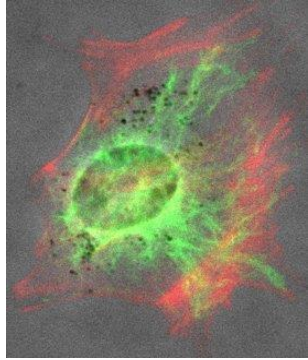


Loops versus lines and the compression stiffening of cells



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Dept. of Physics, Syracuse University, USA

Katarzyna Pogoda

Institute of Nuclear Physics, Polish Academy of Sciences, Poland

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Leiden Academic center for drug research, Netherlands

T. A. Engstrom

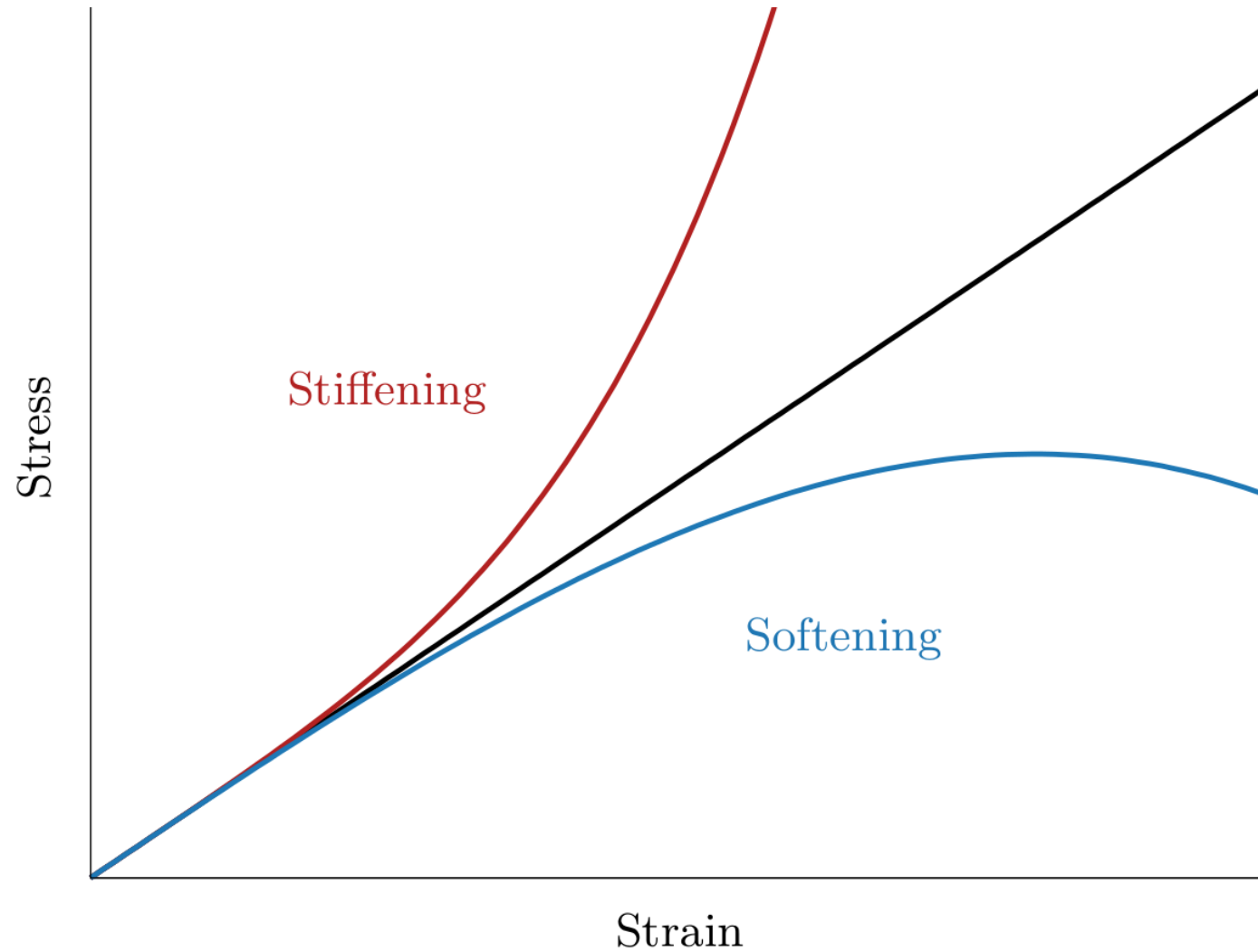
Dept. of Physics, Hobart & William Smith Colleges, USA

P. A. Janmey

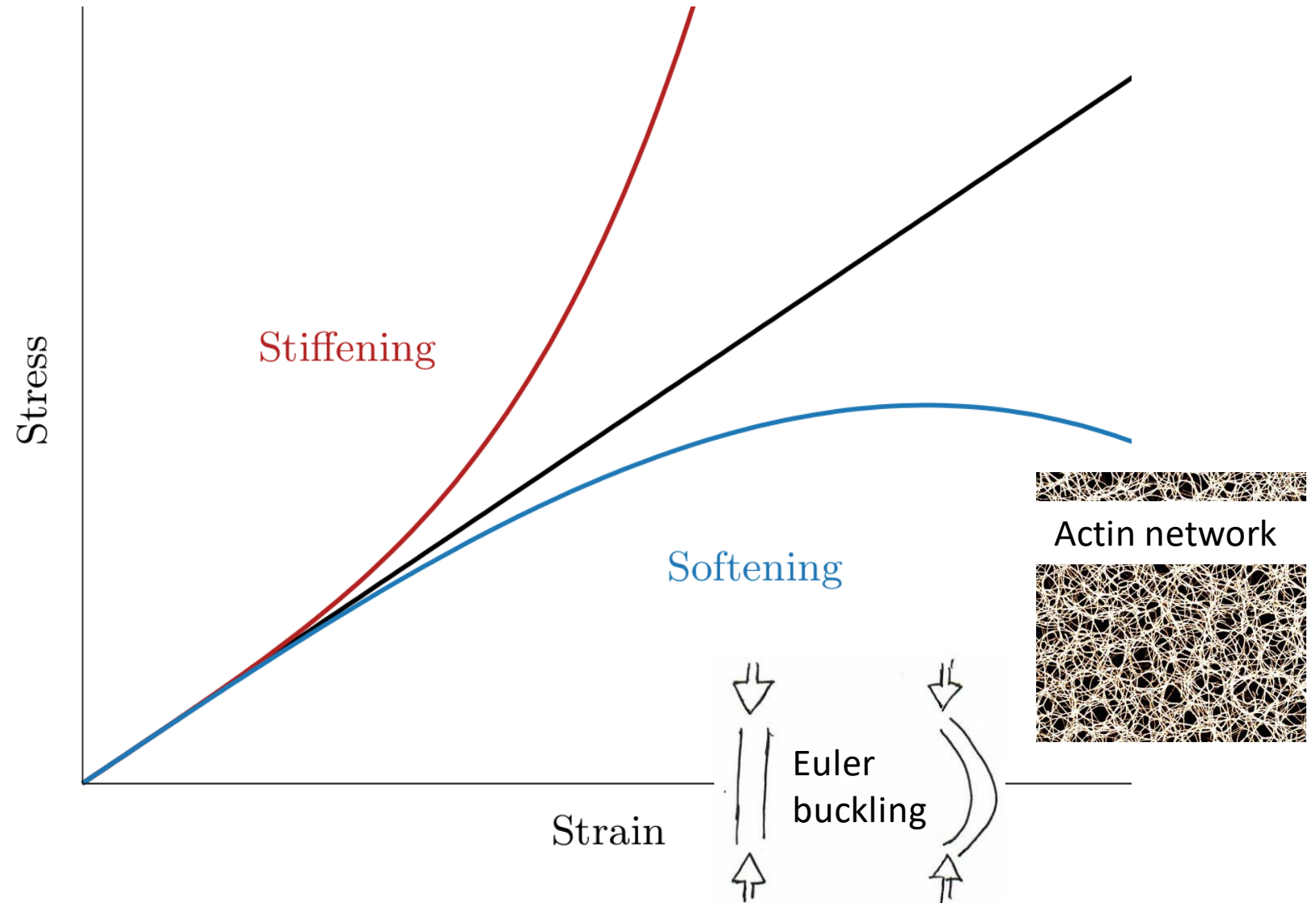
Departments of Physiology and Physics & Astronomy, University of Pennsylvania, USA



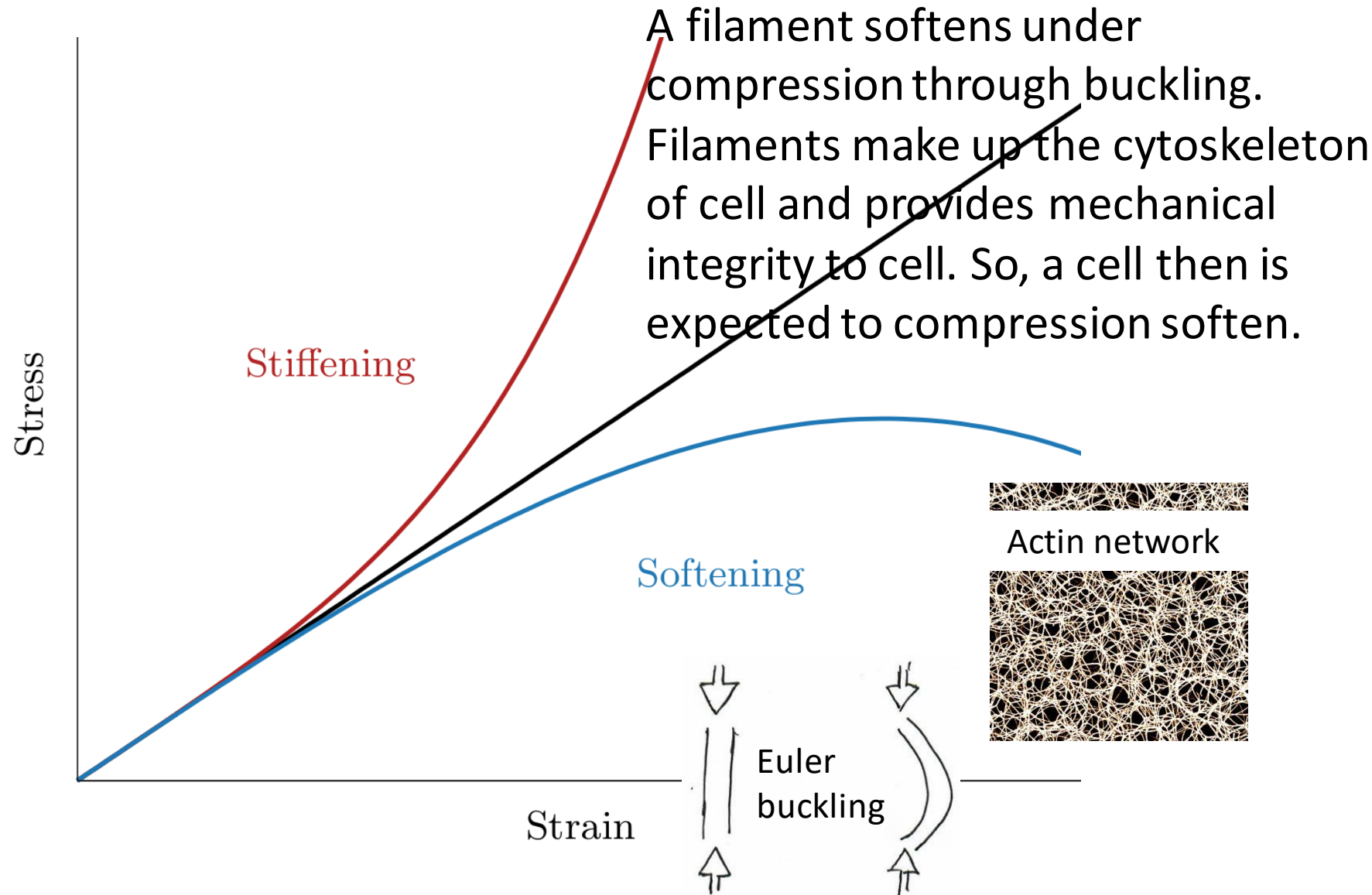
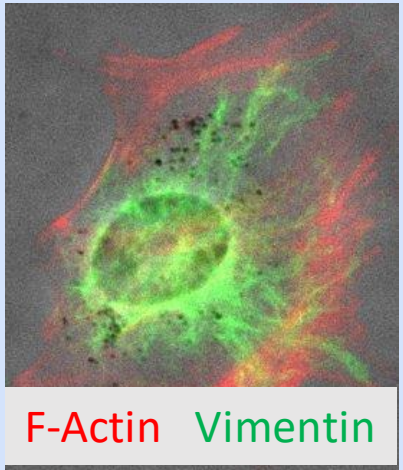
What will happen if you compress anything?



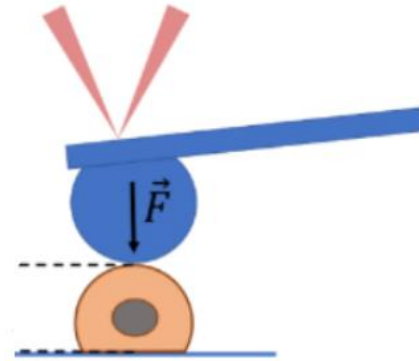
What will happen if you compress anything?



What will happen if you compress a cell?

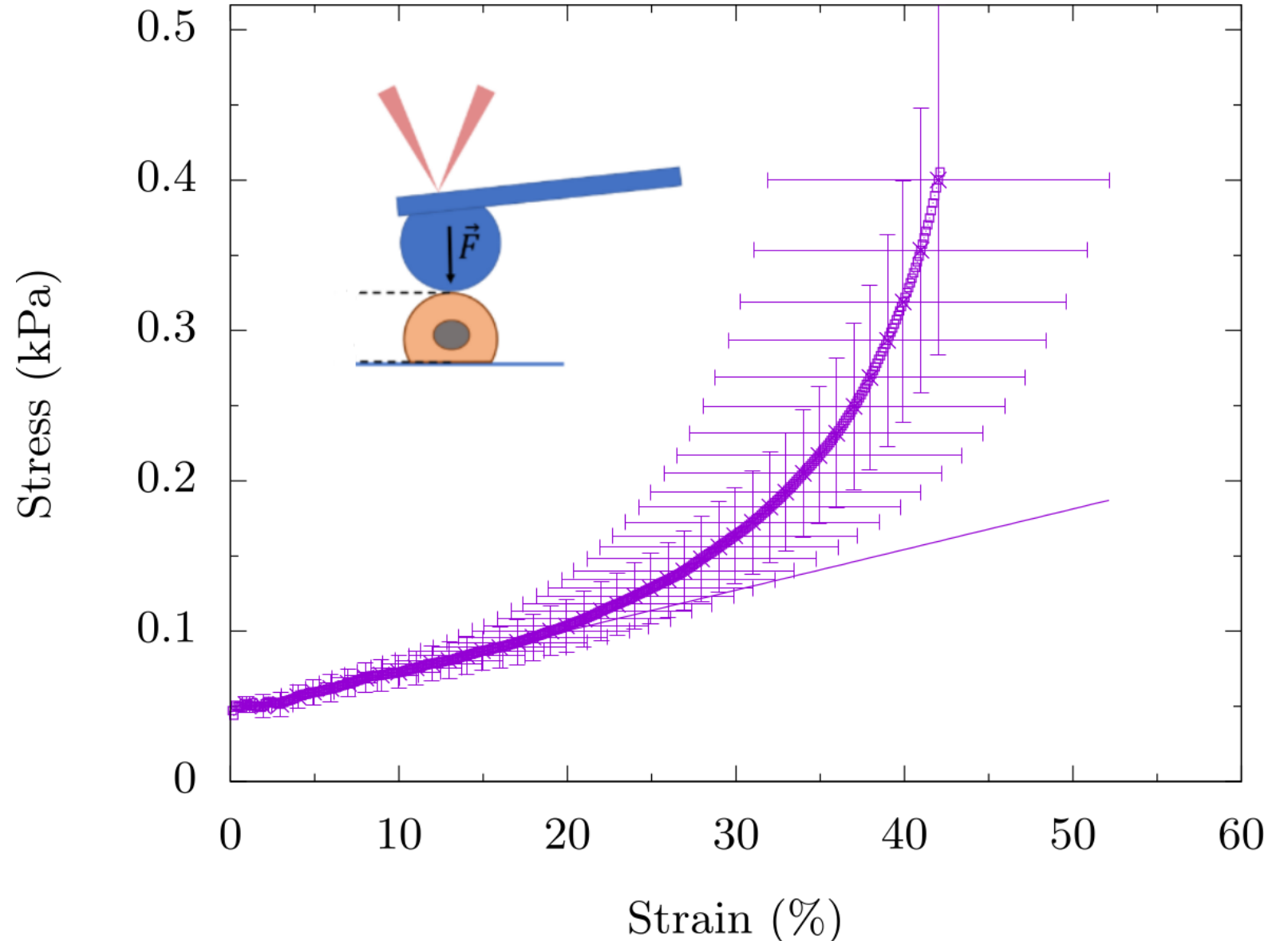


Atomic force microscopy of mouse embryo fibroblast (mEF)



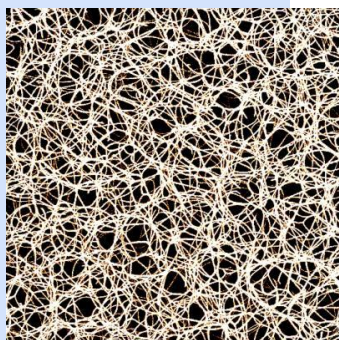
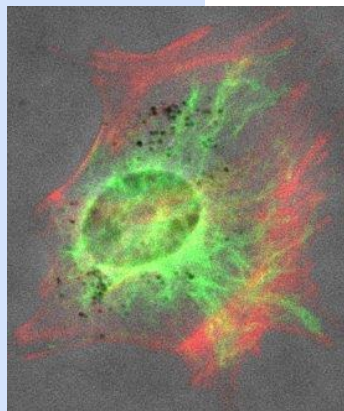
Atomic force
microscopy of
mouse
embryo
fibroblast
(mEF)

Compression
stiffening

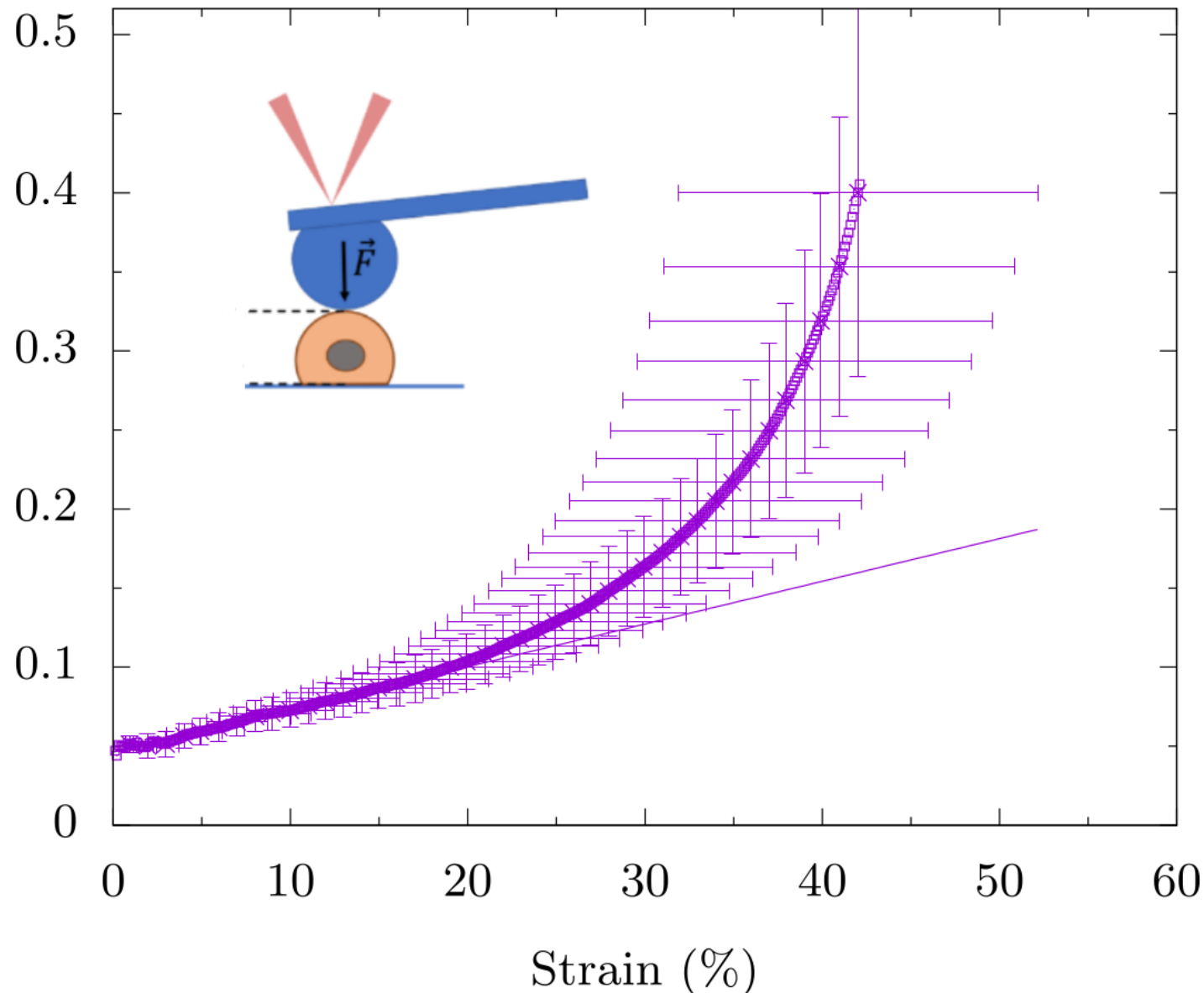


QUESTION

How can a cell
compression
stiffen when
fiber
networks
compression
soften?

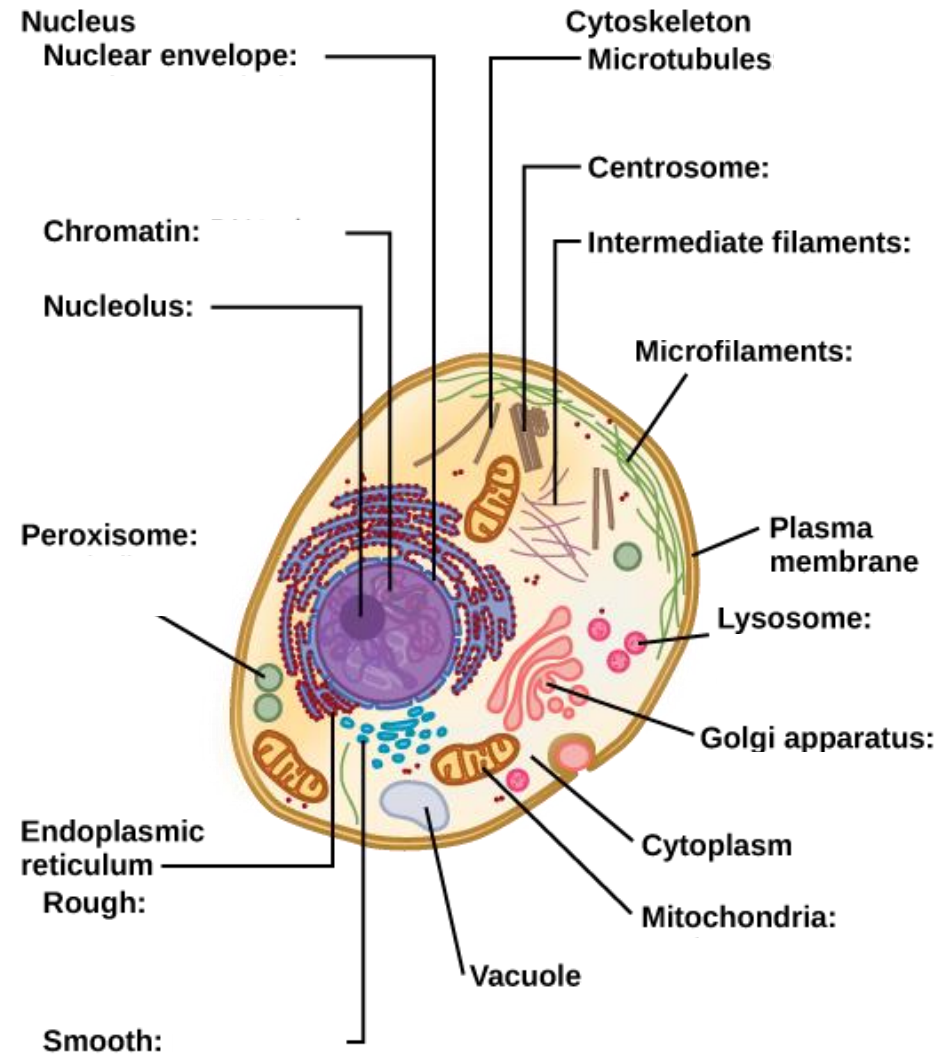
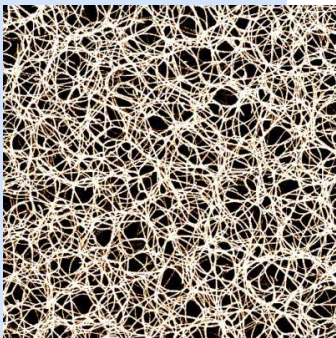


Stress (kPa)



Cell is more than a cytoskeletal network

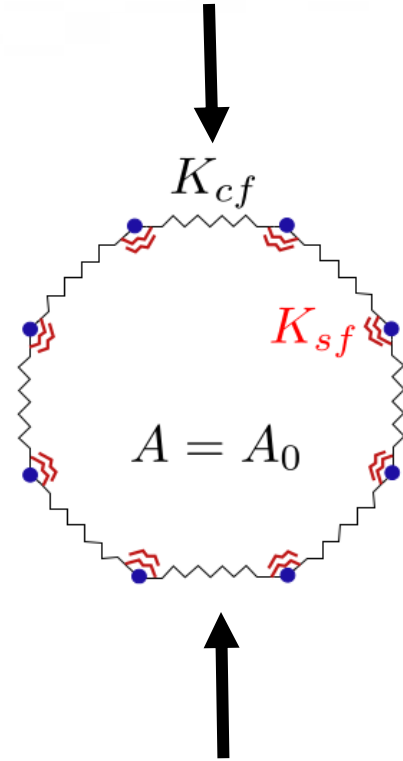
How can a cell
compression
stiffen when
fiber
networks
compression
soften?



One Loop

$$H = \frac{1}{2} K_{cf} \sum_{\langle ij \rangle} (l_{ij} - l_o)^2 + \frac{1}{2} K_{sf} \sum_{\langle ijk \rangle} (\theta_{ijk} - \theta_o)^2 + \lambda (A - A_0),$$

$$\tilde{\kappa} = \frac{K_{cf} l_0^2}{K_{sf}}$$

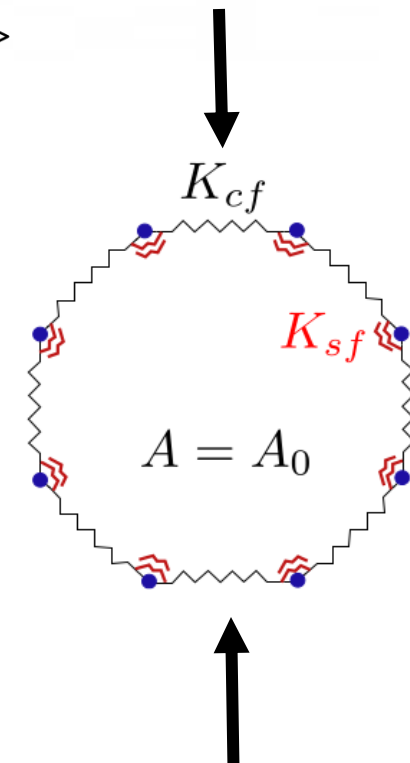
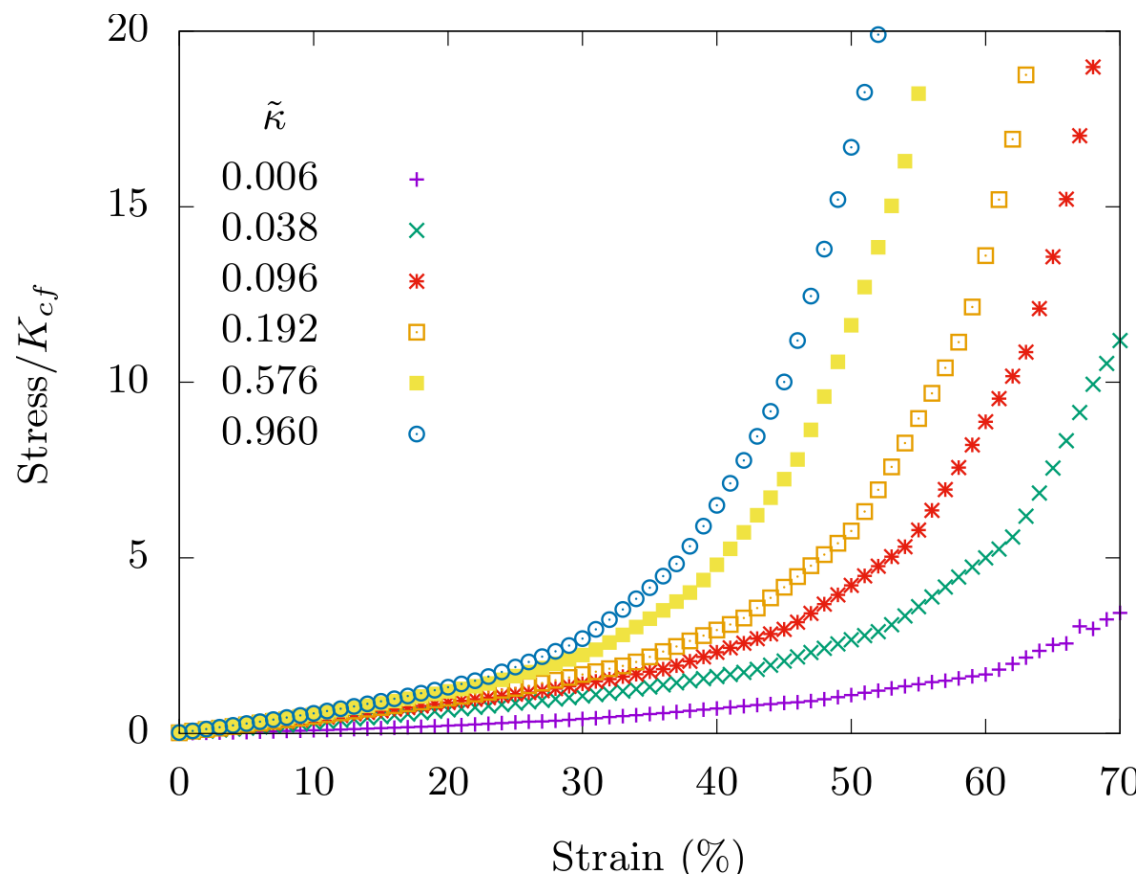


One Loop

Compression stiffening determined by $\tilde{\kappa}$

$$H = \frac{1}{2} K_{cf} \sum_{\langle ij \rangle} (l_{ij} - l_o)^2 + \frac{1}{2} K_{sf} \sum_{\langle ijk \rangle} (\theta_{ijk} - \theta_o)^2 + \lambda (A - A_0),$$

$$\tilde{\kappa} = \frac{K_{cf} l_0^2}{K_{sf}}$$

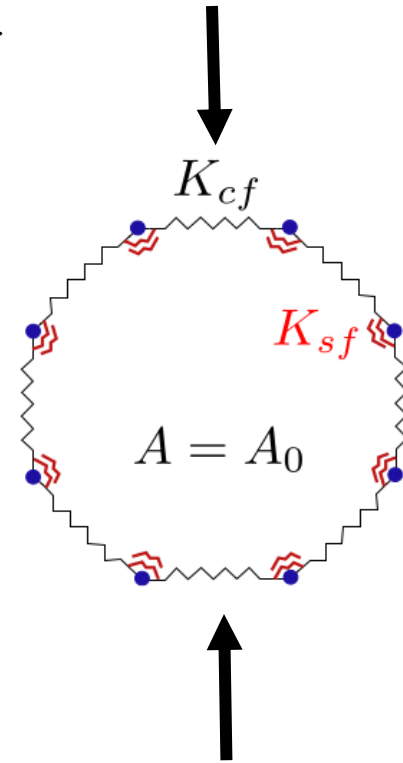
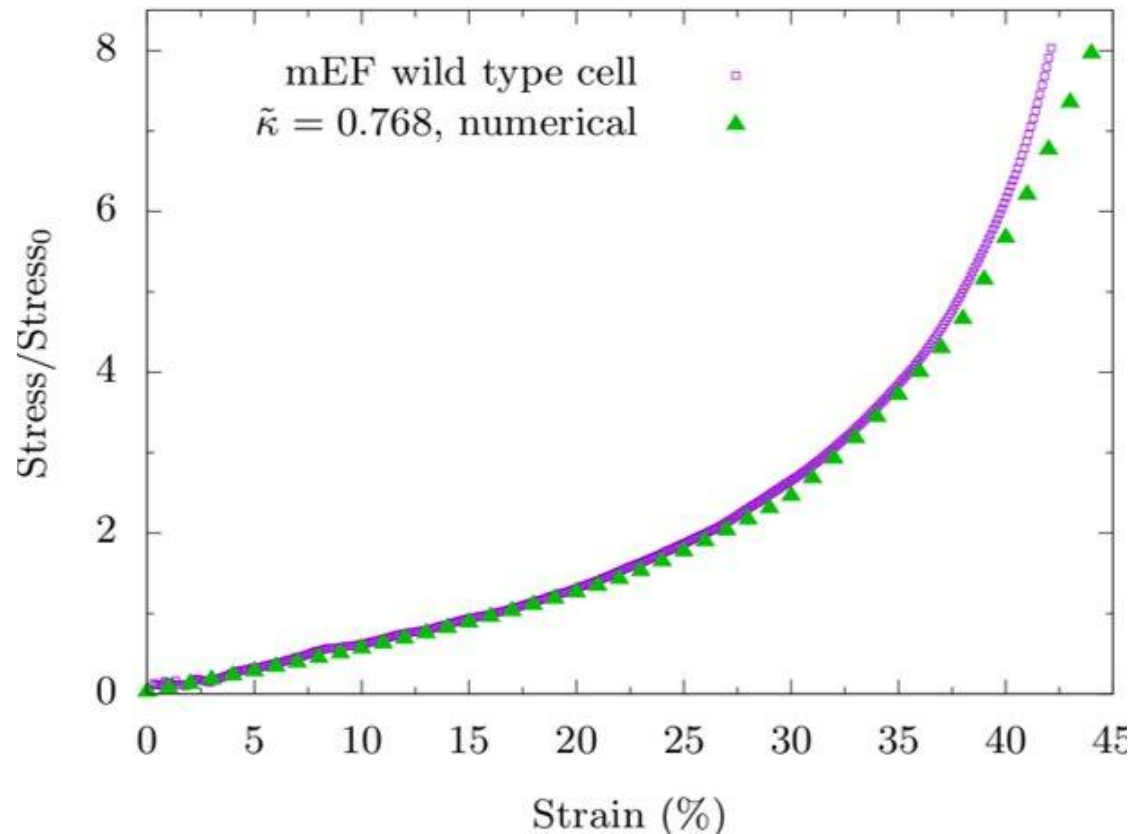


One Loop

"Quantitative"
agreement
with
experiment

$$H = \frac{1}{2} K_{cf} \sum_{\langle ij \rangle} (l_{ij} - l_o)^2 + \frac{1}{2} K_{sf} \sum_{\langle ijk \rangle} (\theta_{ijk} - \theta_o)^2 + \lambda (A - A_0),$$

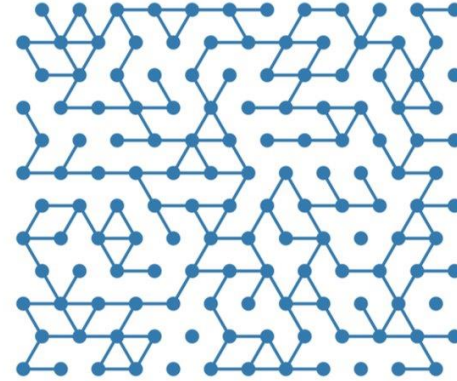
$$\tilde{\kappa} = \frac{K_{cf} l_0^2}{K_{sf}}$$



Fiber networks in the innards of a cell

$$H = \frac{1}{2}K_{cf} \sum_{\langle ij \rangle} p_{ij} (l_{ij} - l_0)^2 + \frac{1}{2}K_{sf} \sum_{ijk=\pi} p_{ij}p_{jk} (\theta_{ijk} - \pi)^2$$

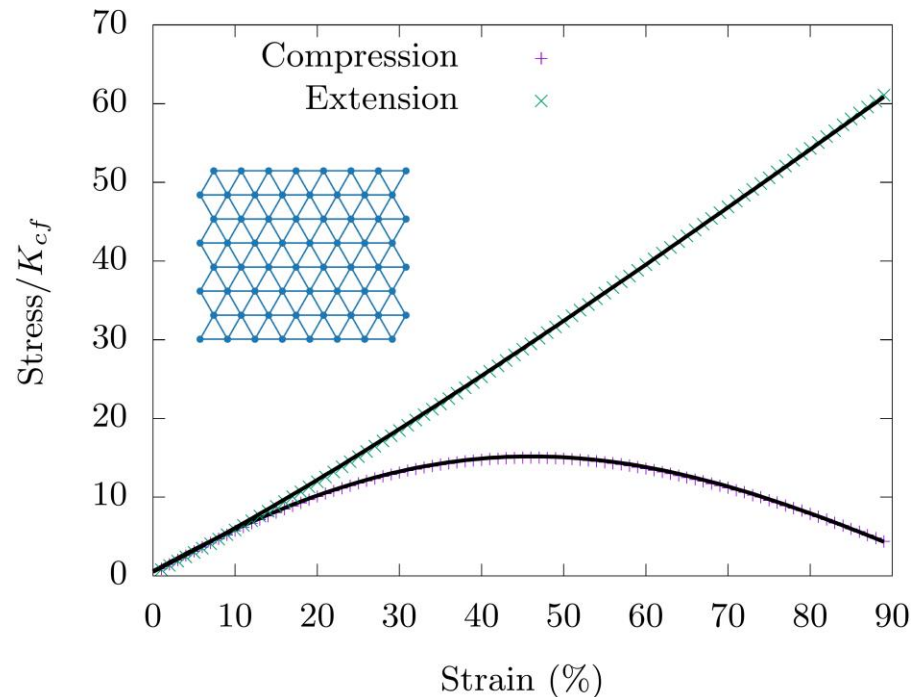
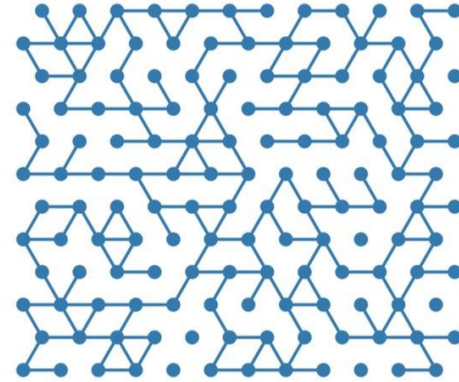
$$p_{ij} = \begin{cases} 1 & \text{with probability } p \\ 0 & \text{with probability } 1 - p \end{cases}$$



Fiber networks in the innards of a cell

$$H = \frac{1}{2} K_{cf} \sum_{\langle ij \rangle} p_{ij} (l_{ij} - l_0)^2 + \frac{1}{2} K_{sf} \sum_{ijk=\pi} p_{ij} p_{jk} (\theta_{ijk} - \pi)^2$$

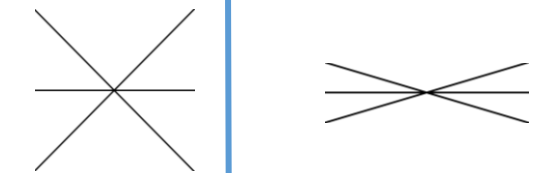
$$p_{ij} = \begin{cases} 1 & \text{with probability } p \\ 0 & \text{with probability } 1 - p \end{cases}$$



Bare network

Affine behaviour

Collapse of springs



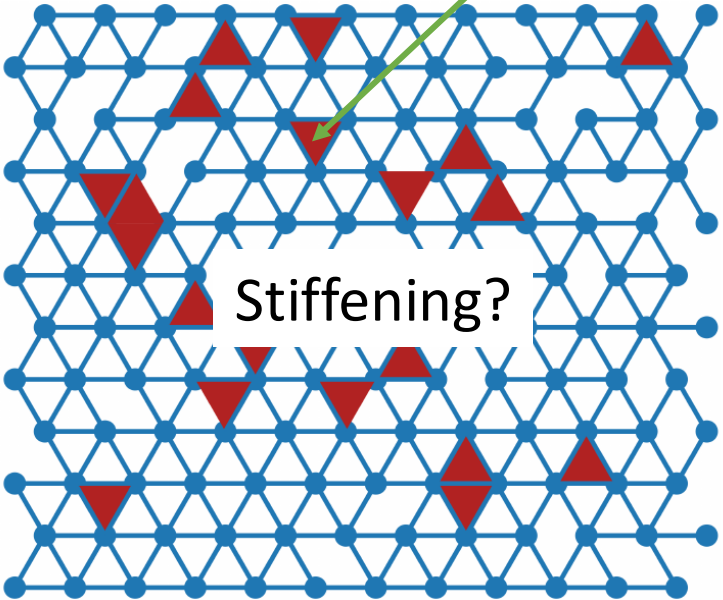
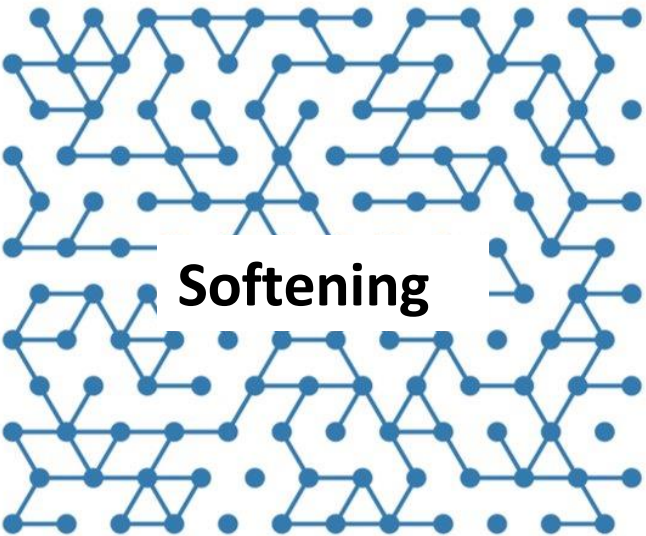
Compression softening

Cell as a collection of organelles within a fiber network

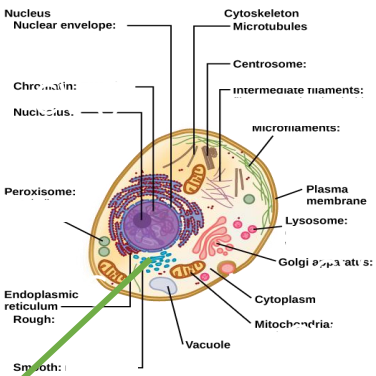


+

=



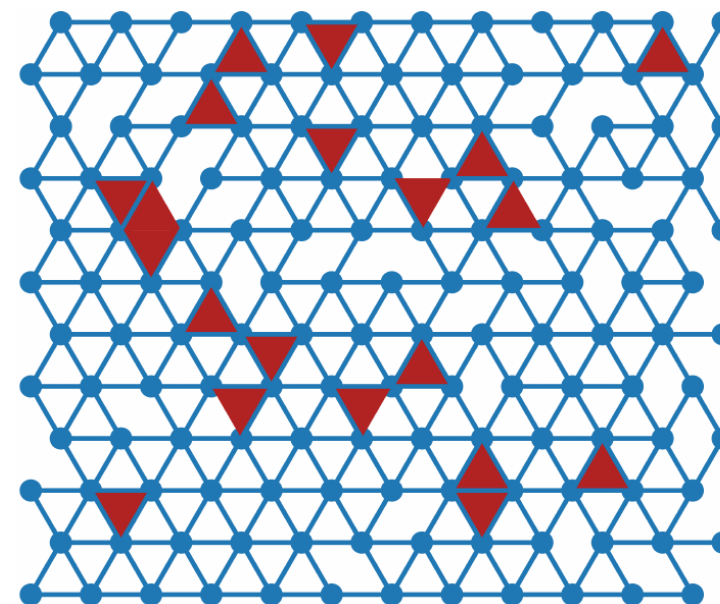
?



N Loop

Add area
conserving
triangles

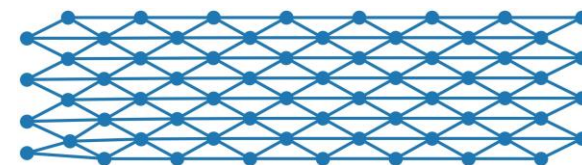
$$H = \frac{1}{2}K_{cf} \sum_{\langle ij \rangle} p_{ij} (l_{ij} - l_0)^2 + \frac{1}{2}K_{sf} \sum_{ijk=\pi} p_{ij}p_{jk} (\theta_{ijk} - \pi)^2 \\ + \frac{1}{2}K_A \sum_{i'=1} q_{i'} (A_{i'} - A_0)^2$$



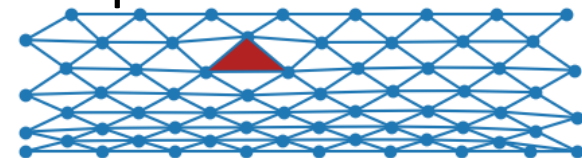
N Loop

Add area
conserving
triangles

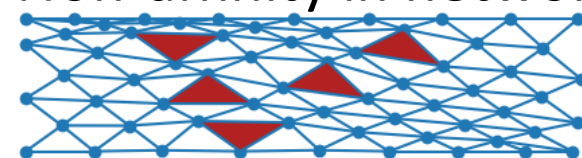
$$H = \frac{1}{2}K_{cf} \sum_{\langle ij \rangle} p_{ij} (l_{ij} - l_0)^2 + \frac{1}{2}K_{sf} \sum_{ijk=\pi} p_{ij}p_{jk} (\theta_{ijk} - \pi)^2 \\ + \frac{1}{2}K_A \sum_{i'=1} q_{i'} (A_{i'} - A_0)^2$$



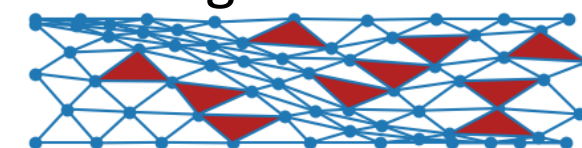
Loops conserve area



Non-affinity in network



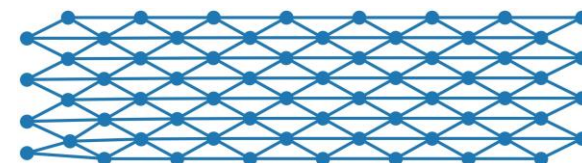
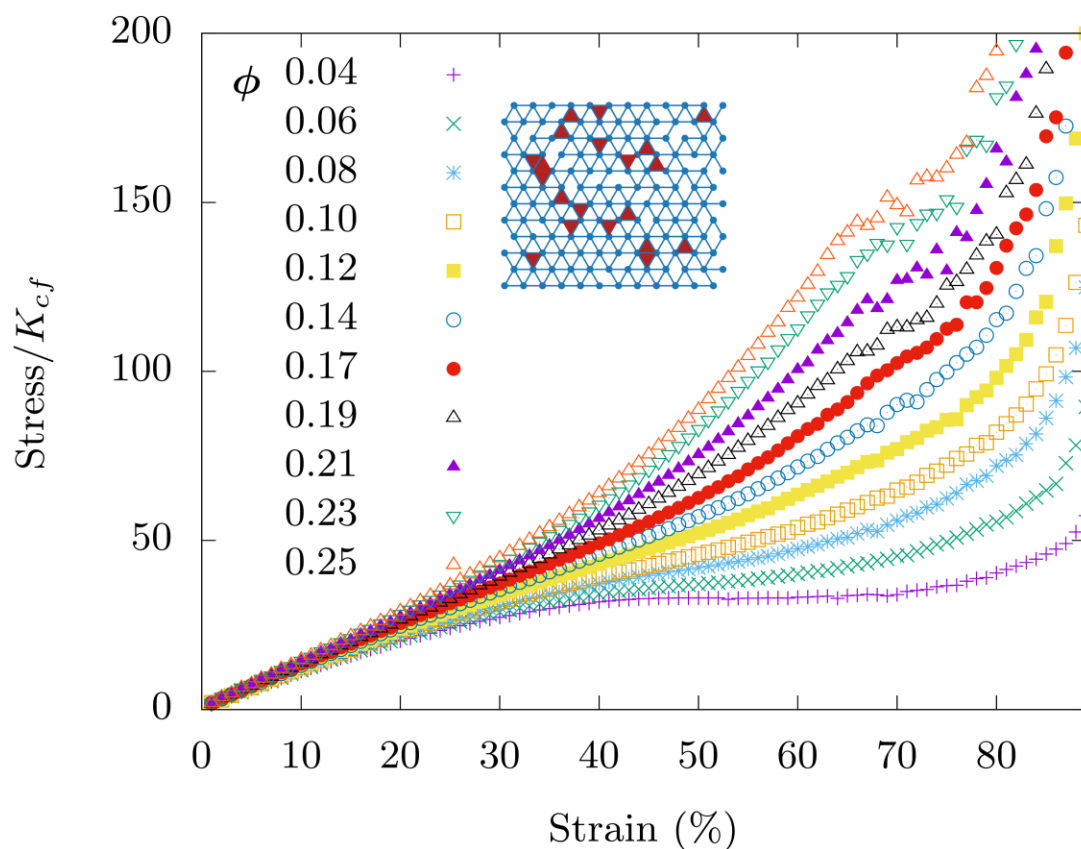
Bending modes



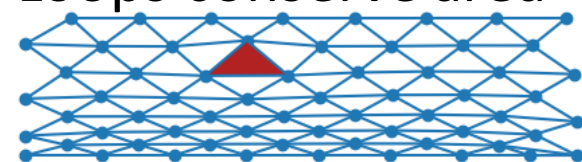
N Loop

Compression
stiffening
determined by
number of loops

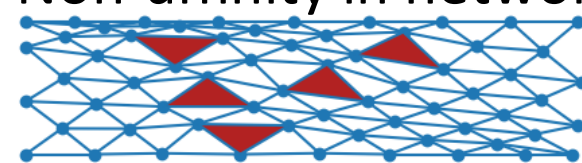
$$H = \frac{1}{2}K_{cf} \sum_{\langle ij \rangle} p_{ij} (l_{ij} - l_0)^2 + \frac{1}{2}K_{sf} \sum_{ijk=\pi} p_{ij}p_{jk} (\theta_{ijk} - \pi)^2 + \frac{1}{2}K_A \sum_{i'=1} q_{i'} (A_{i'} - A_0)^2$$



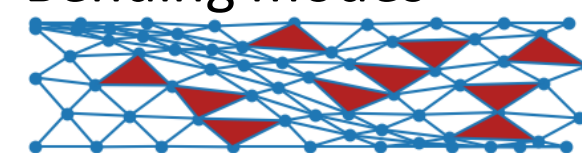
Loops conserve area



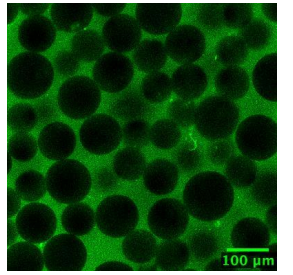
Non-affinity in network



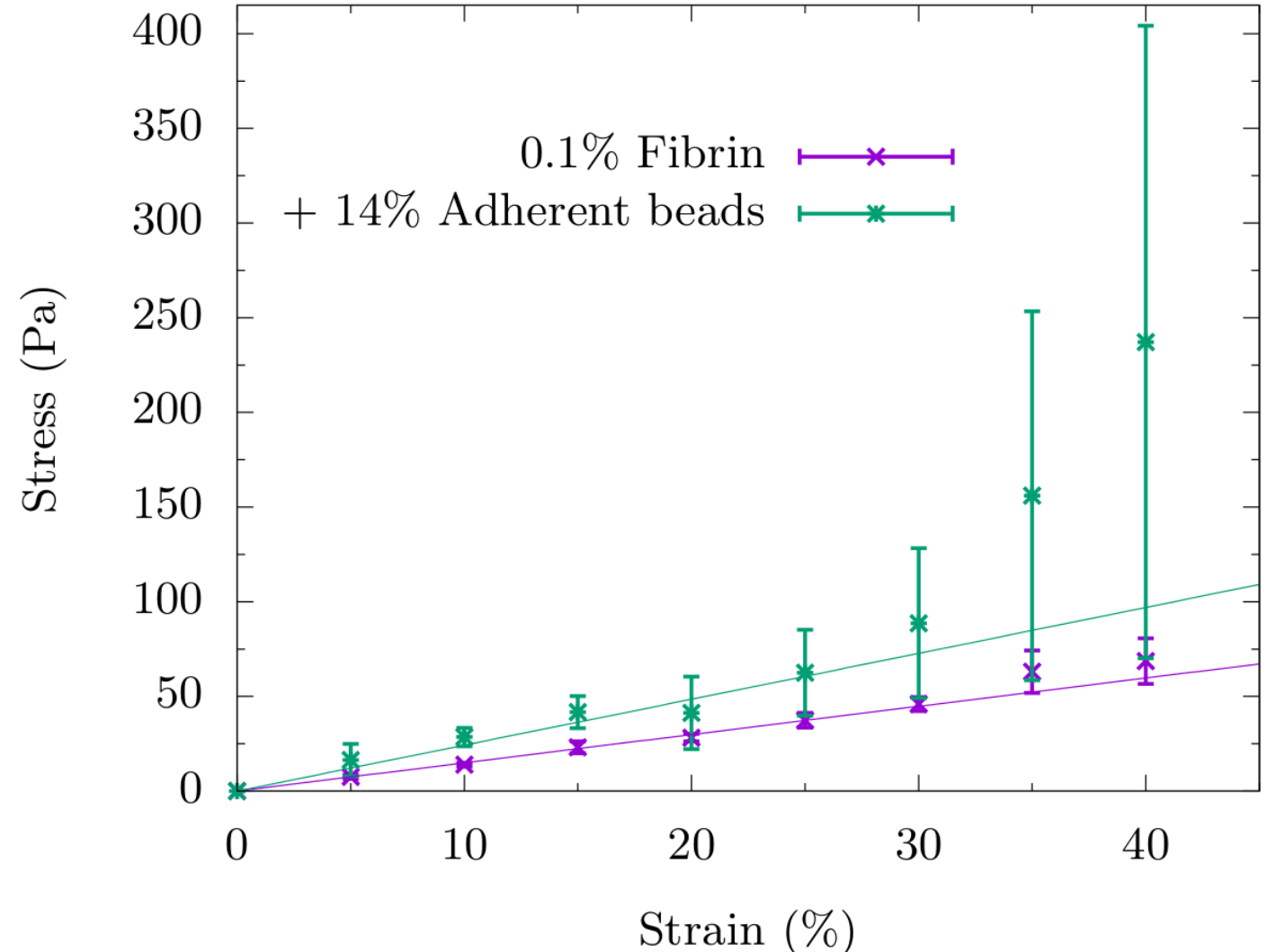
Bending modes



Dextran beads in fiber network

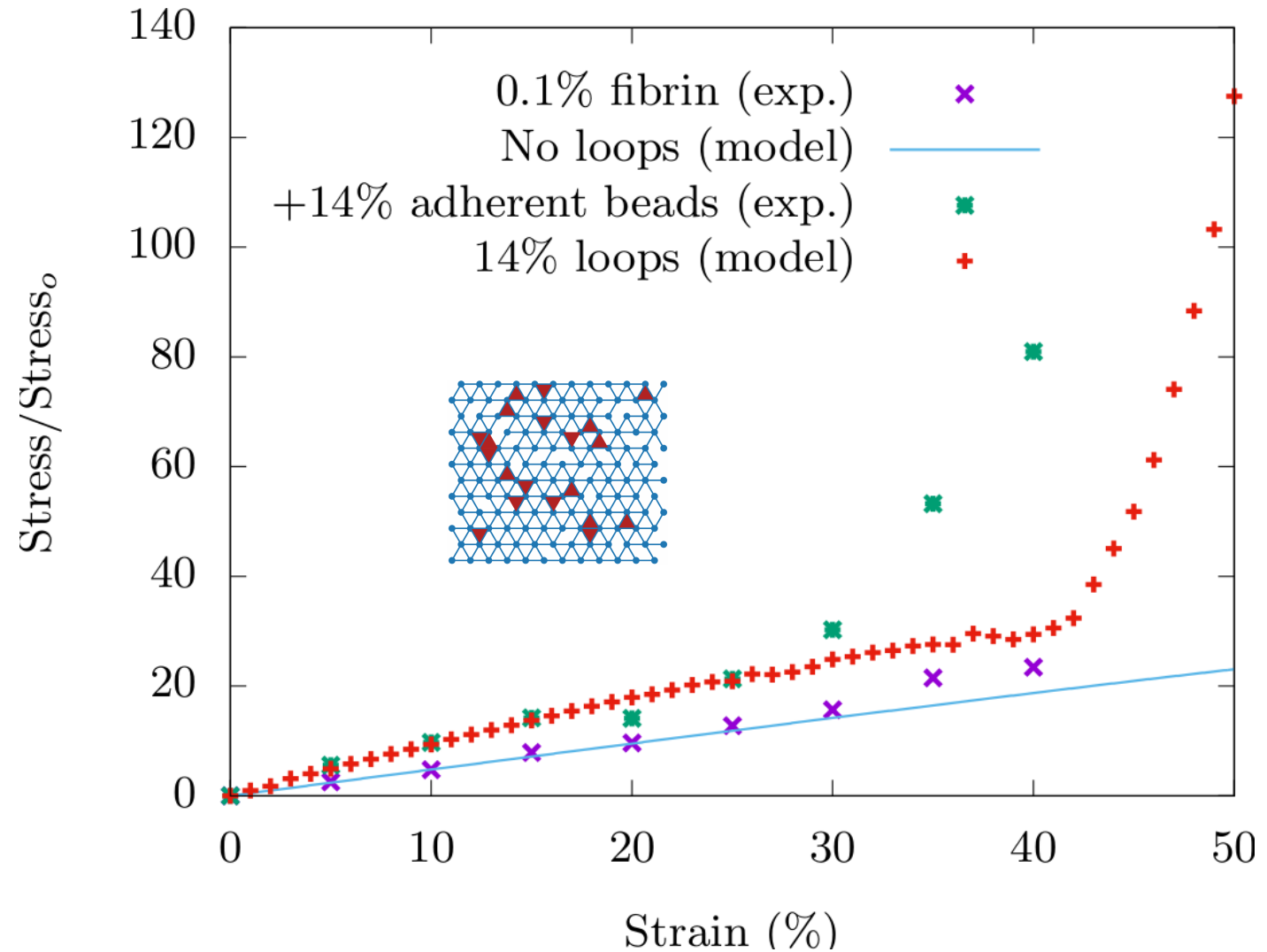
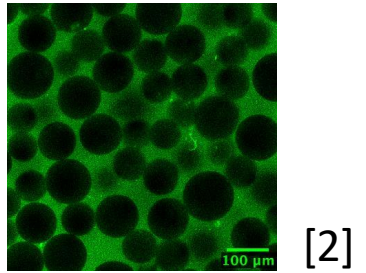


[2]



[2] van Oosten, Anne SG, et al. *Nature* (2019)

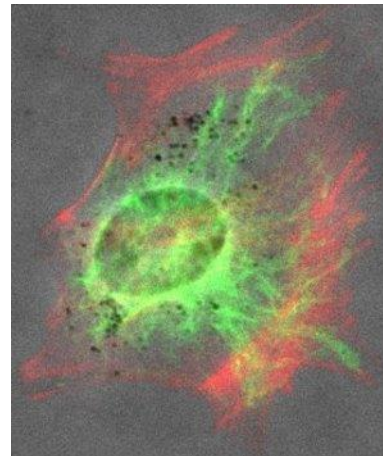
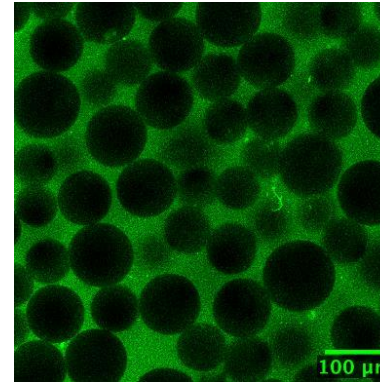
Qualitative
agreement
with
experiment



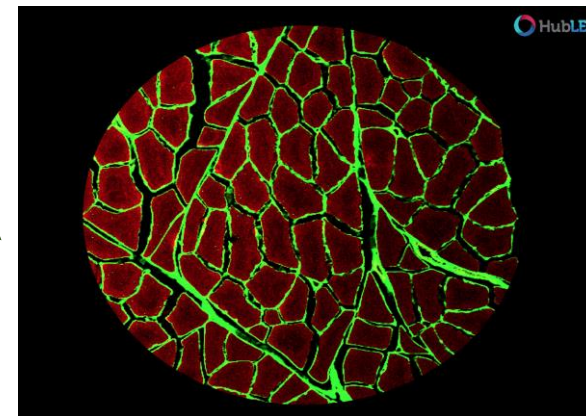
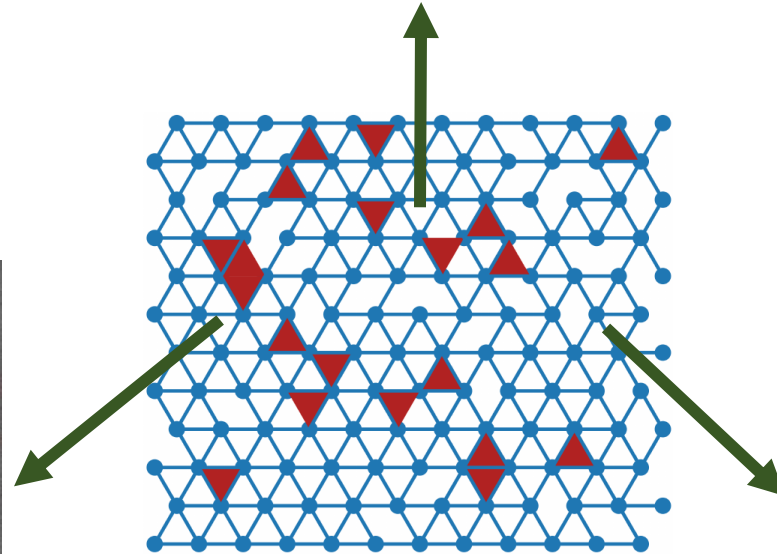
[2] van Oosten, Anne SG, et al. *Nature* (2019)

Compression stiffening across scales

Dextran beads in fibrin [2]



Organelles in cytoskeleton



Cells in extra cellular matrix [4]

[2] van Oosten, Anne SG, et al. *Nature* (2019)

[4] C. Bendzinski and B. Wheatley
– Bucknell University, PA -
<https://www.huble.org/huble-images/>

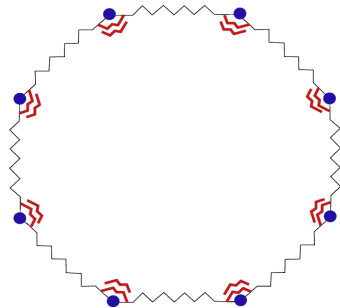
Summary

Question

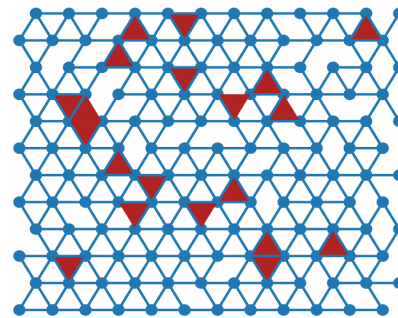
How can a mEF cell **compression stiffen** when fiber networks **compression soften**?

Three potential **compression stiffening** mechanisms proposed:

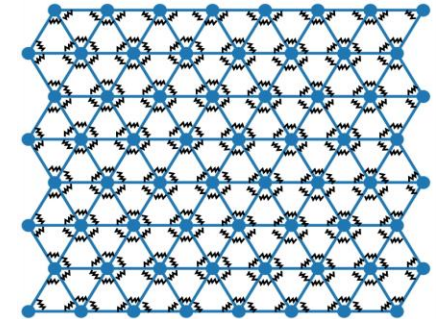
One Loop



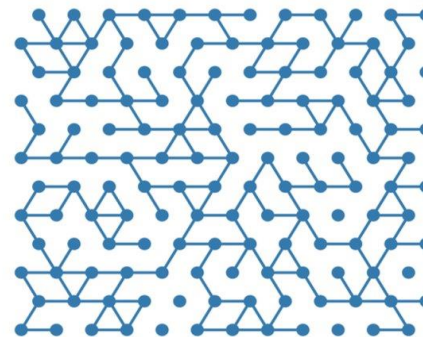
N Loop



Crosslinker Angular Springs



Collapse of springs brings **compression softening** in fiber networks.



References:

- 1) 'Loops versus lines and compression stiffening of cells', *Soft Matter* 2020, **16**, 4389-4406 [arXiv:1908.03725v2](#)
- 2) van Oosten, Anne SG, et al. *Nature* (2019)
- 3) Shivers et al., [arXiv:2002.07220](#)