

In silico avatars of cells to predict cell migration on travelling waves

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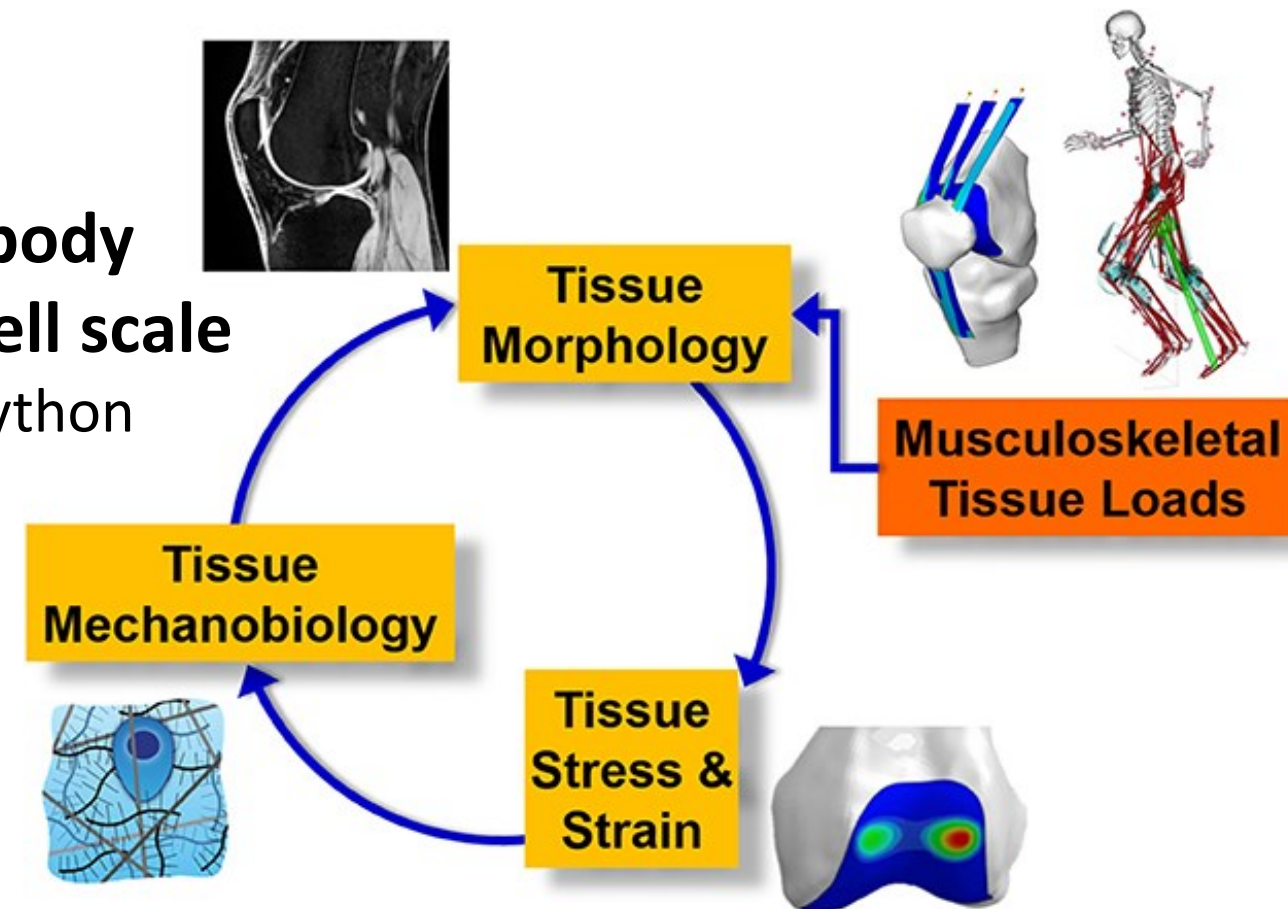
Biomechanics (BMI) Group

-> **integrated models of human body**
from **human movement** to the **cell scale**

Opensim / Febio / Comsol \ python

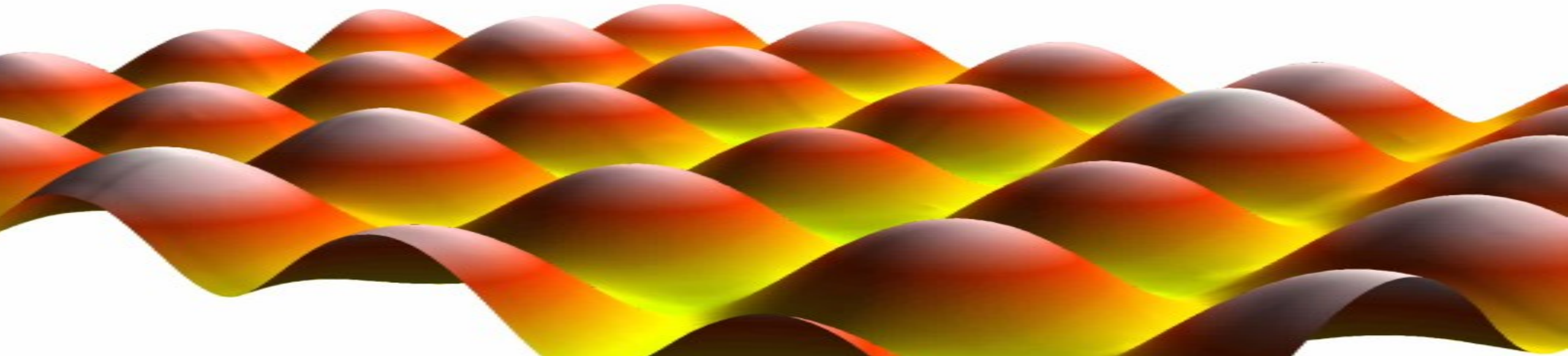
Morphogenesis, Wound healing, ...

-> **Cell migration guidance**



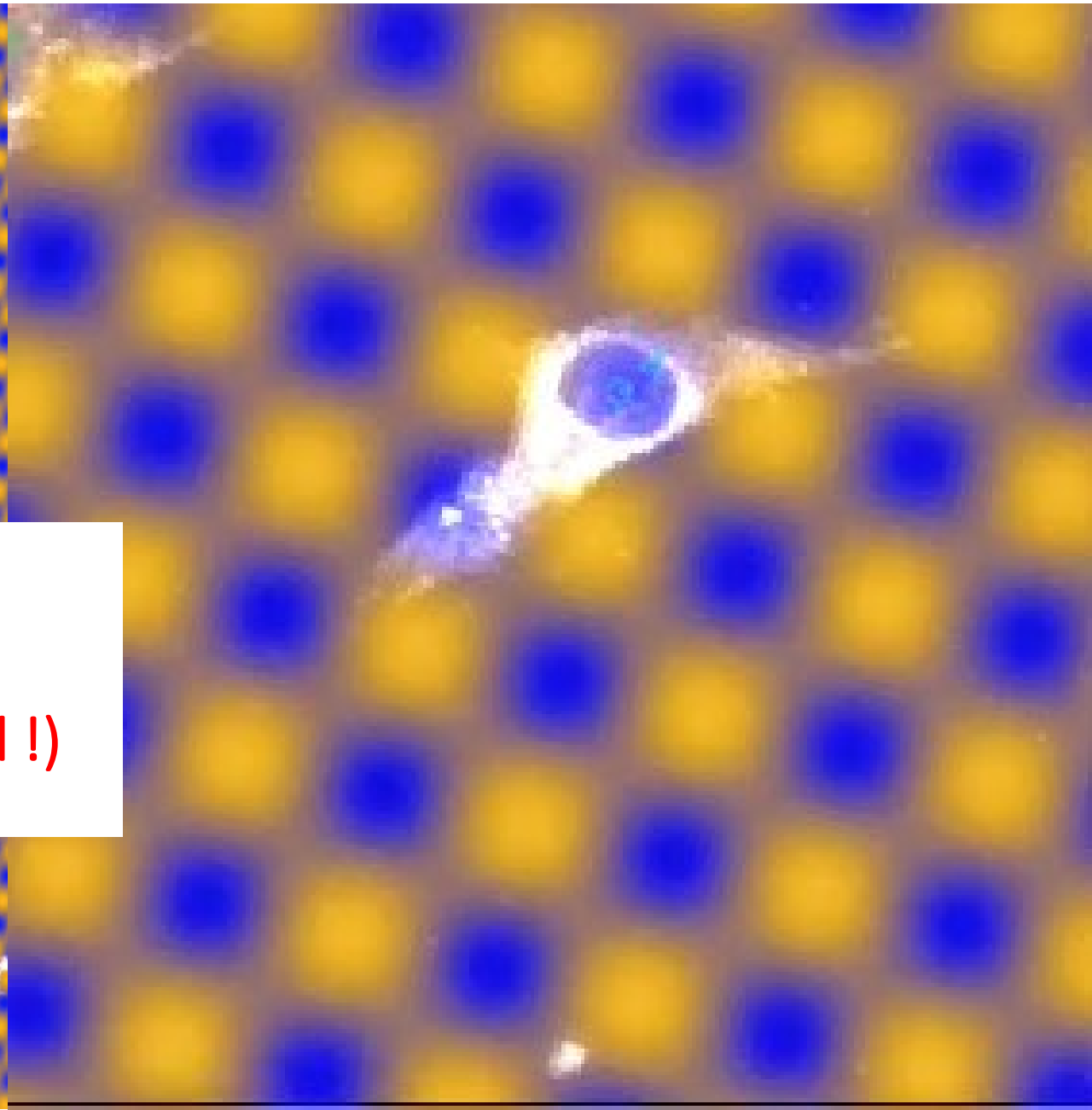
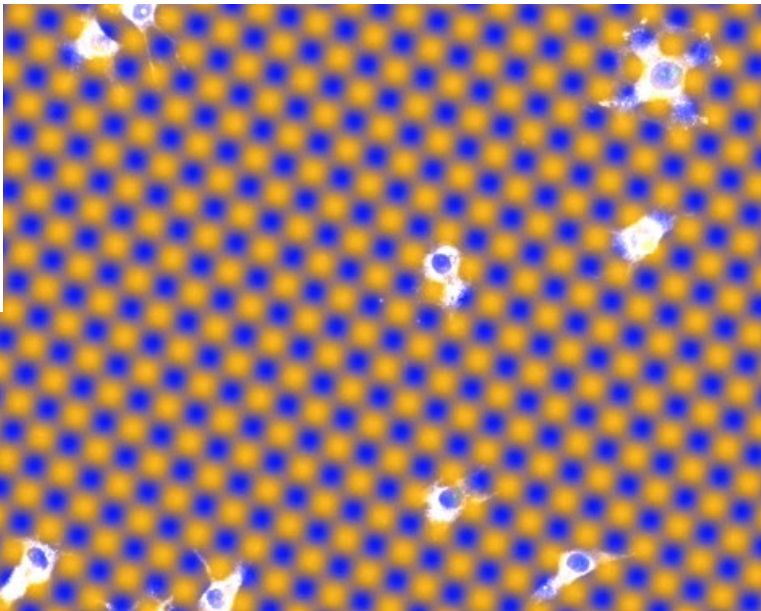
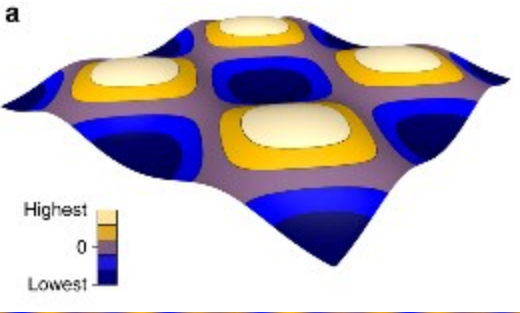
Cell migration guidance by Curvature

-> Cells on **sinusoidal surfaces**



In vitro observations

Karine Anselme & Laurent Pieuchot Mulhouse IS2M



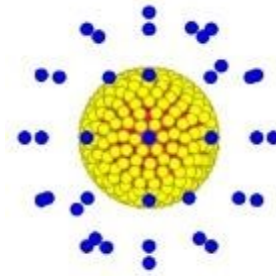
Curvotaxis
(gravity not involved !)

Mechanical explanation of curvotaxis ?

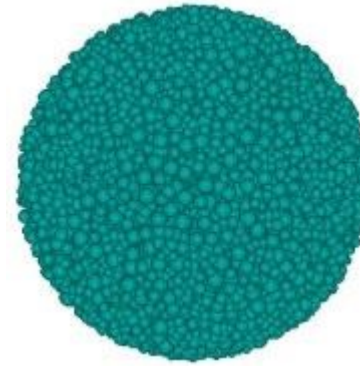
-> 3D Mechanical model of cell & cytoskeleton



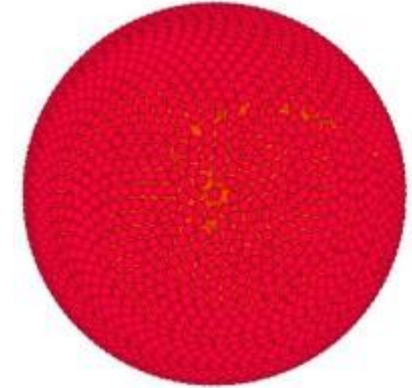
Nucleus core



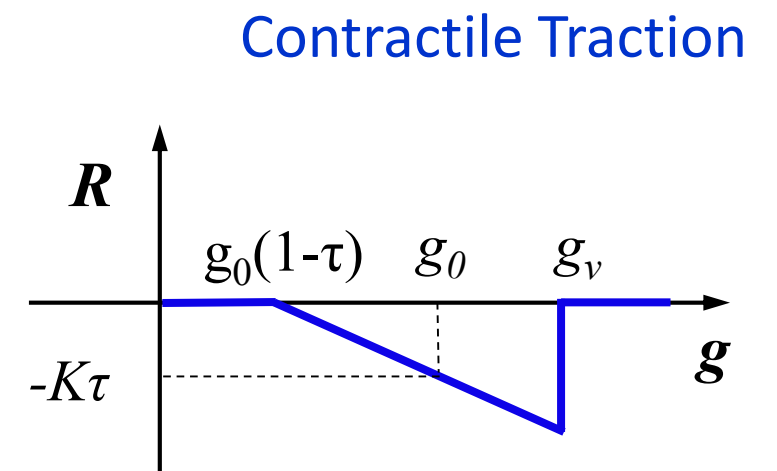
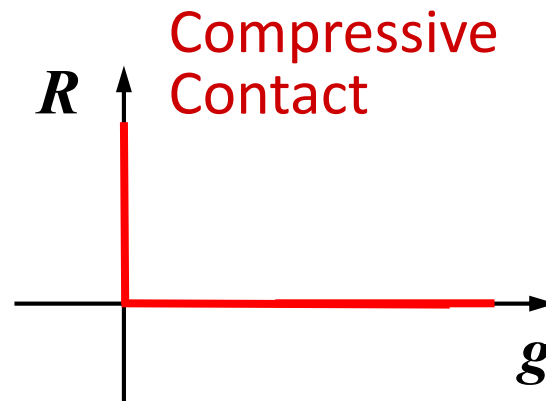
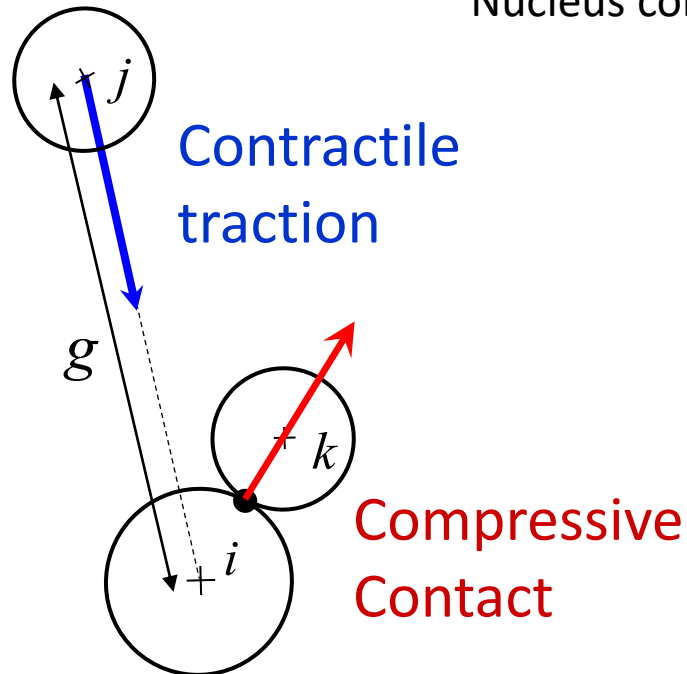
Nucleus membrane



Cell core

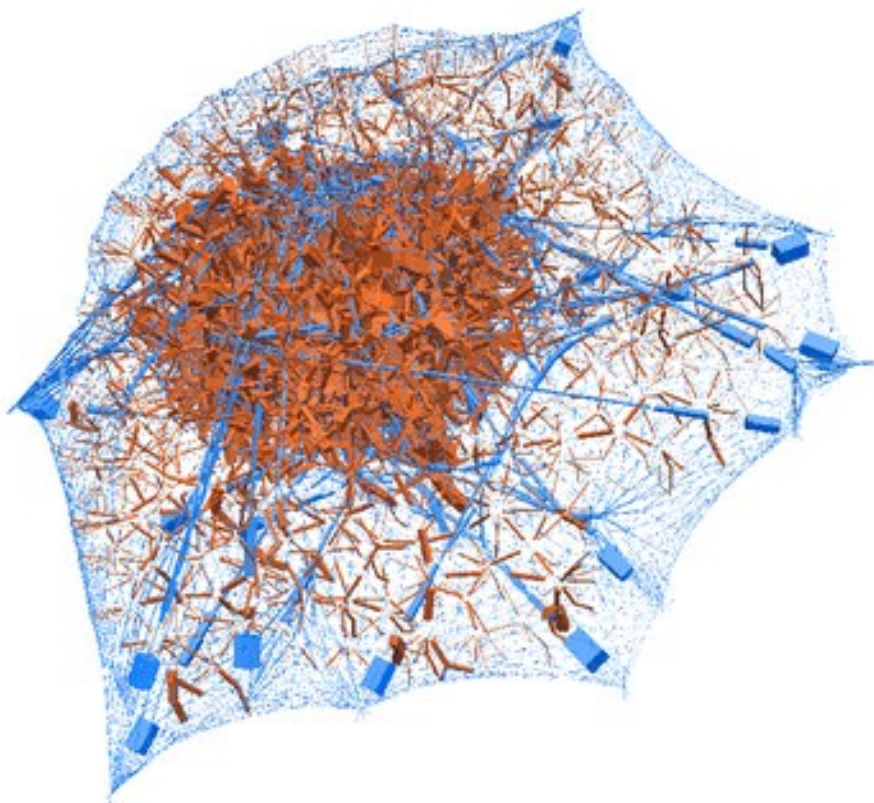


Cell membrane

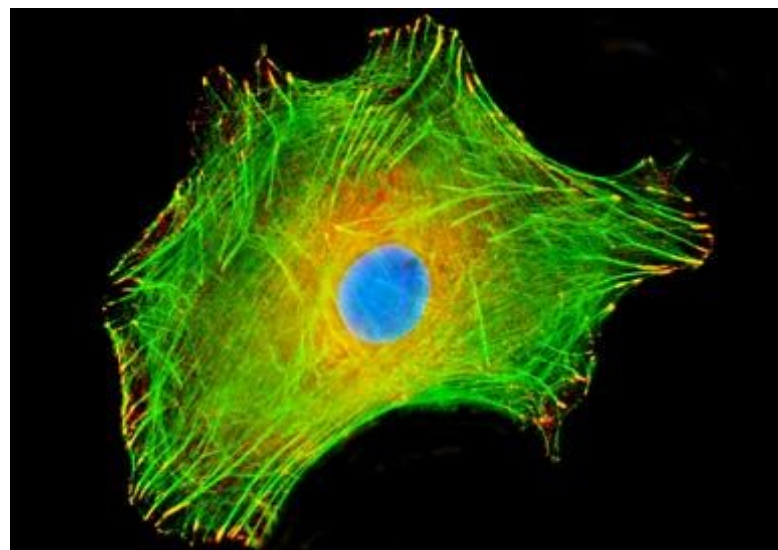


3D Mechanical model of cytoskeleton

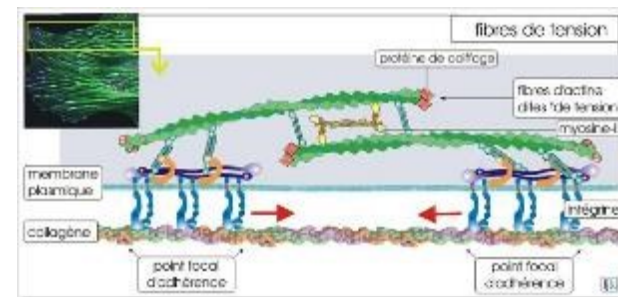
Cytoskeleton = Tension & compression **interactions**



≈



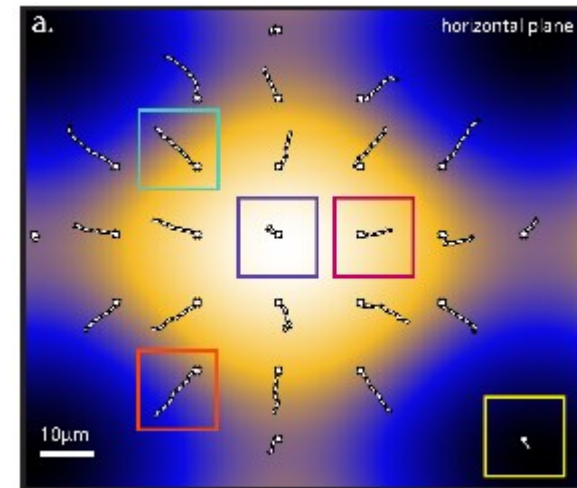
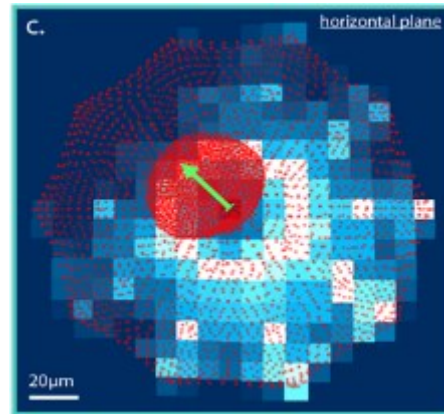
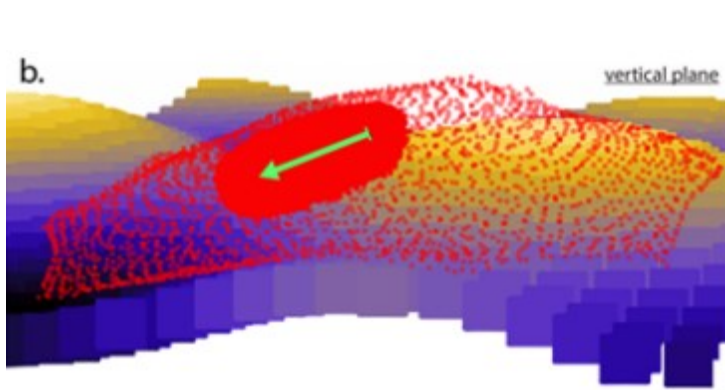
Divided Medium Mechanics using LMG90
(Fred Dubois, LMGC, Montpellier)



Actin filaments & Myosin motors

Adhesion of the model on Sinus Surfaces

Post-Doc
Maxime Vassaux
CR CNRS 2022



The cytoskeleton (Cortex) squeezes the nucleus et pushes it toward concave regions

-> **Decentering of the nucleus**



Migration of the model on Sinus Surfaces

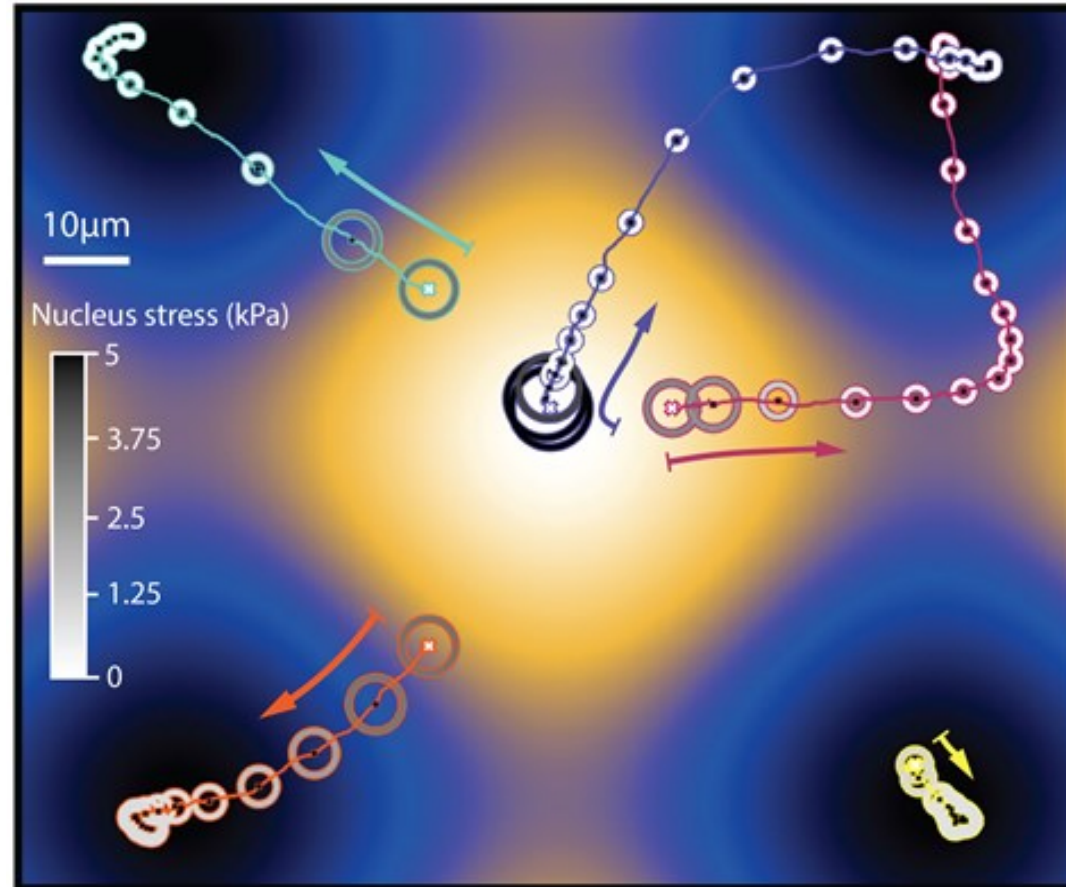
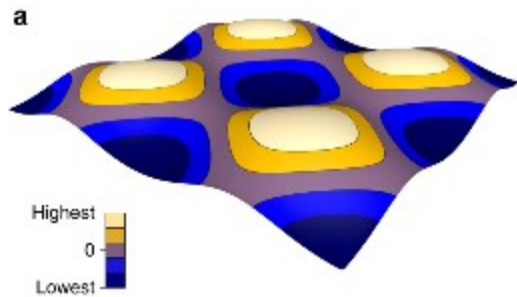
Hypothesis :

- **Nucleus decentering = Migration bias**
≈ « ball and chain » which limits cell migration in some directions

Simulations :

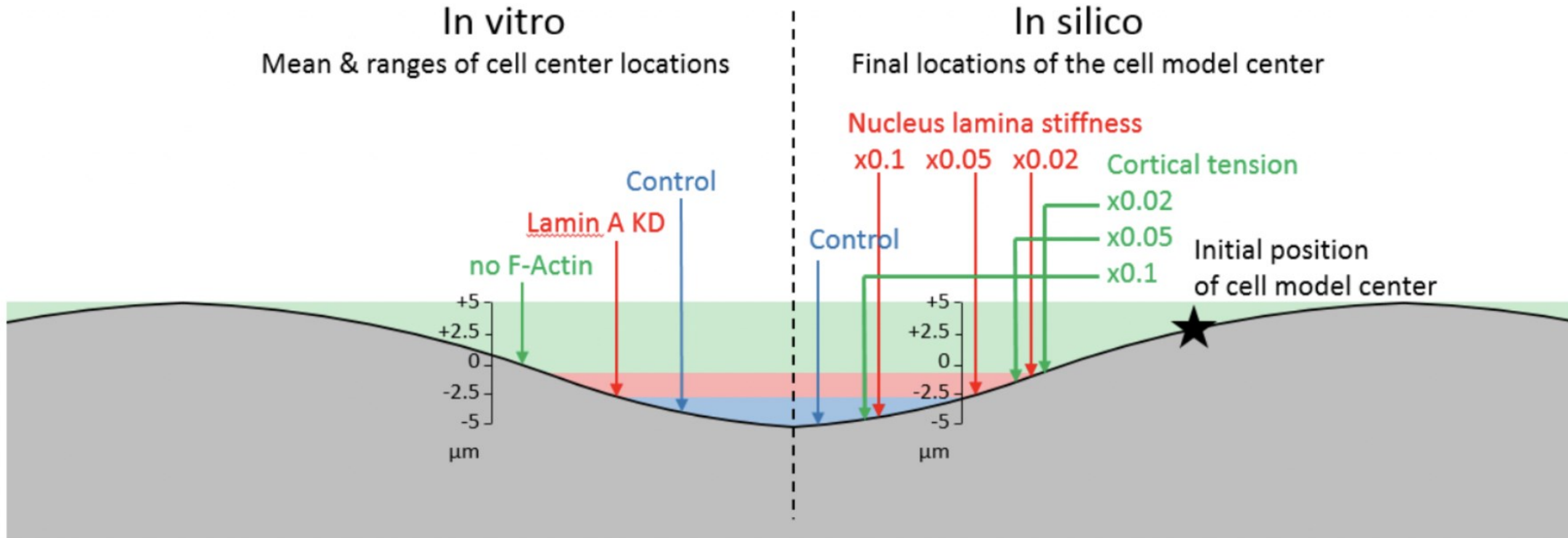
- The model migrates by following the nucleus

Cell model Trajectories based on nucleus mechanosensing



Curvotaxis
allows cells to reach
concave areas
& relaxed
mechanical state

Effect of Cell structure alterations ?



↘ Nucleus stress or stiffness

=>

↘ Curvotaxis sensitivity

↘ Concave-targeting error

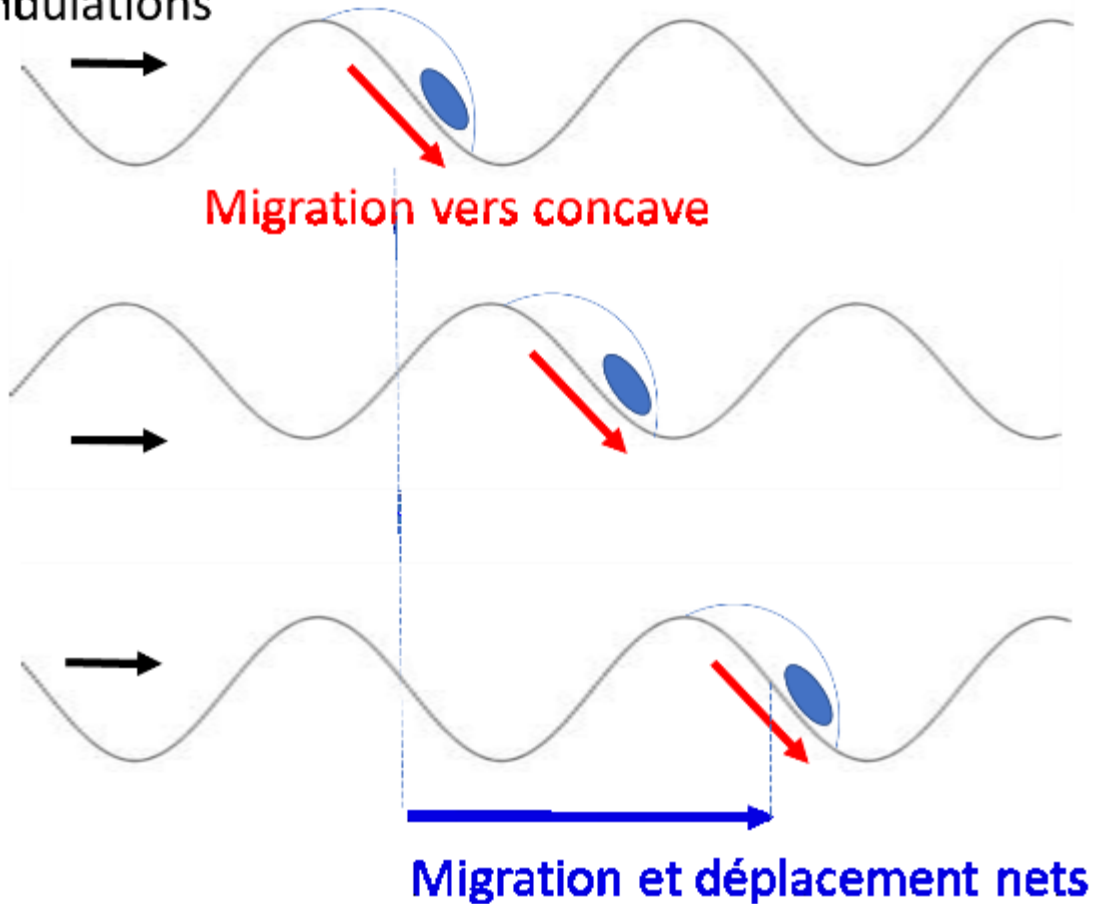
New Problematic

- How guiding cell migration via curvotaxis
continuously & over long distance ?

Guide cell migration via Dynamic Curvotaxis

-> generate travelling waves

Vitesse des
ondulations



-> undulations of cell layers during
development [Harmand 2021]

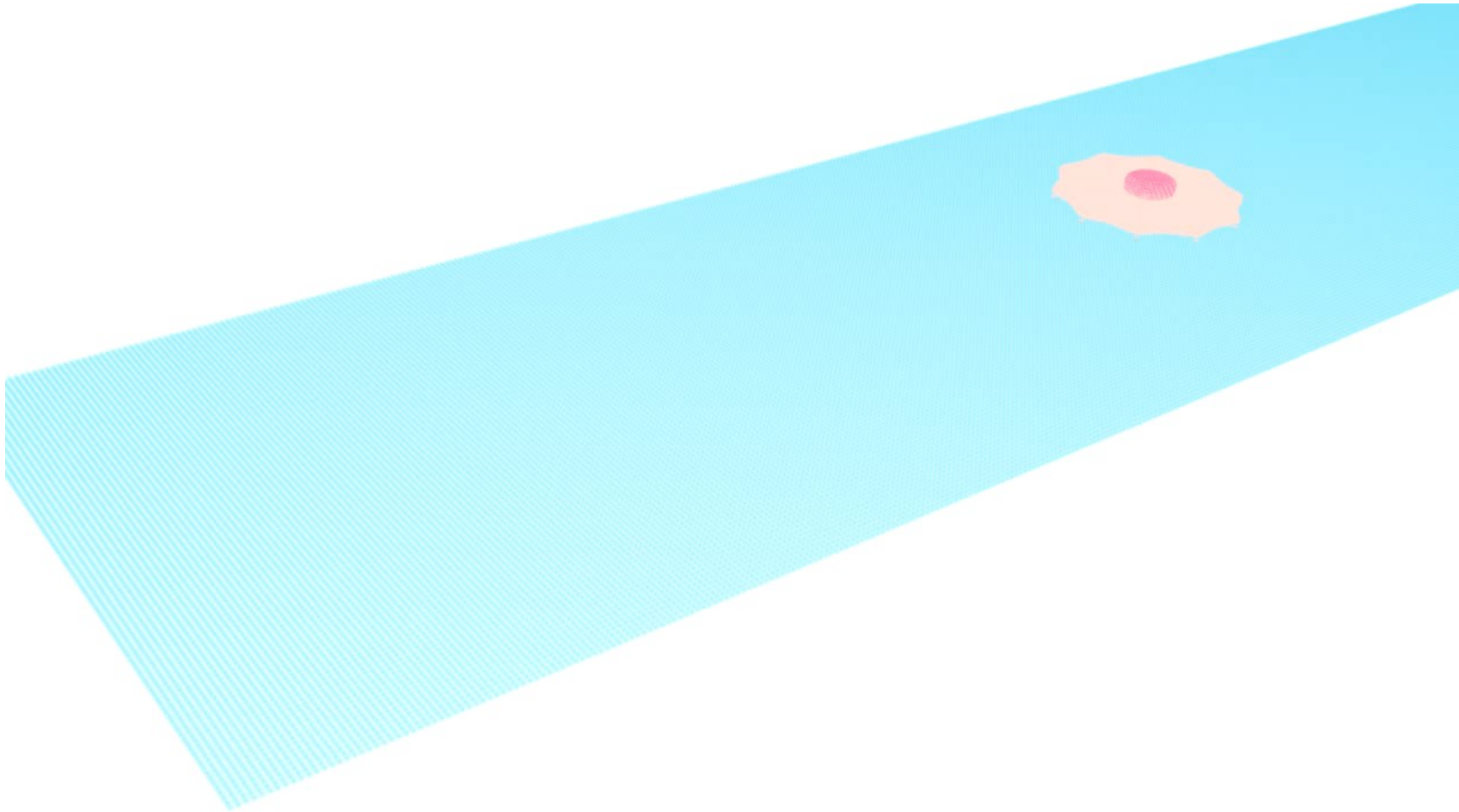
Advantage of the model

Simulate what we can't do
experimentally

Guide cell migration by Dynamic Curvotaxis -> **generate travelling waves**

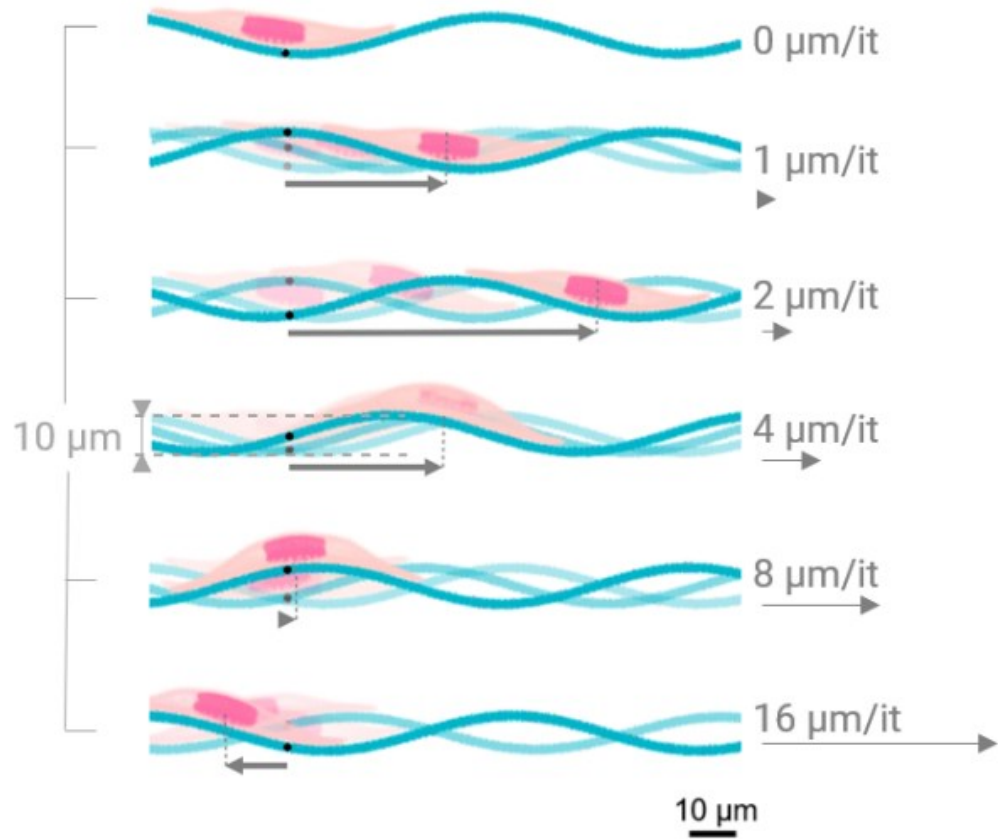


Ian Manificier
(Post- Doc)

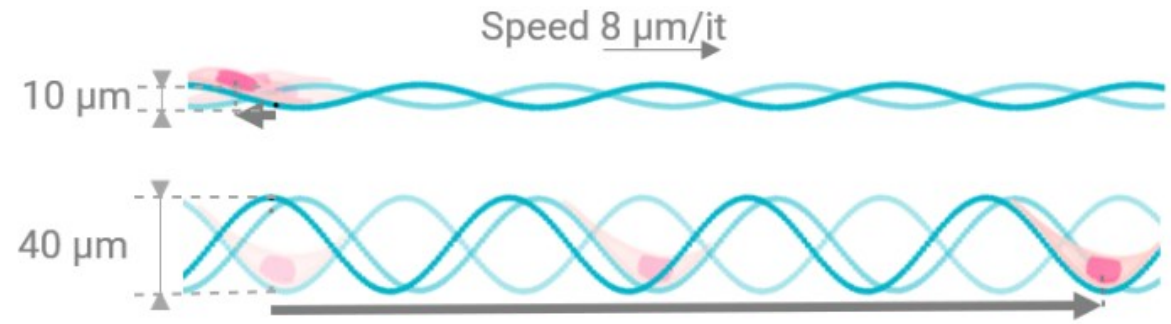


ANR MovingCells 2022-26
Led by In silico BMI Group

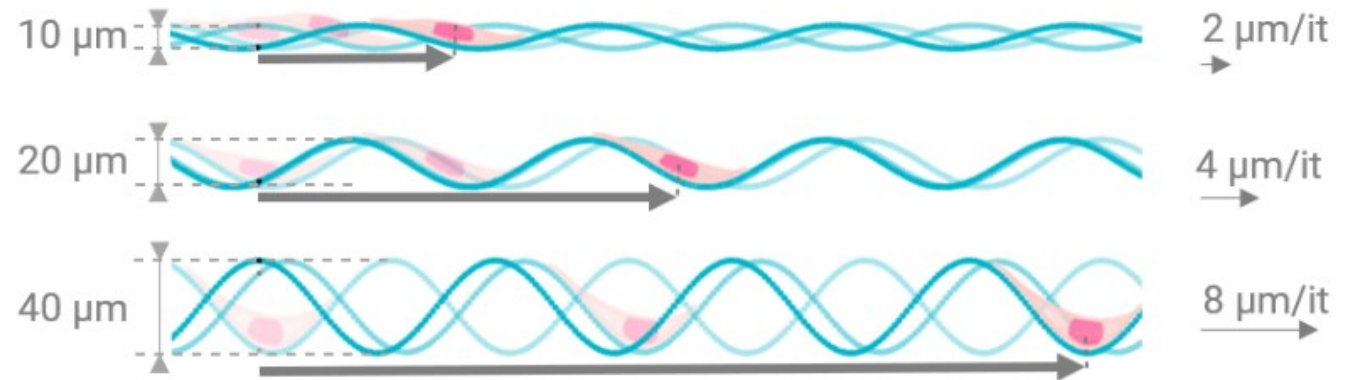
Wave speed influence ?



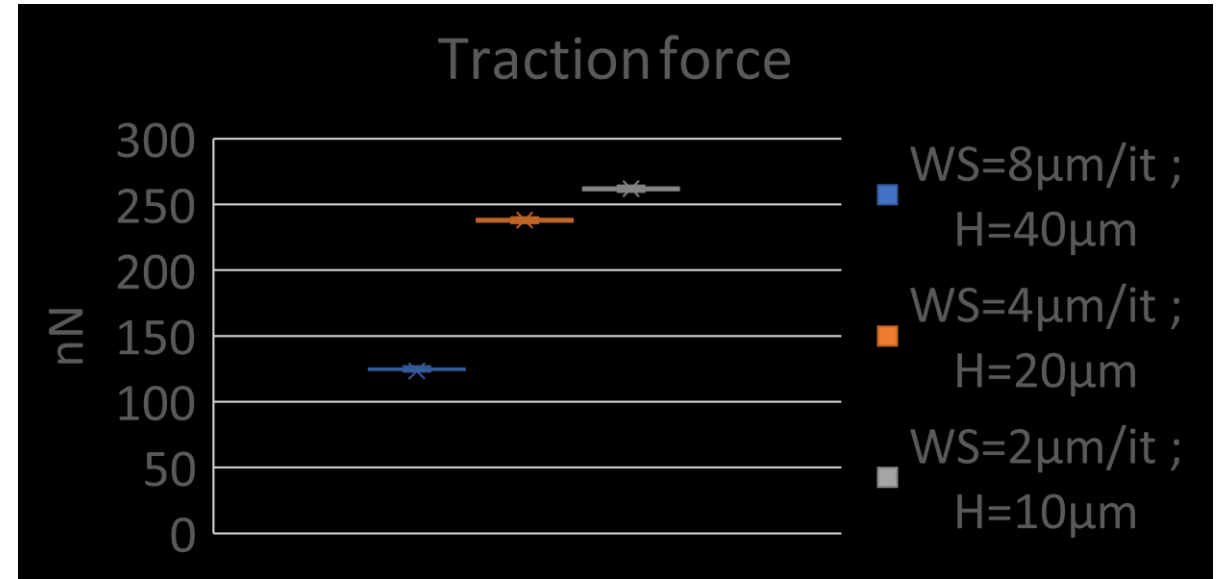
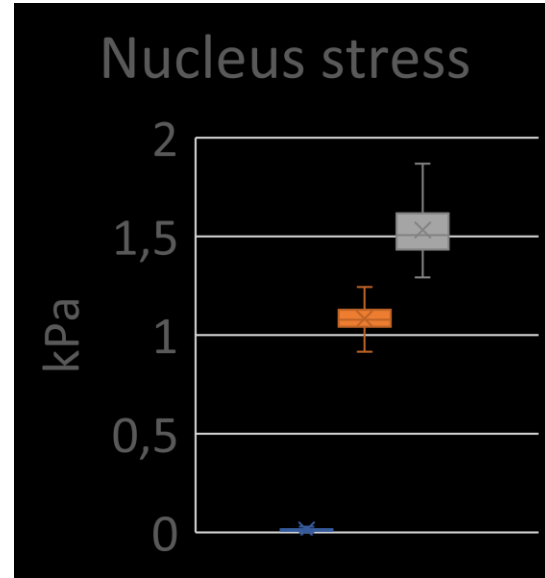
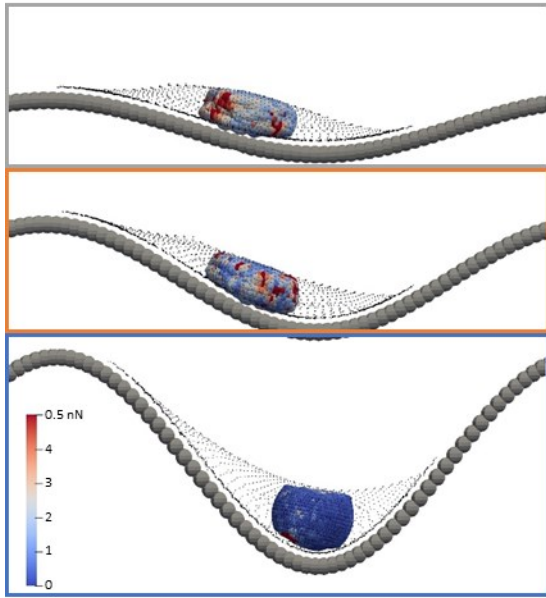
Wave height influence ?



Cross influences of Wave speed & height on cell migration



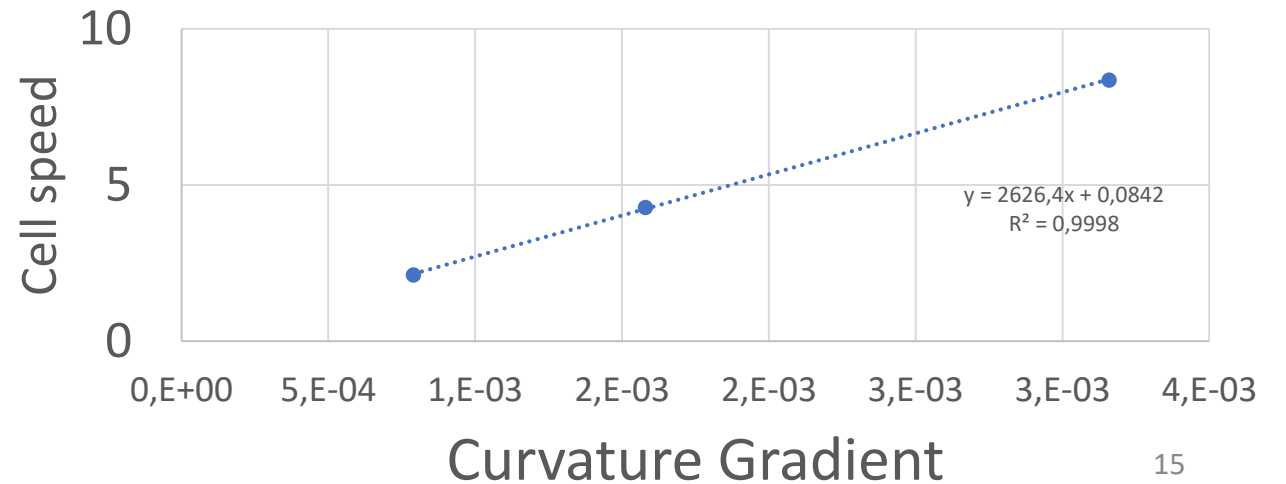
Wave Curvature & Nucleus Stress & Cell speed



$$C(x) = f''(x) \cdot (1 + f'(x)^2)^{-\frac{3}{2}}$$

$$\frac{\Delta C(x)}{\frac{1}{2}WL} = 8 \frac{H \cdot \pi^2}{WL^3}$$

Cell Speed VS curvature gradient



Conclusions

- 1st « proof of concept » of **dynamic chemotaxis**
 - with mechanical understanding

Limits :

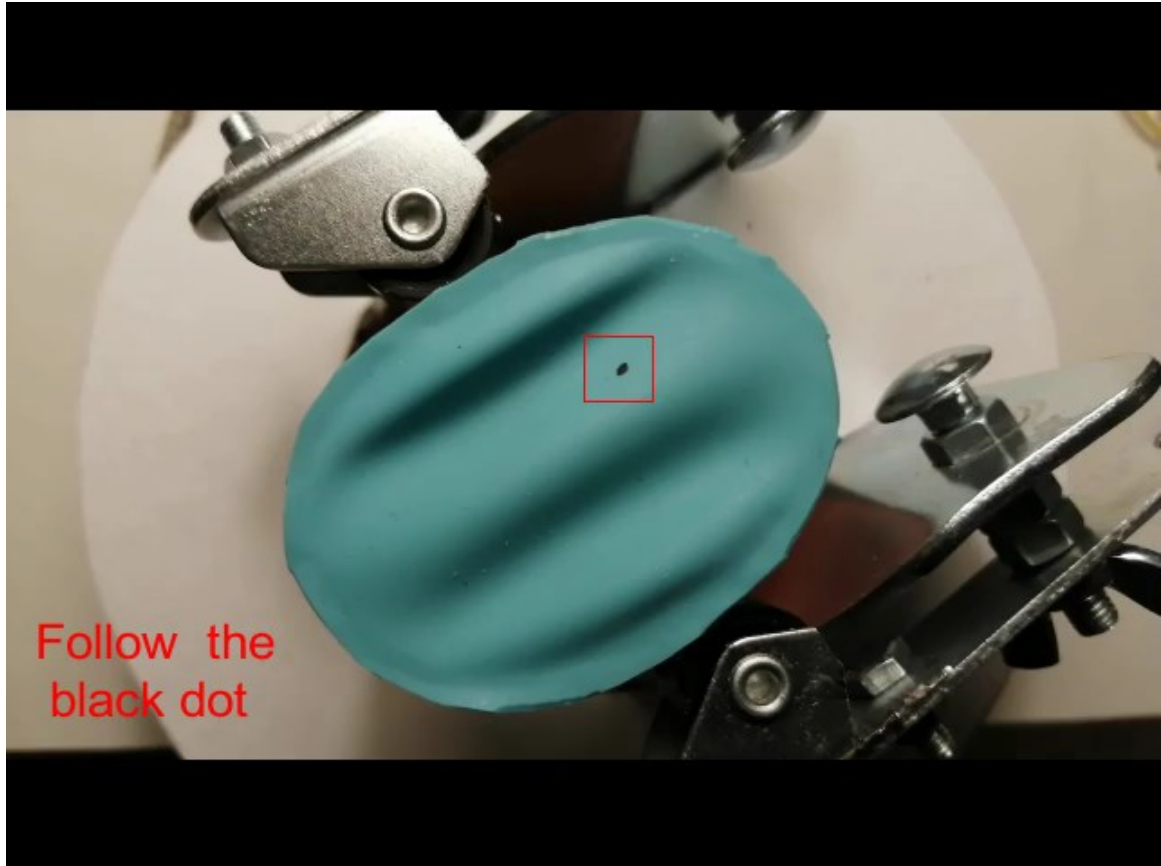
- cell migration machinery not involved (no filopodia, no lamellipodia,...)
 - > cell model is just sliding
 - > Hard to change & remodel cytoskeleton during migration simulation
- Only deterministic, no stochastic
 - > hard to analyze emergence of a given cell behavior

New strategies :

- cell = agent based-model -> agent = cytoskeleton filament
 - real-time modelling & stochasticity
- > **Post Doc Position available**

Technical Solution – Dynamic Surface Waves

Collaboration with Valeriy Luchnikov & Laurent Pieuchot IS2M Mulhouse



Next step:

- Develop the dynamic substrate to run in vitro experiments