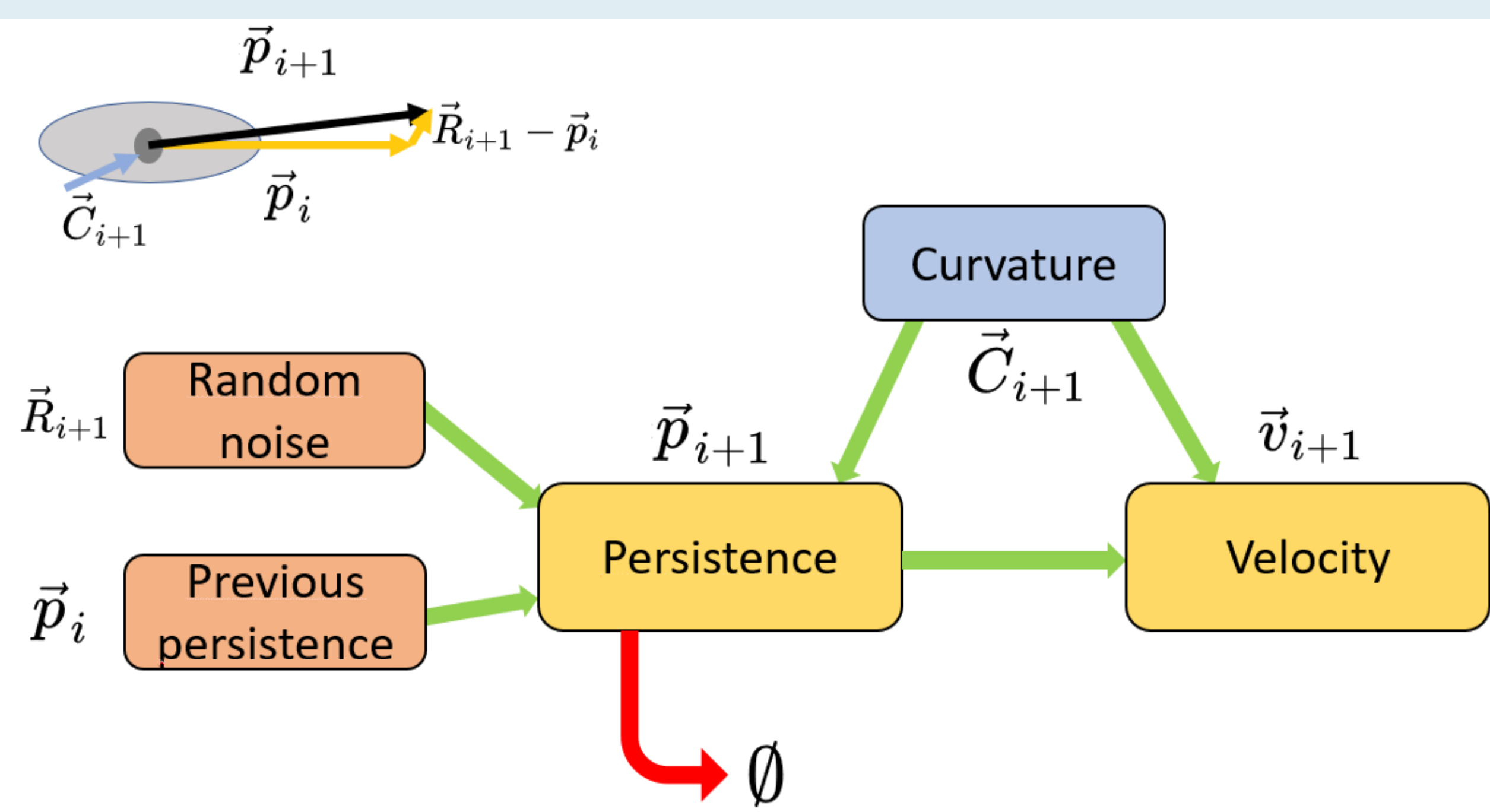
Scale bar : 50µm

The greater the curvature, the greater cell migration is contained in the valleys of the substrate [1]. The cell is triggered by cell-scale curvature, this phenomenon named "curvotaxis" leads cells toward concave areas [2].

Does the curvature triggers inner signal pathways or limits mechanically cell migration?

Development of a stochastic agent-based model

Cell Dynamic



$$\begin{cases} \tau \frac{d\vec{p}}{dt} = v_{\Delta t_r} \hat{\theta} - \vec{p} + \beta \vec{C} \\ \vec{v} = \vec{p} + (1 - \beta) \vec{C} \\ \frac{d\vec{x}}{dt} = \vec{v} \end{cases}$$

Every time step Δt_r :

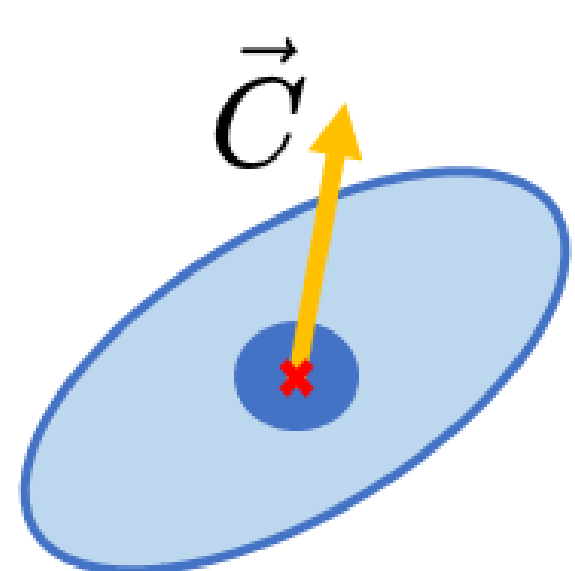
$v_{\Delta t_r}$ is drawn following $\mathcal{U}_{[0, v_m]}$

$\arg(\hat{\theta})$ is drawn following $\mathcal{U}_{[0, 2\pi]}$

What is the strategy of the cell to measure curvature ?

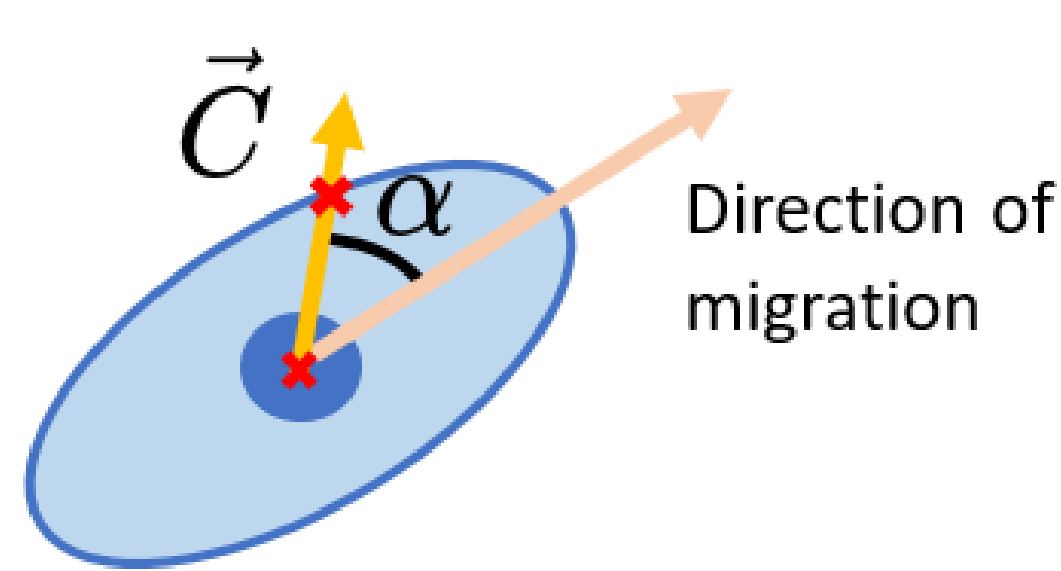
Mean curvature : $H(x, y) = \frac{h_{,xx}}{2(1 + h_{,x}^2)^{3/2}}$

Local metric



$$\vec{C} = \gamma \text{grad} H$$

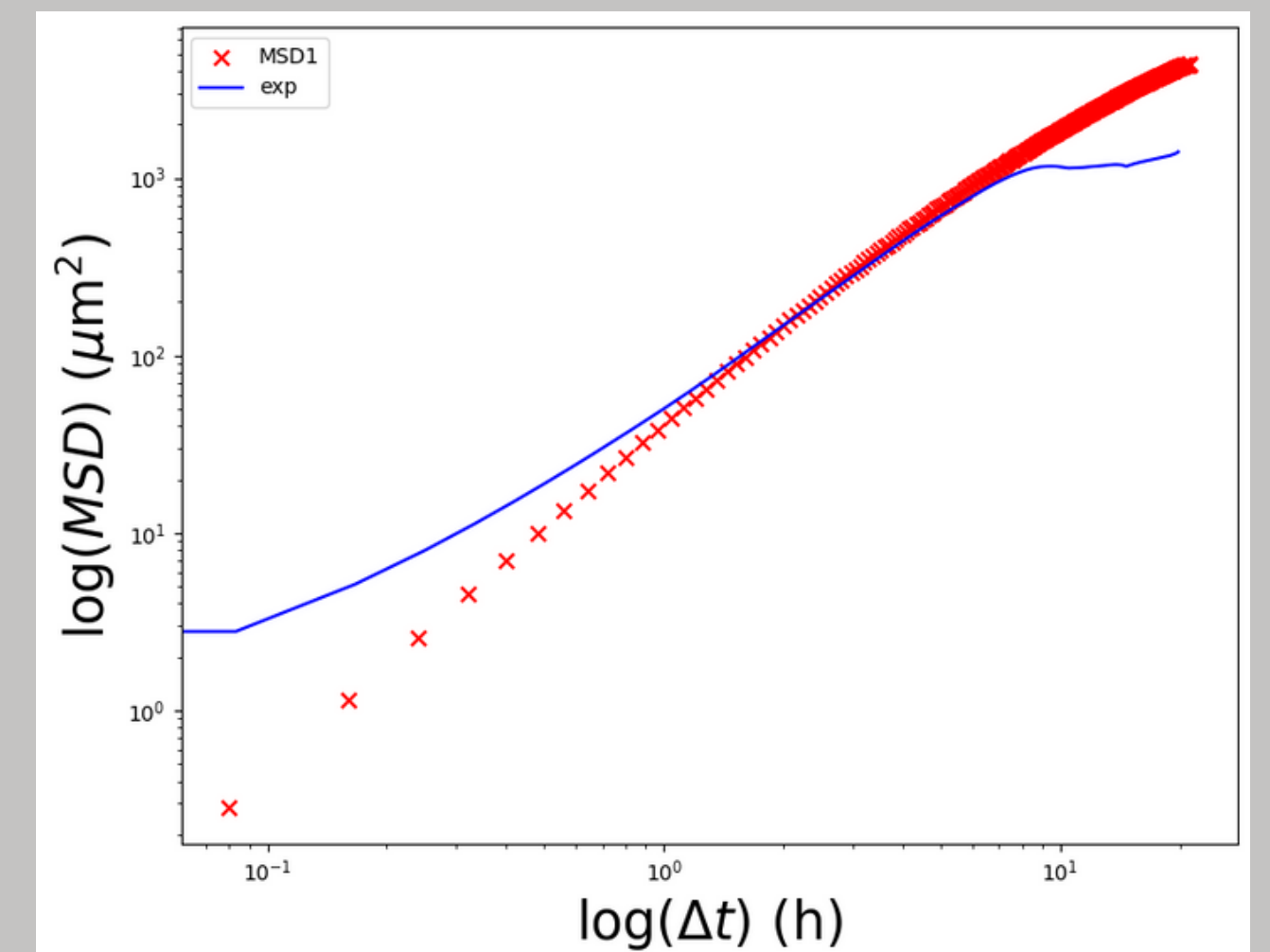
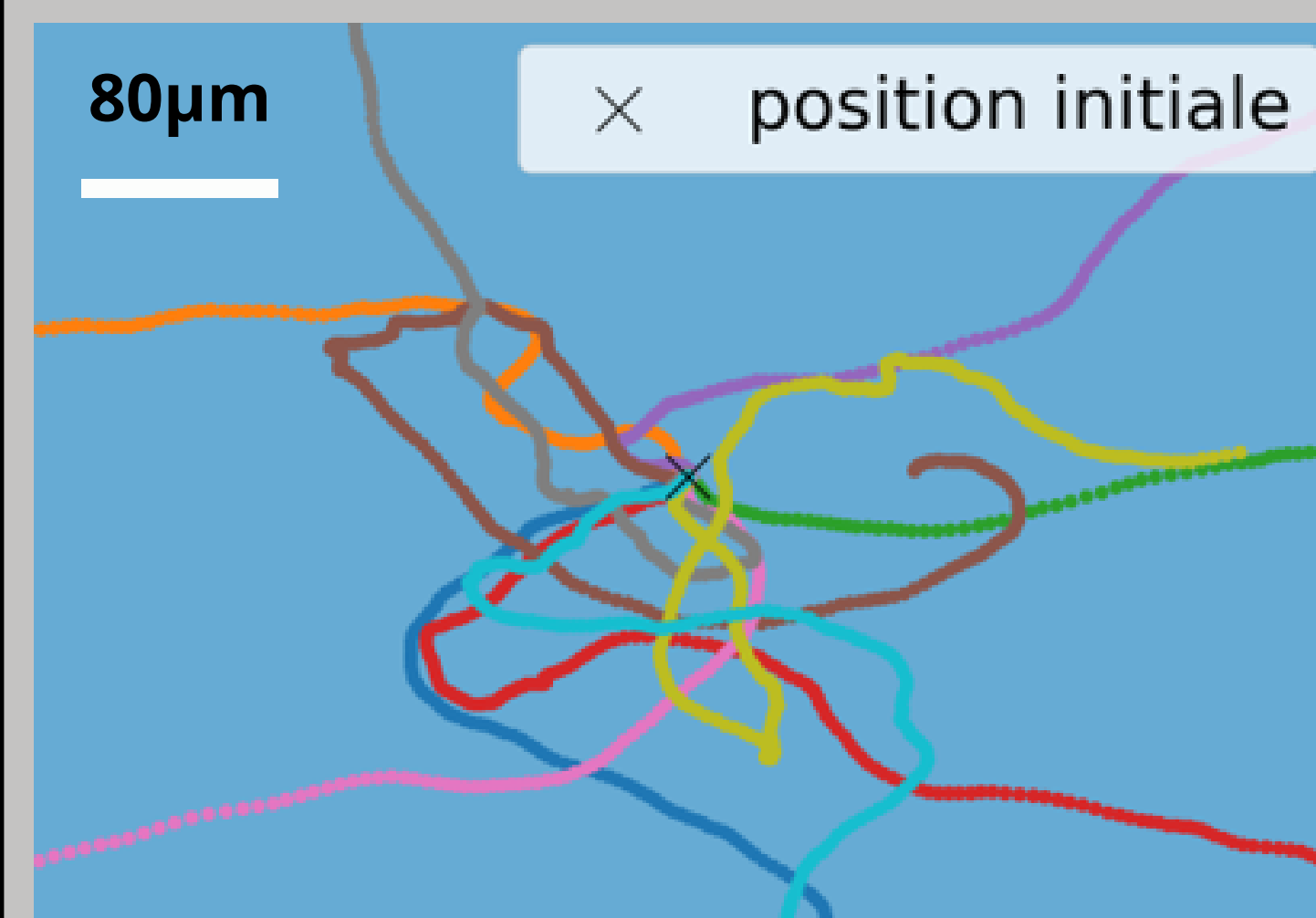
Cell-scale metric



$$\vec{C} = \max_{\alpha} \frac{|H_0 - H_{\hat{n}}|}{a} \hat{n}$$

Results

Does the model behaves like cells ? a flat substrate study

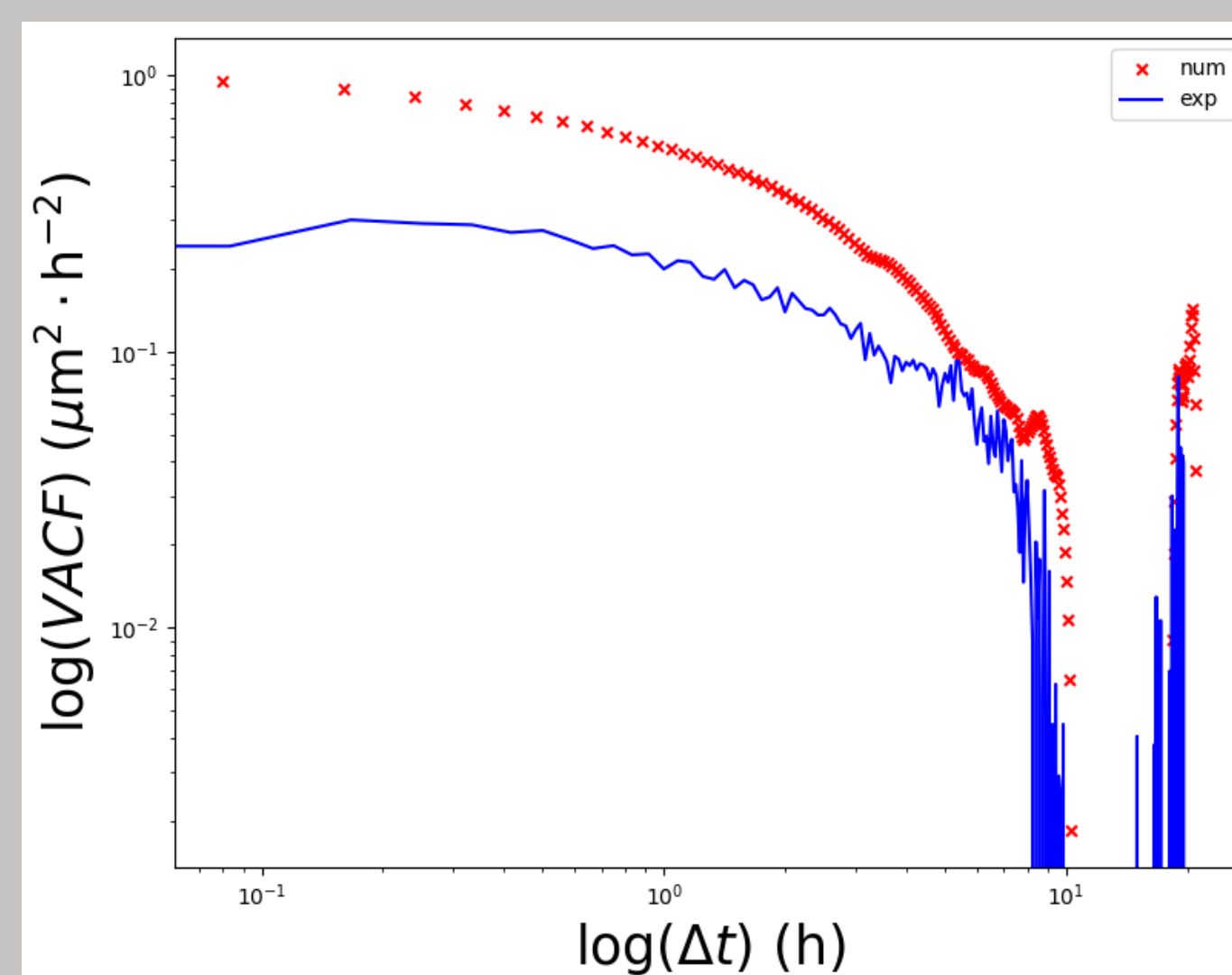


Validation of the model on flat substrate :

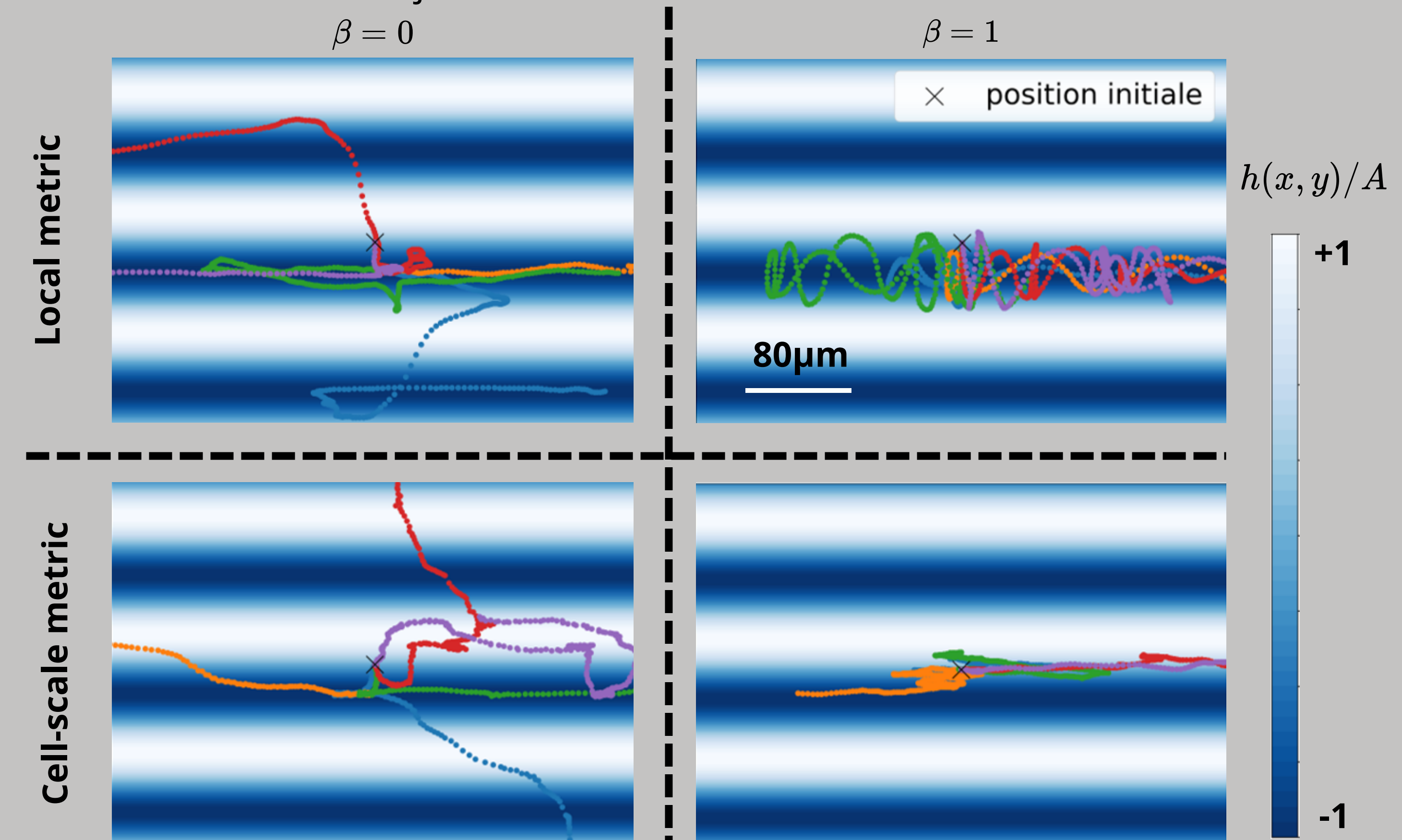
Mean Square Displacement (MSD) and Velocity Autocorrelation Function (VACF) are calculated (red curves) and compared with experimental data (blue curves) [3] --> **the model behaves like cells**

It gives parameters independant with curvature

$$\begin{aligned} \Delta t_r &= 0, 2h \\ \tau &= 2, 5h \\ v_m &= 50 \mu\text{m} \cdot h^{-1} \end{aligned}$$



Does the curvature activates signal pathways ($\beta=1$) or not ($\beta=0$) ? trajectories of cells on curved substrate



[1] K. H. Song, S. J. Park, D. S. Kim, and J. Doh. Sinusoidal wavy surfaces for curvature-guided migration of T lymphocytes. *Biomaterials*, 51 :151–160, 2015.

Ref.

[2] L. Pieuchot, J. Marteau, A. Guignandon, T. Dos Santos, I. Brigaud, P.-F. Chauvy, T. Cloatre, A. Ponche, T. Petithory, P. Rougerie, M. Vassaux, J.-L. Milan, N. T. Wakhloo, A. Spangenberg, M. Bigerelle, and K. Anselme. Curvotaxis directs cell migration through cell-scale curvature landscapes. *Nature Communications*, 9(1) :3995, 2018.

[3] G. Passucci, M. E. Brasch, J. H. Henderson, V. Zaburdaev, and M. L. Manning. Identifying the mechanism for superdiffusivity in mouse fibroblast motility. *PLoS Computational Biology*, 15(2) :e1006732, 2019.