Soft Condensed matter @ Sharif

Single particle activities

Mohammad Reza Ejtehadi

Sharif University of Technology, 2016

Erice, September 2019

The city Tehran

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A Low Reynolds number predator

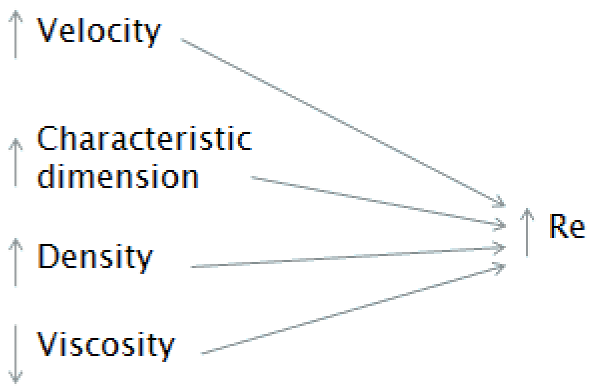
An example of microscopic wolf and rabbit

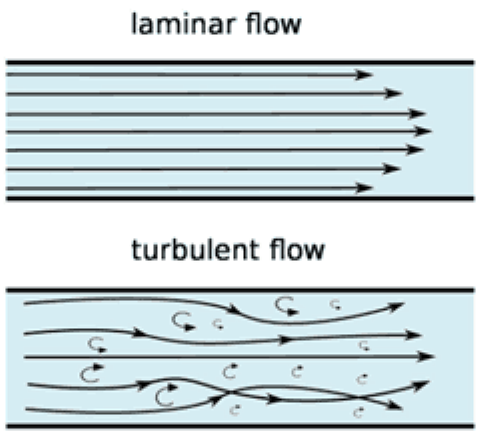
Taken in 1950s by David Rogers at Vanderbilt University

Why does it move?
To find something

Low Reynolds number swimming

$$Re = \frac{\text{inertia forces}}{\text{viscous forces}} = \frac{\rho \,.\, V \,.\, D}{\mu}$$

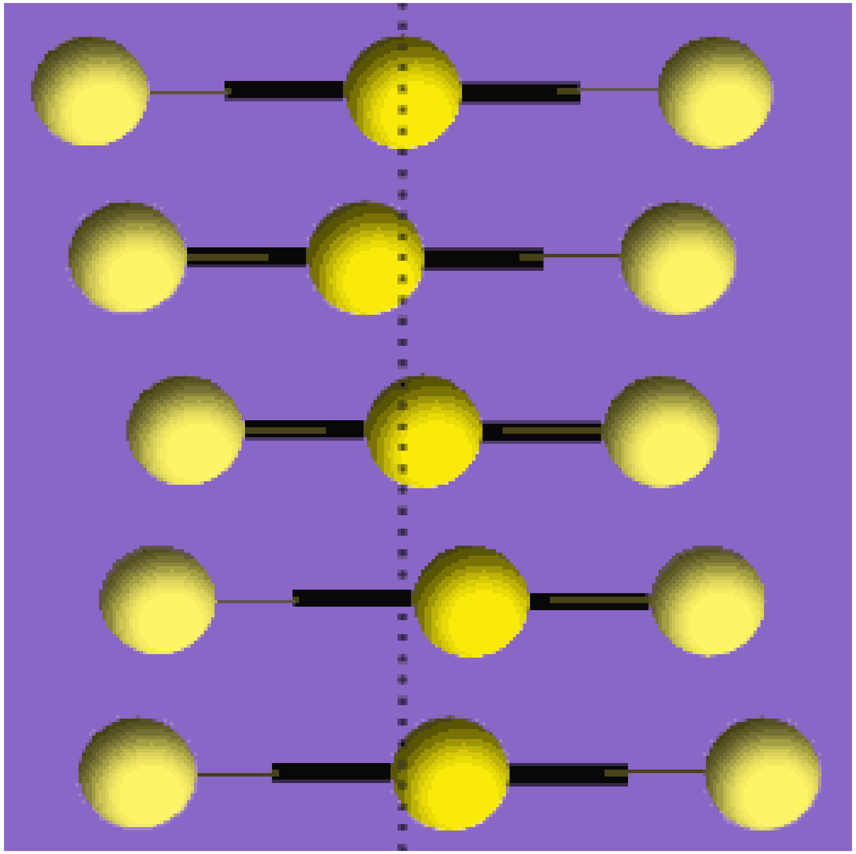




$$\rho\left(\frac{\partial V}{\partial t} + V\cdot\nabla V\right) = \underbrace{\nabla P} + \underbrace{\rho g} + \underbrace{\mu\nabla^2 V}$$

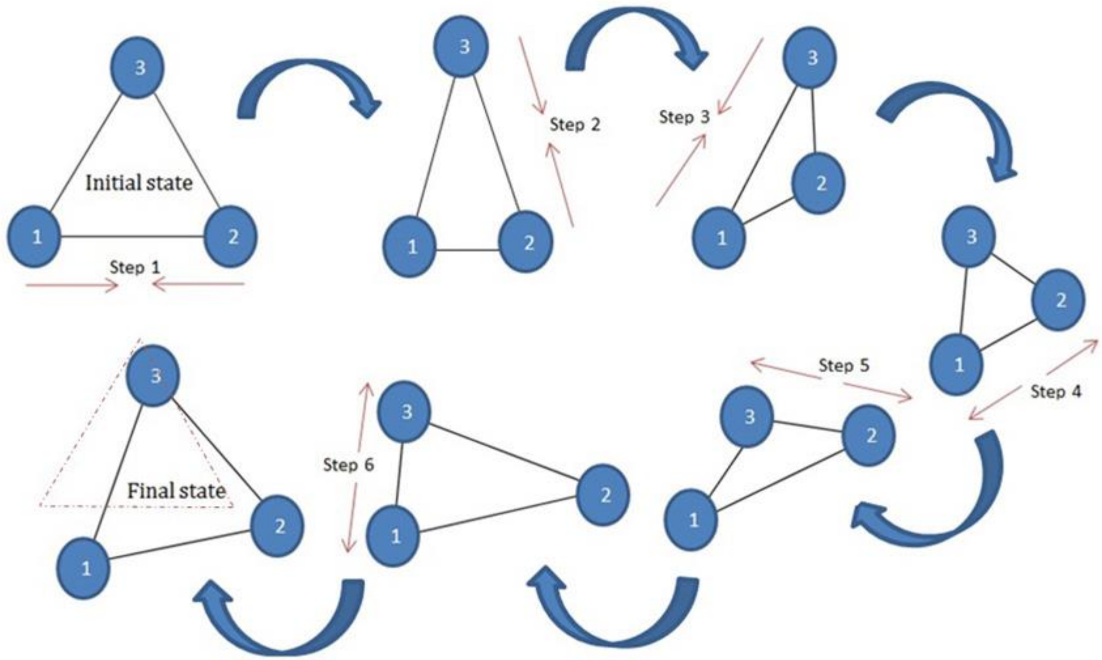
Low Reynolds number swimming is difficult

Najafi-Golestanian swimmer



Najafi, Golestanian, PRE (2003)

Two dimensional active swimmer design

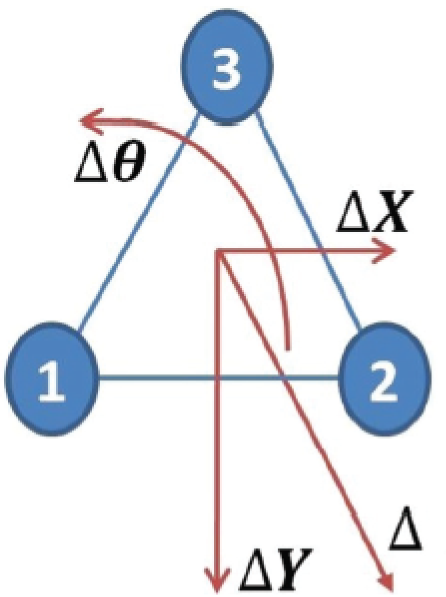


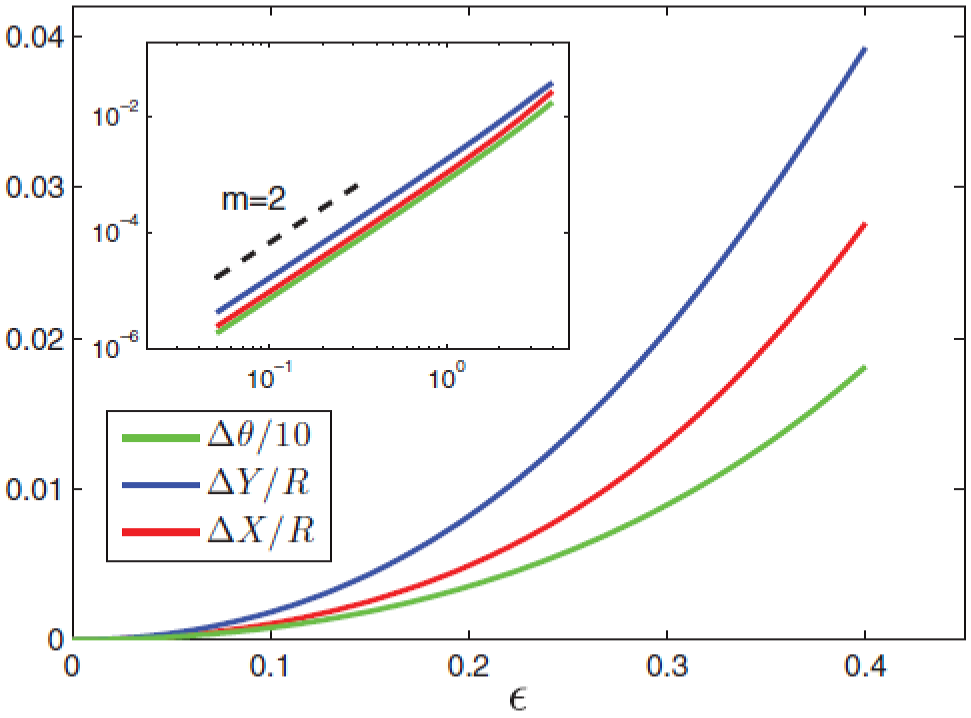
Mehram Ebrahimian

Mohammad Yekezareh

Ebrahimian, Yekezareh, Ejtehadi, Phys Rev E (2015)

Translational and rotational displacements after a full period

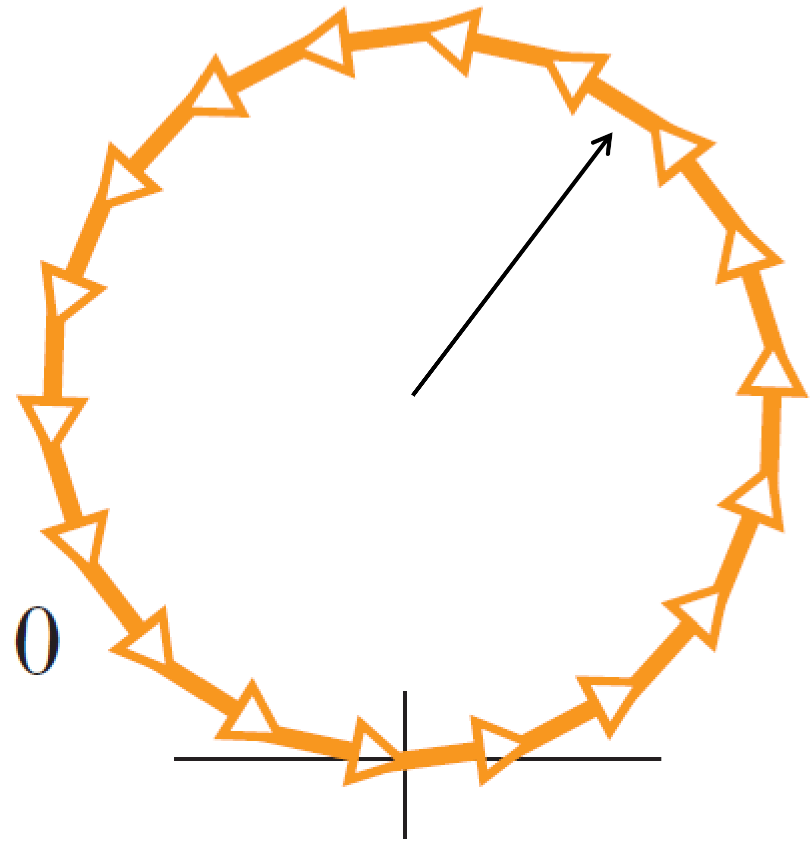




For regular cycles it doesn't go anywhere

$$\rho = \frac{\Delta}{\Delta\theta}$$

For possible values of ϵ :

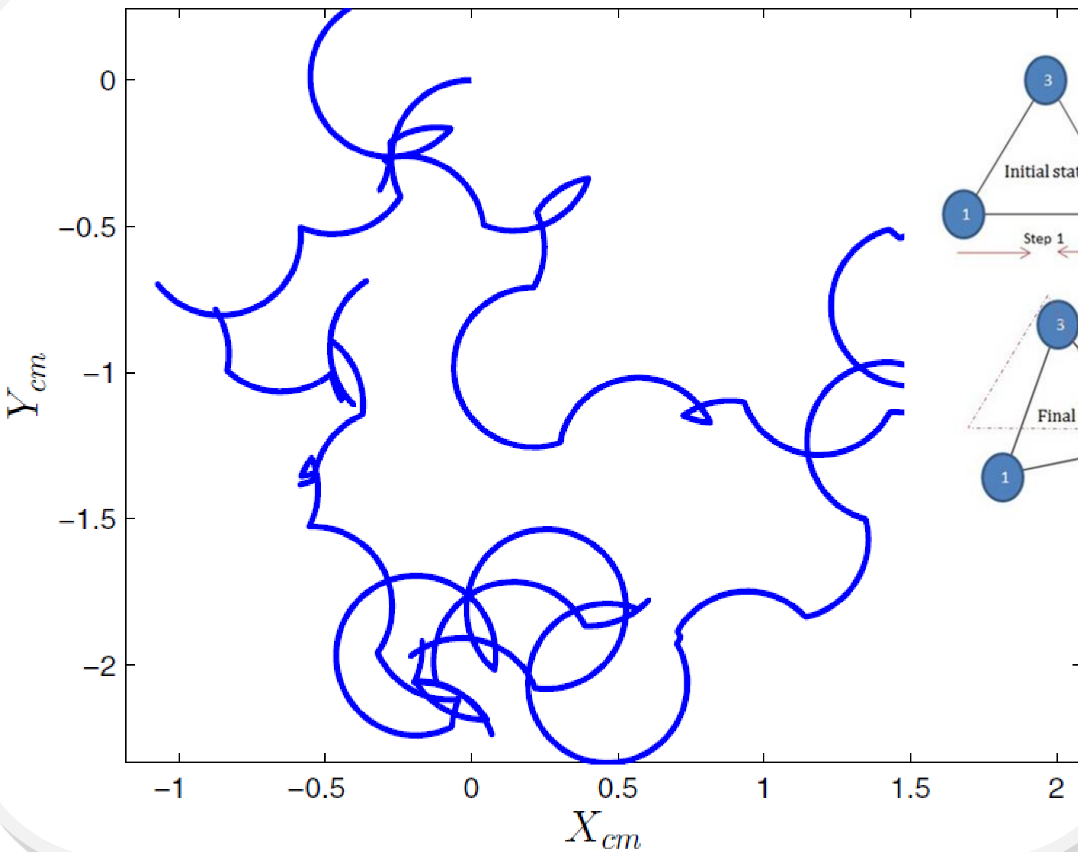


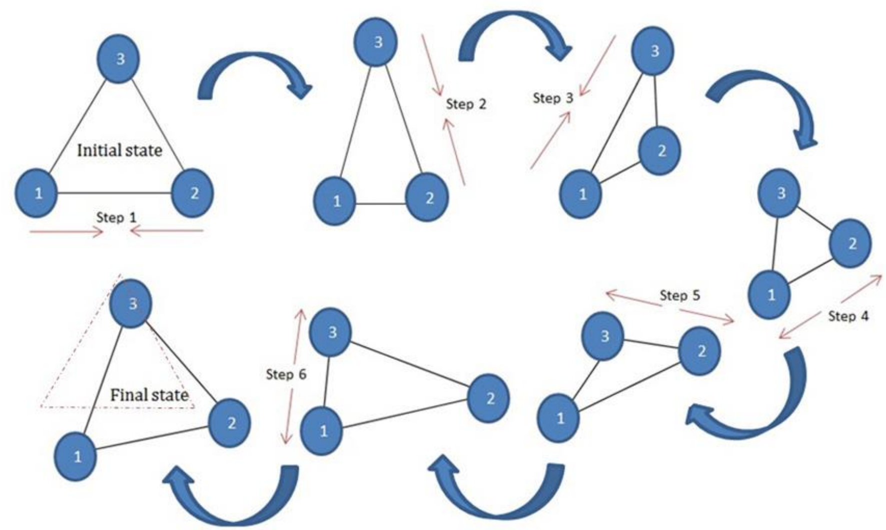
radius of rotation < triangle size

Then

It is almost a rotor

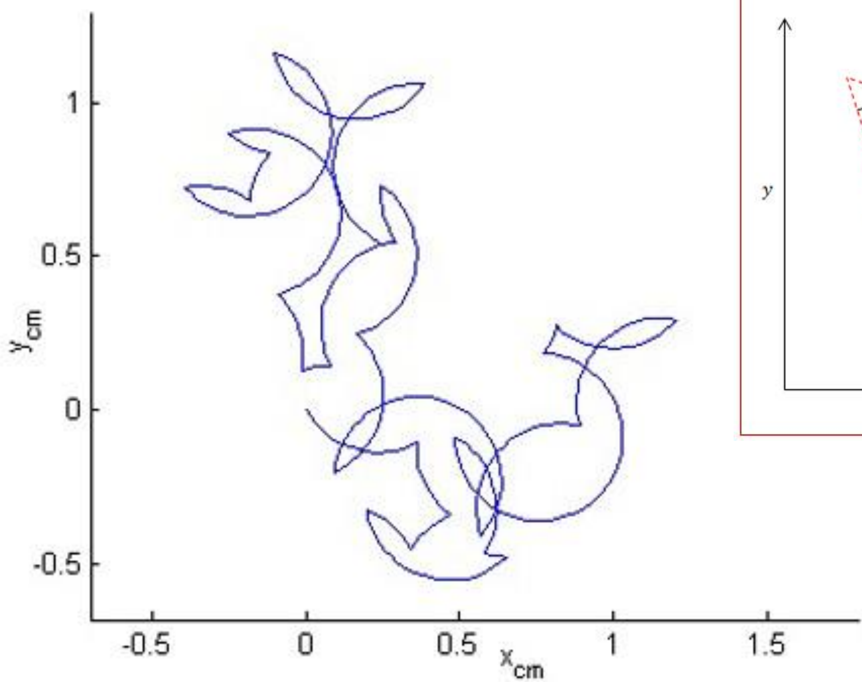
Introduction of the noise

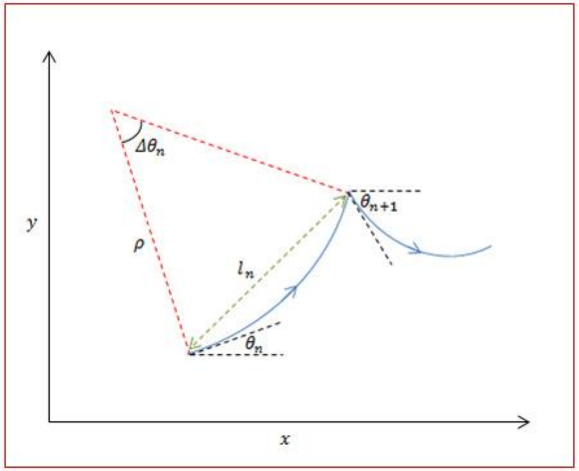




Run & Tumble :
Curved runs & 120^o tumbles

Chiral Run and Tumble – Arc and Tumble





For small tumble probability

$$p \ll 1$$

and tumble rate

$$\eta = \frac{p}{\Delta\theta}$$

$$D = \frac{1}{2}\omega\,\rho^2\,\frac{\eta}{(\eta^2+1)}$$

Ebrahimian, Yekezareh, Ejtehadi, Phys Rev E (2015)

If linkers act independently

It is more realistic to assume any linker as an individual molecular motor which acts independently in response to chemicals

$$S + E \underset{k_3}{\overset{k_1}{\rightleftharpoons}} SE \xrightarrow{k_2} E + P$$

SE : arm in extended state

E : arm in shrank state

Characteristic times:

$$t_o = \frac{1}{k_2+k_3}$$

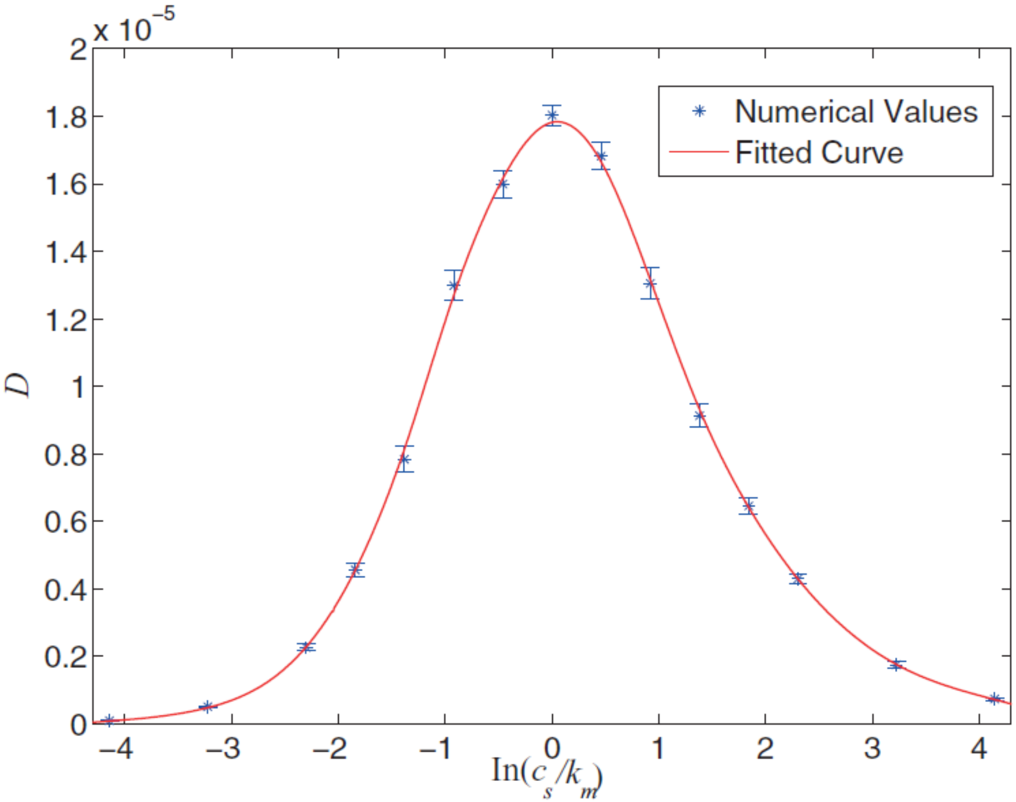
$$t_c = t_0 \frac{k_m}{C_s} \qquad k_m = \frac{k_2 + k_3}{k_1}$$

Optimized concentration of the chemicals

If $C_s \ll k_m$ then $t_c \gg t_0$,

or if $C_s \gg k_m$ then $t_c \ll t_0$

almost all the link length changes are reversible and there is no movement



Chemotaxis

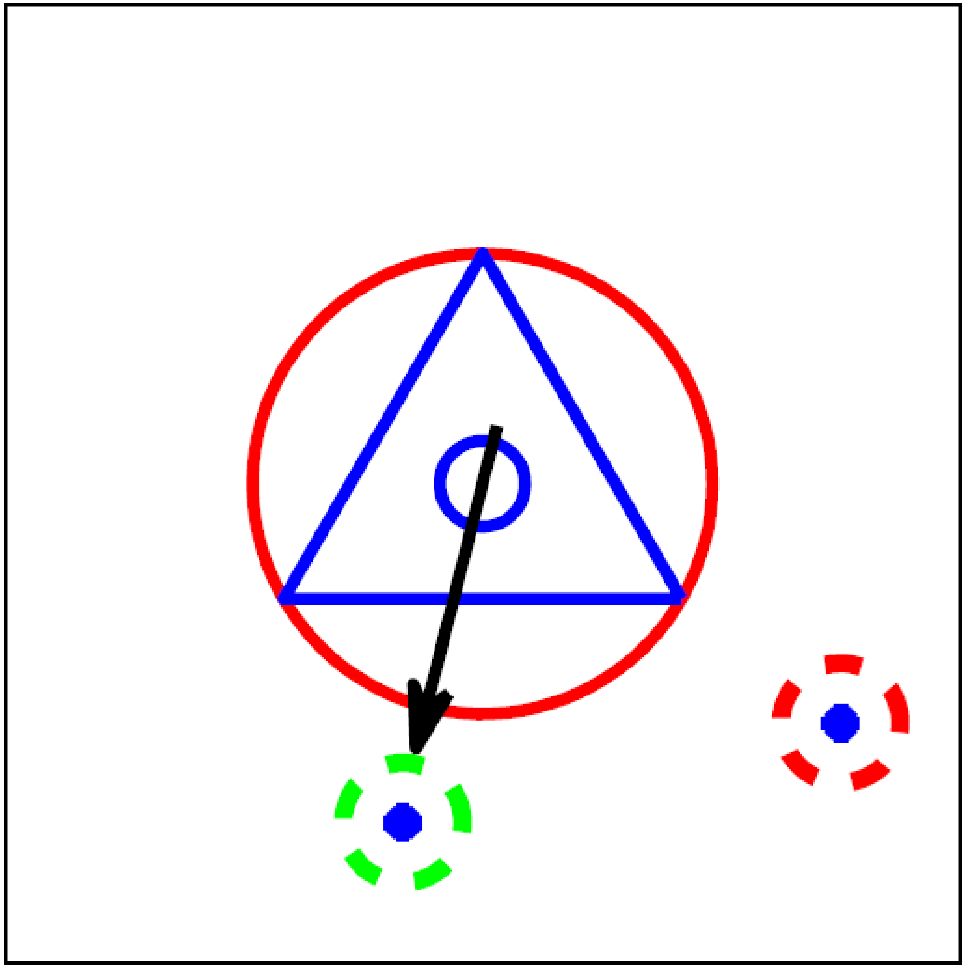
Drift velocity depends on both gradient of the concentration and concentration of the chemicals itself.

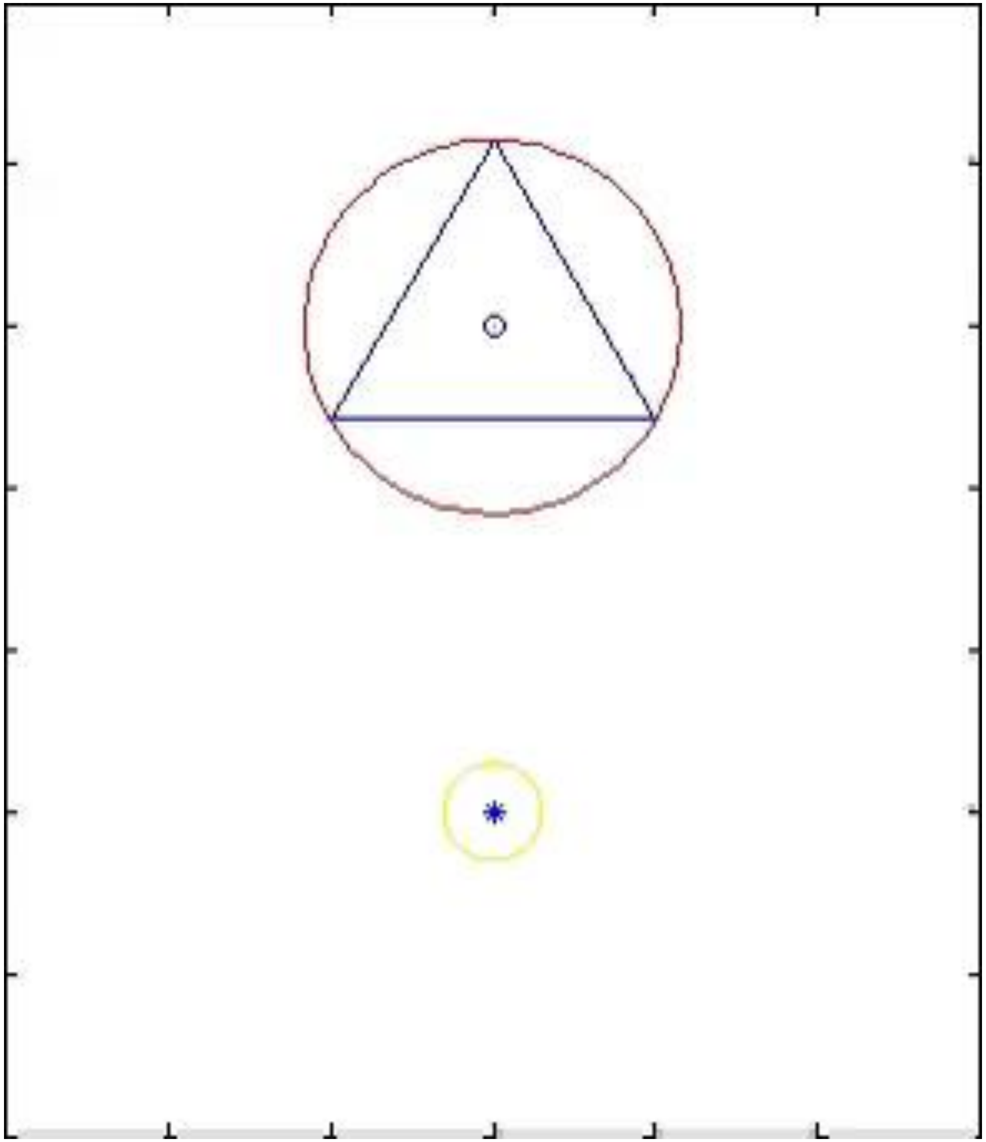
$$\boldsymbol{v} = f(c)\,\boldsymbol{\nabla} c$$

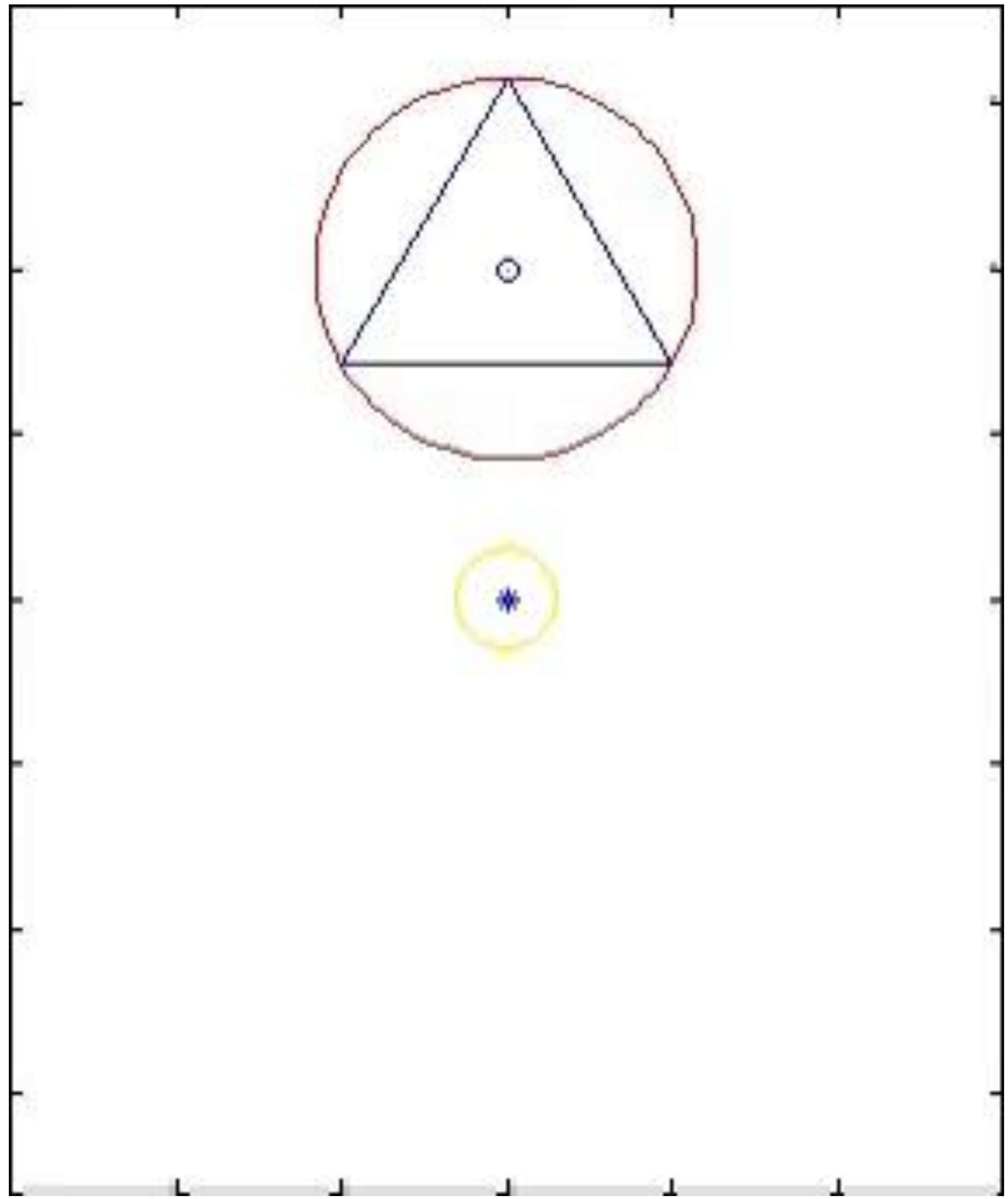
Prey and Predator

To introduce the predator it is supposed that the prey is a source of chemicals which affect the linkers dynamics.

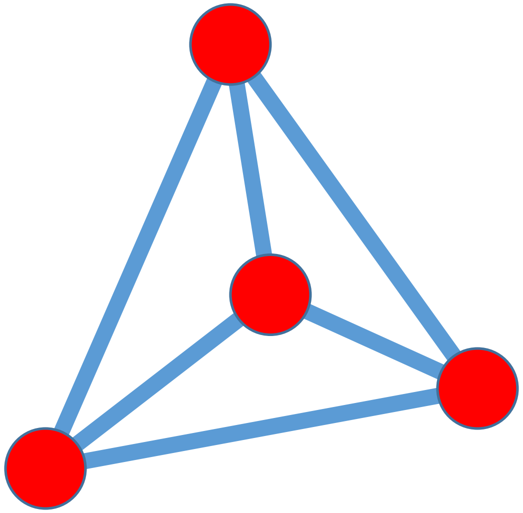
The large red and small blue circles indicate the size and COM of predator, respectively. The arms of the predator swimmer are presented by blue triangles. The prey is the blue point with green circle.

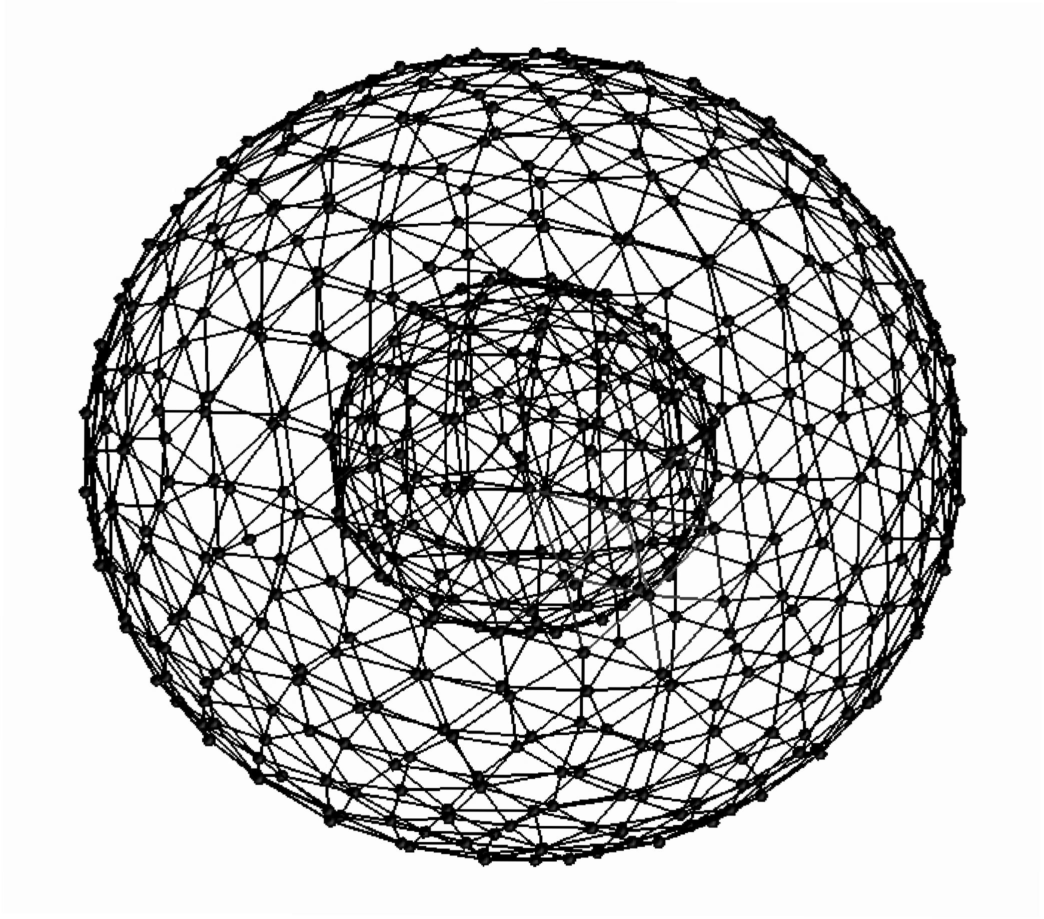






Straightforward generalization to three dimensions





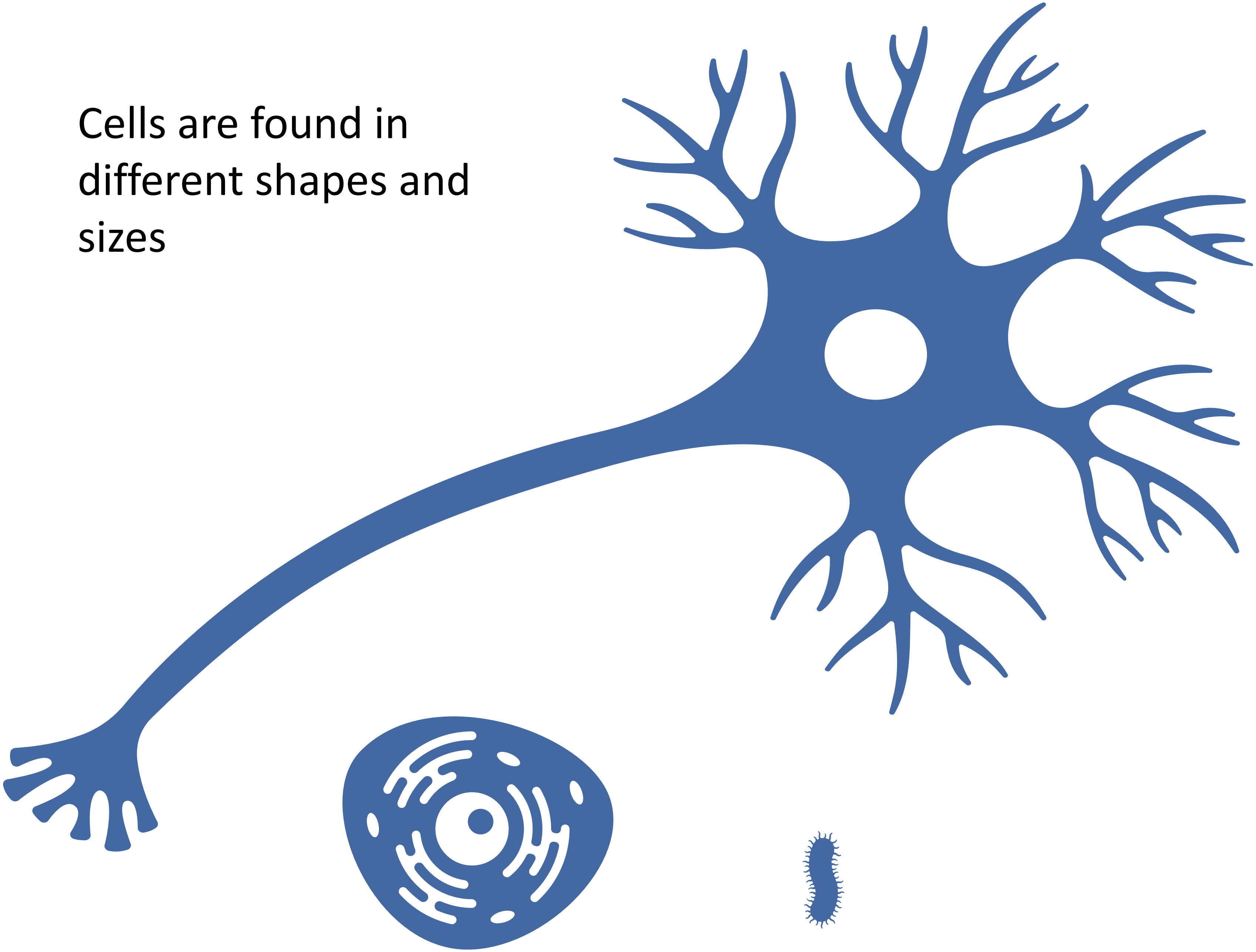
Soft Condensed matter @ Sharif

Mechanical response of cells to substrate topography

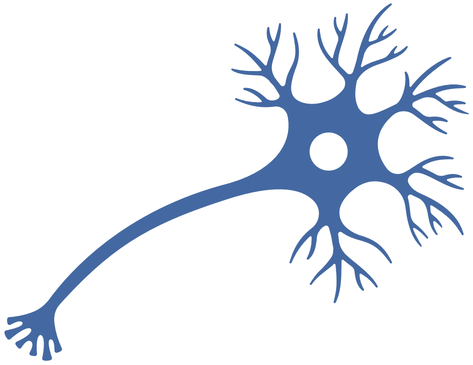
Cells are soft and flexible

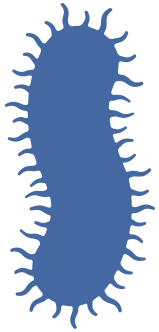
- They responses to deformations and external forces
- But in much larger time and size scales in compare to macromolecules inside.
- Large deformation could be harmful and nonreversible.

Cells are found in different shapes and sizes

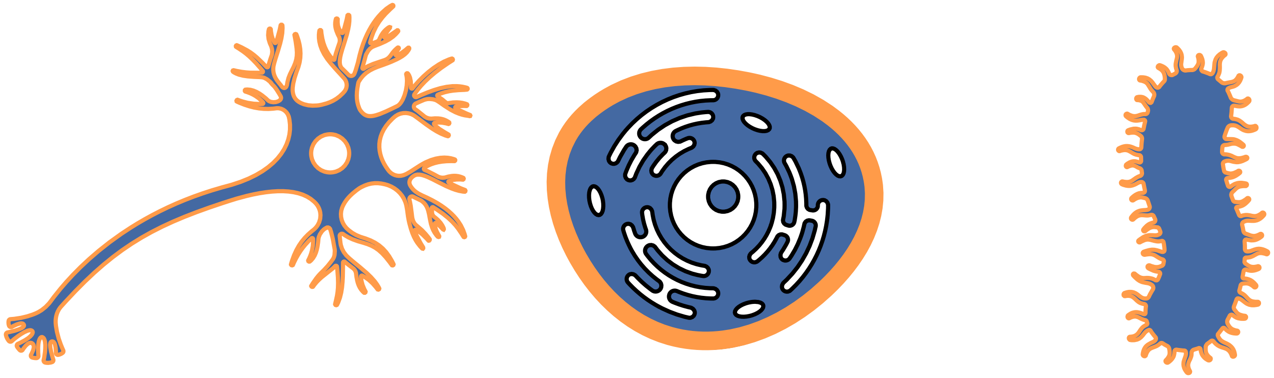


Basic structural elements



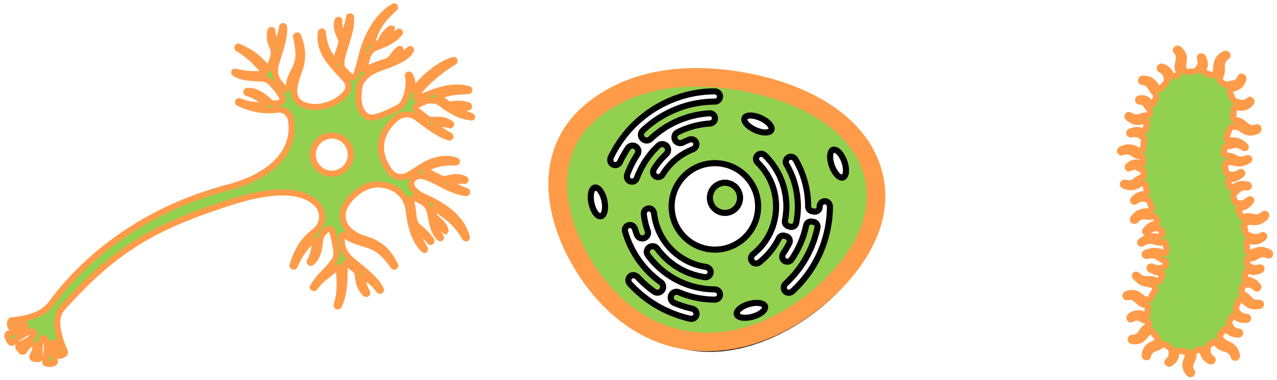


Basic structural elements



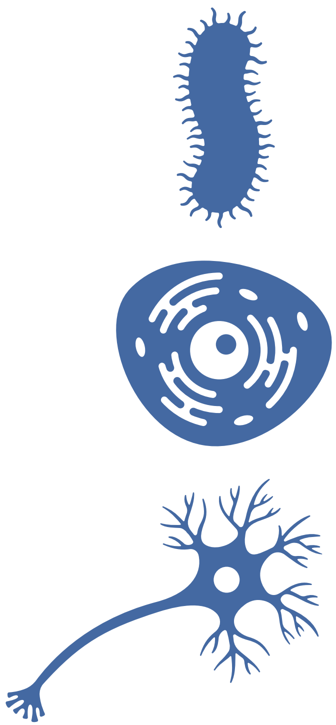
Membrane

Basic structural elements



Filament network

Physicist's perspective



How does a cell maintain/change its shape?

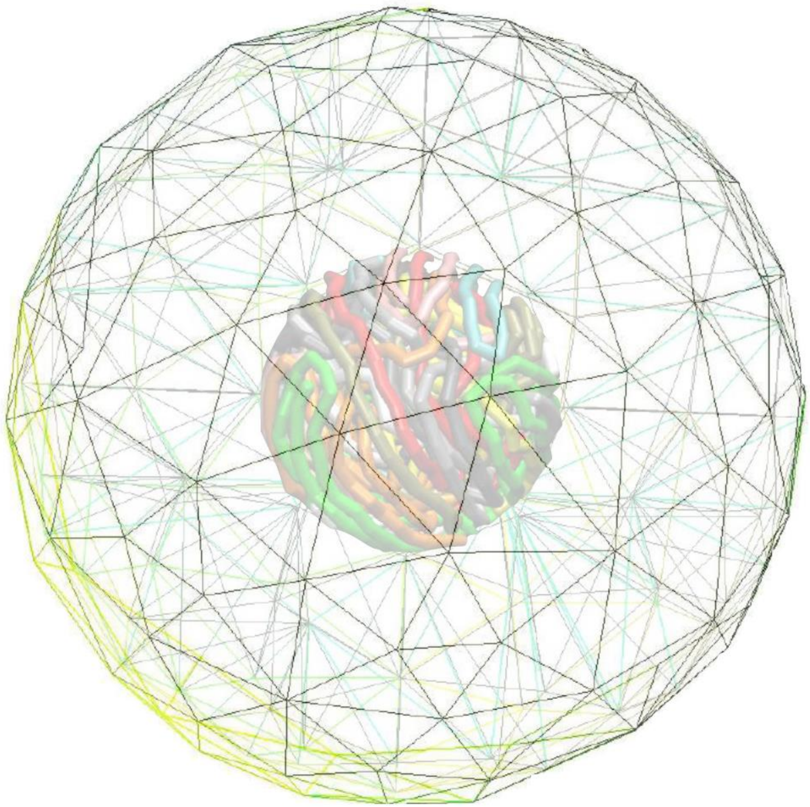
How does the shape change if we apply force (stress)?

How does it affect the shape of the nucleus?

What about the chromatins inside?

How they affect their biological functions?
(mechanotransductions)

THE VIRTUAL CELL



Maziar Heidari

Tiam Heydari

Ali Farnudi

Shahrzad Zareh, Oveis Sheibani, Hoda Shirzad, ……

https://afarnudi.github.io/Membrane_OBJ/

The Virtula Cell Model

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The Virtual Cell Model Software Package

Breif Introduction

The Soft Condensed Matter Group at Sharif university of Technology lead by Prof. Mohammad Reza Ejtehadi has developed a unifying computational framework to create a multicomponent cell model, called the **Virtual Cell Model** (VCM) that has the capability to predict changes in whole cell and cell nucleus characteristics (in terms of shape, direction, and even chromatin conformation) on cell substrates. Modelling data used in the package are correlated with cell culture experimental outcomes in order to confirm the applicability of the models and to demonstrate their ability to reflect the qualitative behaviour of different cells. This may provide a reliable, efficient, and fast high-throughput approach for the development of optimised substrates for a broad range of cellular applications including stem cell differentiation. Since the VCM is designed to mimic properties of soft matter in the micro scale, it can be used to study a verity of physical problems. Mechanical properties of thin film near or attached to other objects.

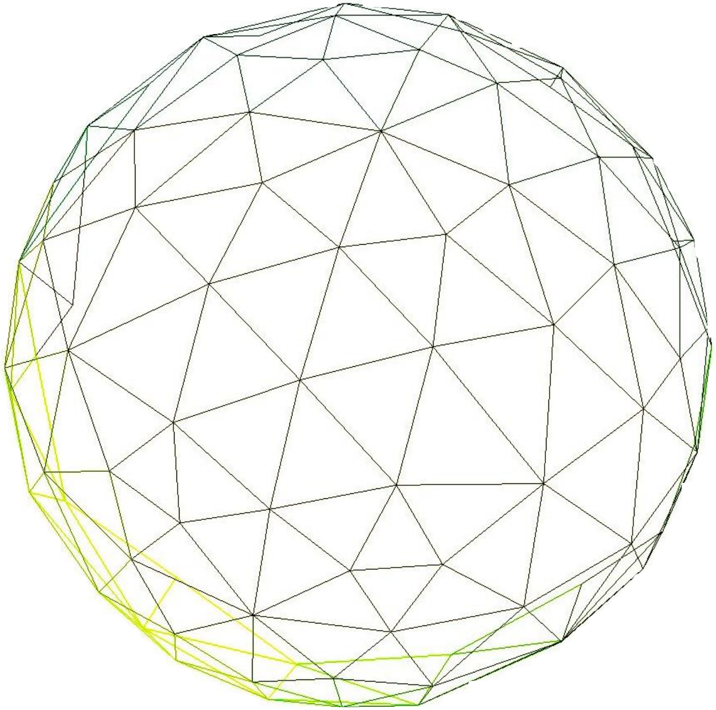
The VCM utilises 4 basic parts that are the membrane, the actin network, the nucleus, and the substrate.

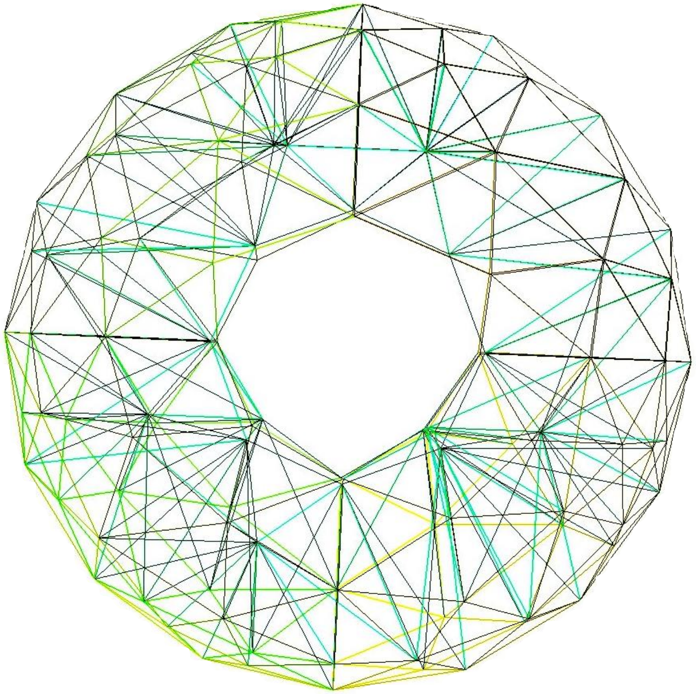
The Membrane

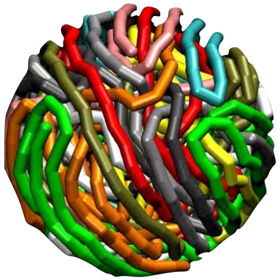
The membrane is made of a series of nodes (x, y, and z coordinates of points in space) and a list of node pairs that are imported into the software. The VCM package can automatically import mesh files[^1] generated by the GMSH software.

[^1]: The current version is compatible with the gmsh version II file style. The option is also available in gmsh versions 2 and above.

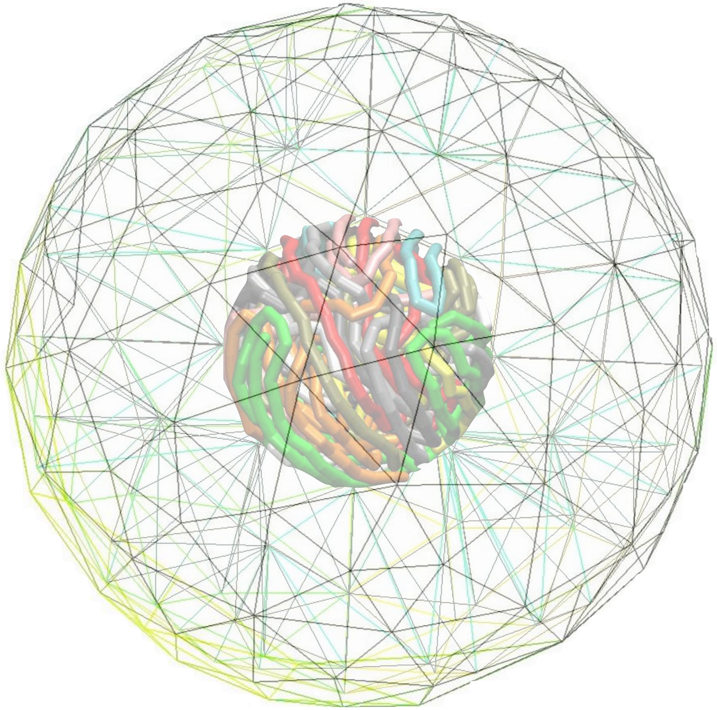
The Virtual Cell: Components

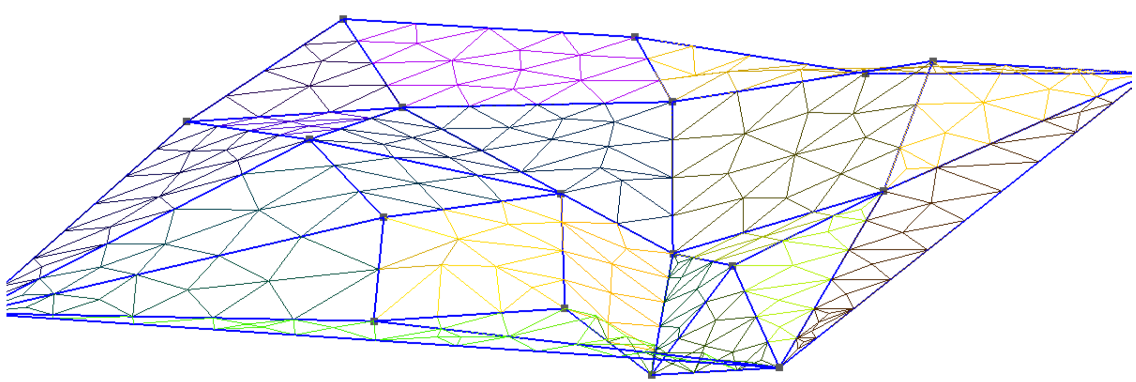




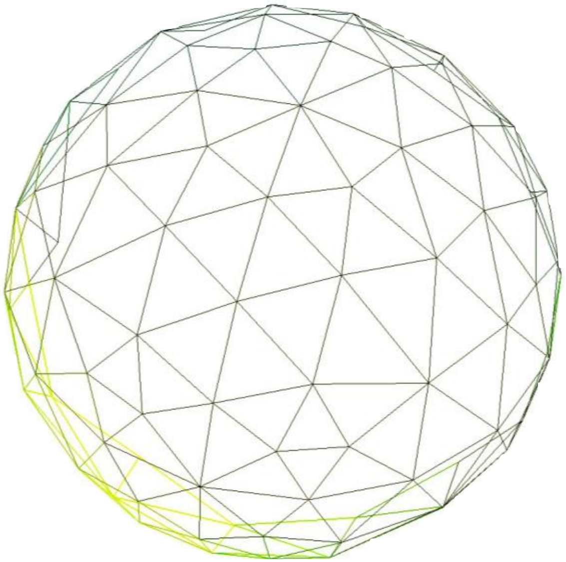


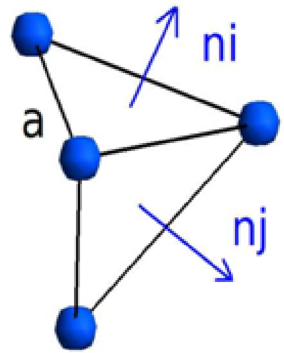
The Virtual cell model

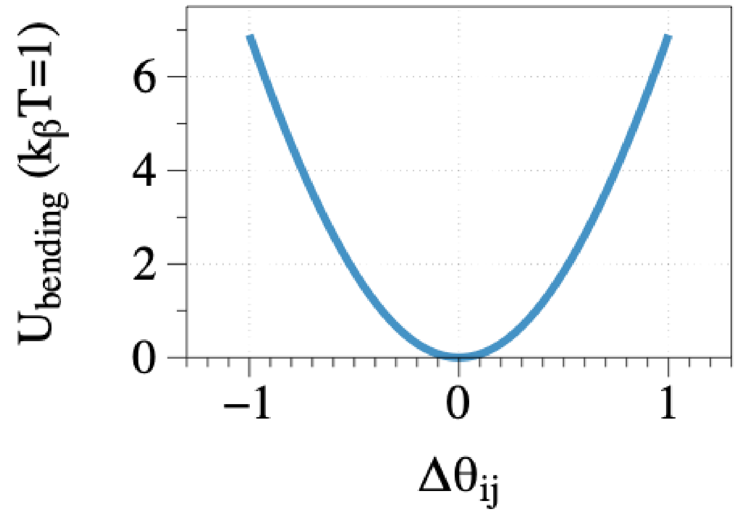


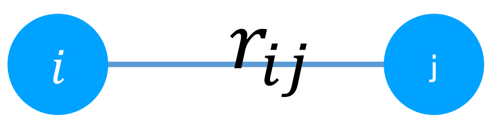


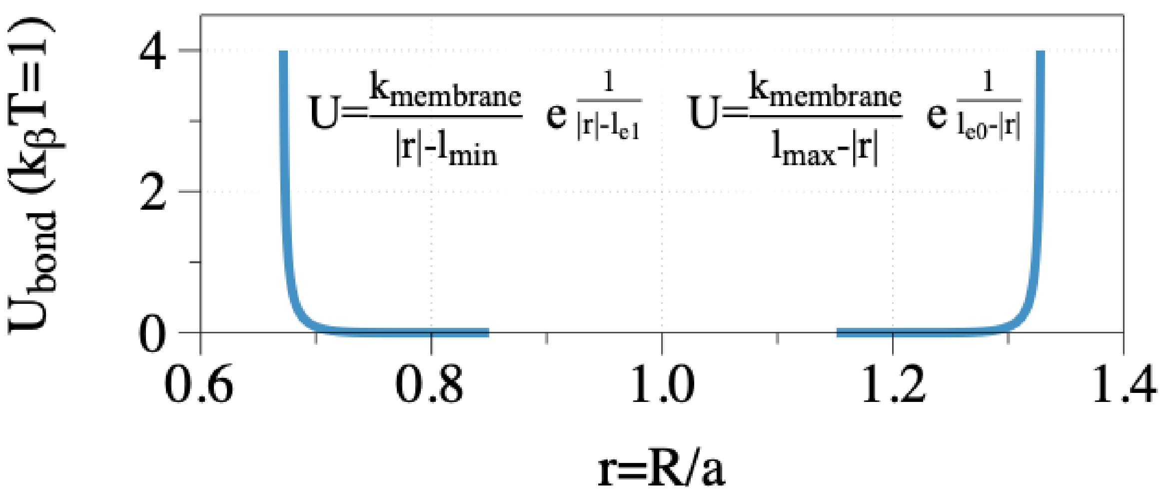
The Virtual Cell: Membranes









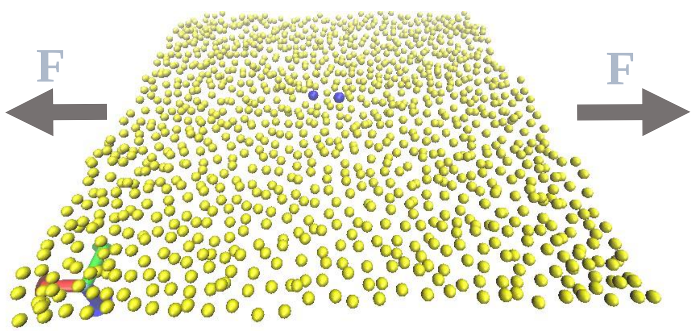


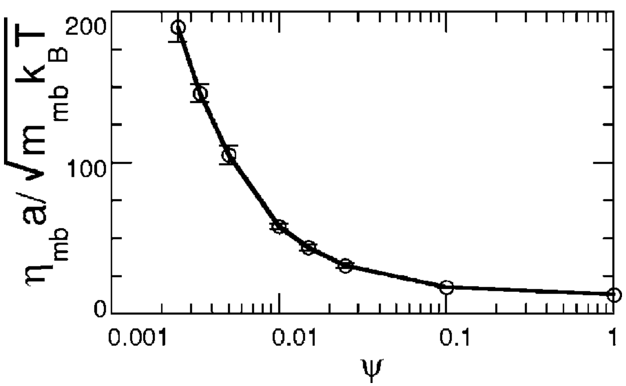
[12] G. Gompper and D. M. Kroll. Triangulated-surface models of fluctuating mem- branes. In D. R. Nelson, T. Piran, and S. Weinberg, editors, Statistical Mechanics of Membranes and Surfaces, chapter 12, pages 359–426. **World Scientific, Singapore, 2nd edition**, **2004**
.

The Virtual Cell: Membranes

Diffusion of membrane nodes

$$Prob(\pi_{new} \rightarrow \pi_{old}) = e^{-\left(\frac{U_{new}-U_{old}}{k_B T}\right)}$$





Gompper, gerhard and Kroll, Daniel, "in Statistical Mechanics of Membranes and Surfaces" Edited by D. R. Nelson, T. Piran, and S. Weinberg, 2nd ed.: World Scientific Publishing Company, 2004.

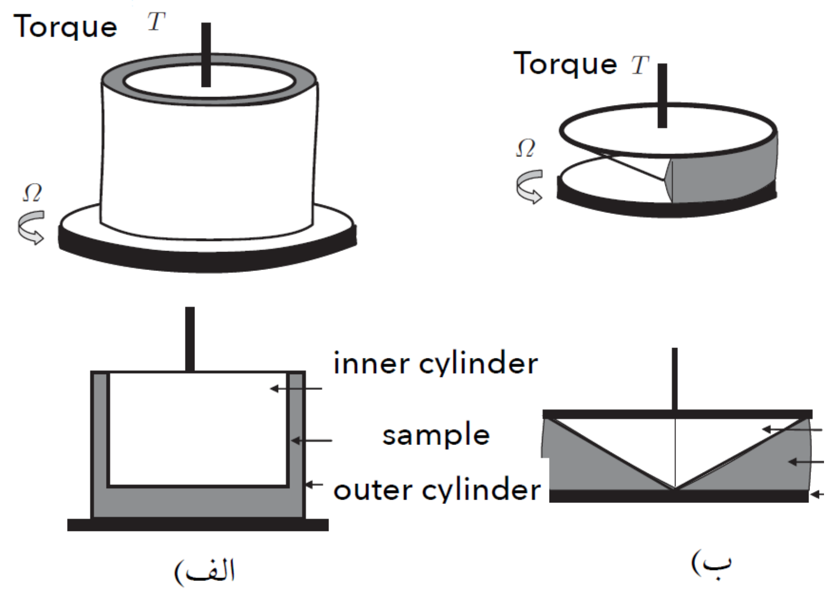
The Virtual Cell: Cytoscleton

$$\gamma(t) = \gamma_0 \cos \omega t.$$

$$\sigma(t) = -\int_{-\infty}^{t} dt' G(t-t')\gamma_0 \omega \sin \omega t$$

$$= -\int_{0}^{\infty} dt' G(t')\gamma_0 \omega \sin \omega (t-t')$$

$$= \gamma_0 \left[G'(\omega)\cos \omega t - G''(\omega)\sin \omega t\right]$$

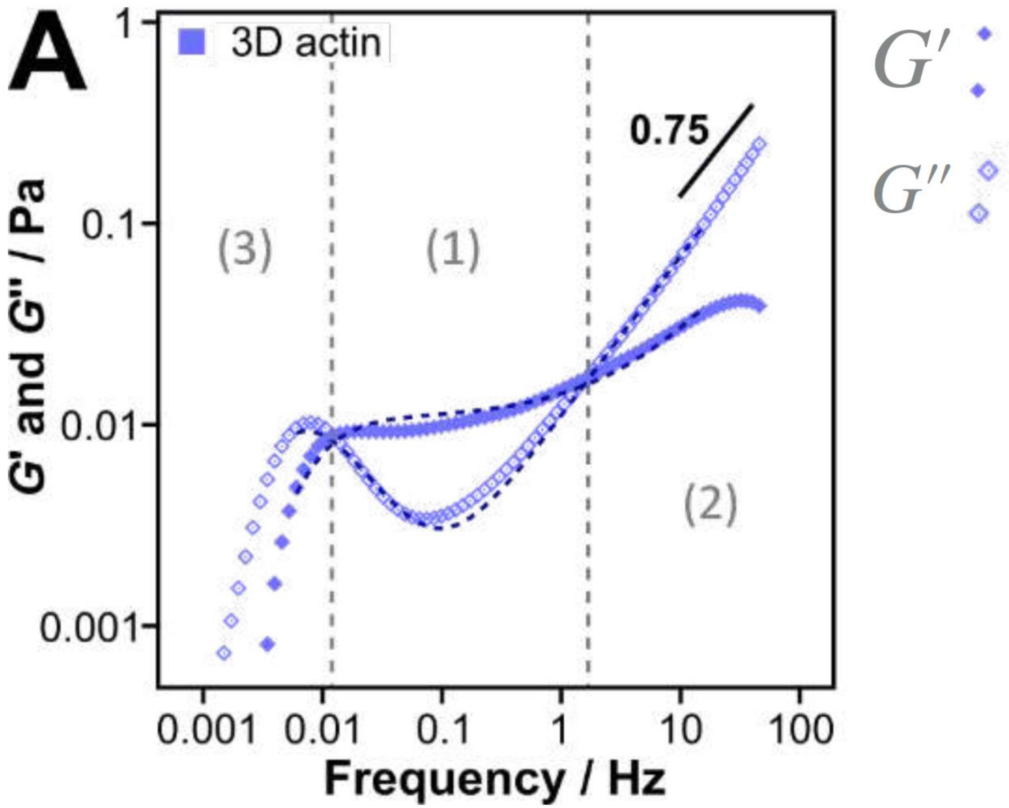


$$G'(\omega) = \omega \int_{0}^{\infty} dt \sin \omega t G(t)$$

$$G''(\omega) = \omega \int_{0}^{\infty} dt \cos \omega t G(t)$$

$$G^*(\omega) = G'(\omega) + iG''(\omega).$$

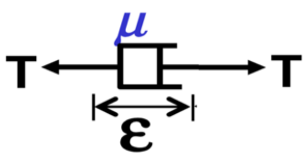
Viscoelastic solids



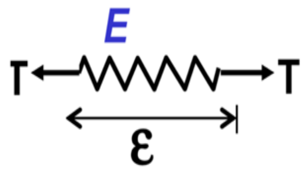
[10] H. Nöding, M. Schön, C. Reinermann, N. Dörrer, A. Kürschner, B. Geil, I. Mey, C. Heussinger, A. Janshoff, and C. Steinem, "Rheology of membrane- attached minimal actin cortices," *The Journal of Physical Chemistry B*, **2018**

The Virtual Cell: Cytoscleton

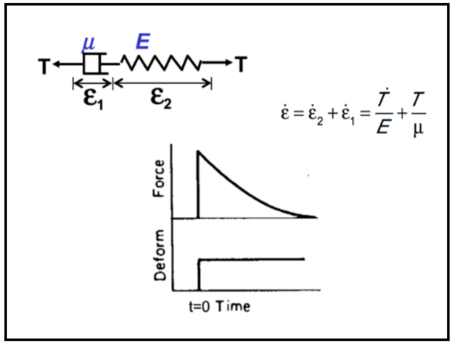
Viscoelastic elements:

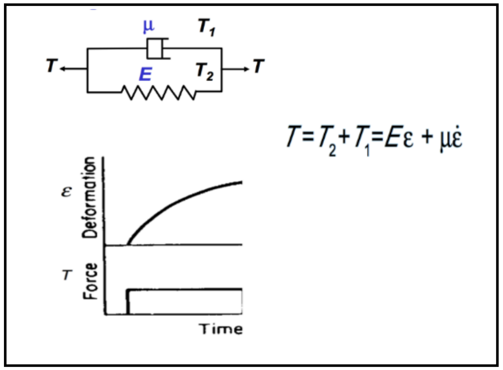


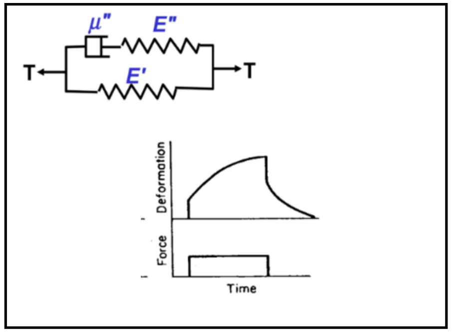
$$\dot{\varepsilon} = T/\mu$$



$$\varepsilon = T/E$$

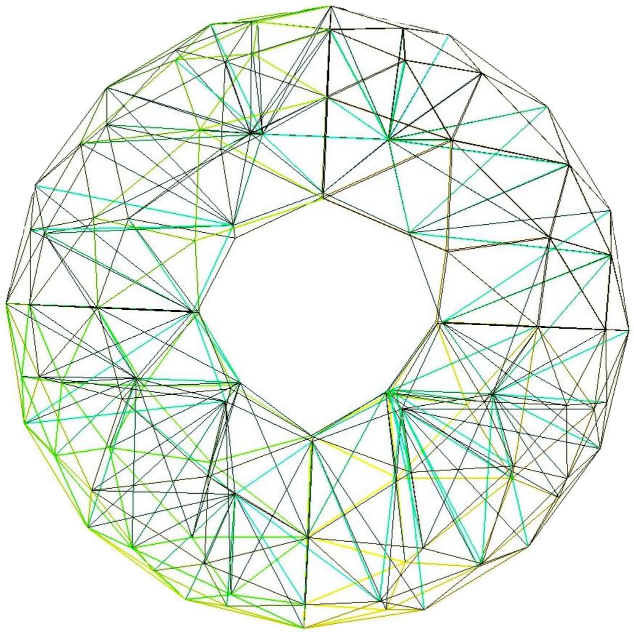


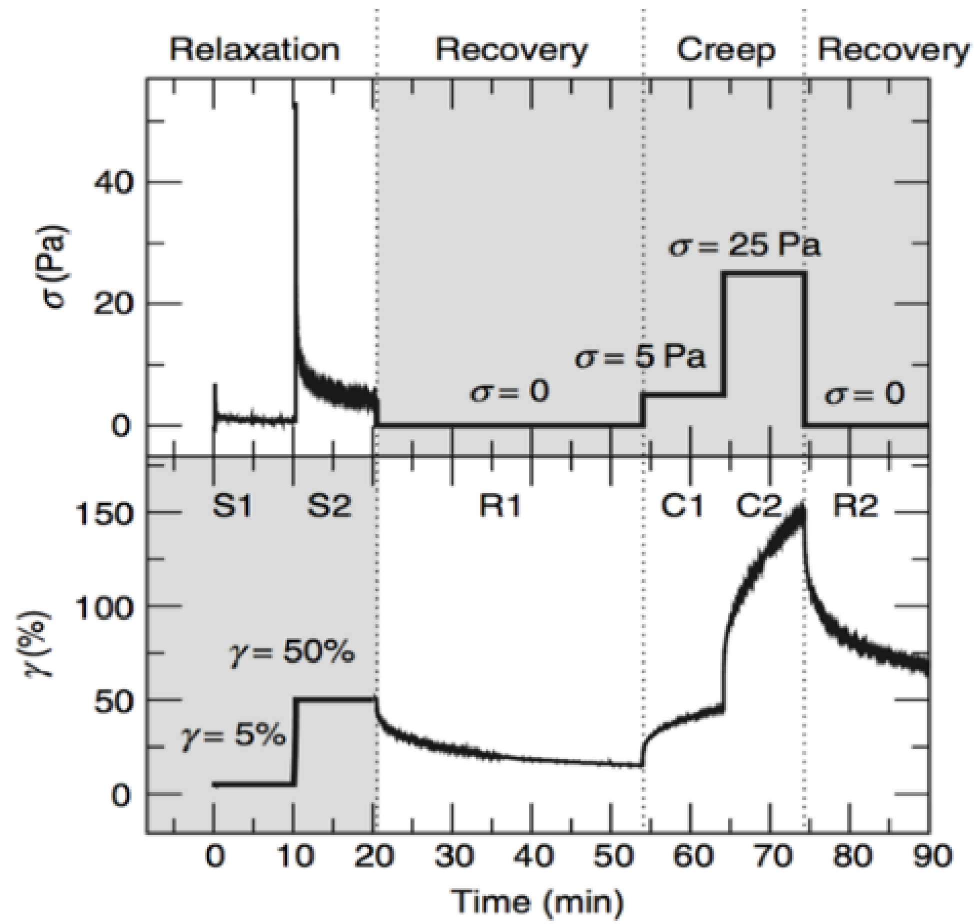


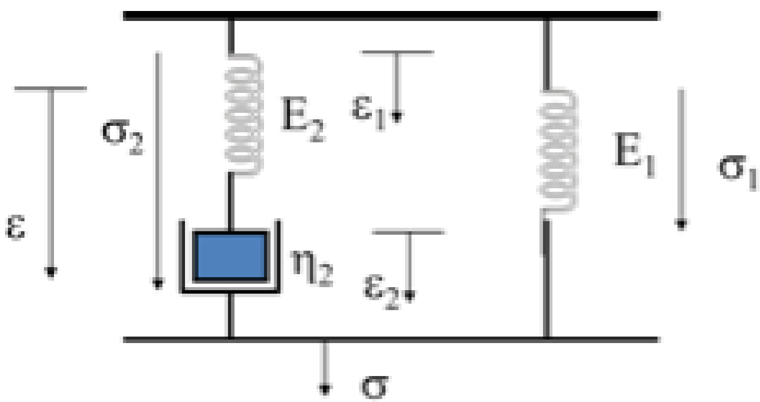


Lewandowski, R. & Chorążyczewski, B. Identification of the parameters of the Kelvin–Voigt and the Maxwell fractional models, used to modeling of viscoelastic dampers. *Computers & Structures* 88, 1-17 (2010).

The Virtual Cell

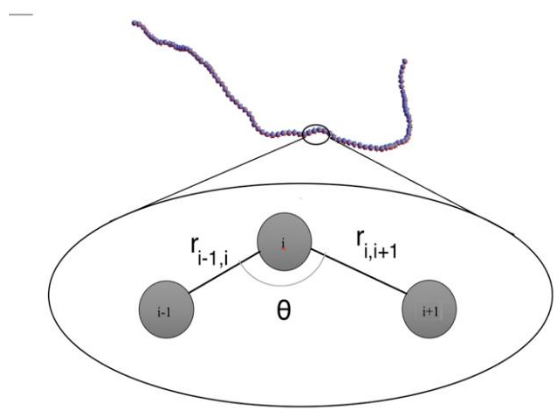






[13] Fernández, Pablo, et al. "Shear rheology of a cell monolayer." **New Journal of Physics** 9.11 **2007**

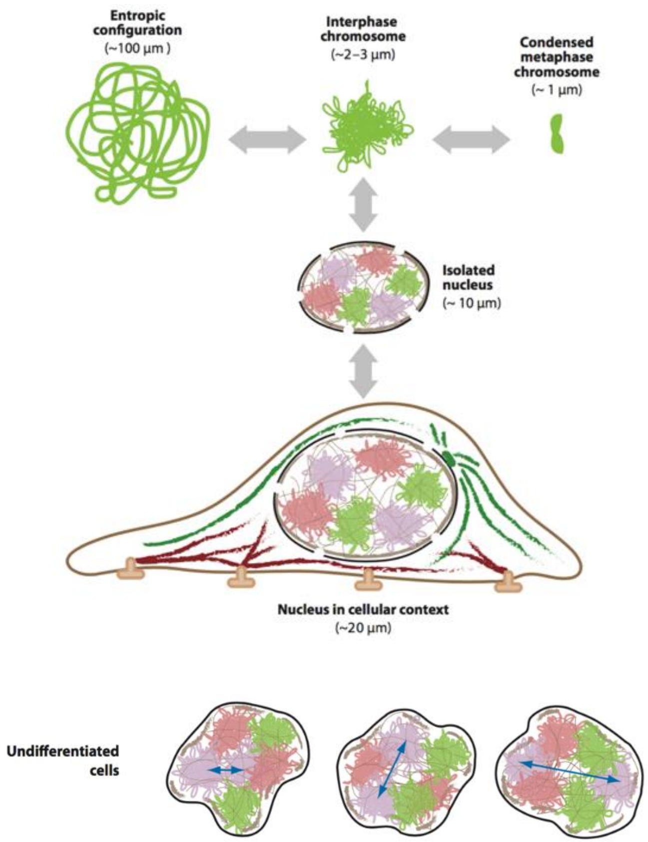
Inside nucleus: Bead-Spring to model Chromatin fibers



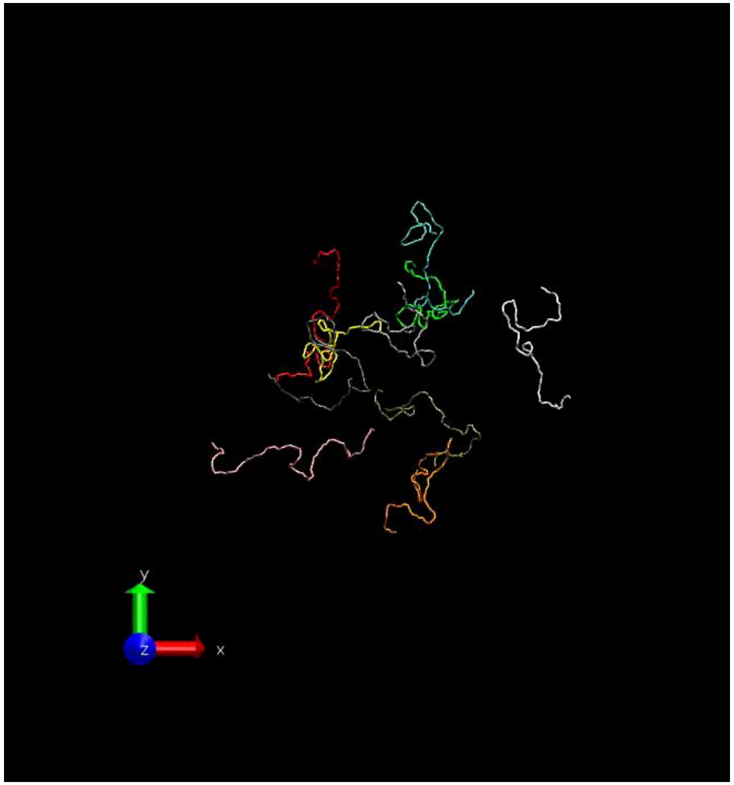
$$U_{bond} + U_{bending} + U_{excludedvuolume} = \frac{\kappa_{bonding}}{2}\sum_{i=1}^{N_c}\sum_{j=1}^{N_i-1}\left(r^{i}_{j,j+1} - r_0\right)^2 + \frac{\kappa_{bending}}{2}\sum_{i=1}^{N_c}\sum_{j=1}^{N_i-2}\left(\theta^{i}_{j,j+1} - \theta_0\right)^2 + \sum_{\substack{<i,j> \\ i<j,\, r_{ij}<\sigma_{ch}}} 4 \in_{ch} \left\{\left(\frac{\sigma_{ch}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ch}}{r_{ij}}\right)^{6}\right\}$$

Mashinchian, Omid, et al. "Cell-imprinted substrates act as an artificial niche for skin regeneration." ACS applied materials & interfaces (2014).

Chromatins inside the nucleus



Shivashankar, G. V. "Mechanosignaling to the cell nucleus and gene regulation." Annual review of biophysics 40 (2011): 361-378.

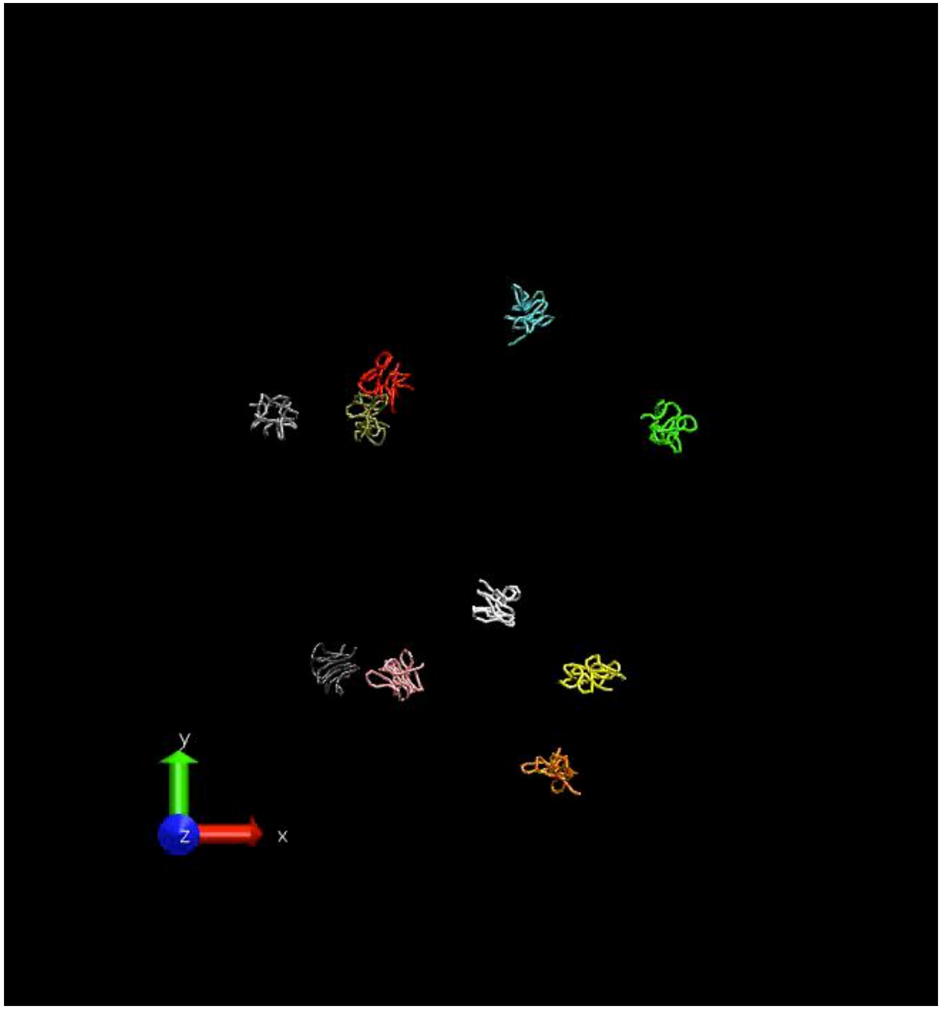


Mashinchian, Omid, MRE, et al. "Cell-imprinted substrates act as an artificial niche for skin regeneration." ACS applied materials & interfaces 6.15 (2014): 13280-13292.

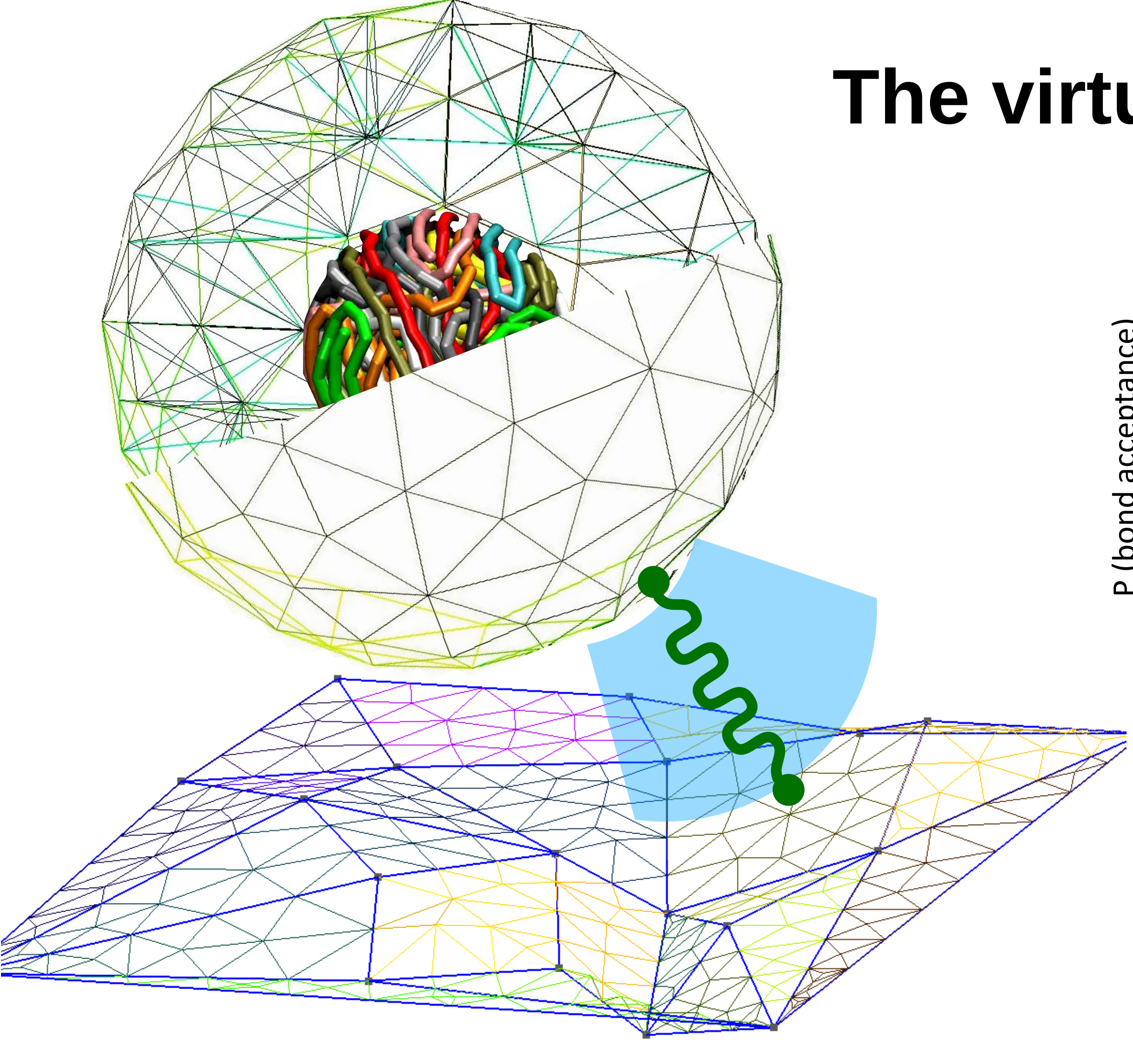
Ring chromosomes

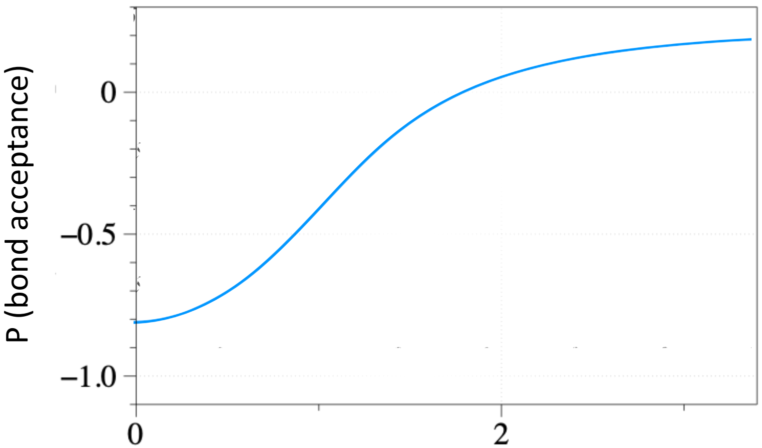
Chromosomes should be on unknotted state to perform their biological function

Rosa, Everaers,
PloS Computational Biology (2008)



The virtual cell: Substrates





$$r = R/a$$

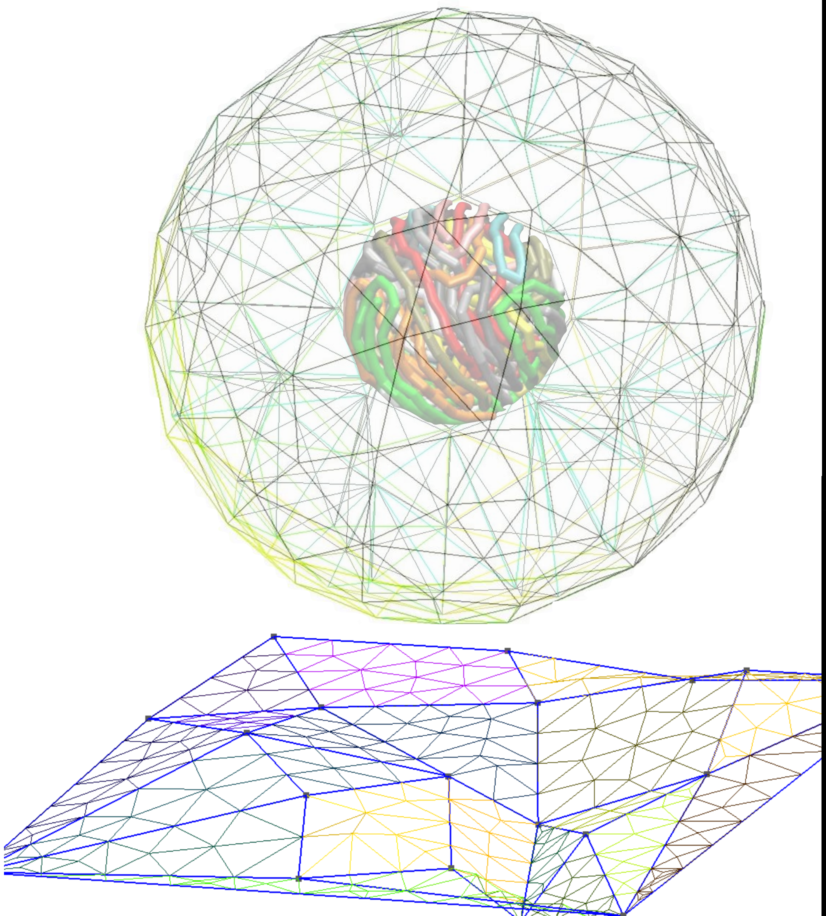
$$F_R = \frac{k_B T}{r} \ln \frac{F' r}{k_B T F_{off}},$$

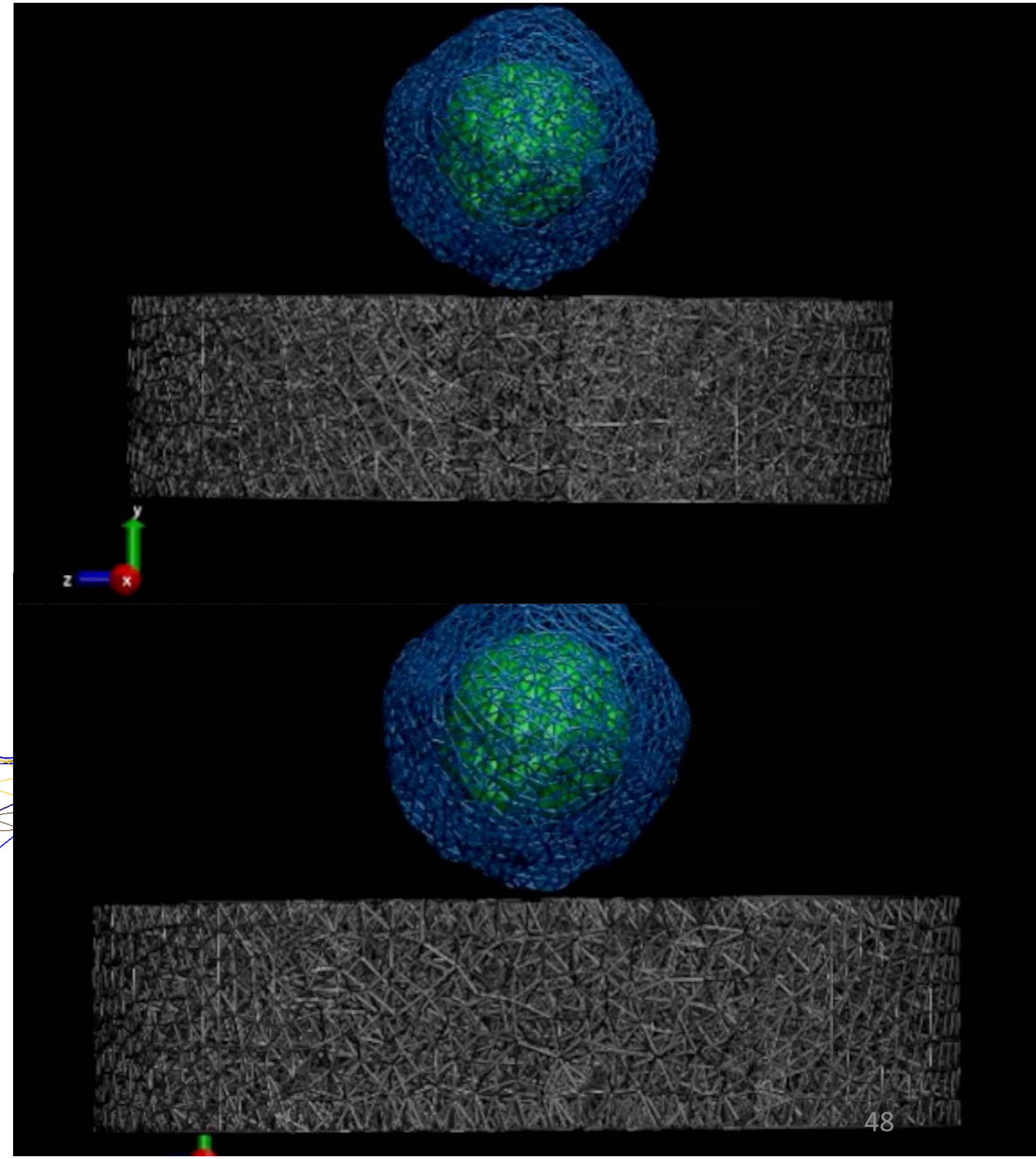
$$F(r) = \frac{4\sigma}{\epsilon}\left[\left(\frac{\epsilon}{r}\right)^5 - \left(\frac{\epsilon}{r}\right)^3\right]\frac{\vec{r}}{r}$$

Shaofan Li, Bohua Sun, Advances in Soft Matter Mechanics, Springer Berlin Heidelberg (2012)

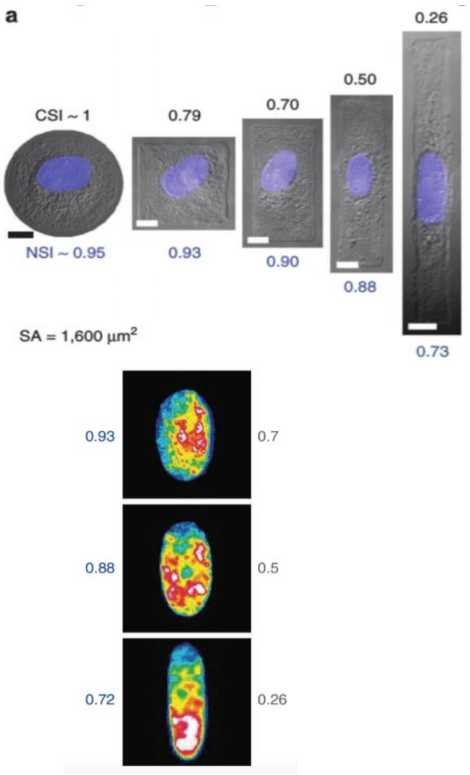
Emily B. Walton, Sunyoung Lee, and Krystyn J. Van Vliet, Biophys J (2008)

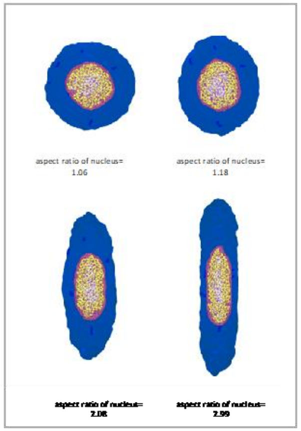
VIRTUAL CELL AT WORK

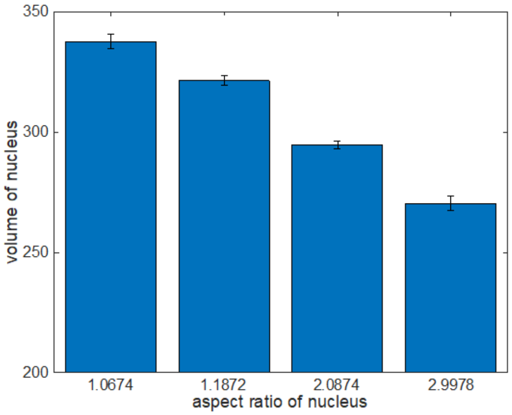


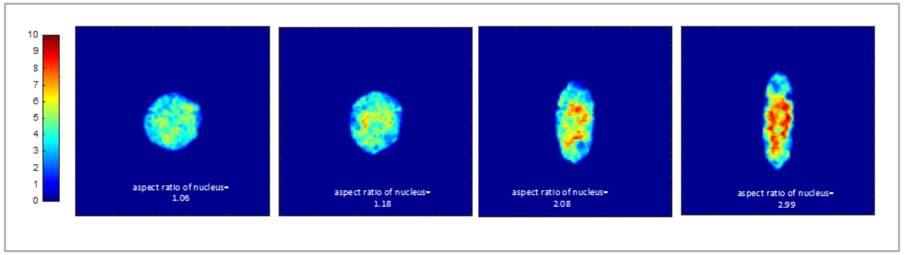


Chromatin condensation



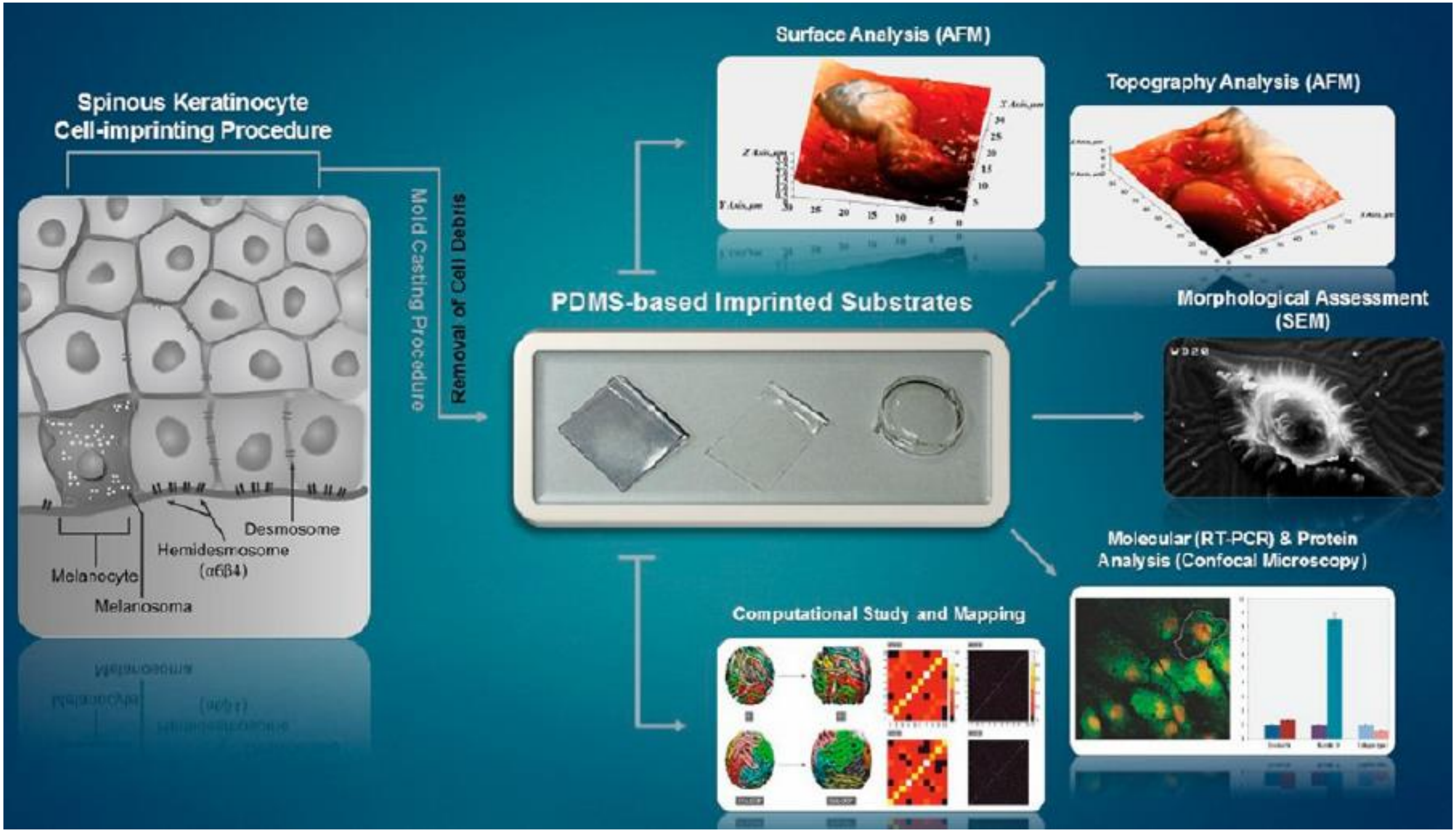






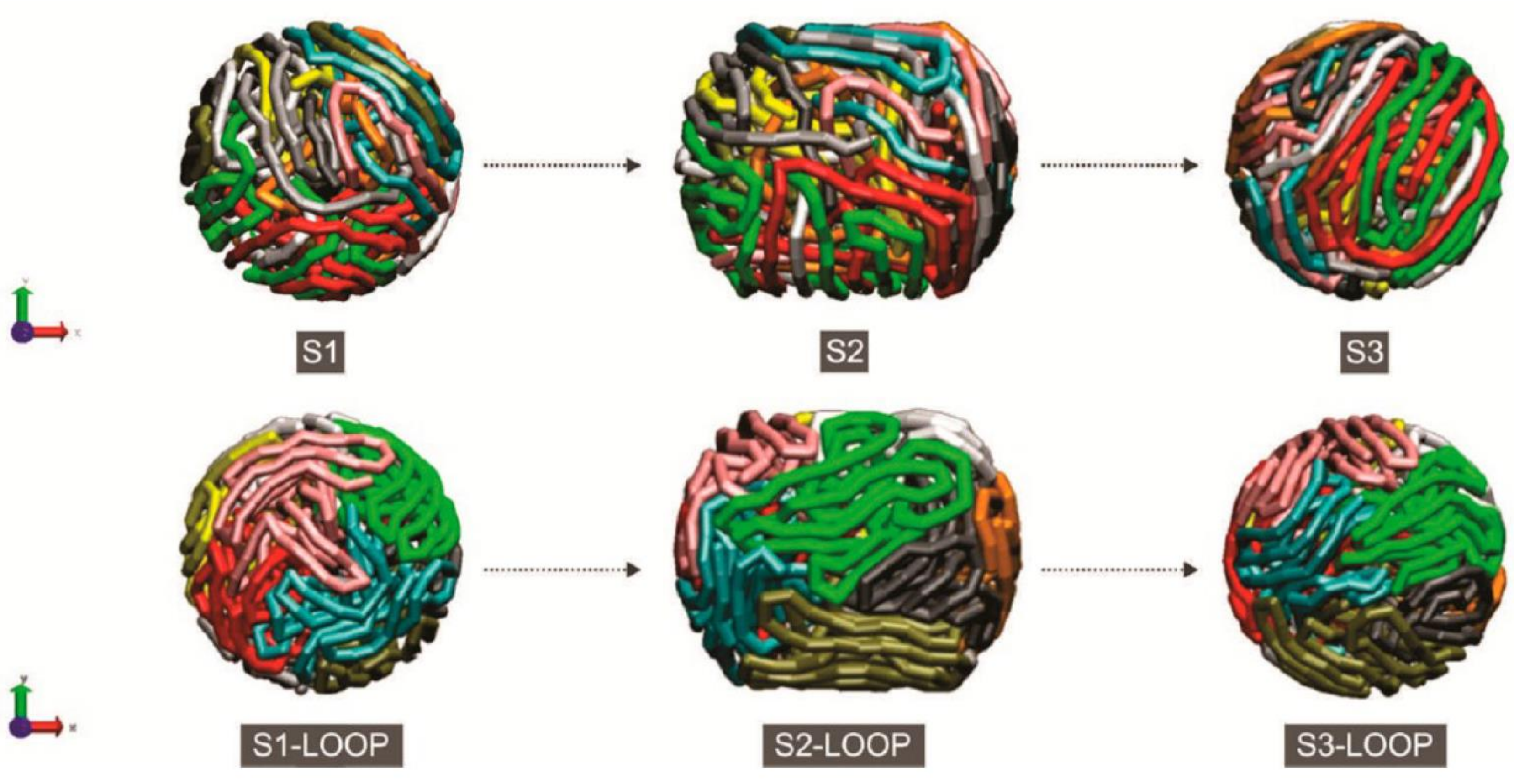
Versaevel, Marie. et al, Nature Commun. 3:671 (2012)

Mechanotransduction



[O. Mashinchian, MR Ejtehadi and et al,
ACS Applied Materials and Interfaces (2014)]

Closed or Open chains



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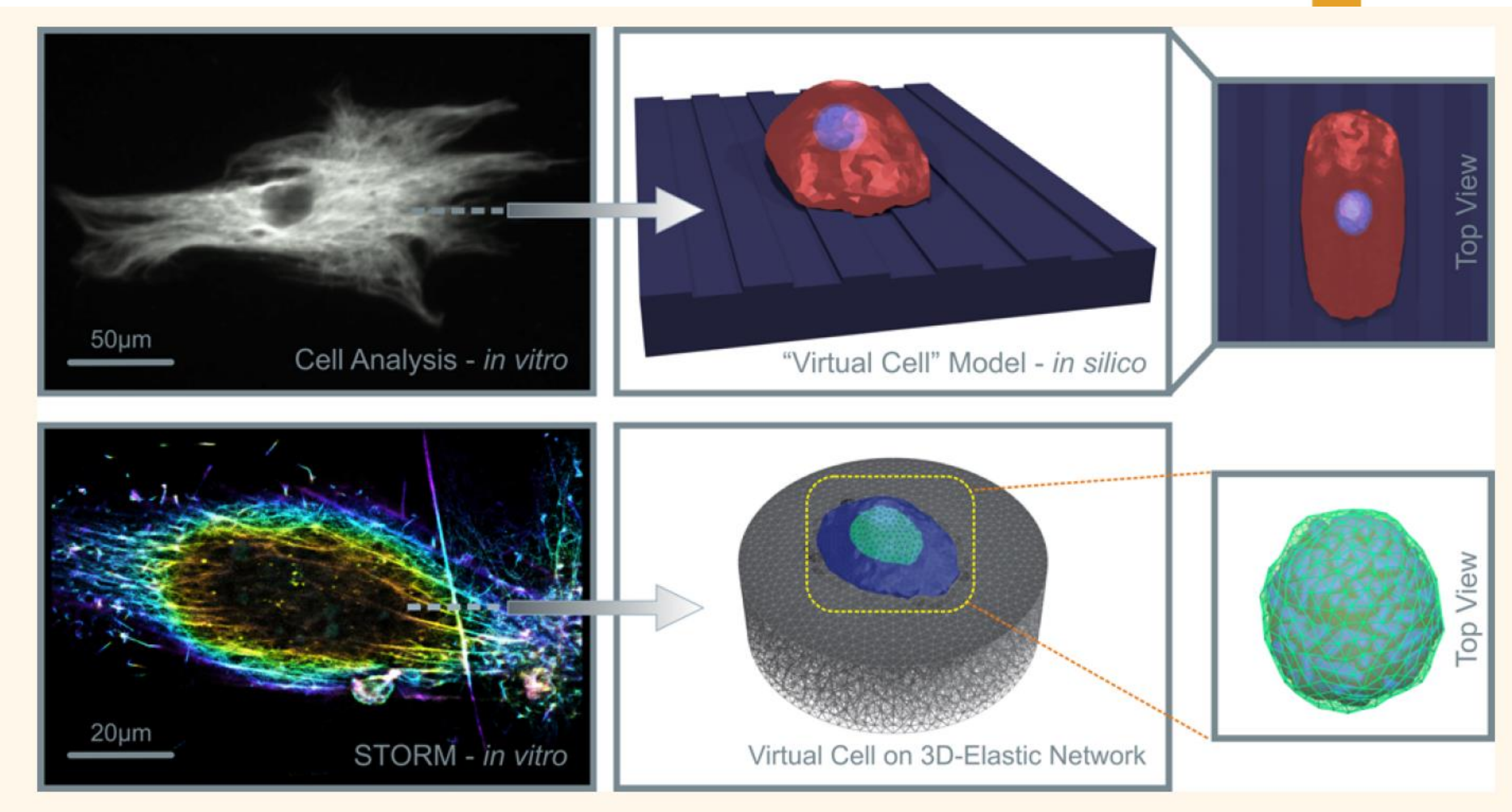
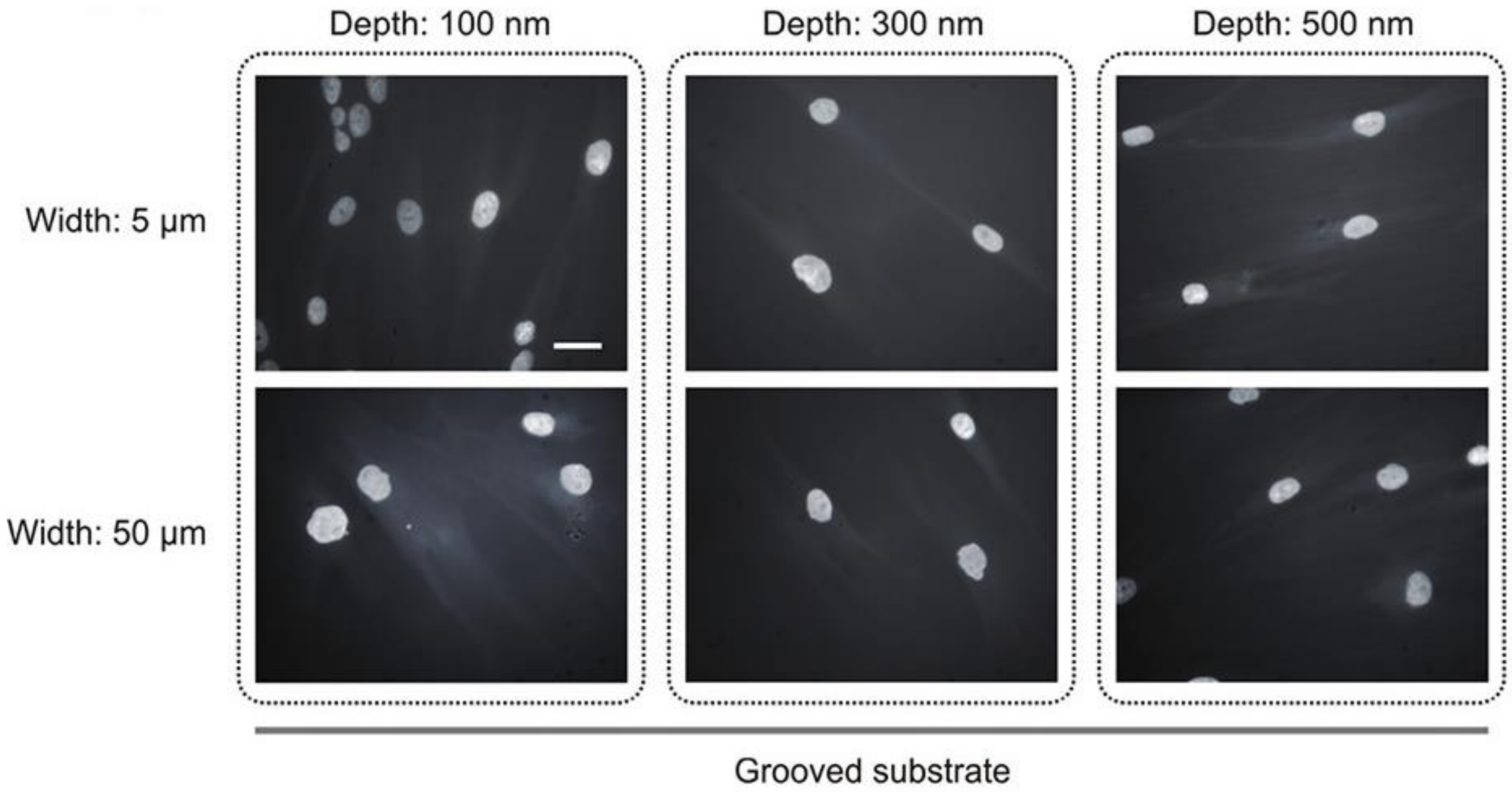
ARTICLE

Development of a Virtual Cell Model to Predict Cell Response to Substrate Topography

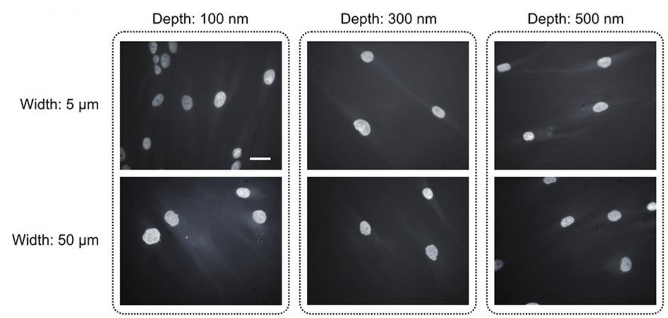
Tiam Heydari,[†] Maziar Heidari,[‡] Omid Mashinchian,[§,⊥] Michal Wojcik,[∥] Ke Xu,[∥,□] Matthew John Dalby,[#] Morteza Mahmoudi,[*,△,▽] and Mohammad Reza Ejtehadi[*,†]

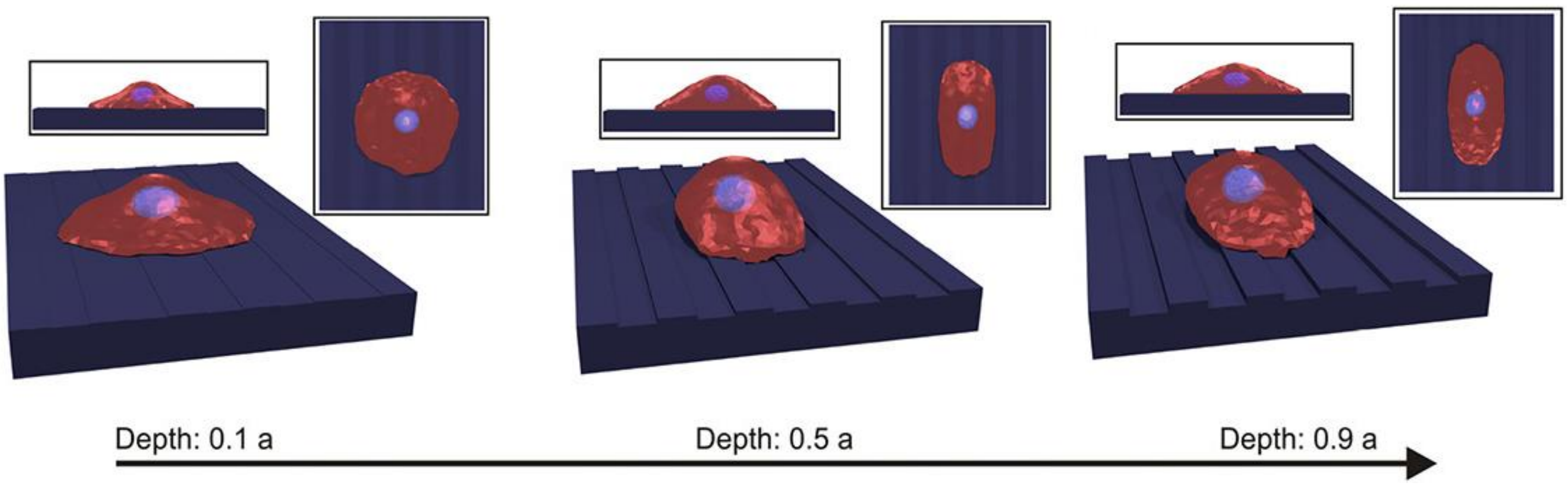


m e s e n c h y m a l   s t e m   c e l l s

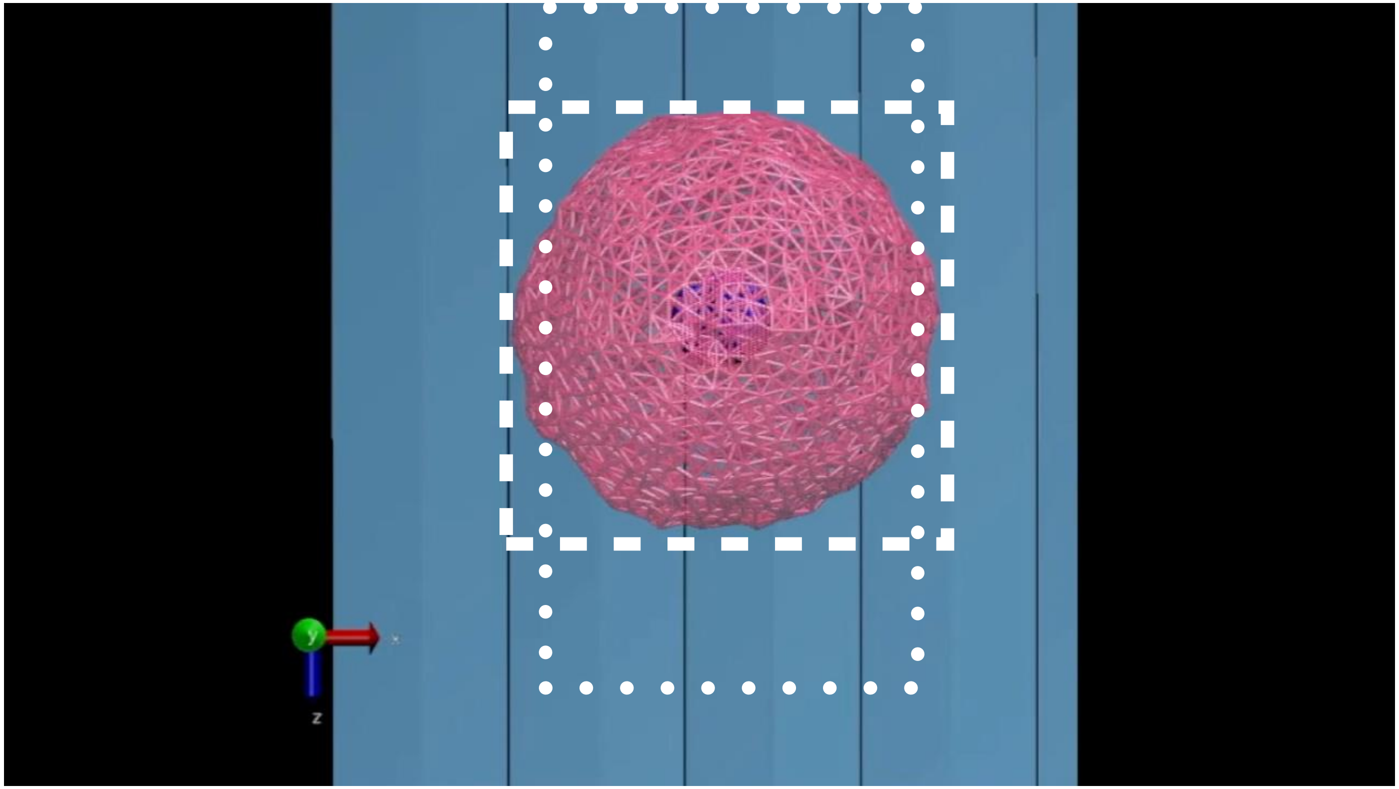


mesenchymal stem cells

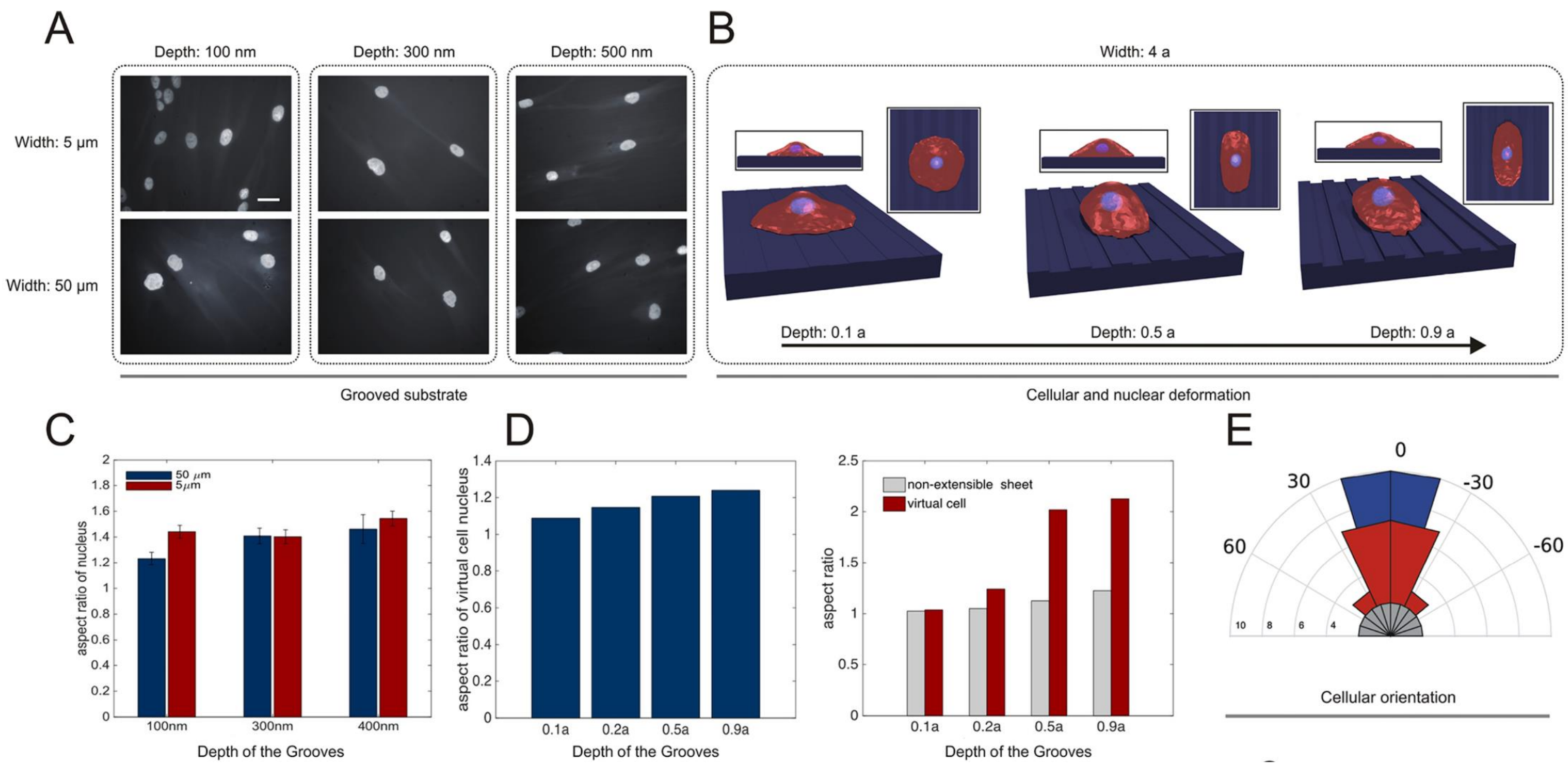


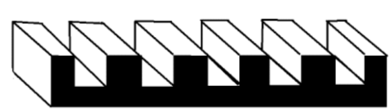


The Virtual Cell Model

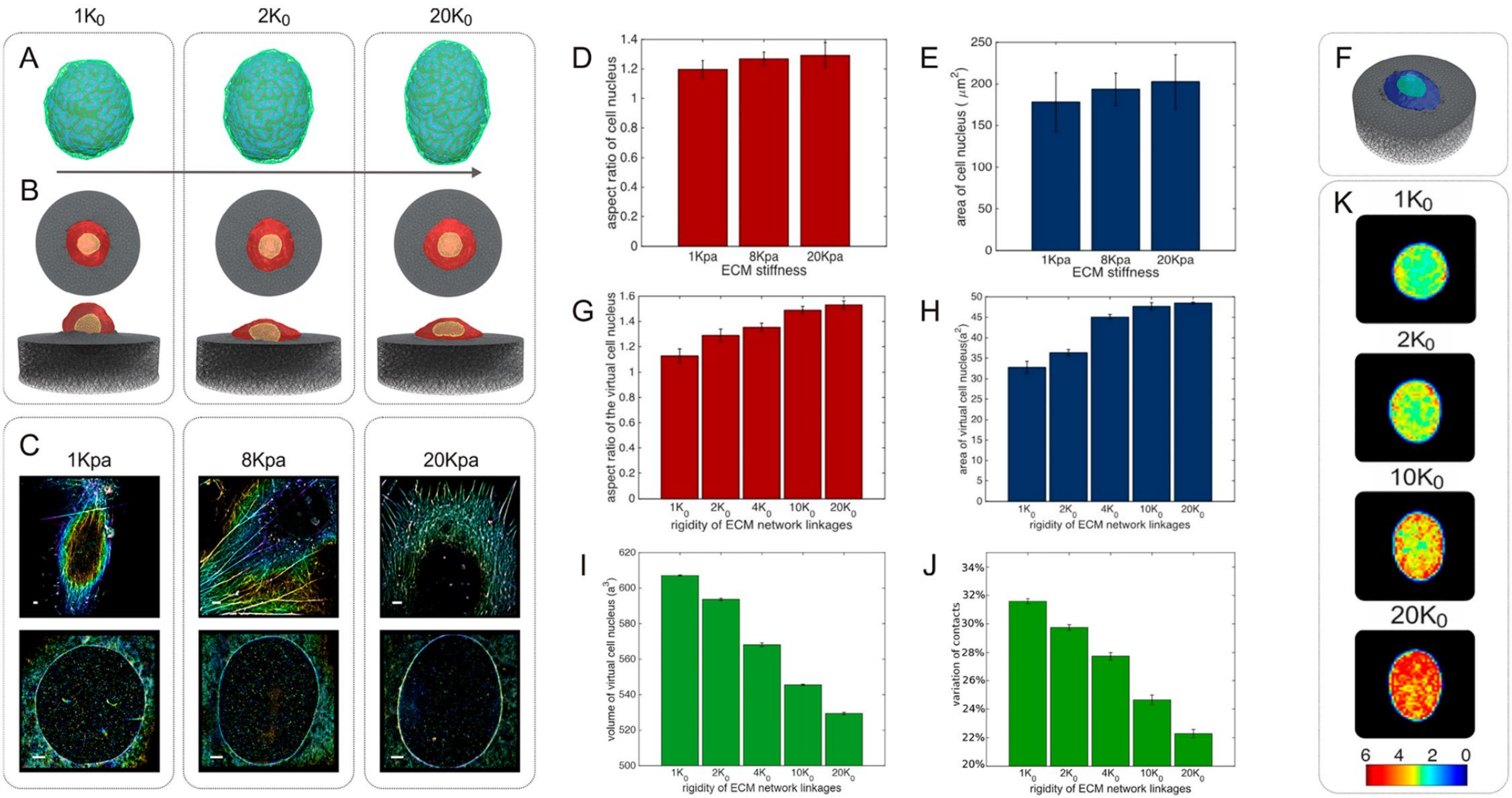


Cell on Grooved substrate

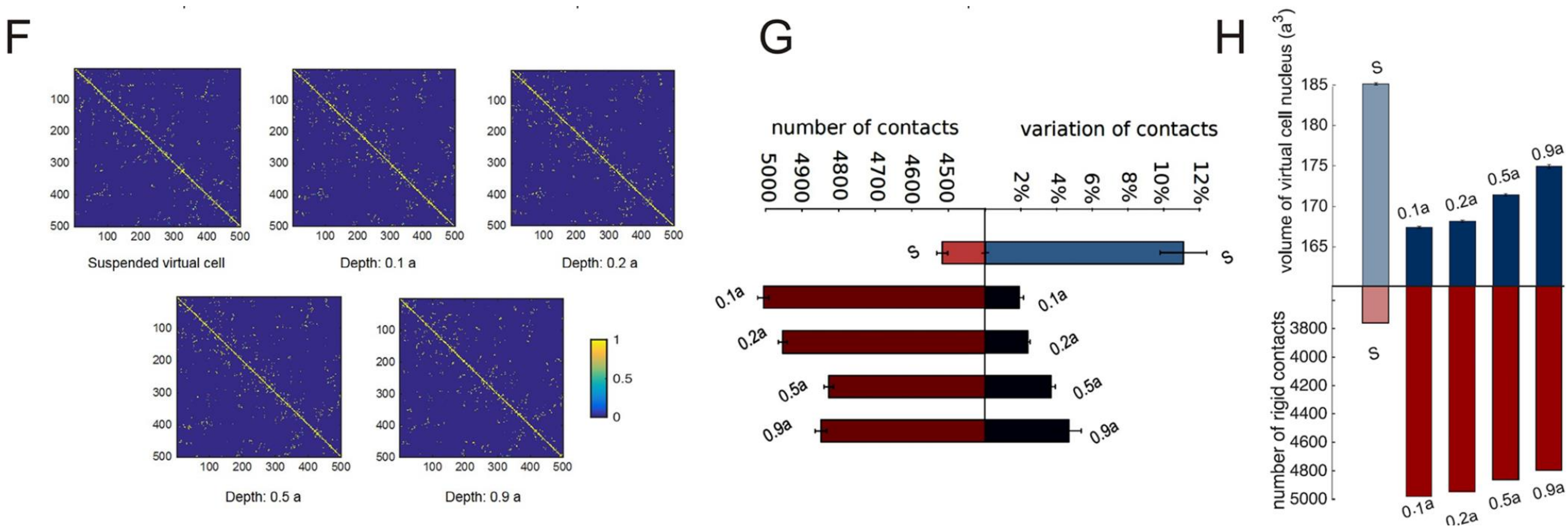




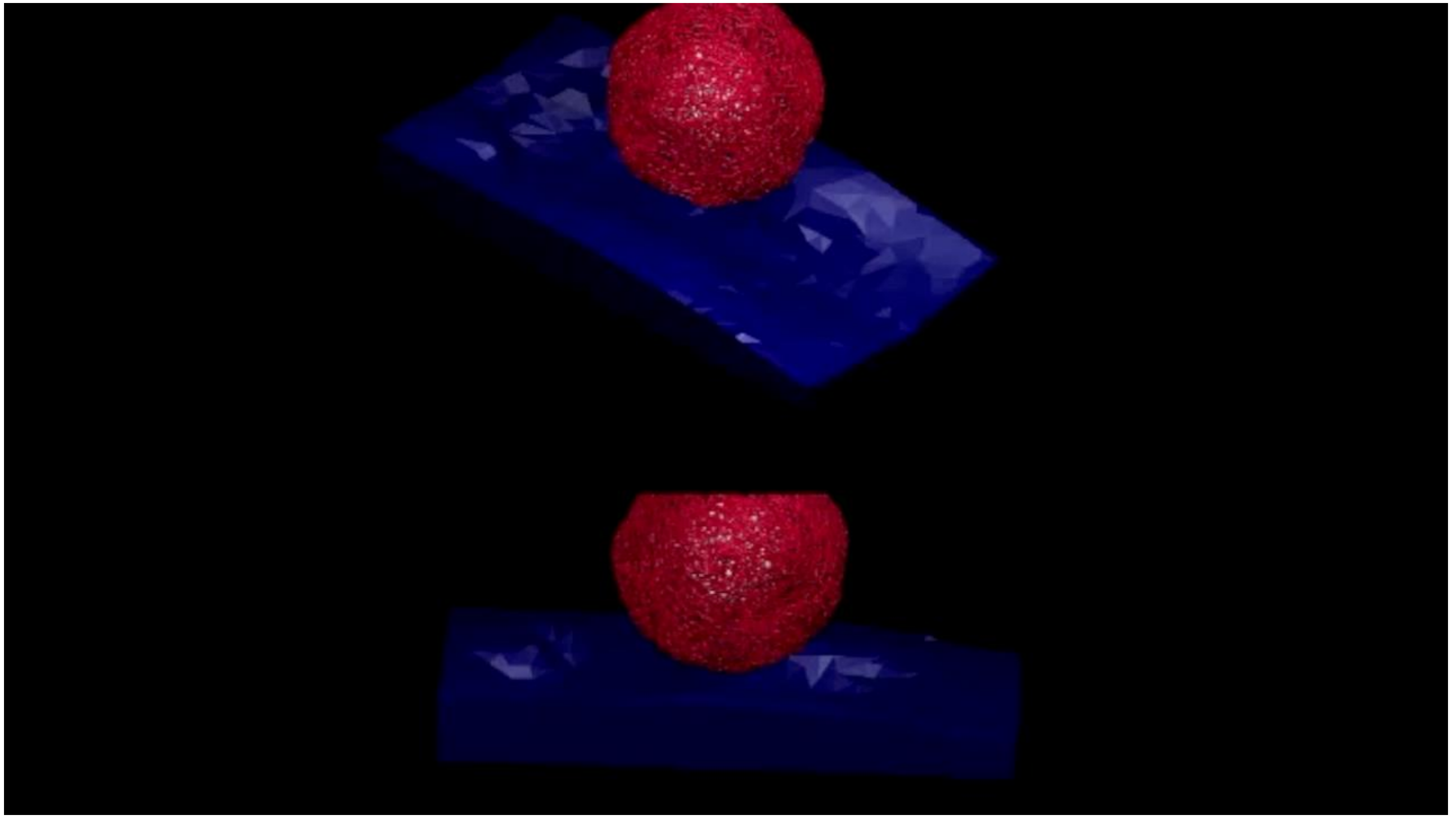
Mesenchymal stem cells



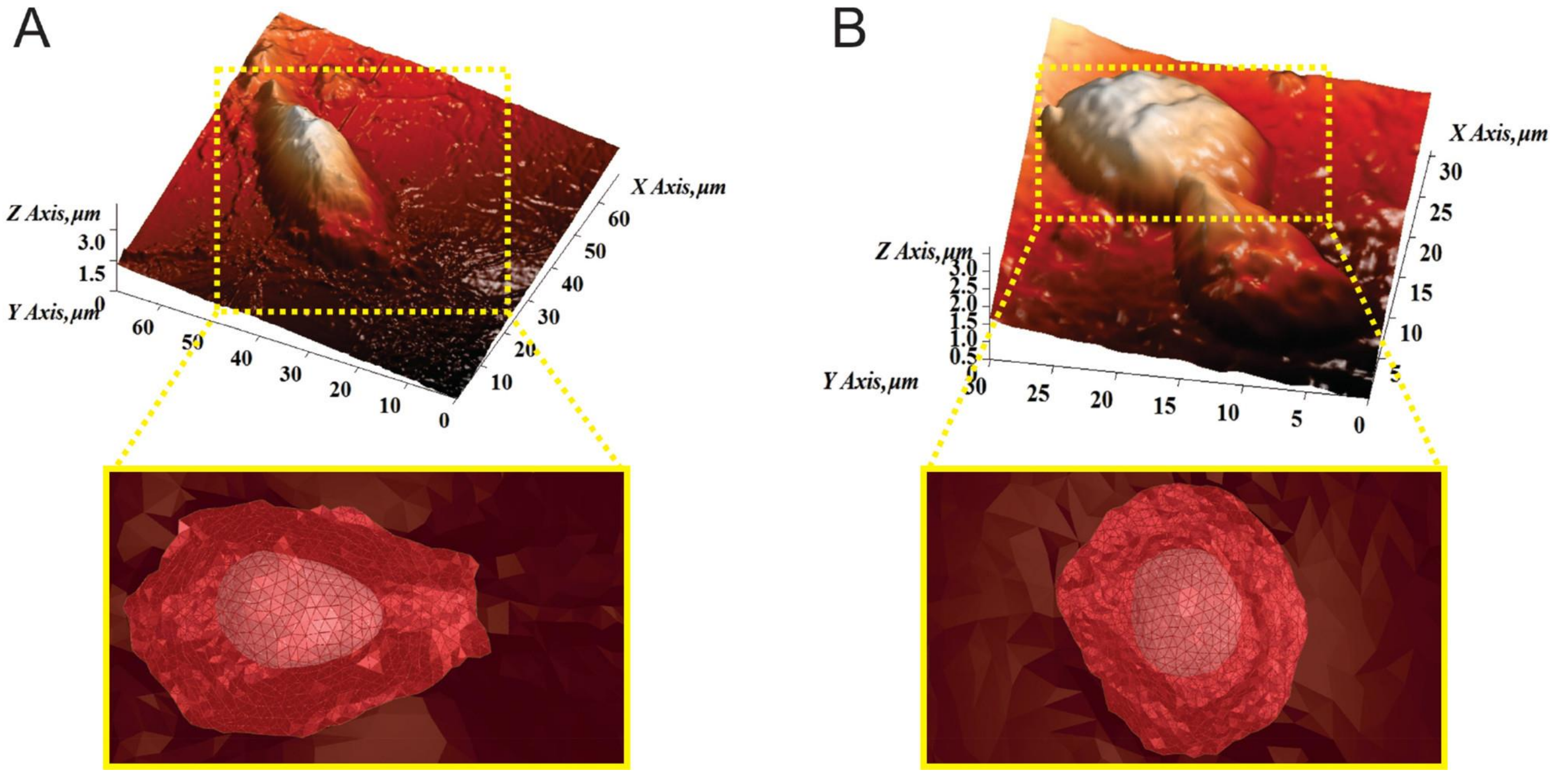
Chromatin interaction network



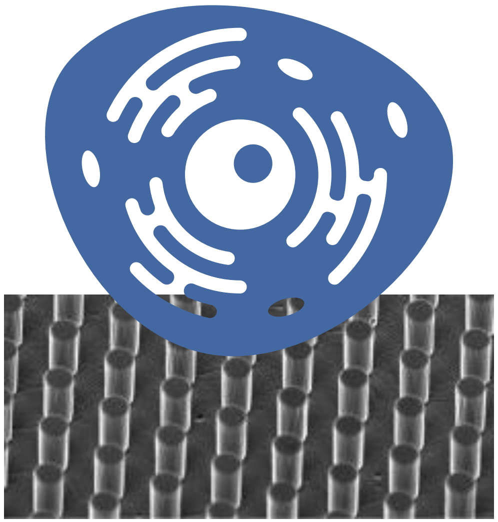
more complicated substrates

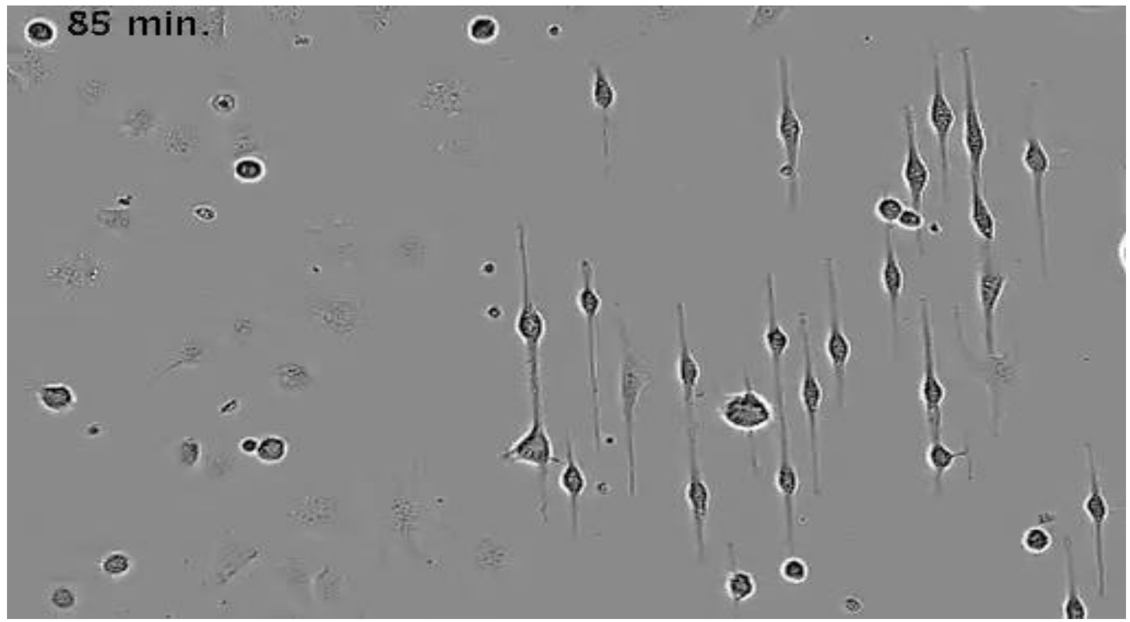


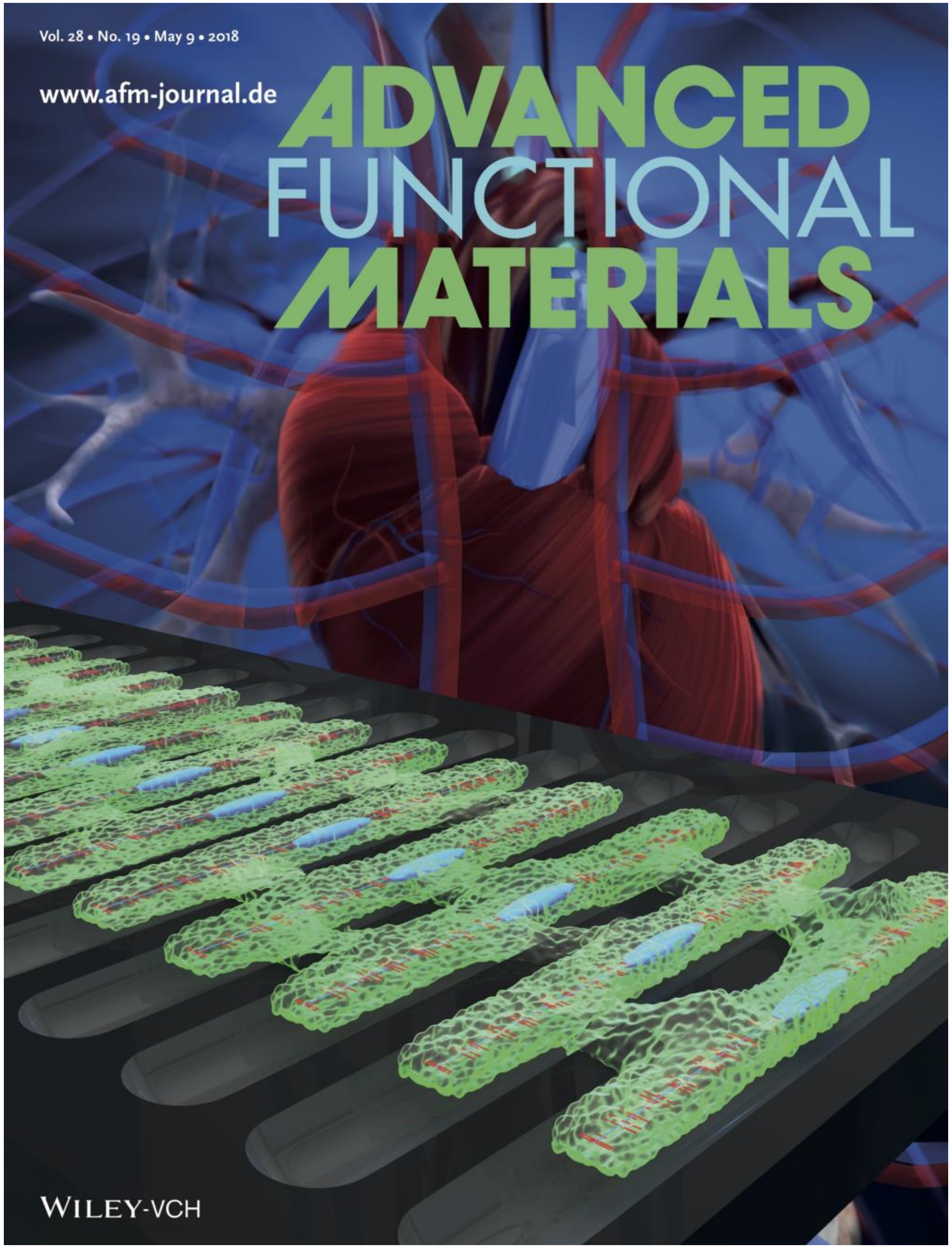
STEM CELL BEHAVIOUR ON A CELL-IMPRINTED SUBSTRATE



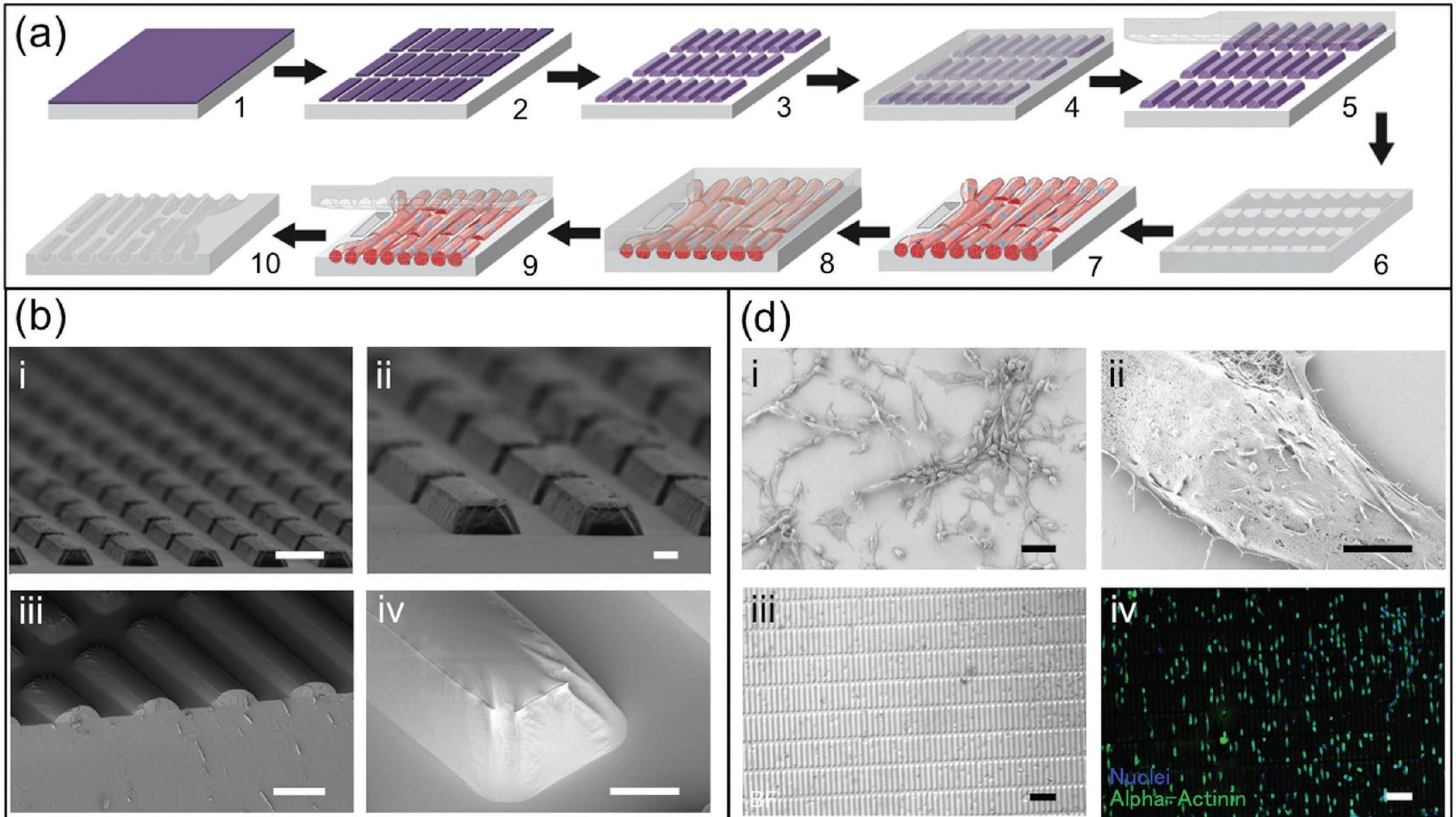
ENGINEERED SUBSTRATES

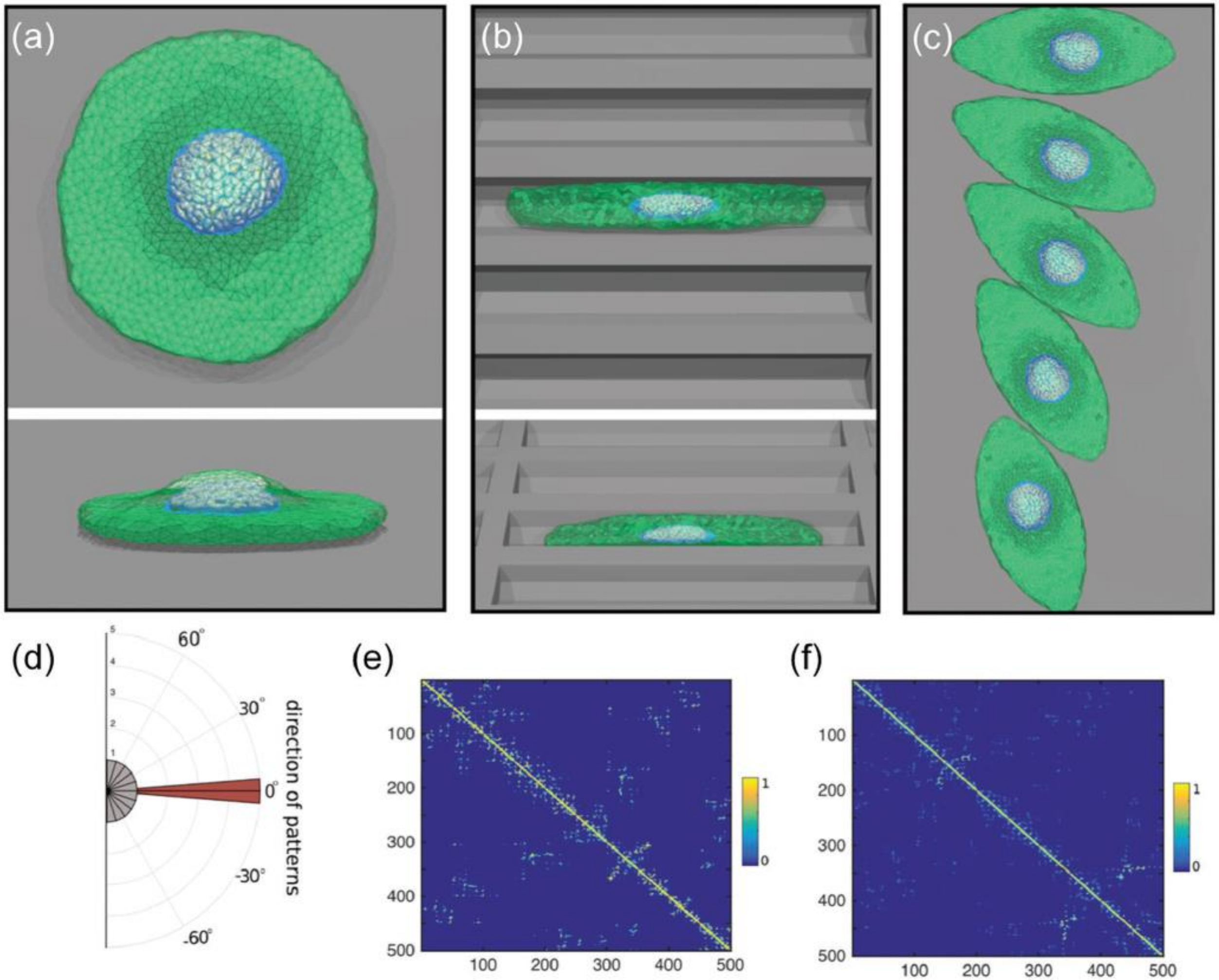




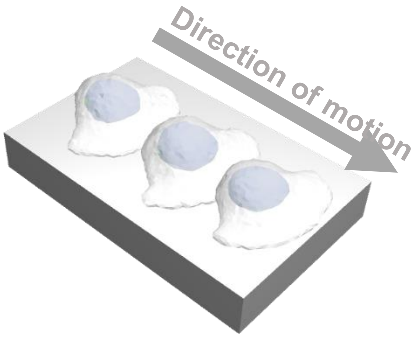


P. P. S. S. Abadi, J. C. Garbern, S. Behzadi, M. J. Hill, J. S. Tresback, T. Heydari, **M. R. Ejtehadi,** N. Ahmed, E. Copley, H. Aghaverdi, R. T. Lee, O. C. Farokhzad, M. Mahmoudi, Adv. Funct. Mater. 2018

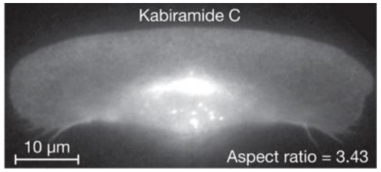

(a)
1
2
3
4
5
6
7
8
9
10
(b)
i
ii
iii
iv
(d)
i
ii
iii
BF
iv
Nuclei
Alpha-Actinin


(a)
(b)
(c)
(d)
60°
30°
0°
-30°
-60°
direction of patterns
(e)
(f)
100
200
300
400
500
1
0

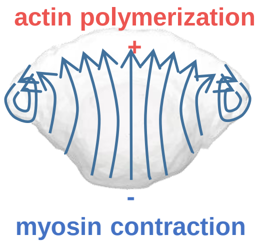
Modeling cell Chemotaxis

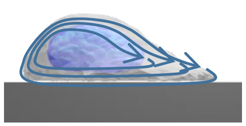


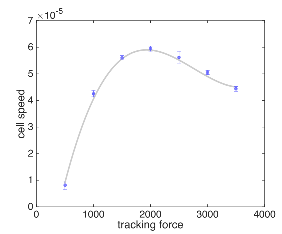
- To have very minimal model of the activity of the cytoskeleton at the cell periphery of the migrating cell, the direction of the generated force is considered normal to the periphery of the cell membrane and the distribution of the force is scaled by $|\cos(\propto)|^{\frac{1}{8}}\, sign(\cos(\propto))$, where $\propto$ is the angel between the polarity direction and the point on the cell periphery.



Keren, Kinneret, et al. "Mechanism of shape determination in motile cells." *Nature* 453.7194 (2008): 475-480.





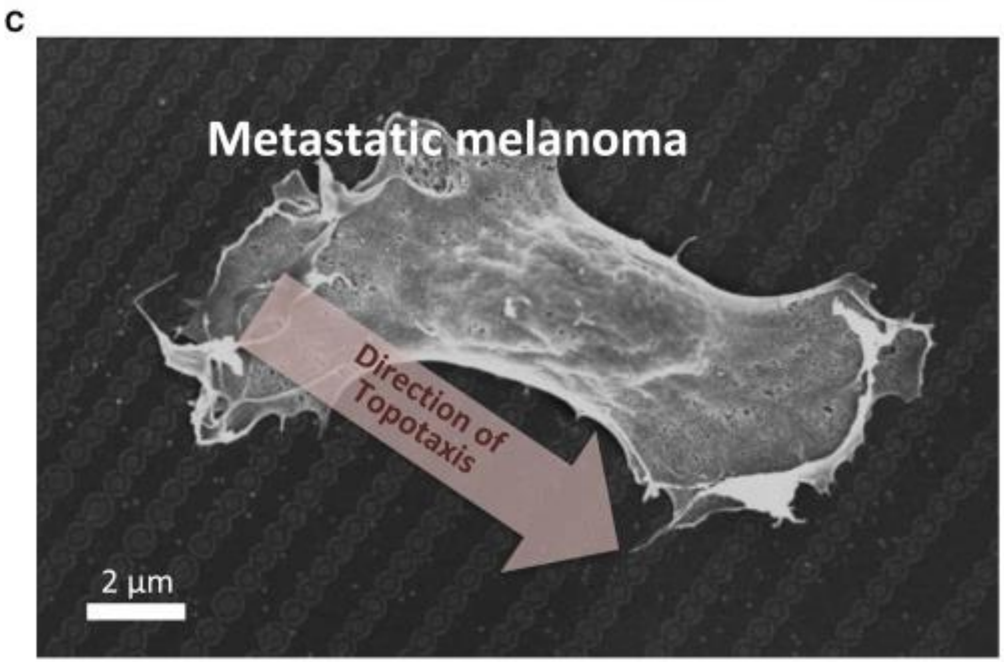


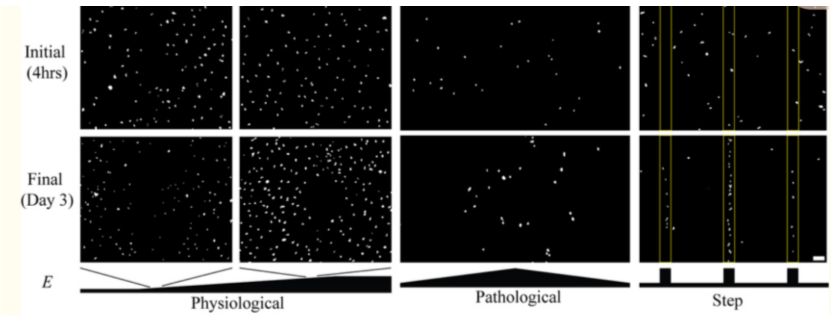
Cell motility

Projects in hand

Topotaxis

Durotaxis

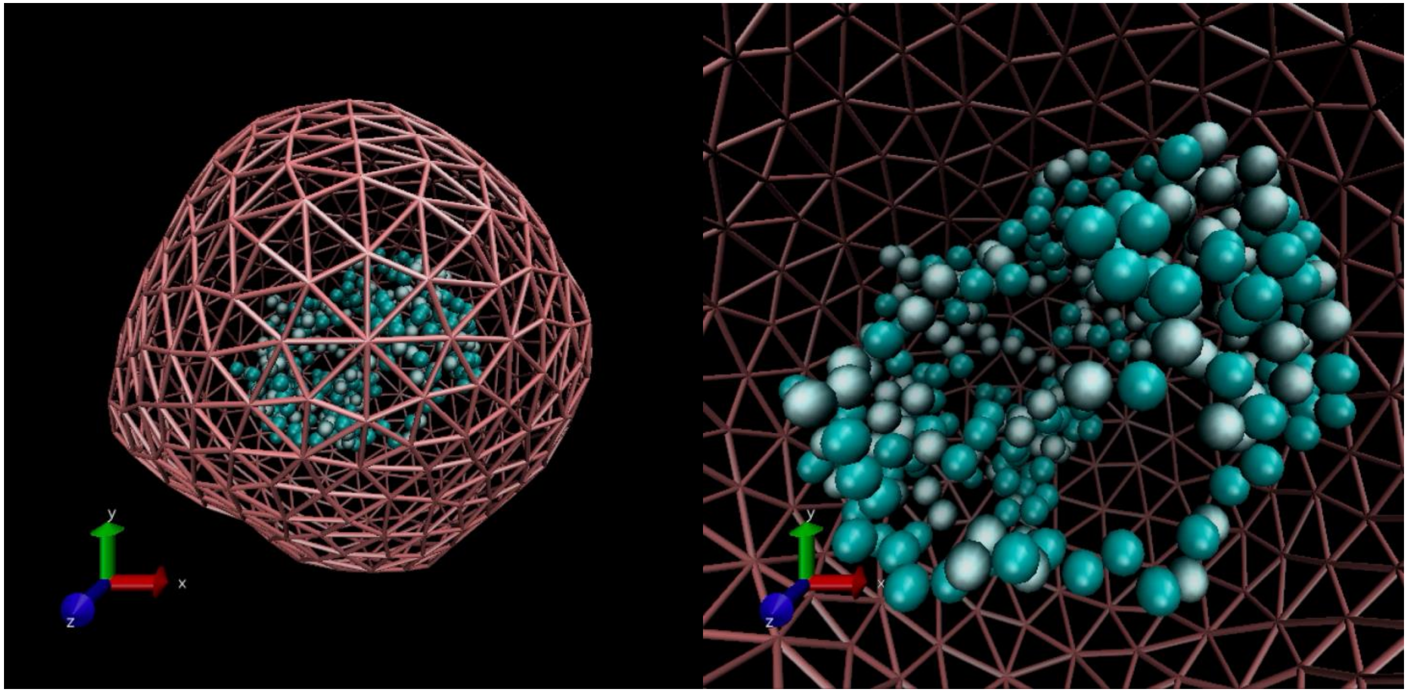




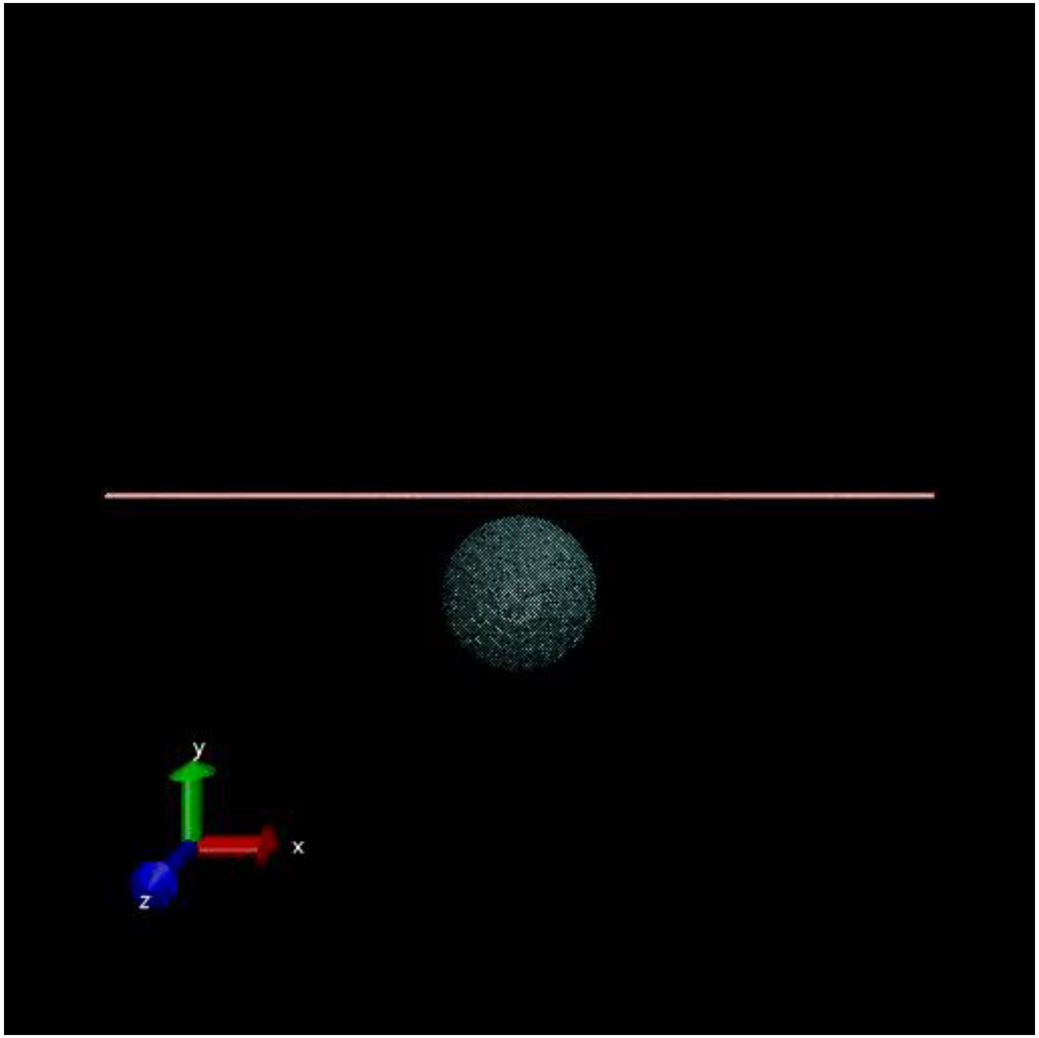
LG Vincent, YS Choi, B Alonso-Latorre, JC del Álamo, and AJ Engler, Biothech J (2013)

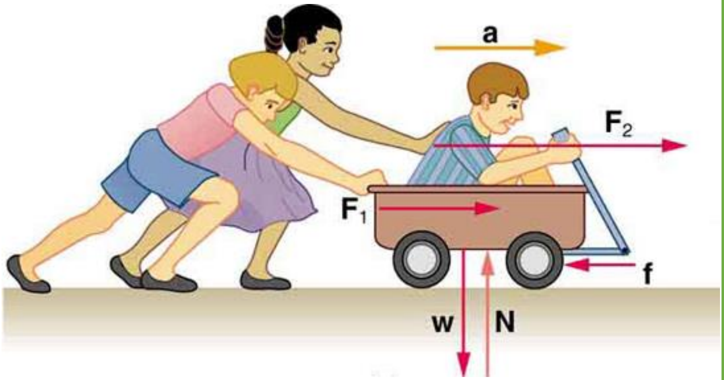
JS Park, DH Kim, and A Levchenko, Biophys J (2018)

Chromosomes in flexible confinements



Graphene wrapping bacteria





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Naeimeh Naseri