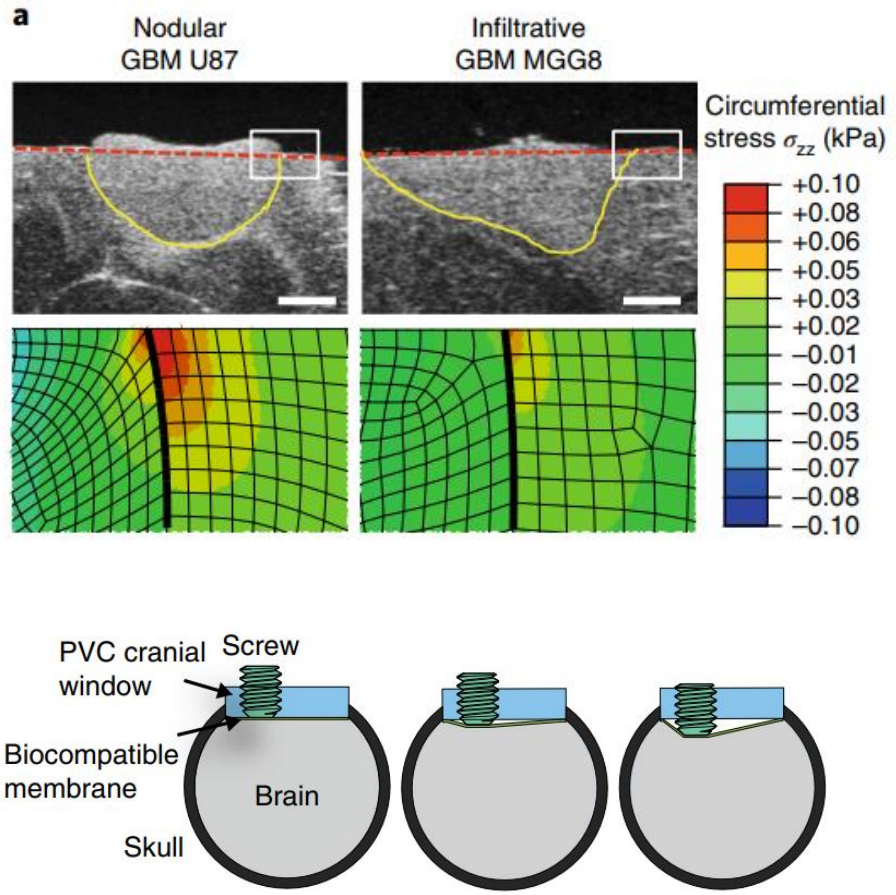
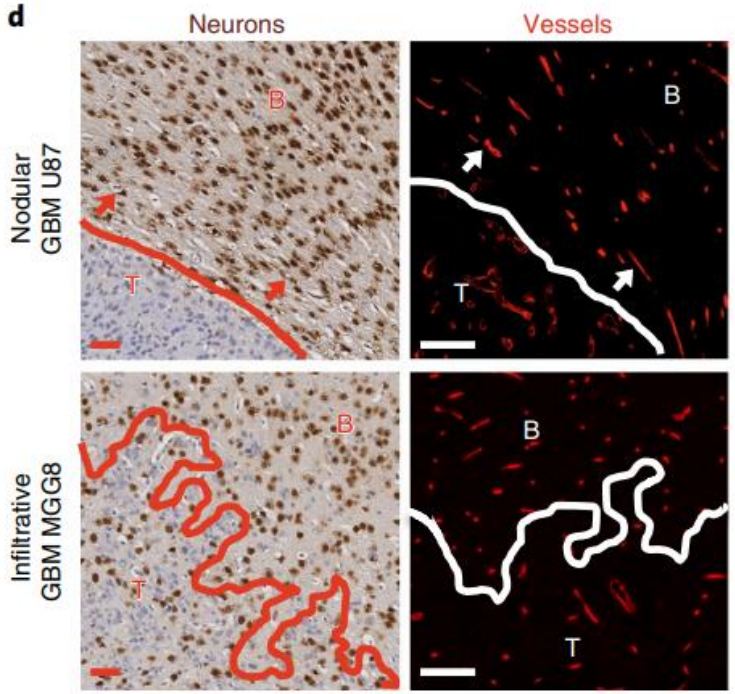
Rheological phenomena in biological systems

Katarzyna Pogoda

25th of February 2021

Solid stress in brain tumours cause neurological dysfunction





Seano et al. *Nature Biomedical Engineering* (2019)

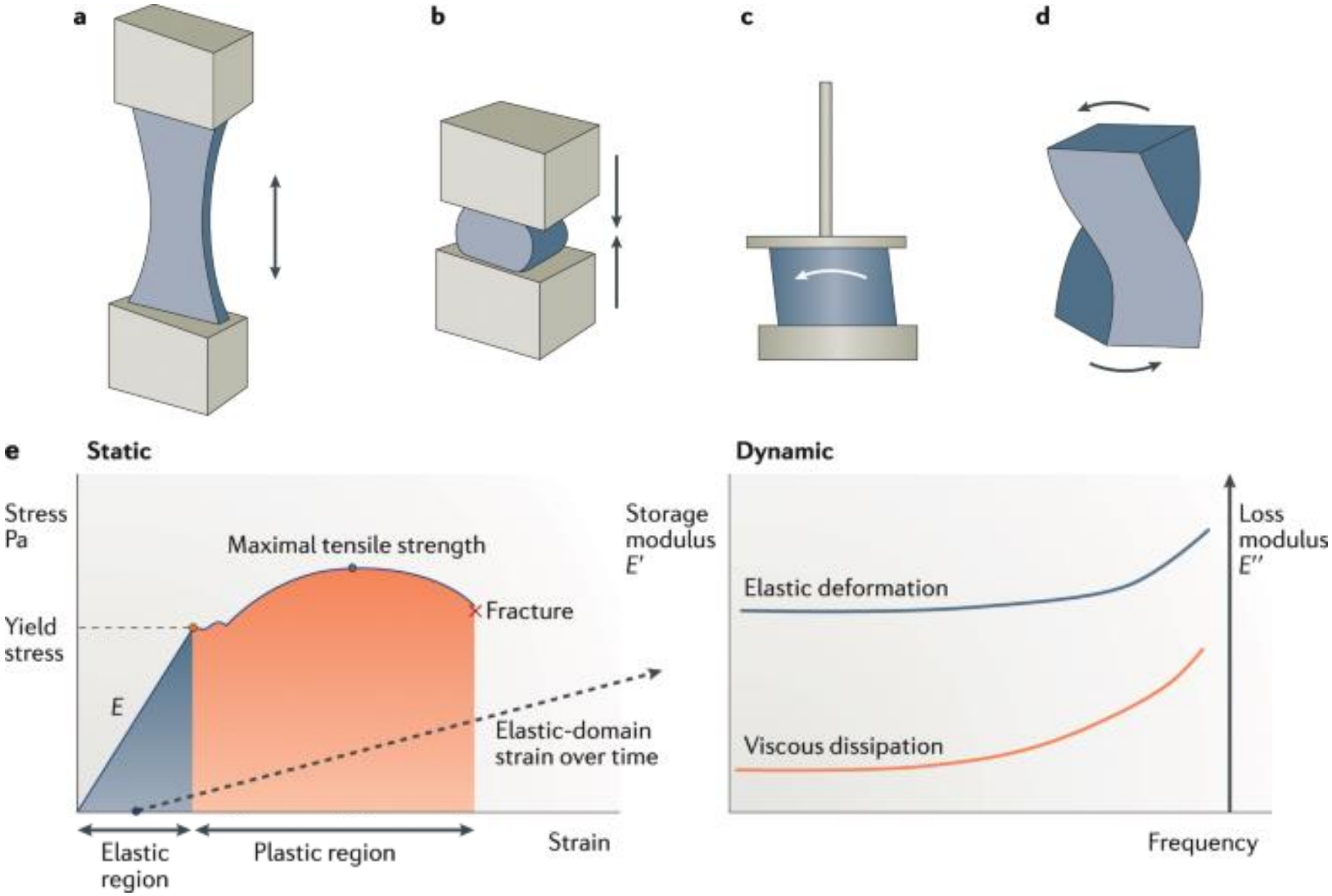
Motivation

- How can we understand the mechanical response of the tissues and cells?
- How is this response derived form the different components of the tissue?
- What is mechanopathology?

Physical problem to be solved:

- The source of mechanical properties in biological systems?
- What happends with cells and tissues under mechanical stress ?
- How to simulate mechanical stress *in vitro*?

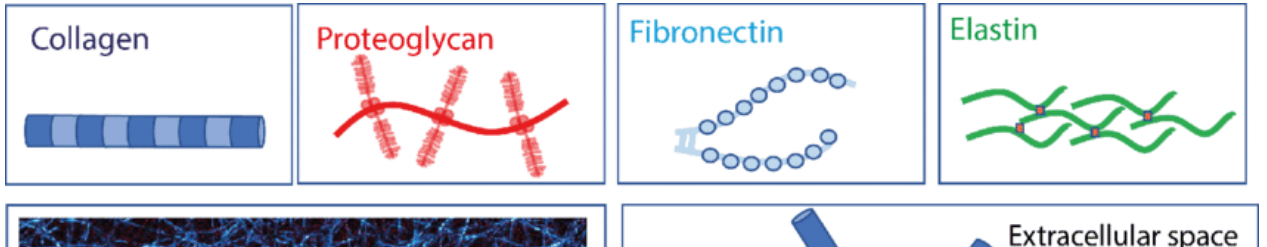
Forces in biological systems



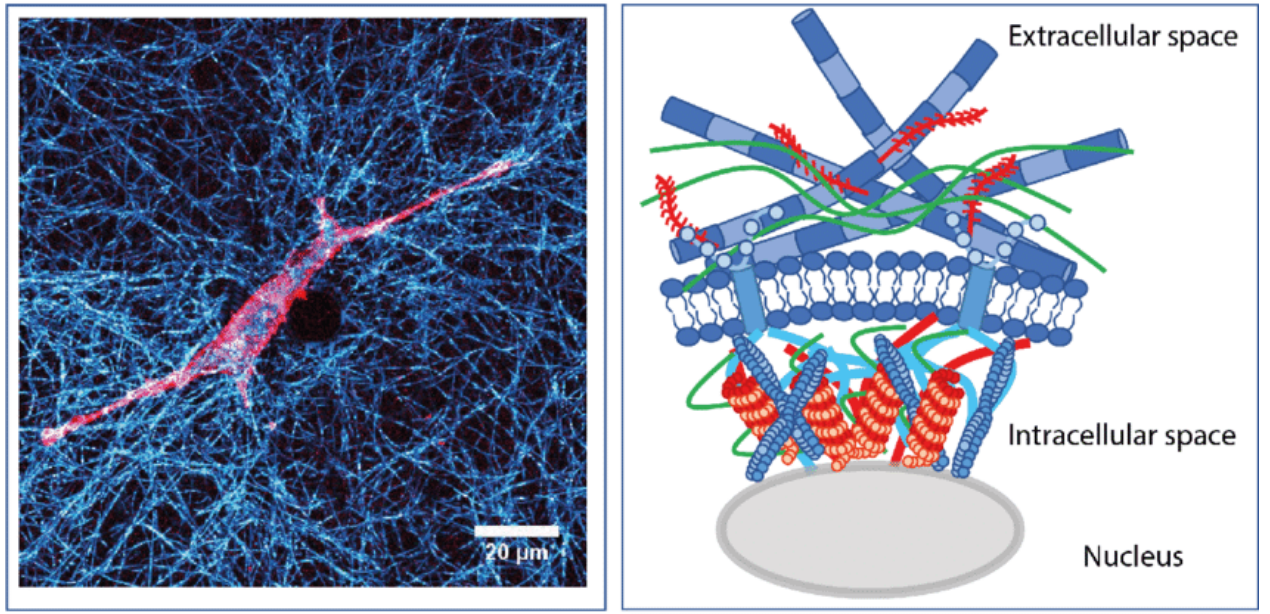
Guimarães et al., *Nature Reviews Materials* (2020)

Tissues are active materials with particular rheological properties

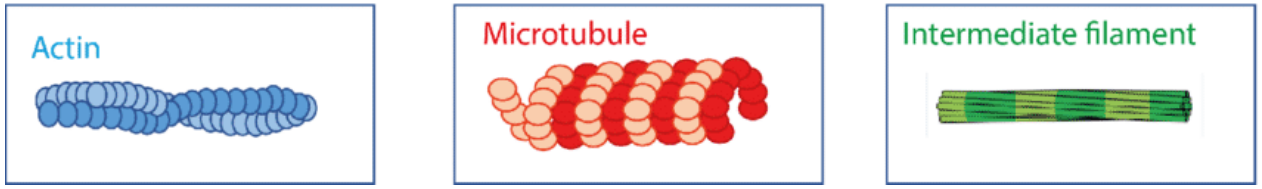
Extracellular biopolymers



Cell embedded in 3D biopolymer network



Intracellular biopolymers



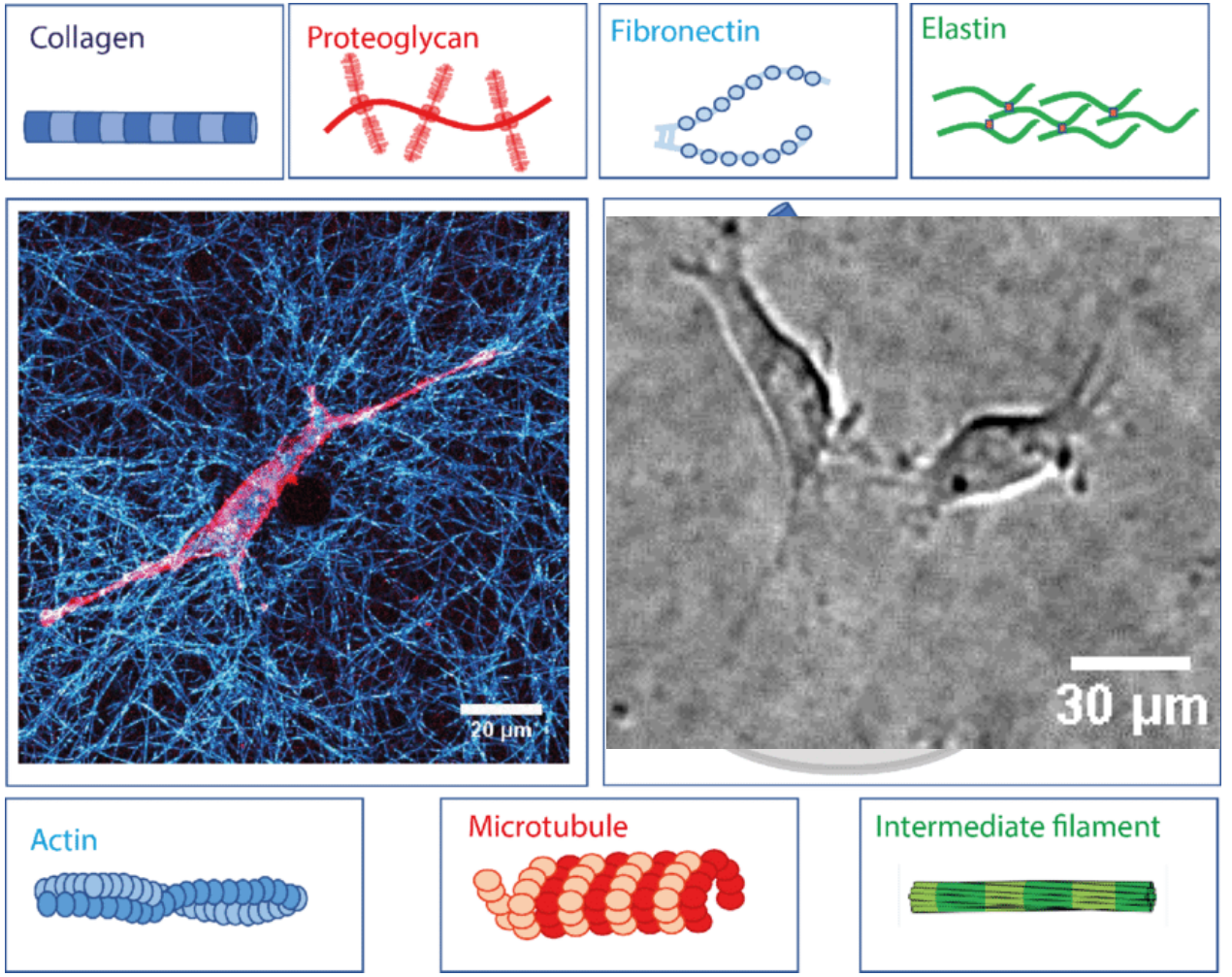
Burla et al., *Nature Reviews Physics* (2019)

Tissues are active materials with particular rheological properties

Extracellular biopolymers

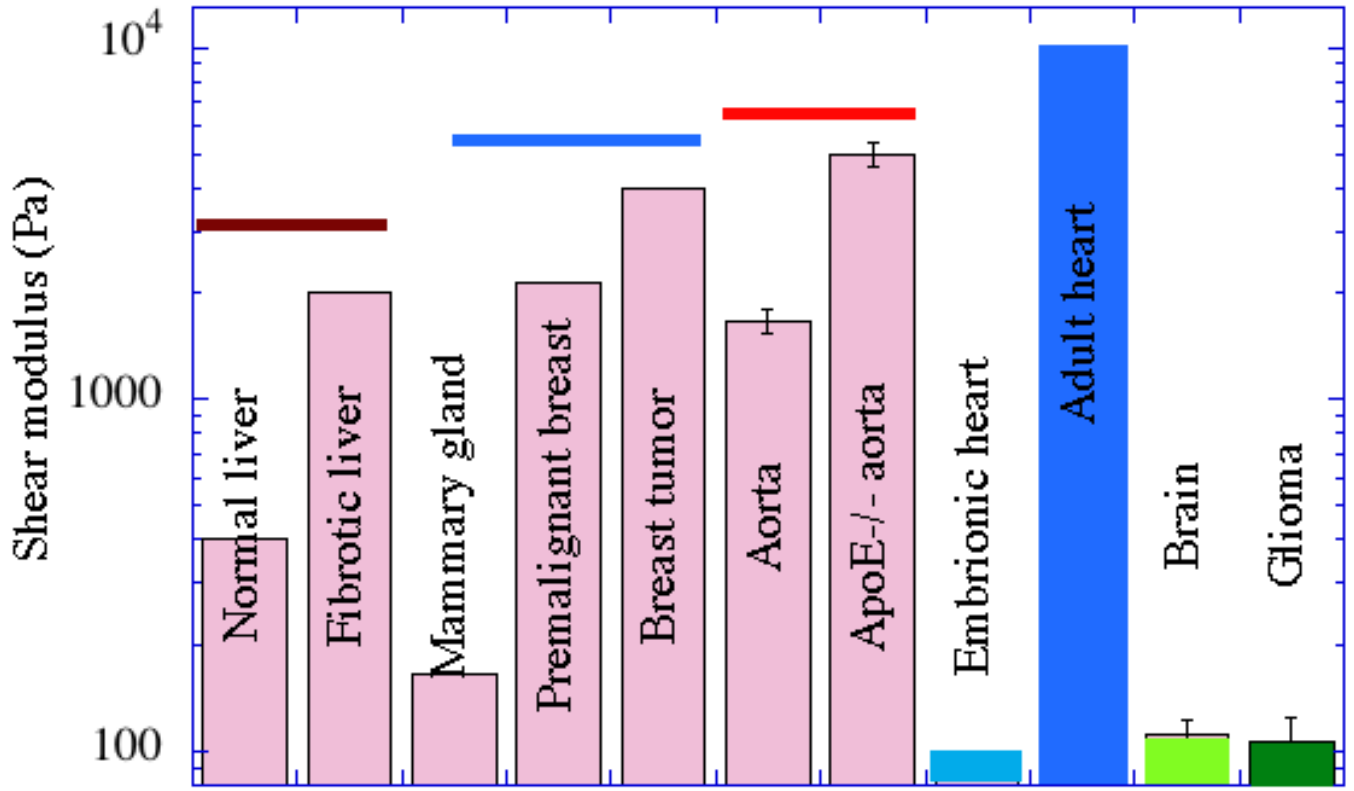
Cell embedded in 3D biopolymer network

Intracellular biopolymers



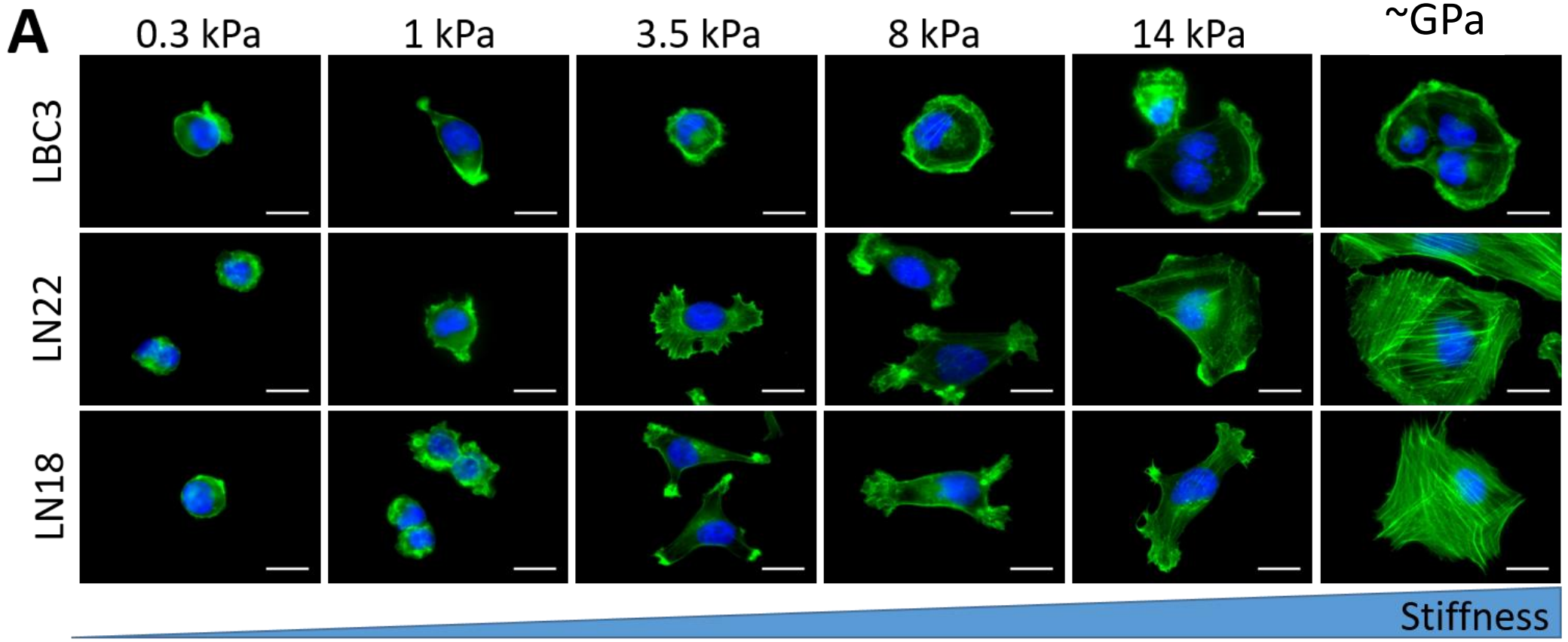
Burla et al., *Nature Reviews Physics* (2019)

Tissue elasticity is well defined



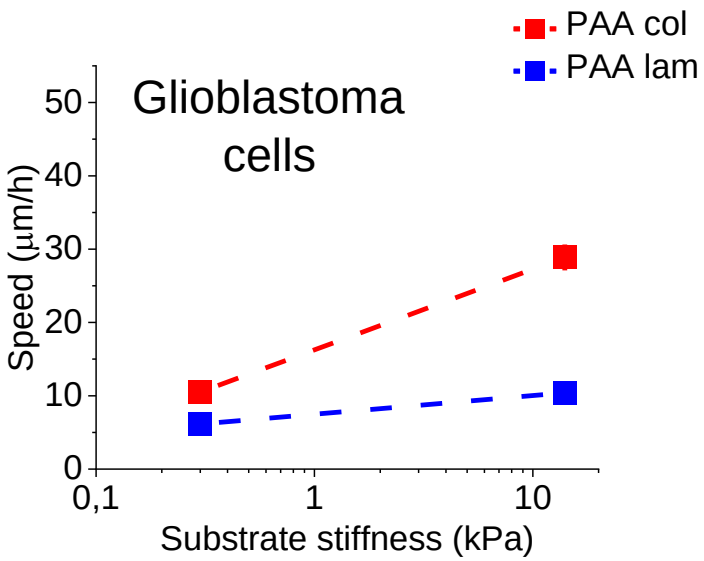
Based on: Levental et al ., *Soft Matter* (2007), Kothapalli et al. *Cell Rep* (2013), Pogoda et al., *New Journal of Physics* (2014)

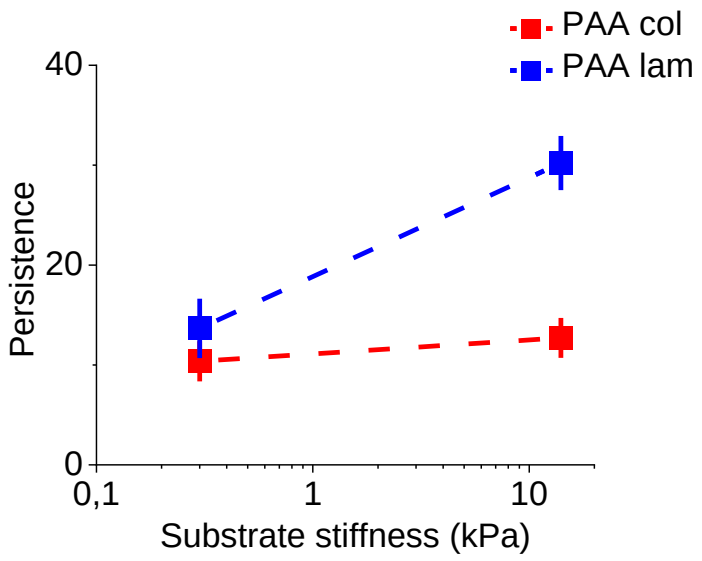
But elasticity of the single cells depeds on their environment

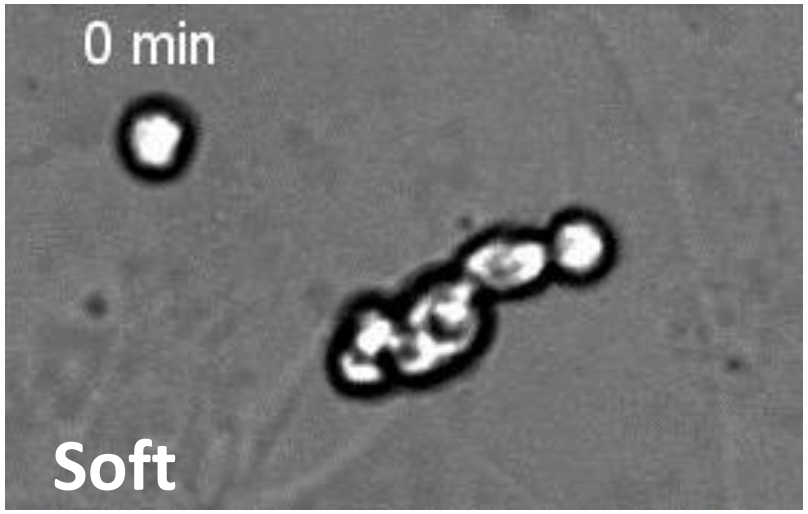


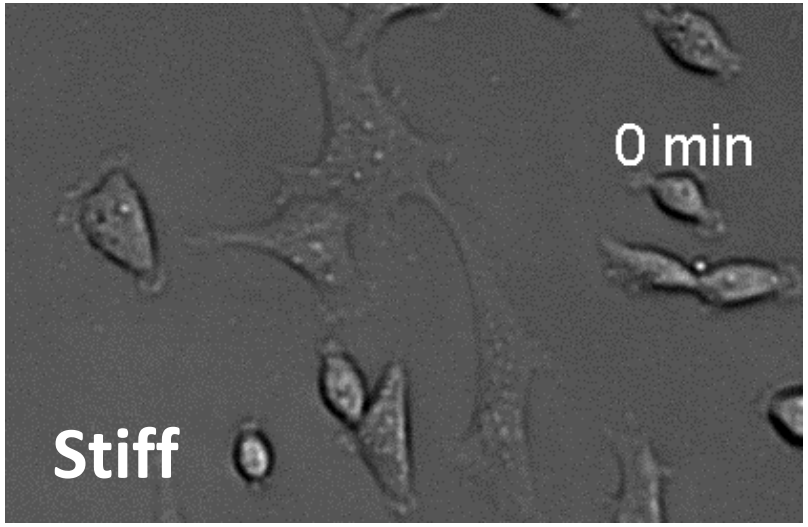
Pogoda et al., *Biomacromolecules* (2017)

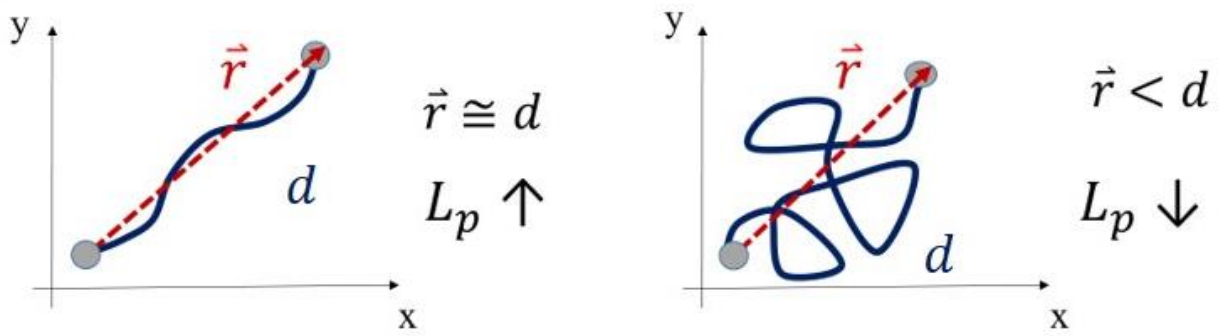
Environmental elasticity alters cell migration





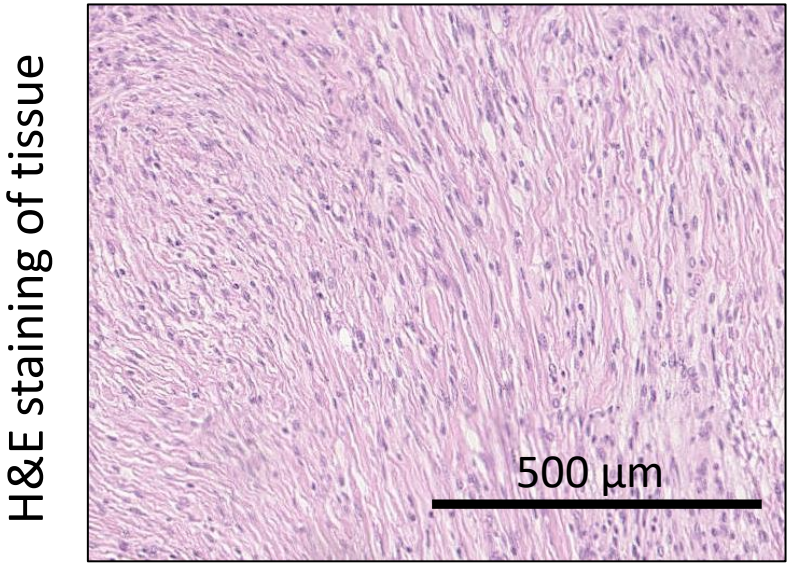




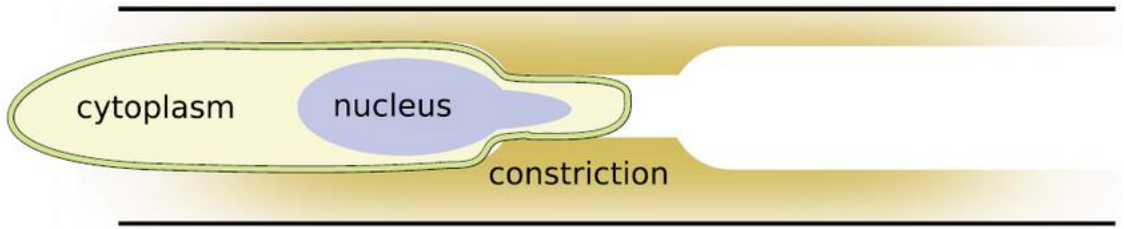


Pogoda et al., *Biomacromolecules* (2017)

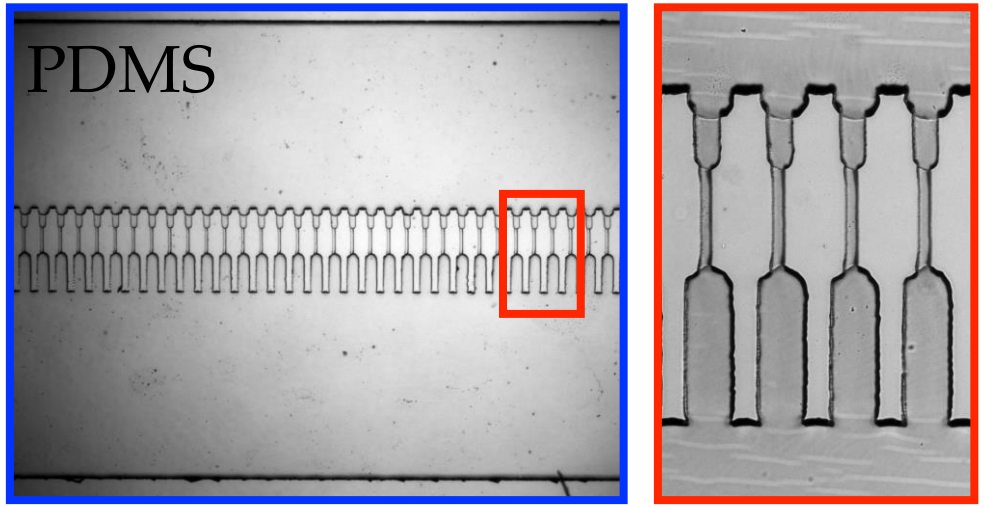
Cell migration is constricted *in vivo*



Cells in the tissue are tightly packed



And their migration is constricted



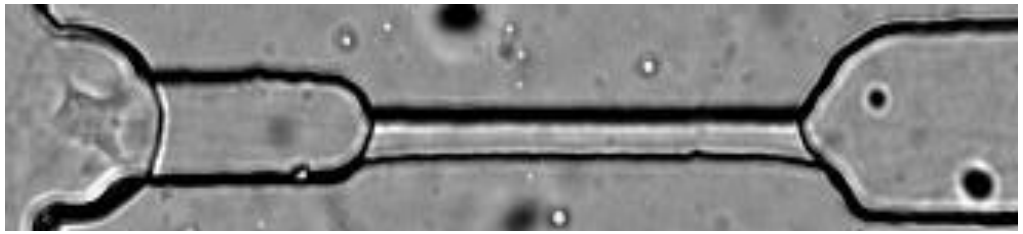
- 10 µm channels
- No applied flow
- No chemical gradient

Cieśluk M, Pogoda K. et al. *International Journal of Nanomedicine* (2020)

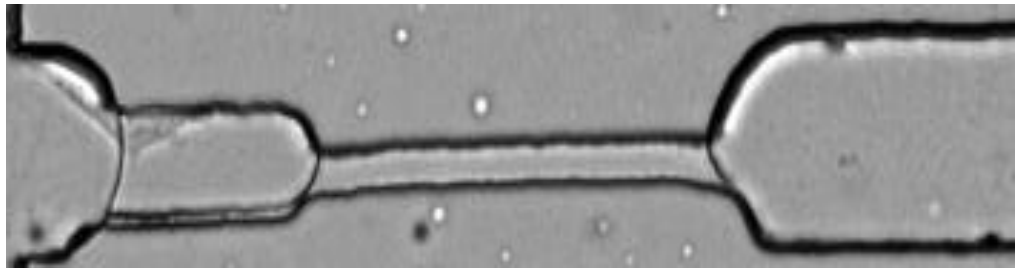
Patteson, A. E., Pogoda, K. et al., *Small* (2019)

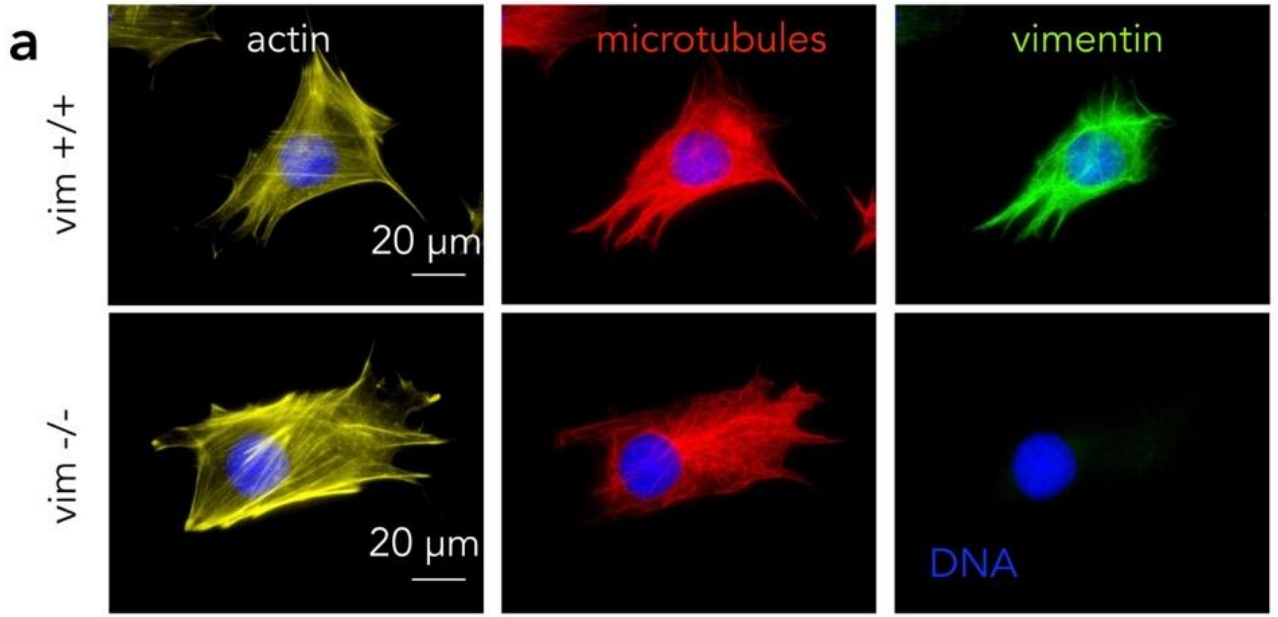
Cell migration in constrictions depends on their elasticity

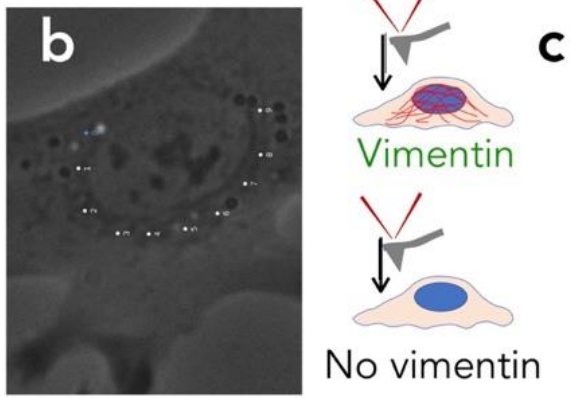
Vimentin positive (+/+)

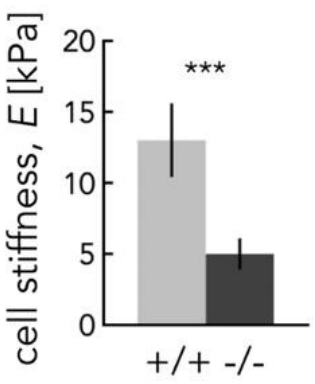


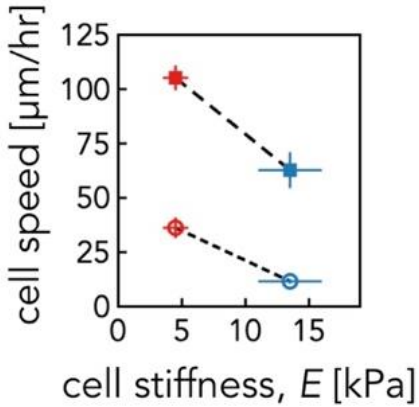
Vimentin negative (-/-)





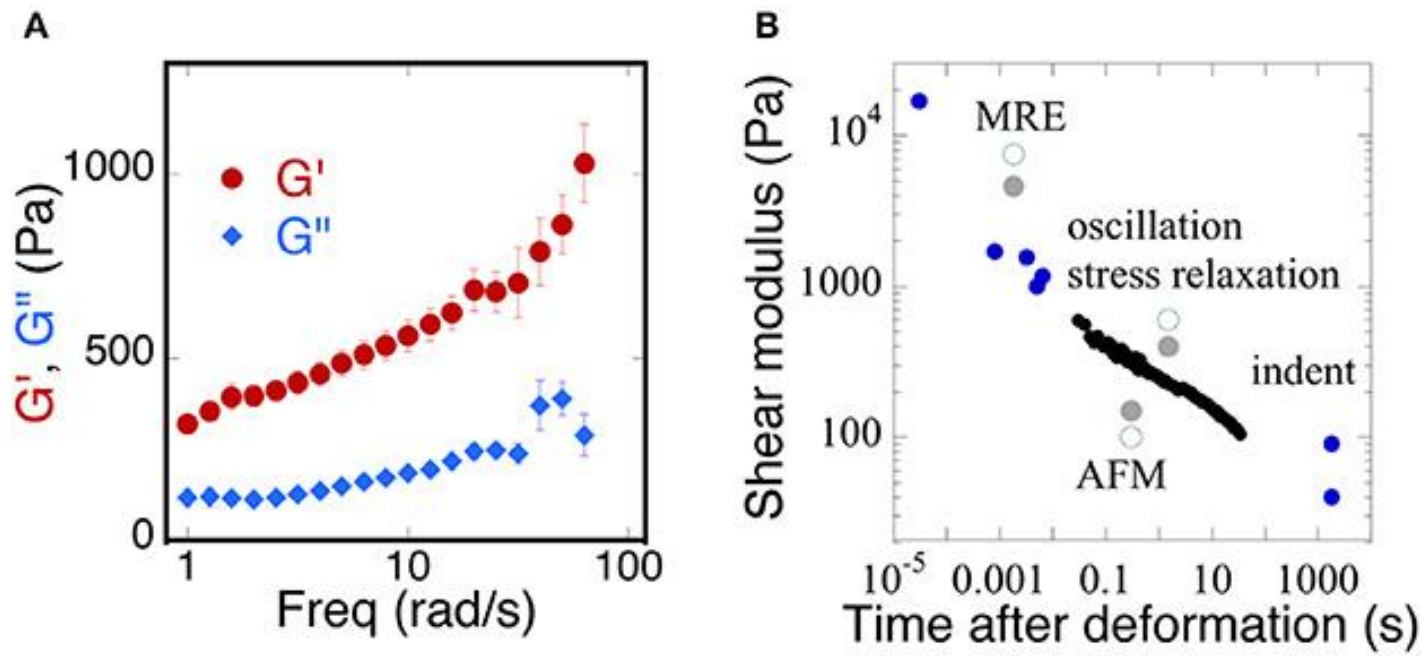






Patteson, A. E., Pogoda, K. et al.,
Small (2019)

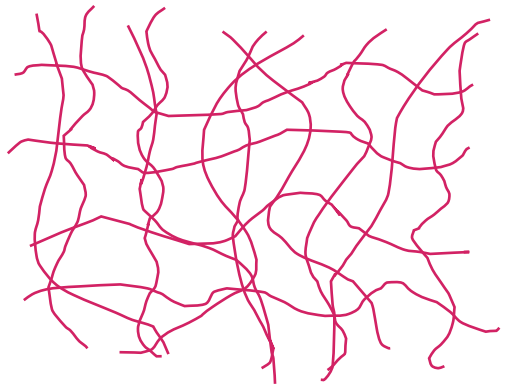
Viscoelasticity in biological systems



Time dependence of the viscoelastic properties of brain tissue

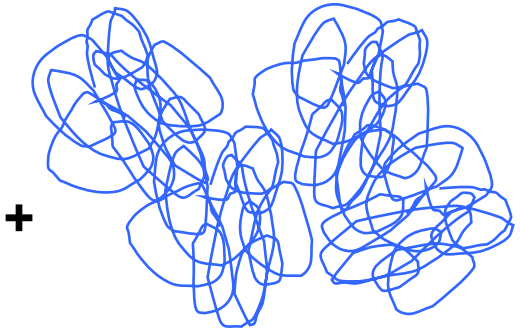
Pogoda, K., & Janmey, P. A. *Frontiers in Cellular Neuroscience* (2018)

How to incorporate viscosity into elastic materials ?

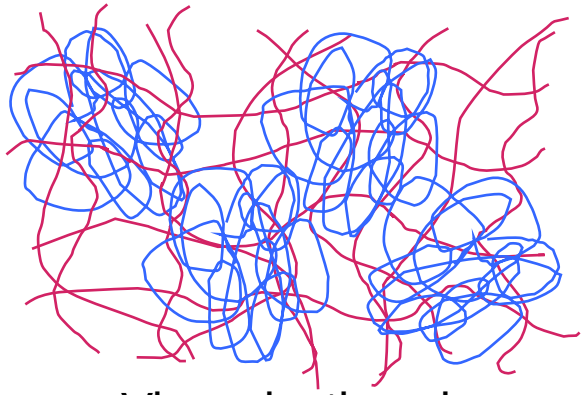


Crosslinked acrylamide 8%
(elastic)
Mesh size = 10nm

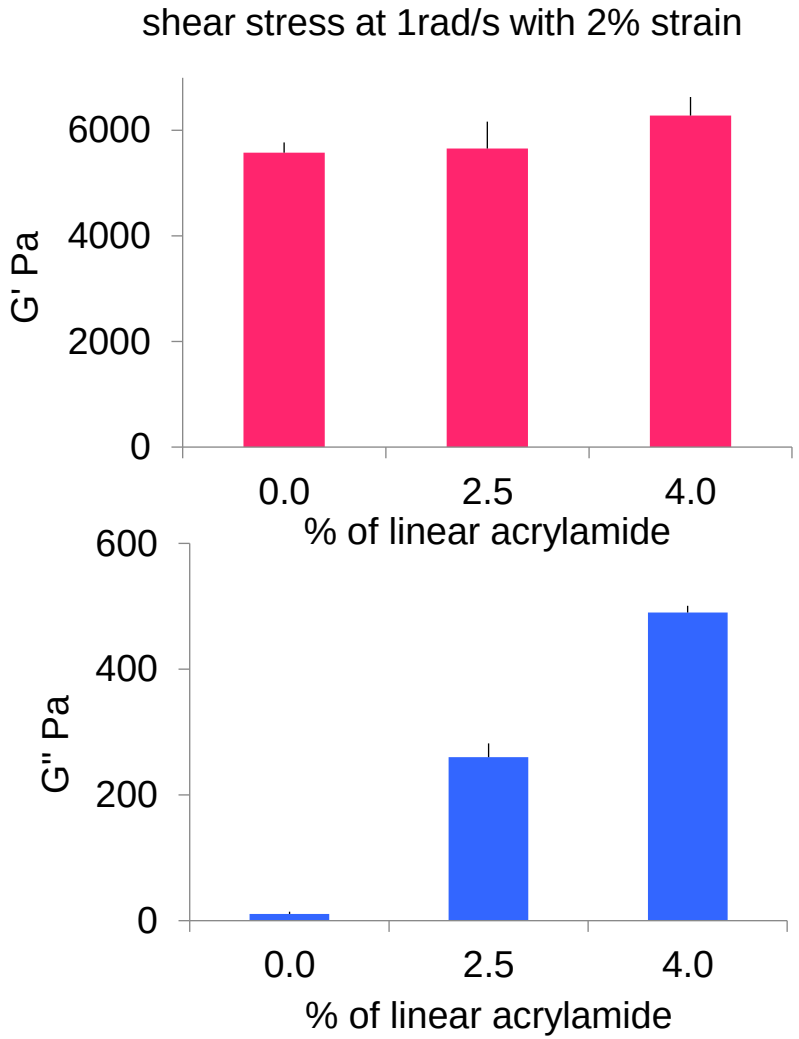
+



Linear acrylamide 5%
(viscous)
Hydrodynamic radius = 40nm



Viscoelastic gel



Charrier, E. E., Pogoda, K., Wells, R. G., & Janmey, P. A. *Nature Communications* (2018)

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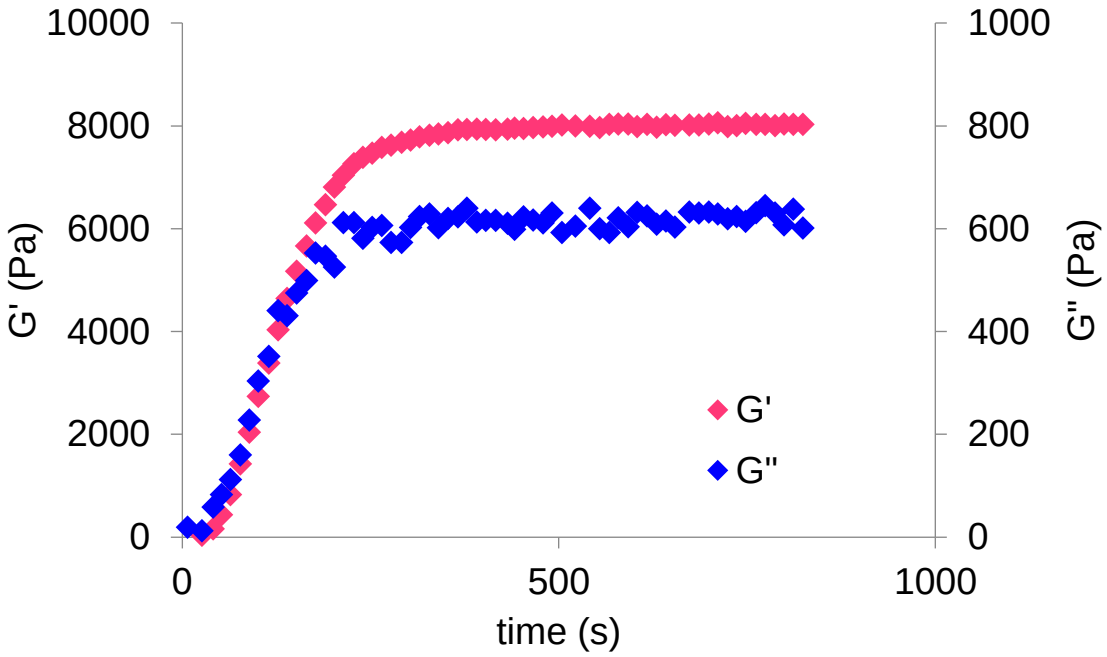
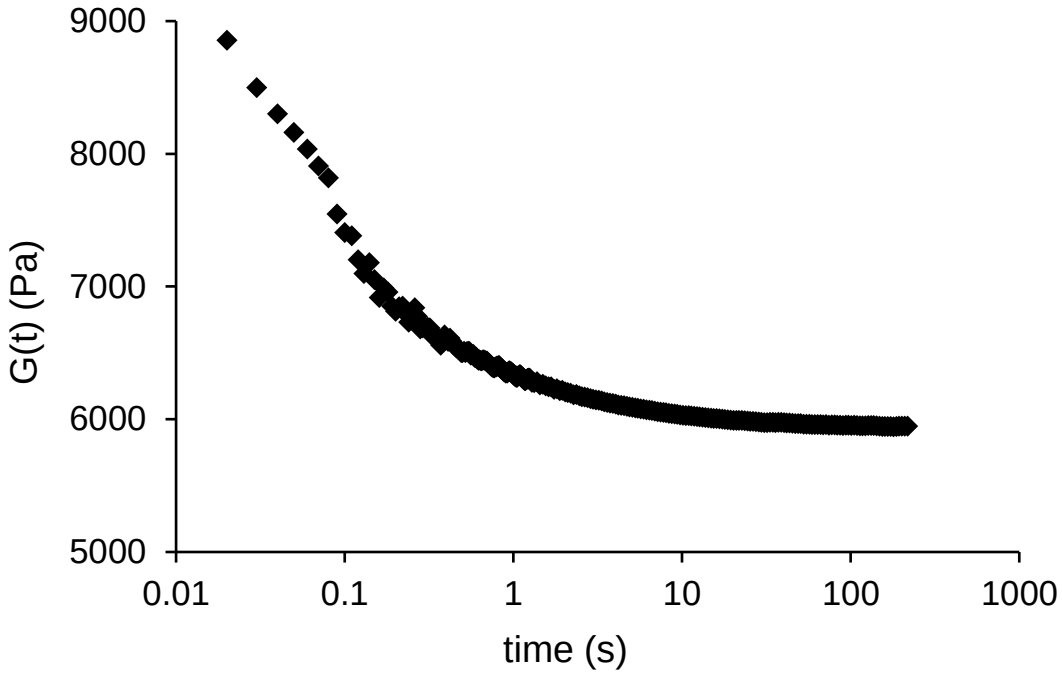


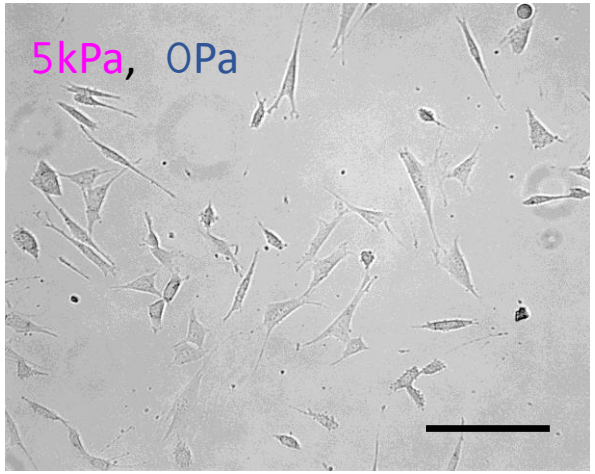
G’ and G” increase during the formation of the gel

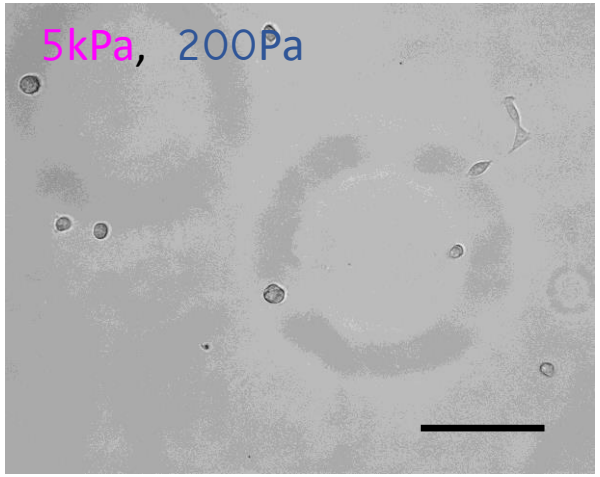


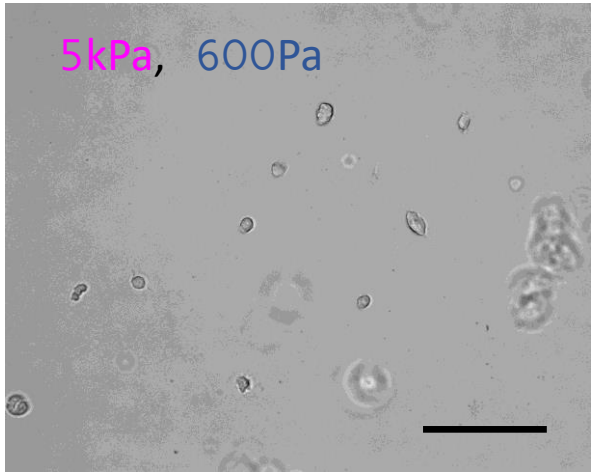
Viscoelastic materials behave in a nonlinear fashion, which is indicated by **stress relaxation**

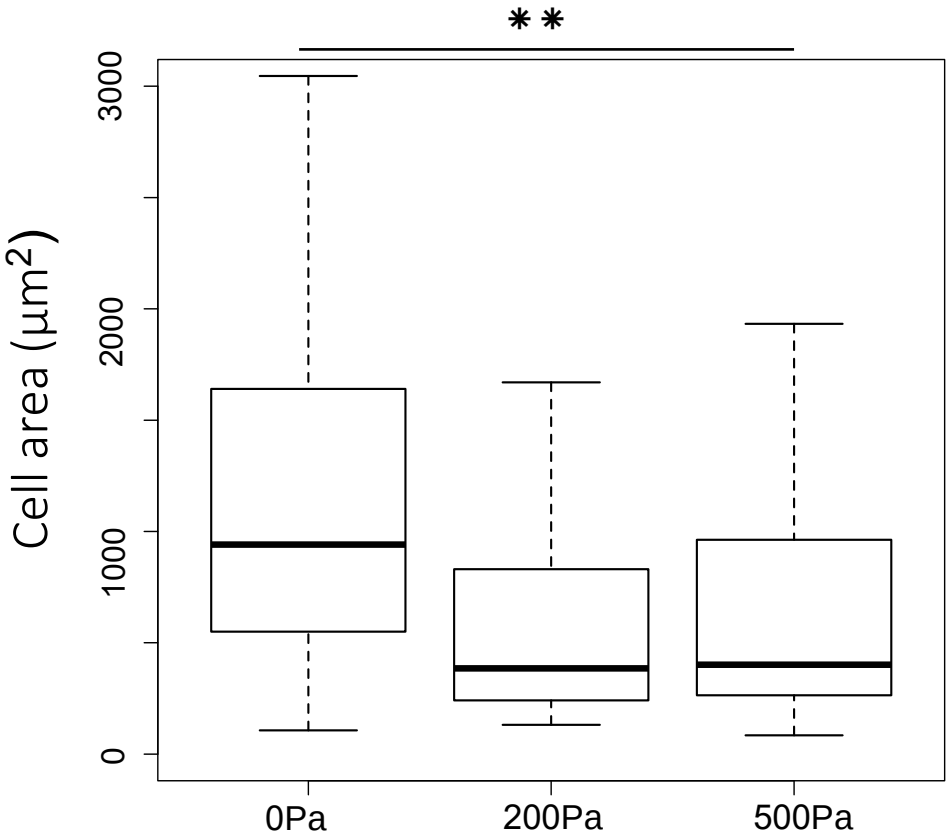
Charrier, E. E., Pogoda, K., Wells, R. G., & Janmey, P. A. *Nature Communications* (2018)

Cell morphology can be controlled by substrates with independently tunable elasticity and viscous dissipation









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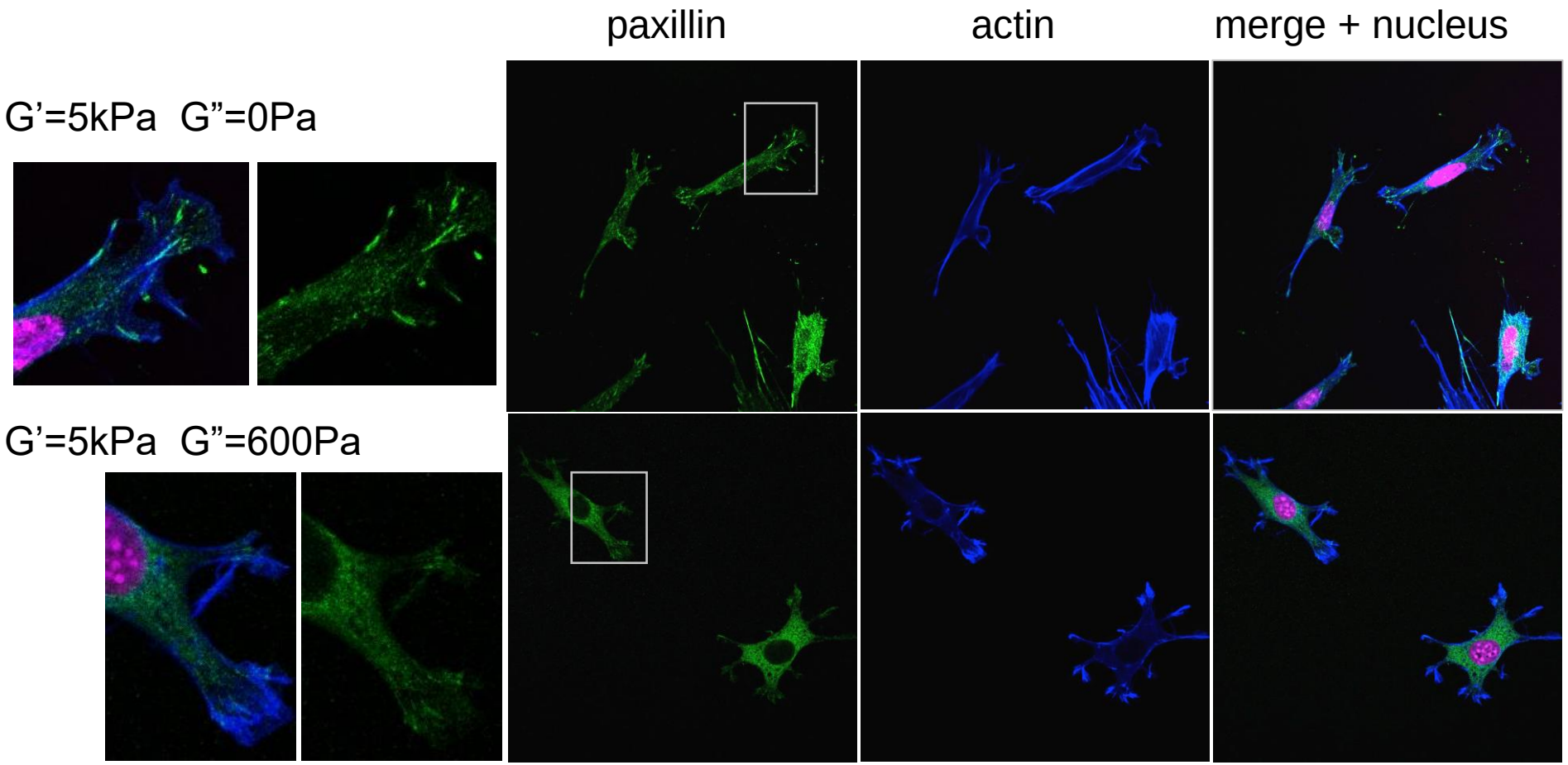
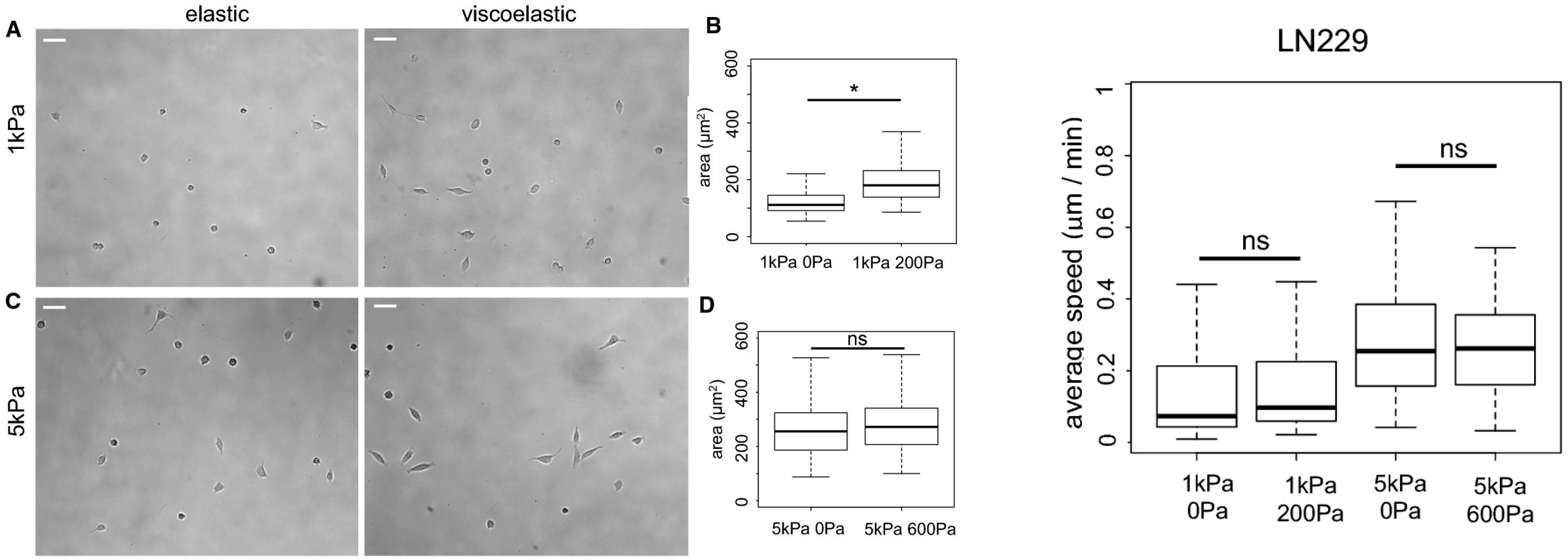


Charrier, E. E., Pogoda, K., Wells, R. G., & Janmey, P. A. *Nature Communications* (2018)

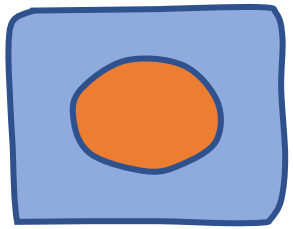
How malignant cells respond to viscous dissipation?



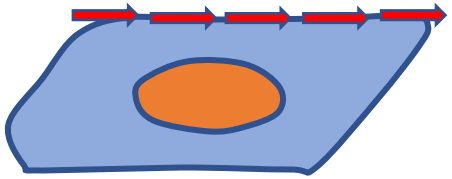
Charrier, E. E., Pogoda, R. Li, K., Wells, R. G., & Janmey, P. A. *Biomech Model Mechanobio* (2021)

Cells under mechanical stress

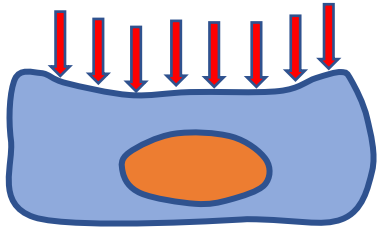
Undisturbed cell



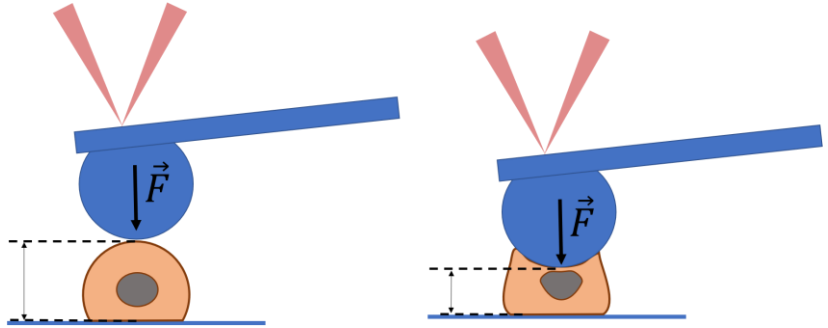
Cell under shear force



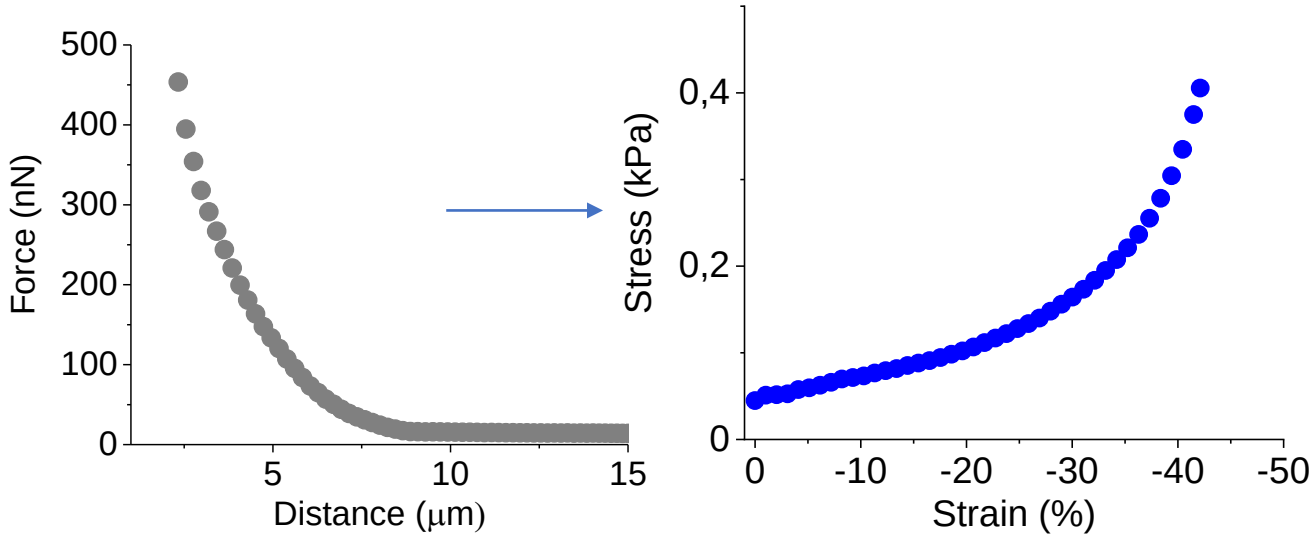
Cell under pressure



Uniaxial compression of the single cell



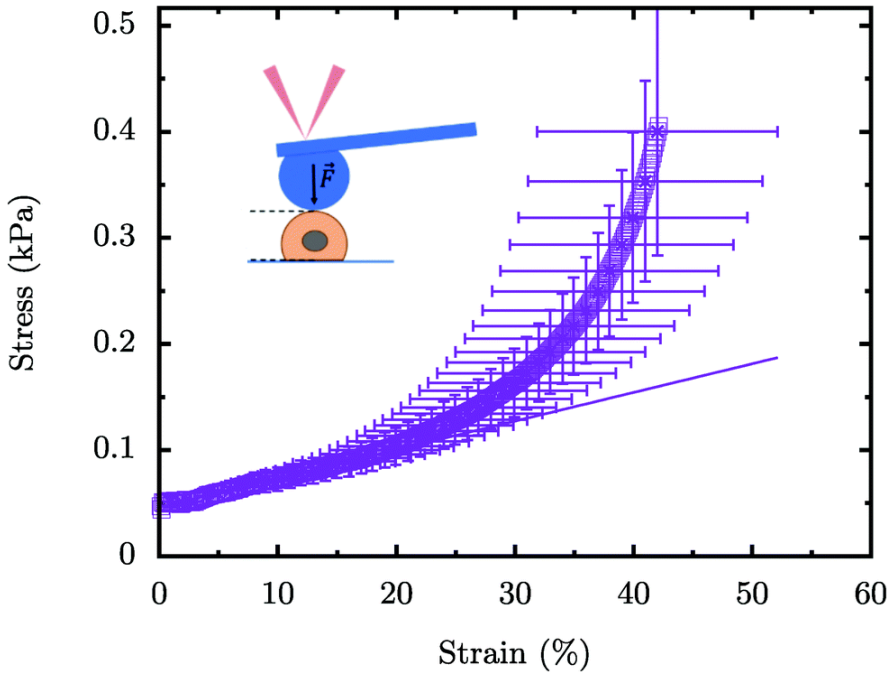
$$Stress = \frac{Force\ (nN)}{Area\ of\ deformation\ (\mu m^2)}$$



Gandikota, M. C., Pogoda, K. et al.,
Soft matter (2020)

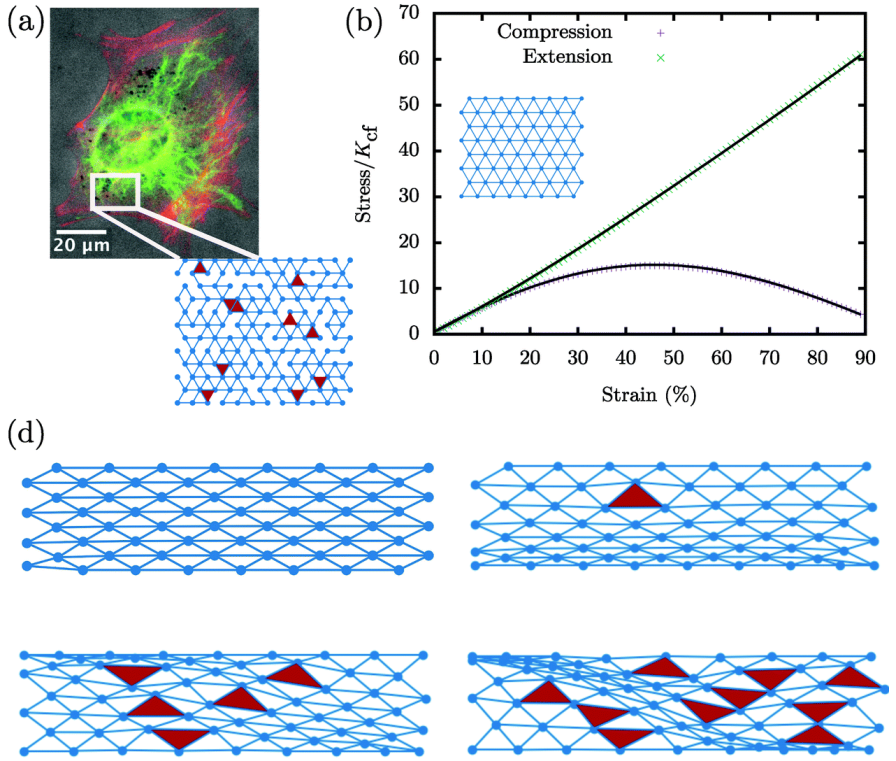
Compression stiffening of cells

Increase in moduli with increasing uniaxial compressive strain



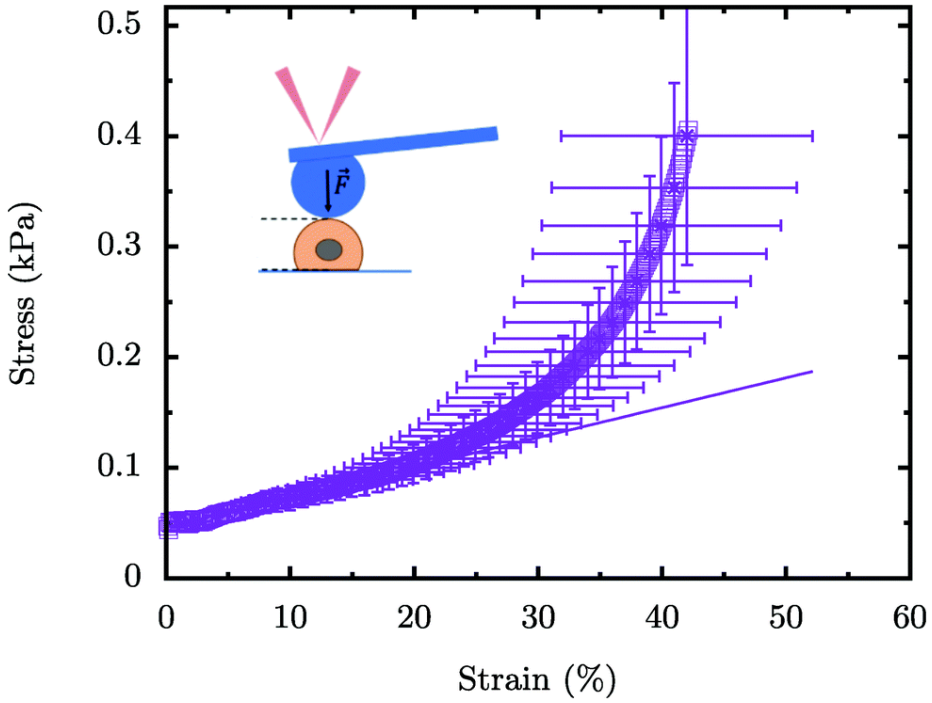
Gandikota, M. C., Pogoda, K. et al.,
Soft matter (2020)

Cell as a collection of organells within a fiber network



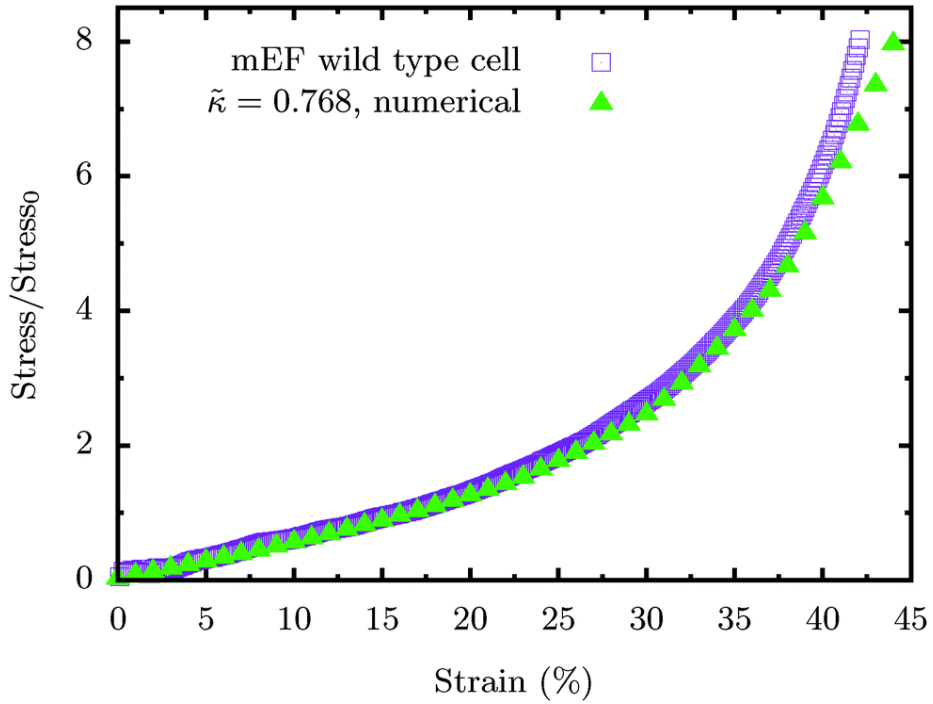
Compression of a fiber network with embedded area-conserving loops

Compression stiffening of cells



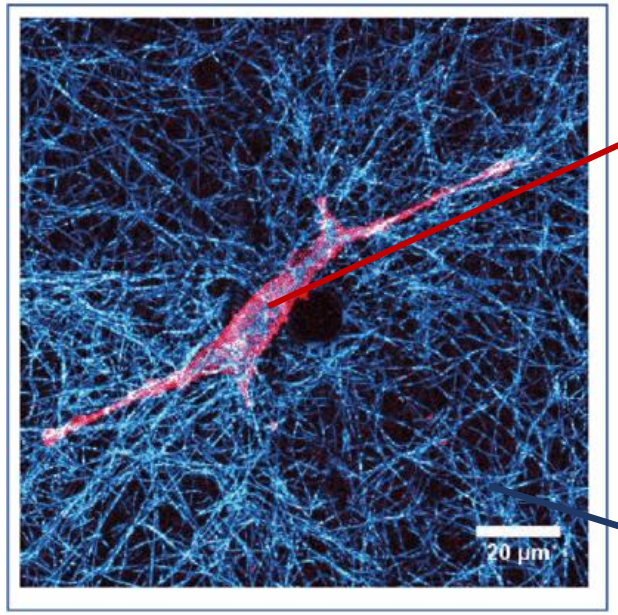
Gandikota, M. C., Pogoda, K. et al.,
Soft matter (2020)

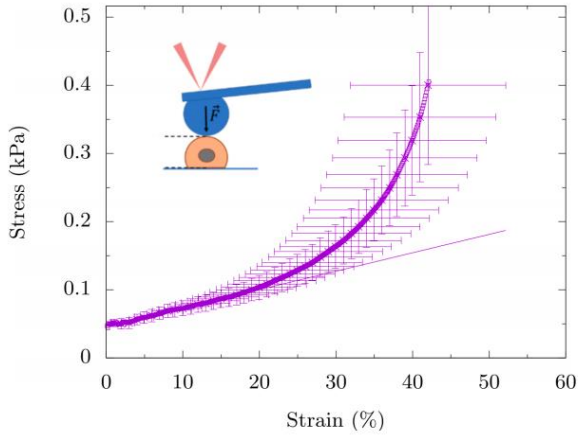
J. M. Schwarz Theory Group
Syracuse University



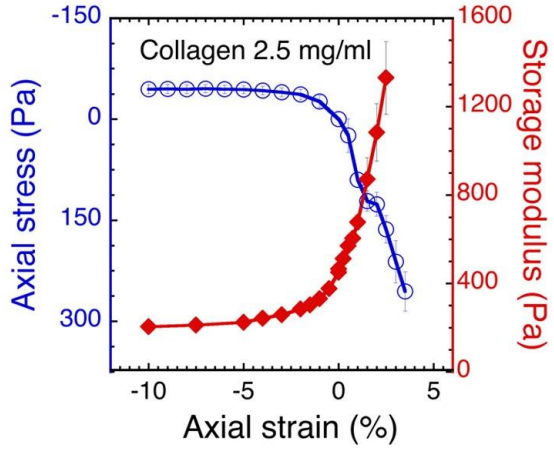
Compression of a fiber network with embedded area-conserving loops

What are the physical principles that define tissue mechanics?





Single cells
compression – stiffen



Biopolymer networks
compression – soften

van Oosten *et al.* *Sci Rep* (2016)

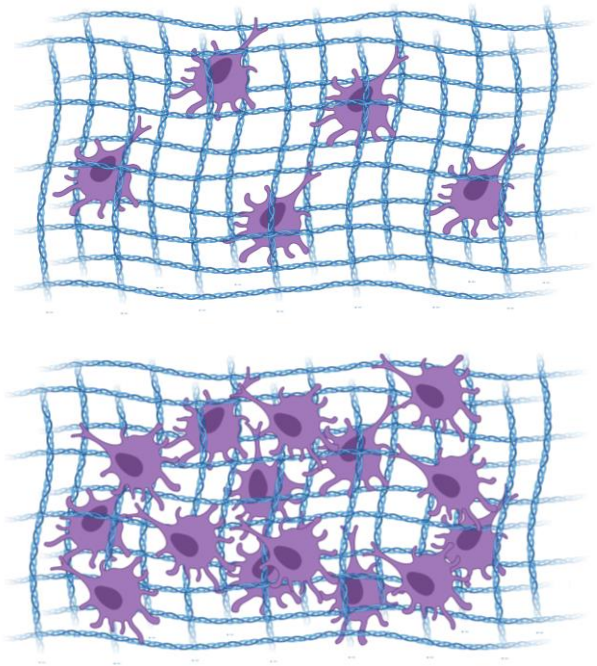
What are the physical principles that define tissue mechanics?

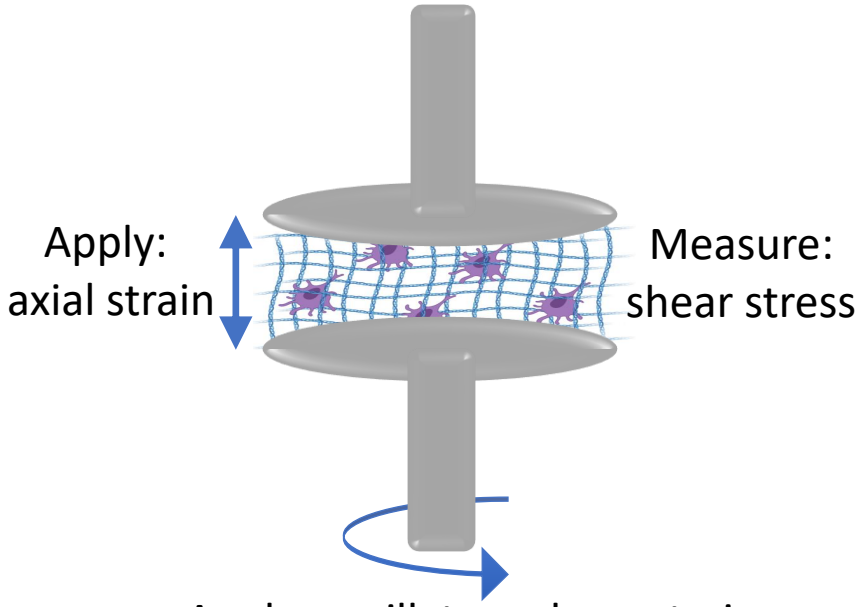
3D collagen network with cells

Glioblastoma cells

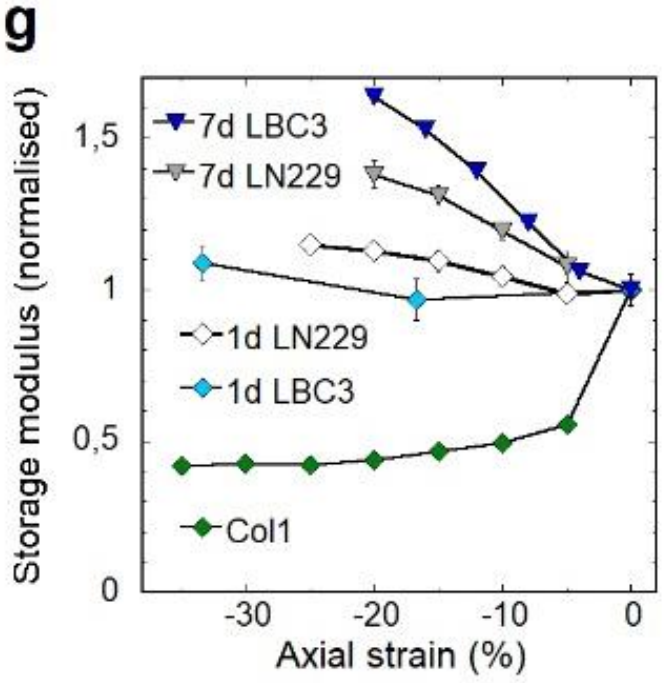
1d

7d



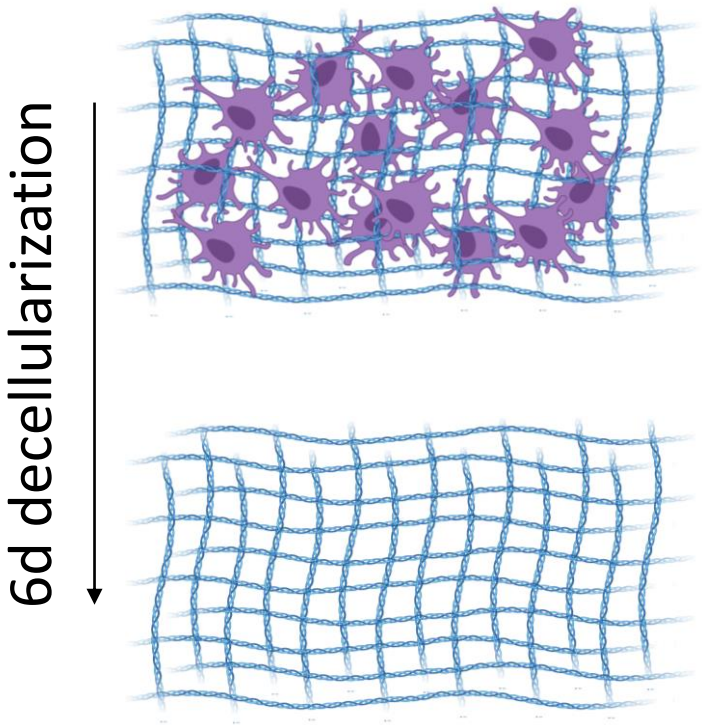


Glioblastoma cells (LN229, LBC3)

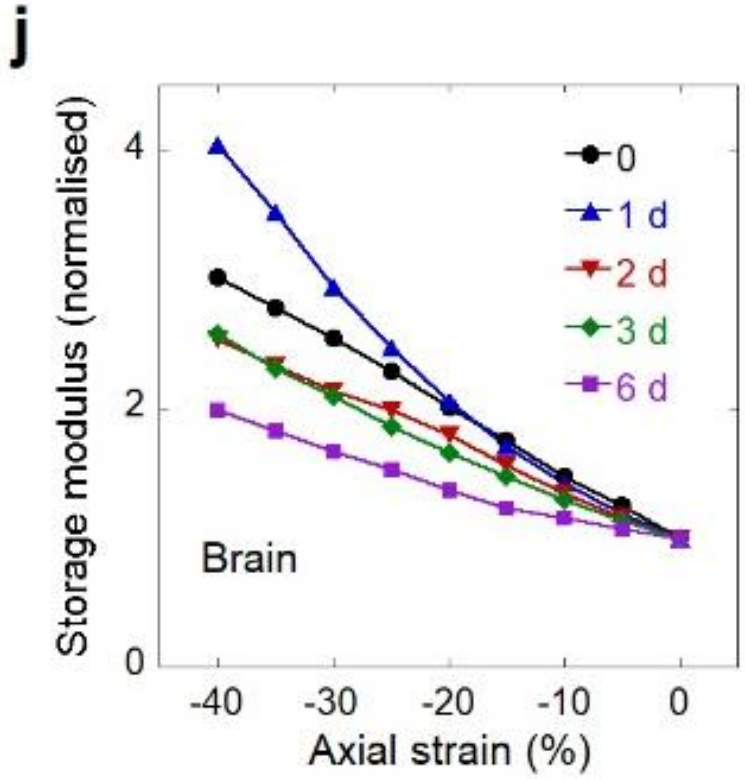


van Oosten, A. S., Chen, X., Chin, L., Cruz, K., Patteson, A. E., Pogoda, K., ... & Janmey, P. A. *Nature (2019)*

What are the physical principles that define tissue mechanics?



Fresh brain tissue



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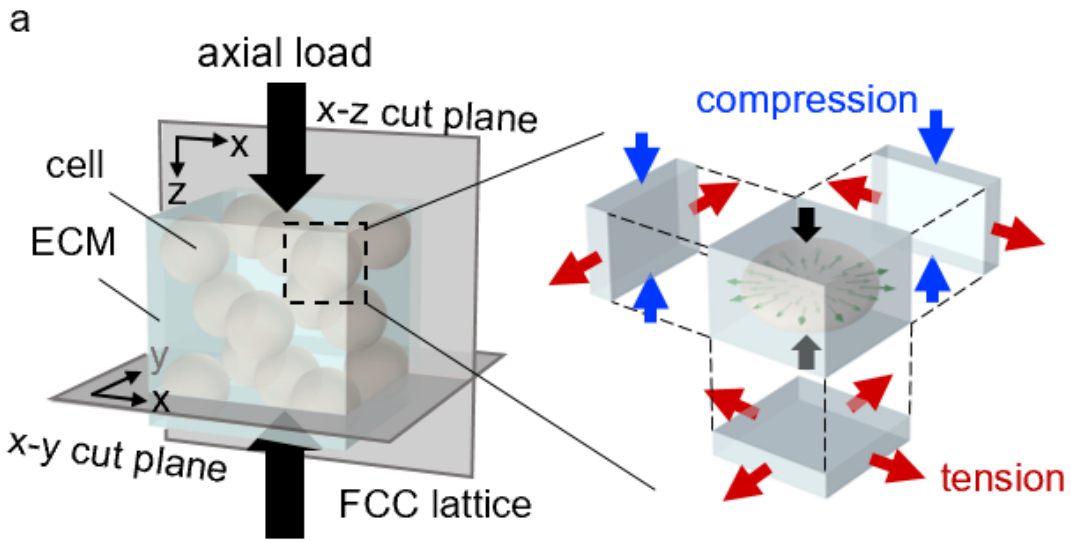
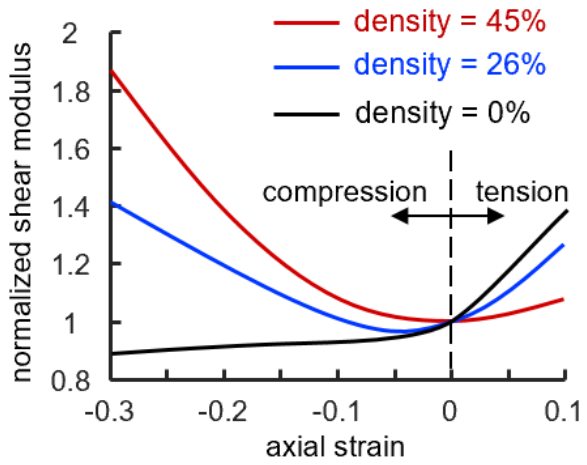
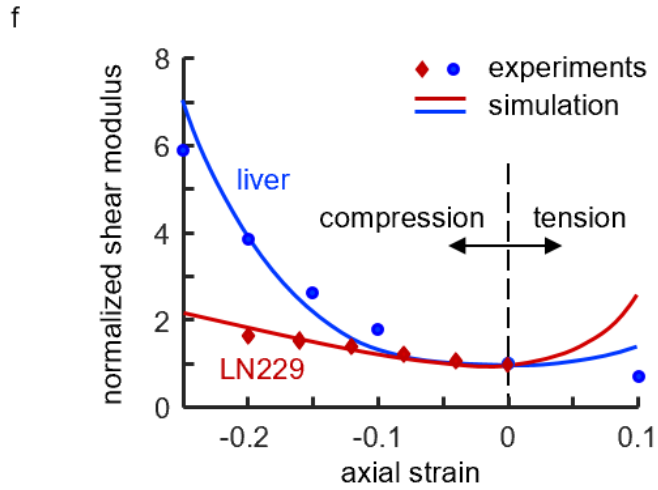
What are the physical principles that define tissue mechanics?







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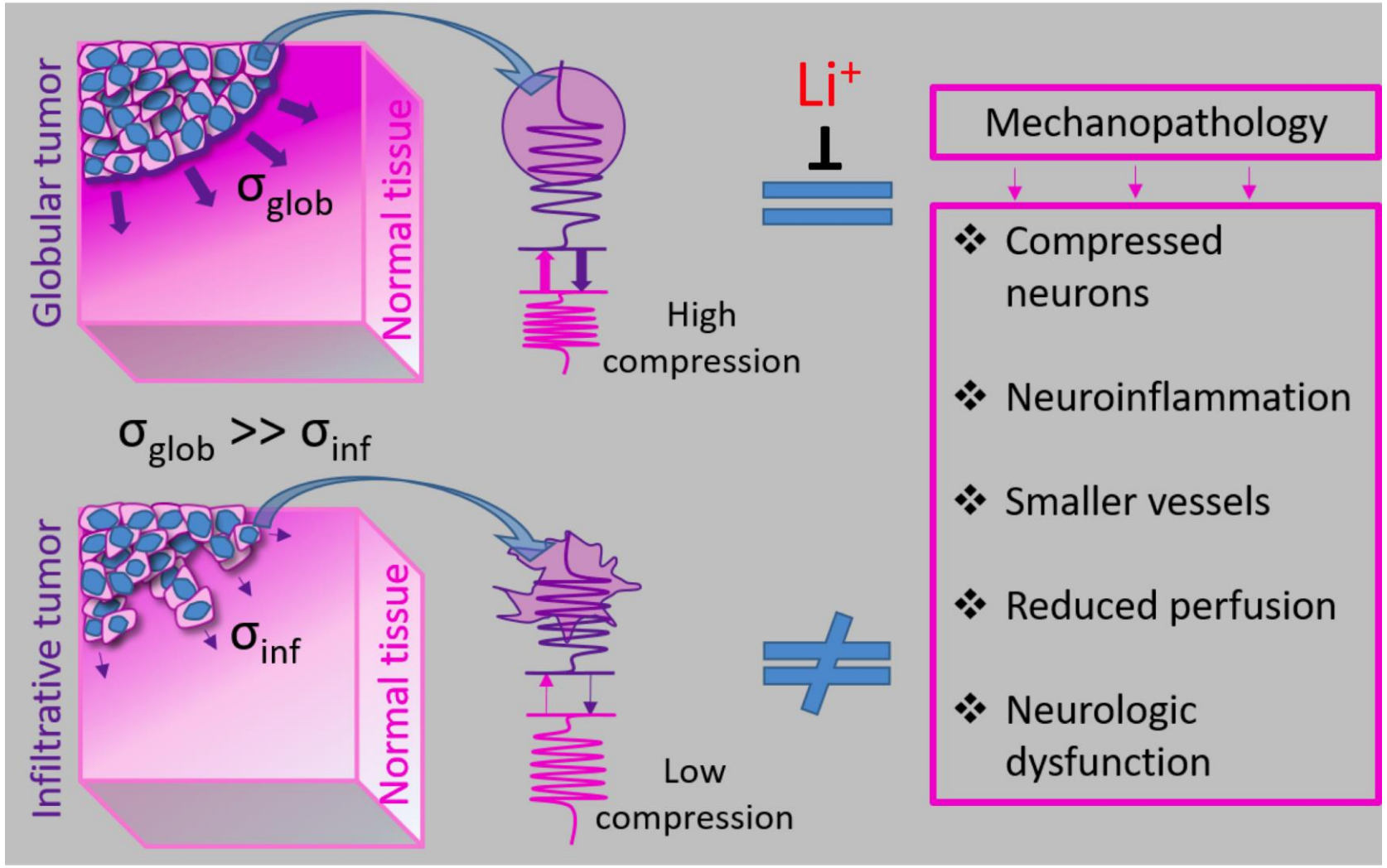
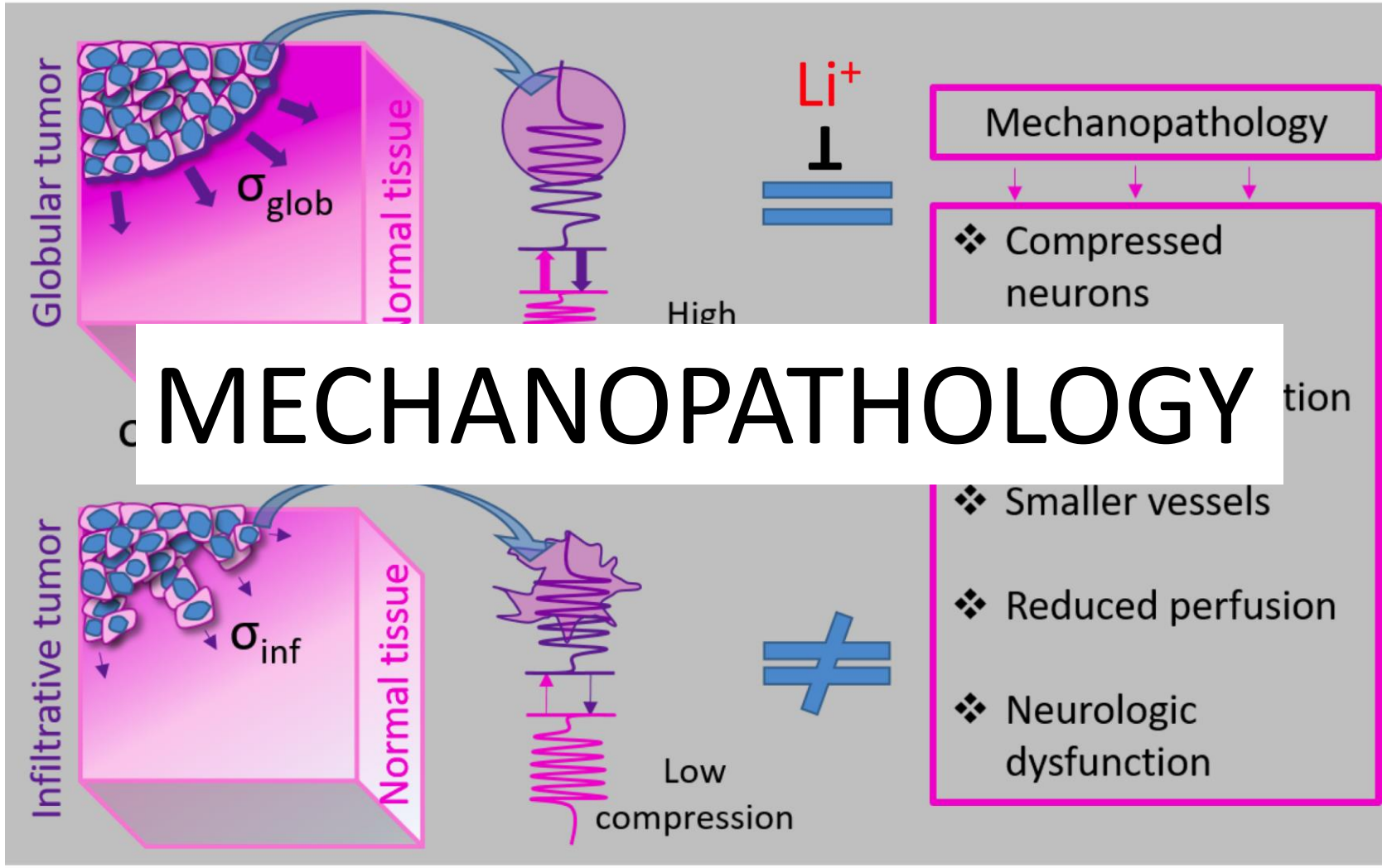
The consequence of compressive stress in tumors



Janmey, P. A., & Pogoda, K. *Nature Biomedical Engineering* (2019)

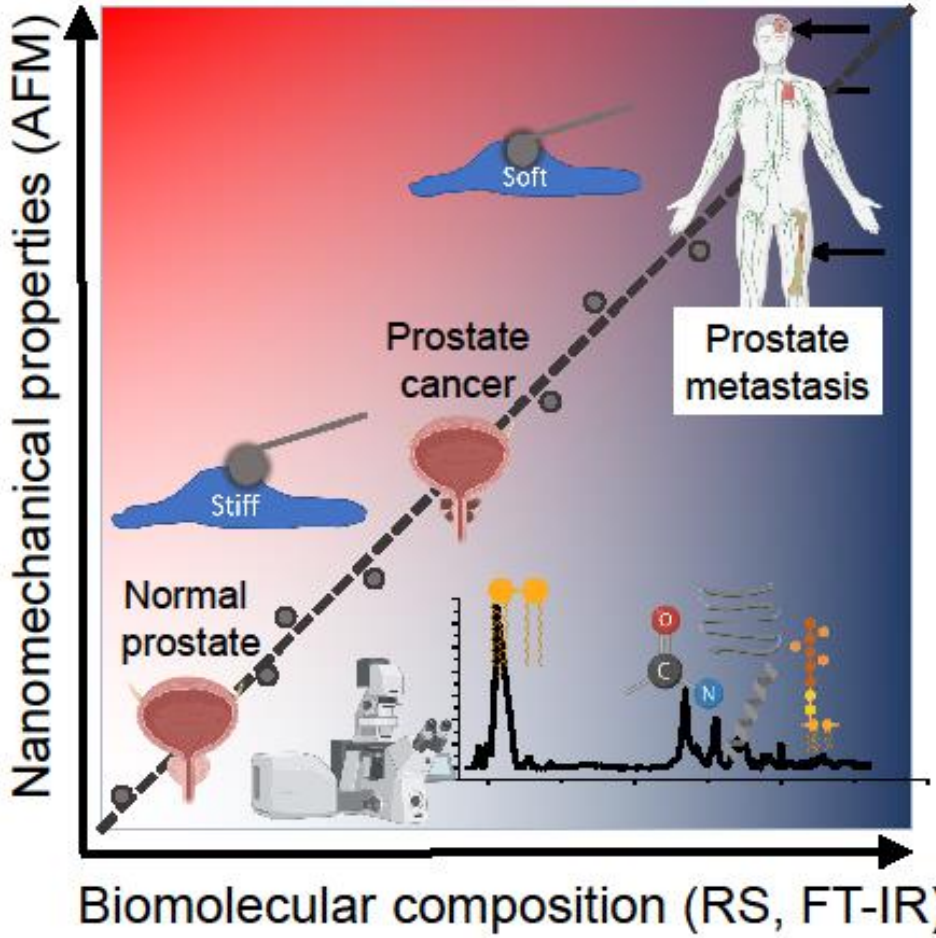
Conclusions



Janmey, P. A., & Pogoda, K. *Nature Biomedical Engineering* (2019)

Future directions

Nanomechanical and biomolecular signatures of the cells can be correlated linearly and relate to their metastatic potential.



Pogoda, K. et al., *Archives of Biochemistry and Biophysics* (2021)

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Paul A Janmey Lab
University of Pennsylvania

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