Mechanical Transitions in Cells and Tissues

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Boulder School 2001: Nonequilibrium Statistical Physics: Glasses, transport & friction, biological systems, and turbulence

July 2-27, 2001

Scientific Coordinators:

E. Bodenschatz (Cornell)
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A. A. Middleton (Syracuse)

Boulder School 2024: Self-Organizing Matter: From Inanimate to the Animate

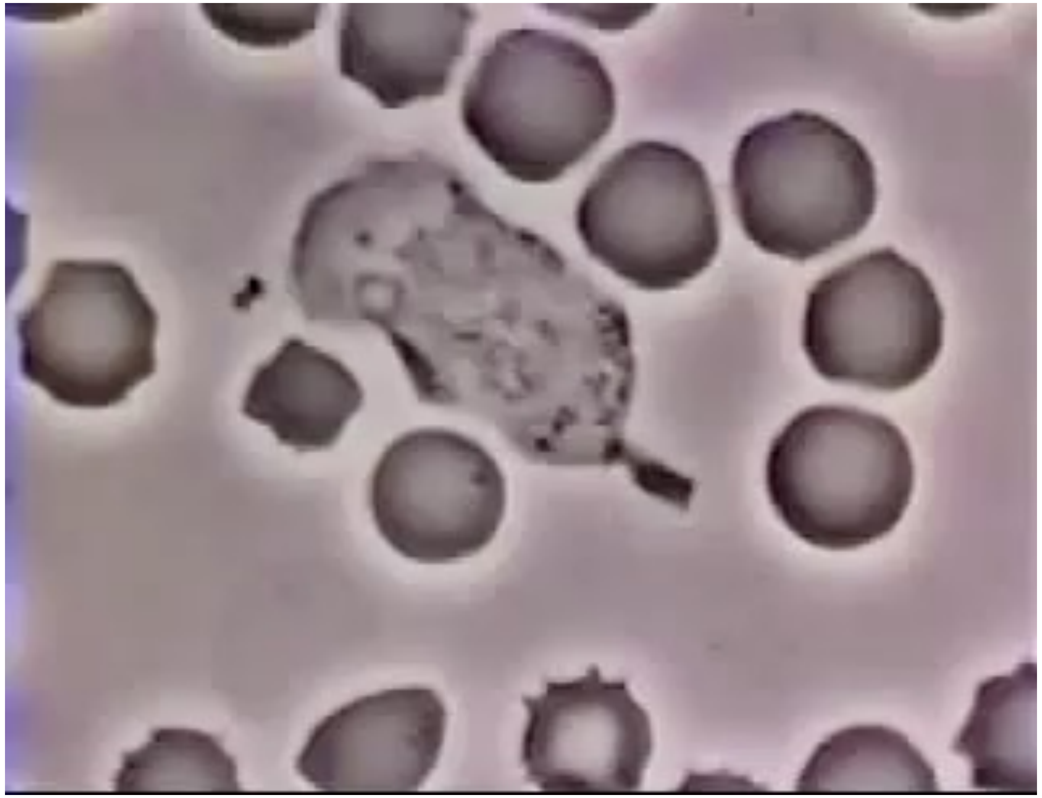
July 1-26, 2024

Scientific Coordinators

Shiladitya Banerjee (Carnegie Mellon)
Andela Saric (IST Austria)
Eric R. Dufresne (Cornell)
Margaret L. Gardel (Chicago)

Trajectory

Cells and tissues are soft and squishy



David Rogers

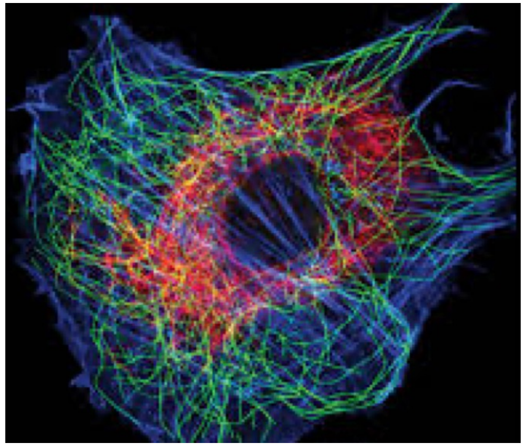
But are resilient and can adapt to different mechanical contexts

Das Group: Why are cells and tissues soft and squishy but robust and resilient?

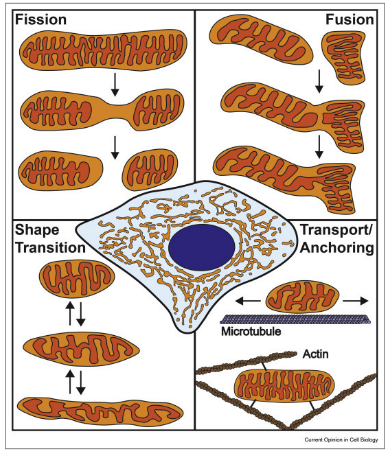
Physics of network-like materials in biological and bio-inspired systems

Cell level systems

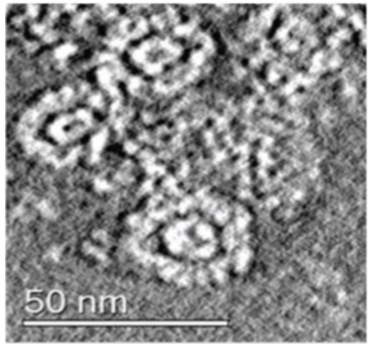
Cytoskeletal networks

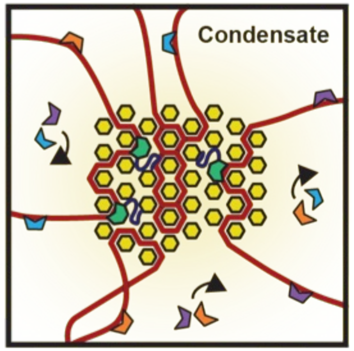


Mitochondria



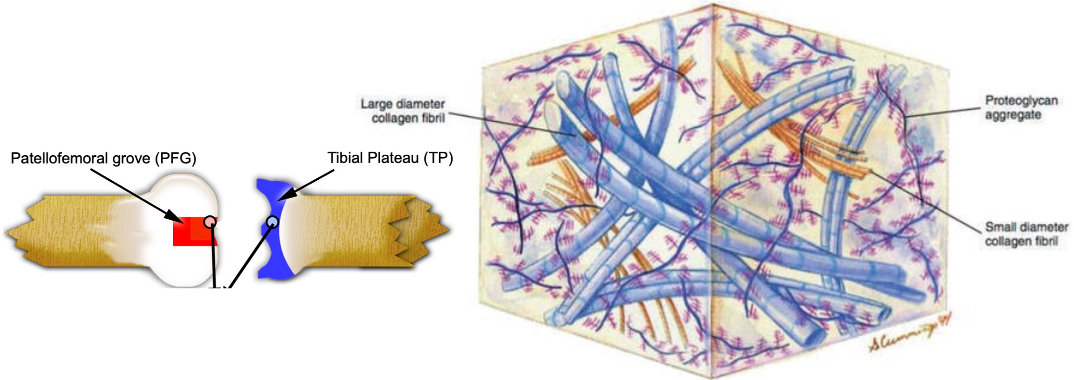
Organization of DNA in starved E. Coli



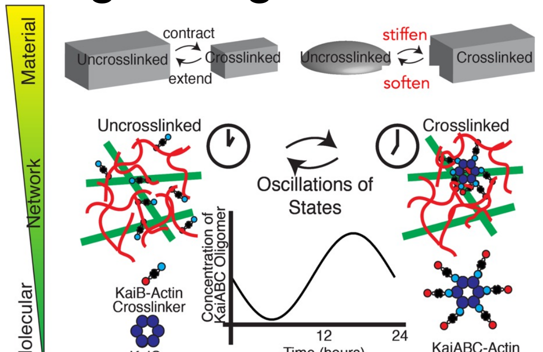


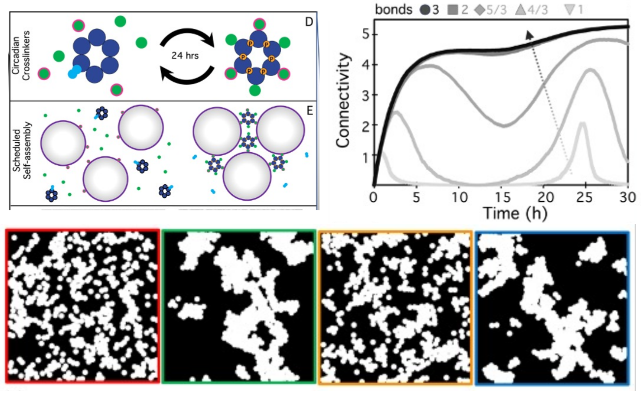
Tissues and synthetic biology

ECM networks in cartilage tissue

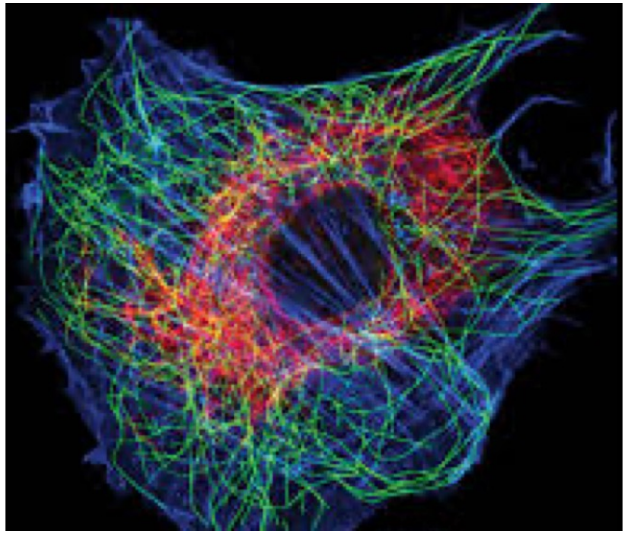


Synthetic biomaterials with programmable properties using biological timers

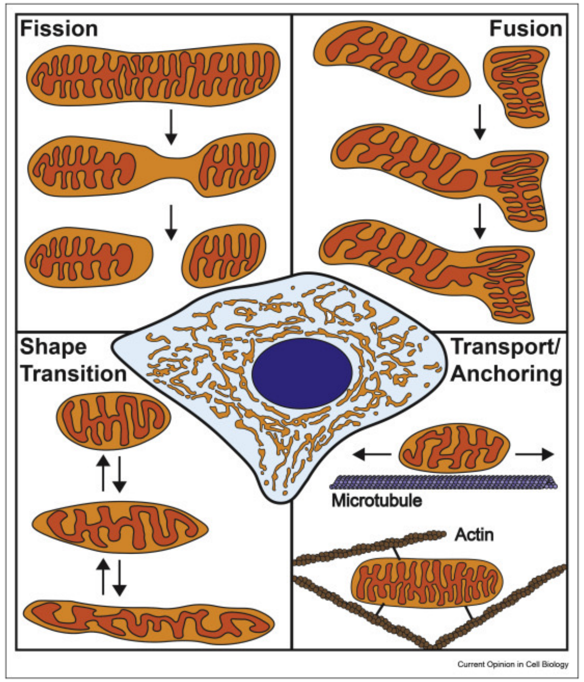




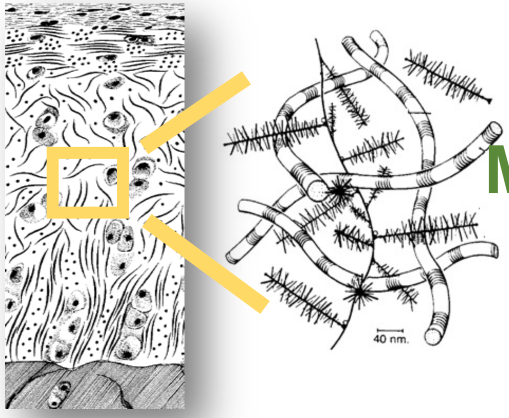
Physics of network-like materials in biological and bio-inspired systems



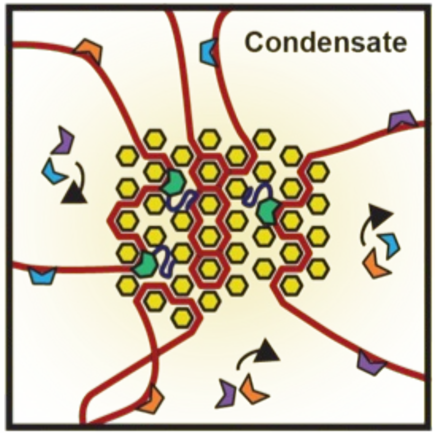
Interplay of mechanics,
statistical mechanics,
Geometry/morphology
(composite morphology/properties
spatial heterogeneity, anisotropy)



Write down Mathematical Models
(Equations of Motion, Free Energies)



Method: Solve ODEs, PDEs, Minimize functions
Solve analytically when feasible
Use Computer simulations when hard



Collaborate with experimentalists to ensure models are realistic

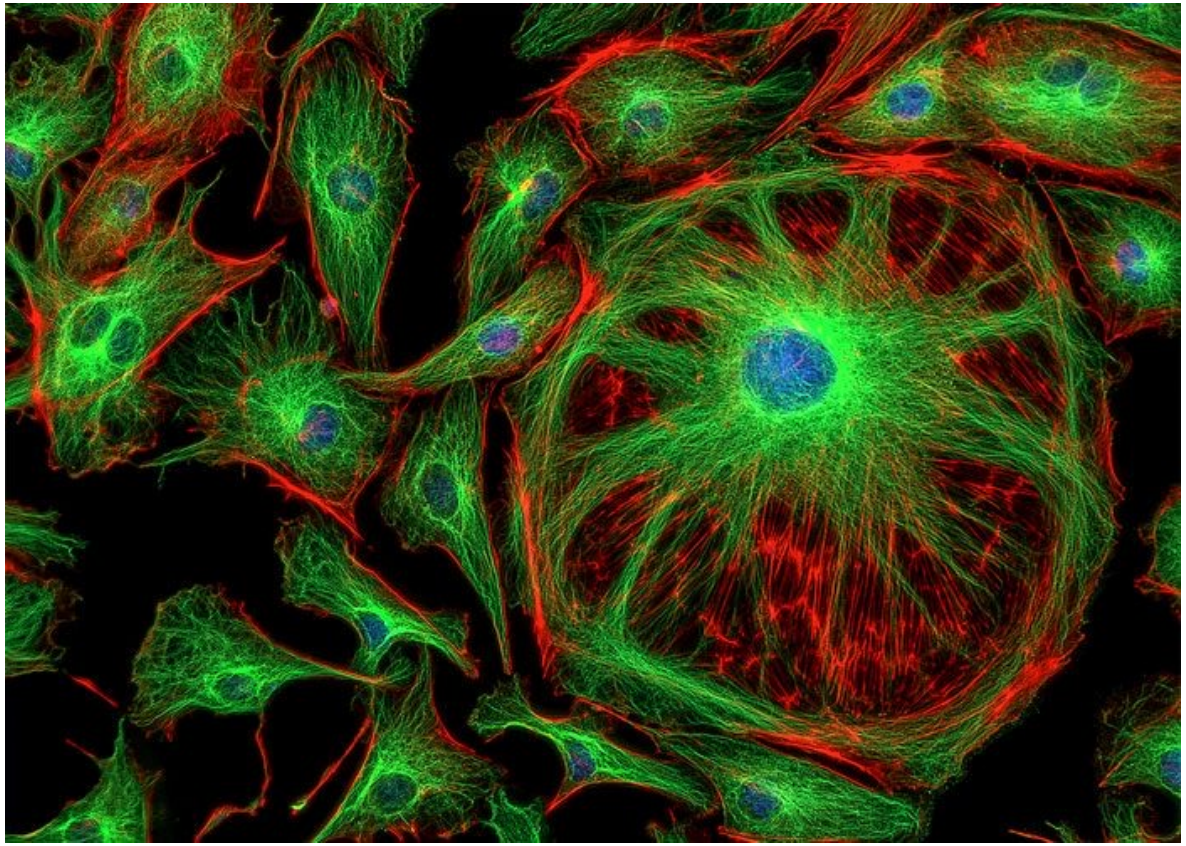
Mechanical Transitions in Cells and Tissues: Outline

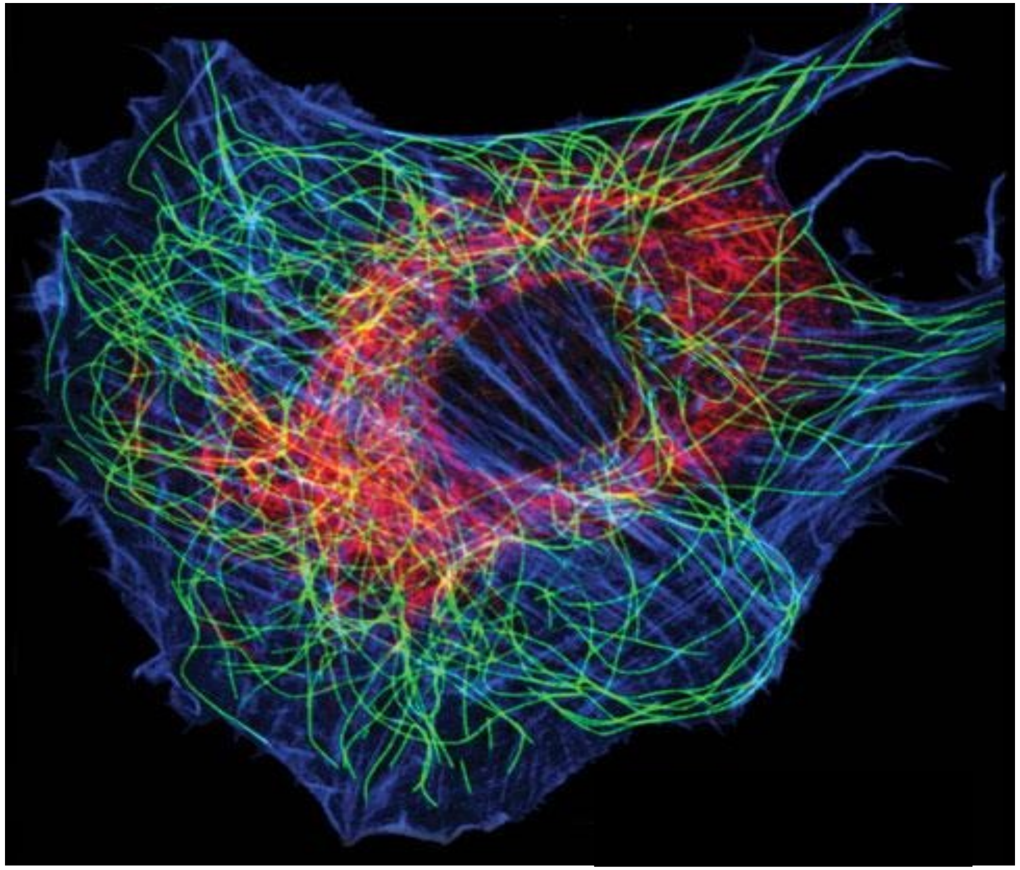
Day 1: Brief introduction to biopolymer networks, how we characterize mechanics (rigidity and rigidity percolation), rigidity percolation in spring networks

Day 2: Mechanics of semiflexible networks (homogeneous and inhomogeneous), applications to mechanical transitions in in-vitro cytoskeletal and extracellular networks

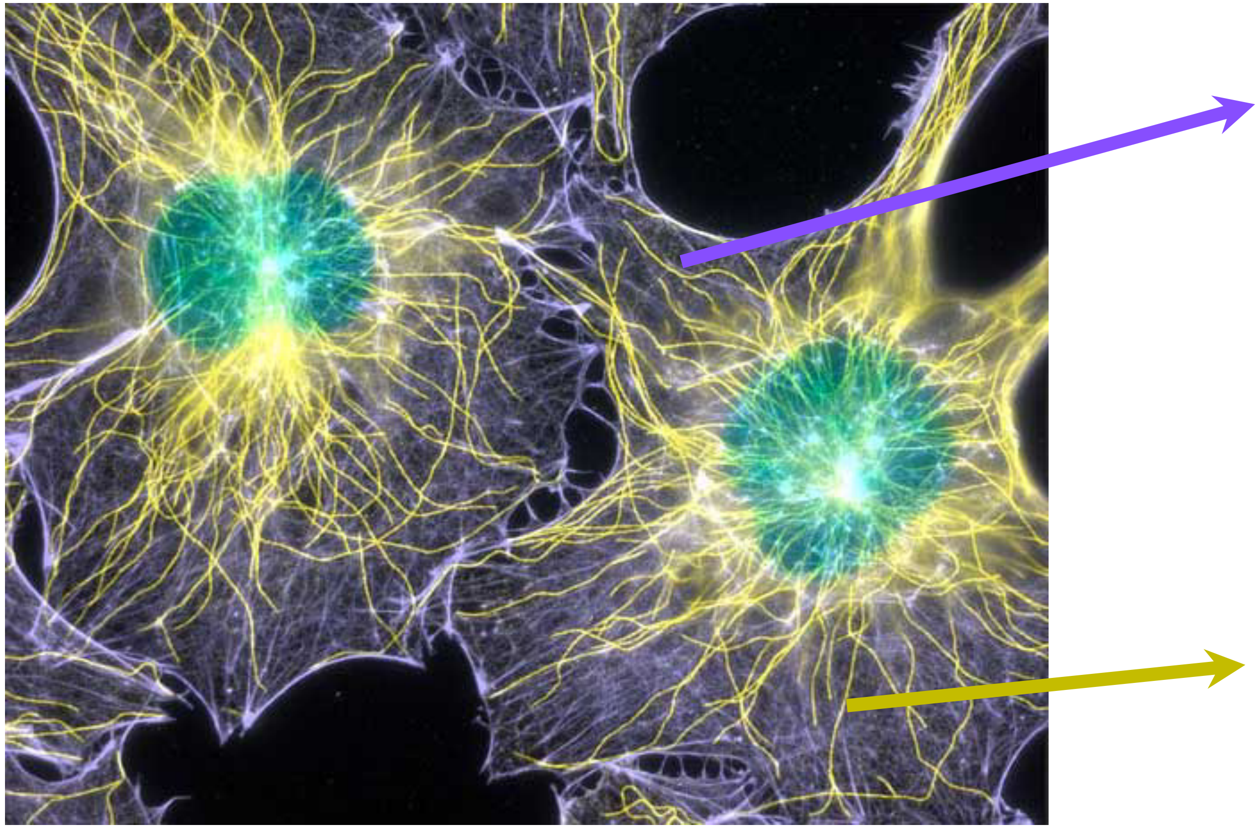
Day 3: Mechanics of composite and active networks, applications to mechanical transitions in cells and tissues

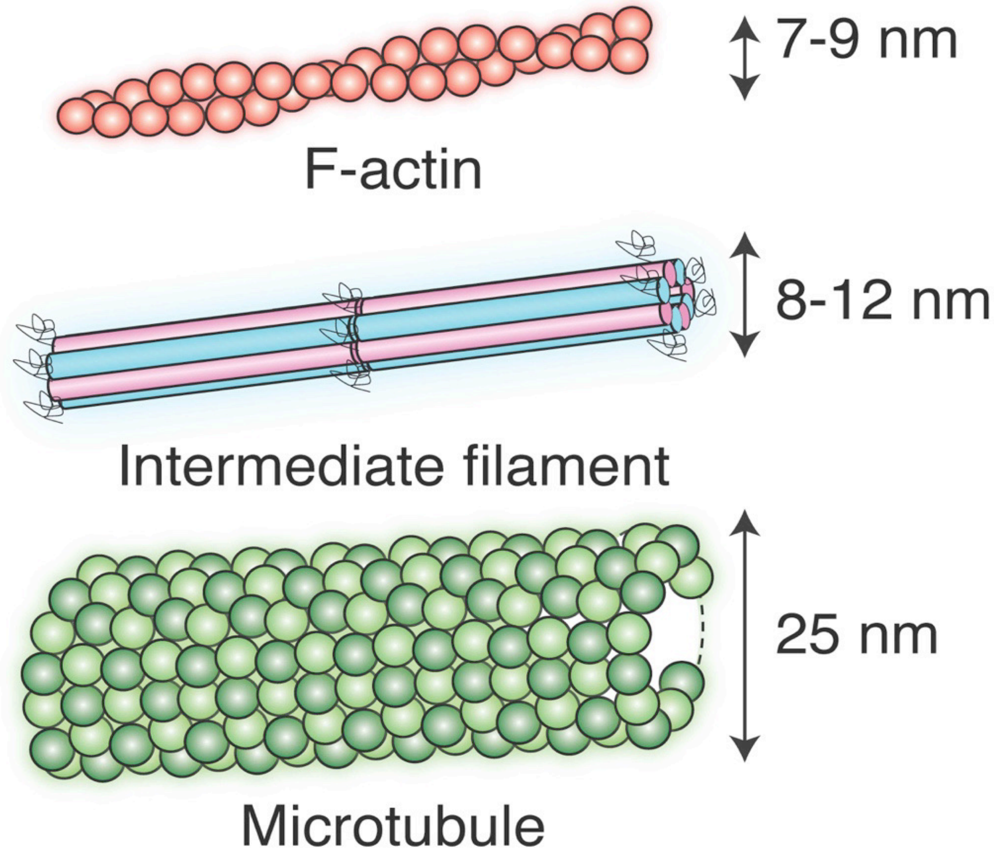
Mechanical Response of Cells is mainly due to the Cytoskeleton





Cytoskeleton



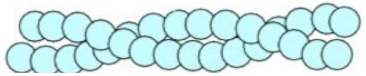


- Three major types of filaments: **filamentous actin (F-actin), intermediate filaments (eg. vimentin), microtubules**

- All are ***semiflexible*** polymers, and form networks

Semiflexible polymers have rigidity intermediate between flexible polymers and rigid rods

Flexible

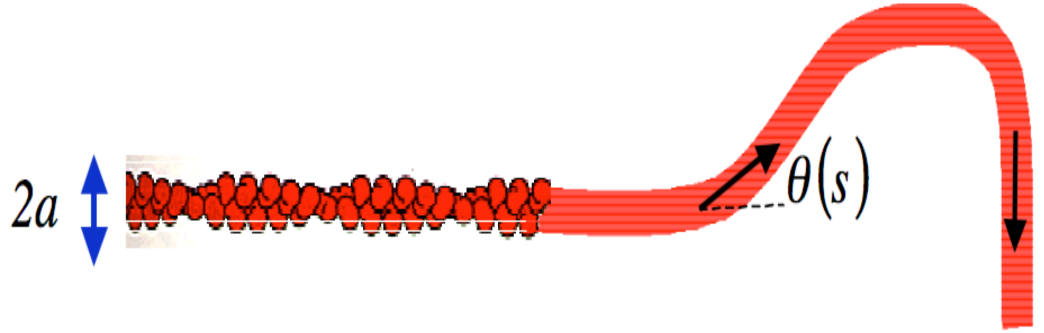


Semiflexible
Biopolymers

Stiff

Stiffness

Mechanics of semiflexible polymers



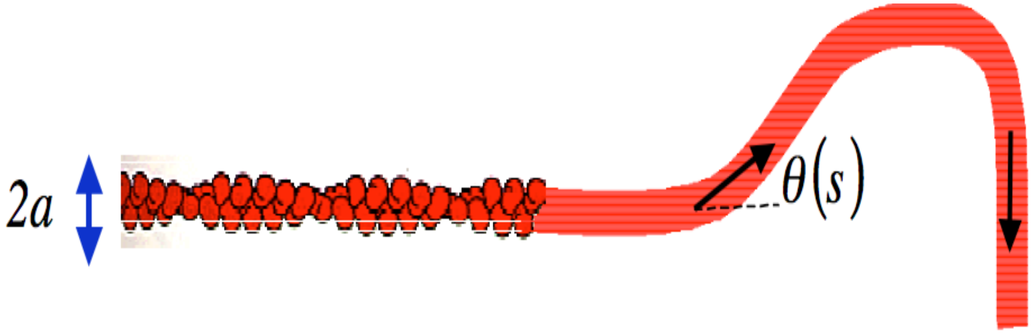
$$E_{\text{bend}} = \frac{1}{2}\kappa\int\left(\frac{\partial\theta}{\partial s}\right)^2 ds$$

Bending rigidity, $\kappa \cong E\,a^4$ E= Young's modulus

$$\langle\cos(\theta(s)-\theta(s'))\rangle = e^{-|s-s'|/\ell_p}$$

Persistence length, $\ell_p = \frac{\kappa}{k_B T}$

Mechanics of semiflexible polymers



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Persistence length, $\ell_p = \frac{\kappa}{k_B T}$

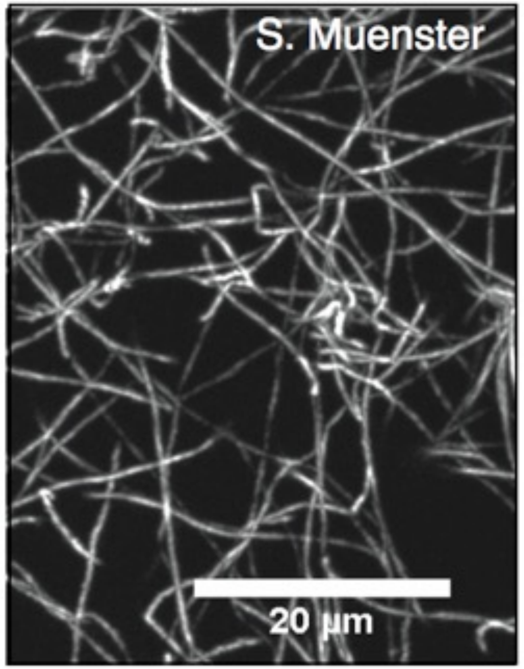
For $E \cong 10^9$ Pa and $a \cong 3$ nm, $\ell_p \cong 10\ \mu$m Actin

$a \cong 10$ nm, $\ell_p \cong 1$ mm Microtubules

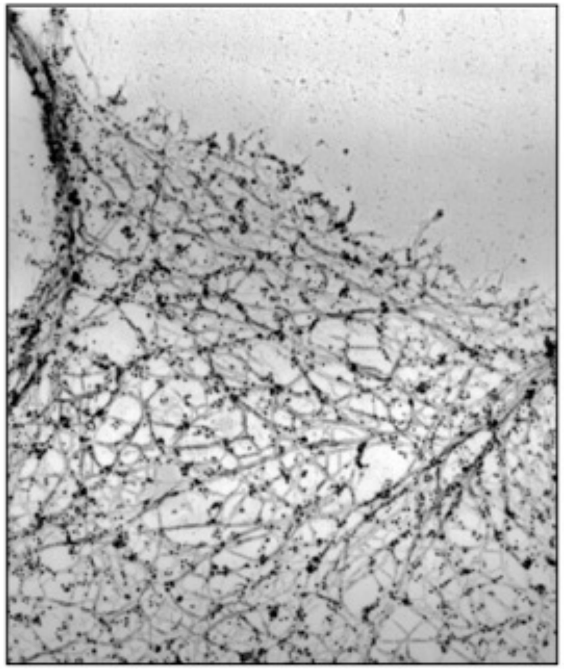
$a \cong 0.2$ nm, $\ell_p \cong 100$ nm DNA

Networks of semiflexible polymers are abundant in cells and tissues

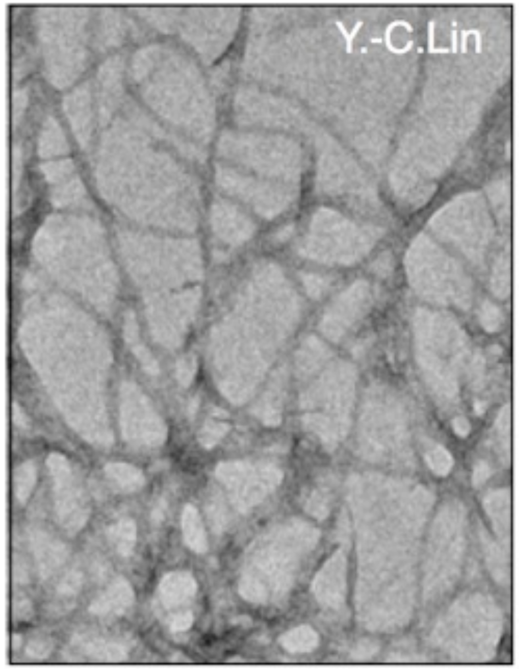
collagen (*in vitro*)



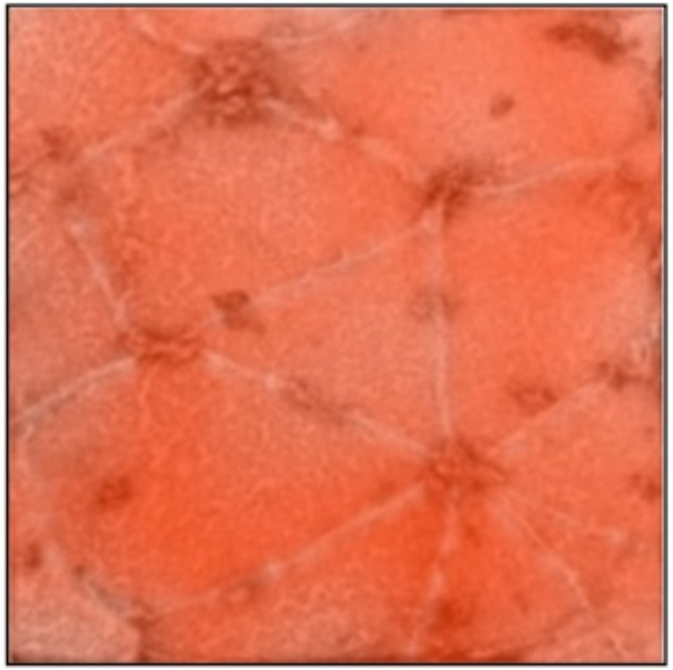
actin-cortex



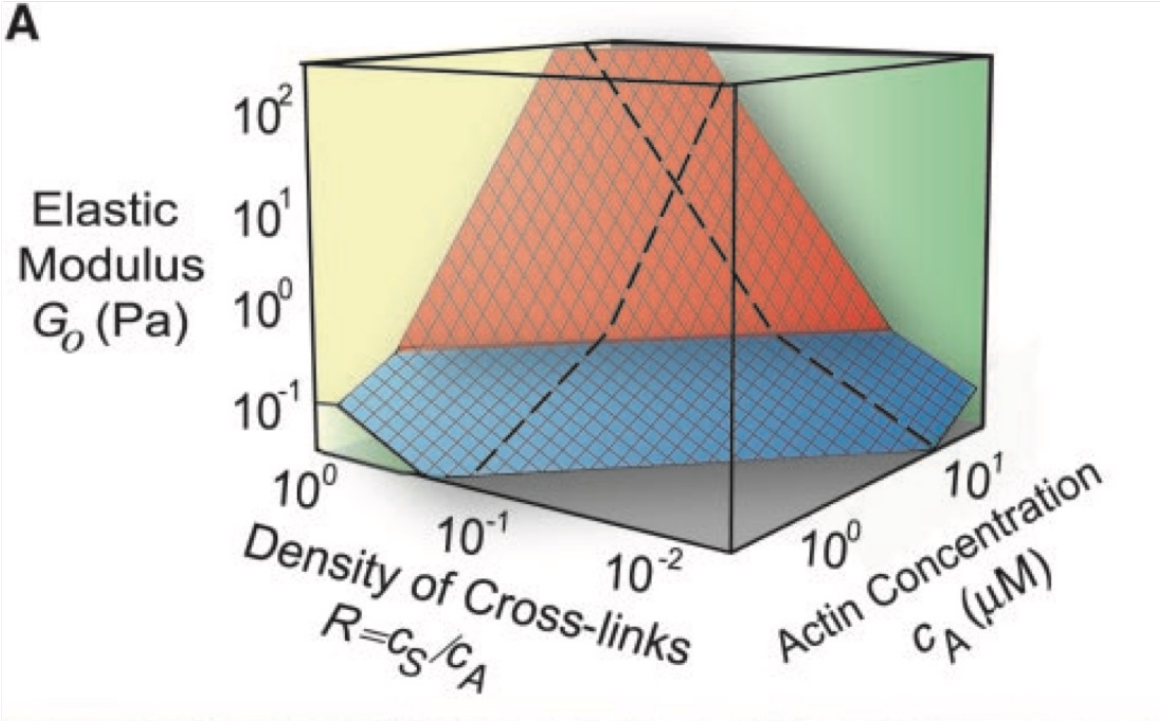
vimemtin (*in vitro*)



red blood cell (actin-spectrin)



Rigidity of biopolymer networks often characterized using their shear modulus, G

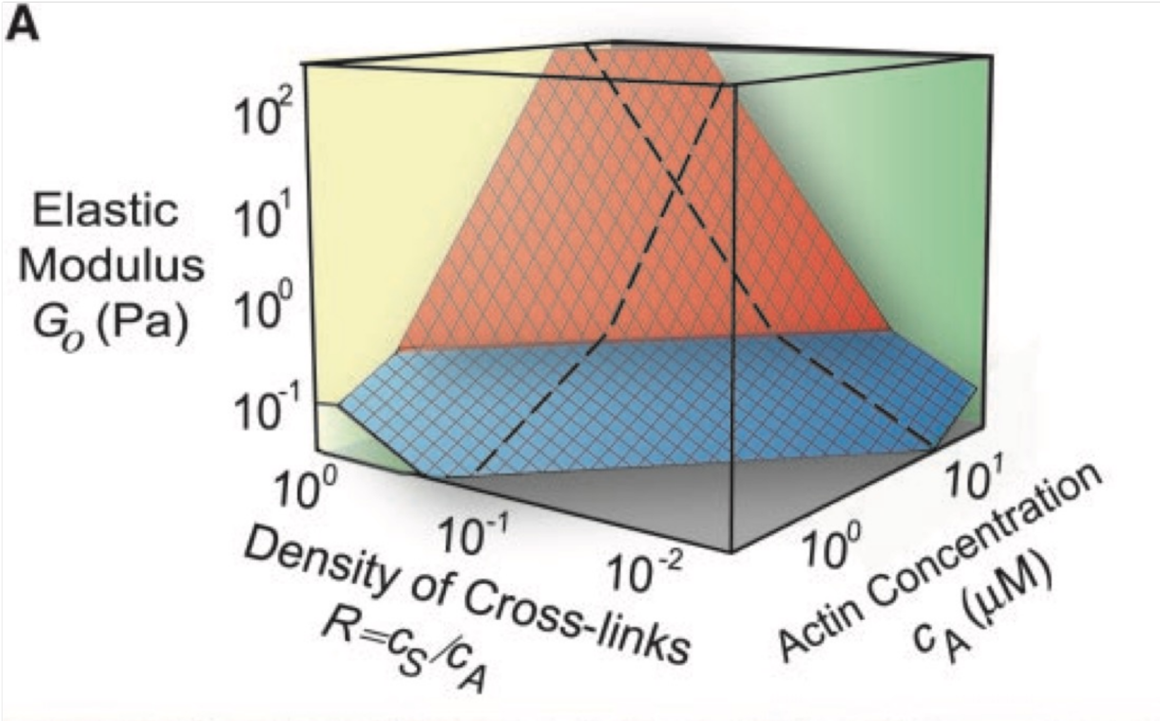


Shear modulus of reconstituted (in vitro) F-actin networks

Gardel *et al.*, Science 2004

- How do we predict whether a network is rigid or not?
- How do predict G for networks of different types of biopolymers, different densities?

Rigidity of biopolymer networks often characterized using their shear modulus, G



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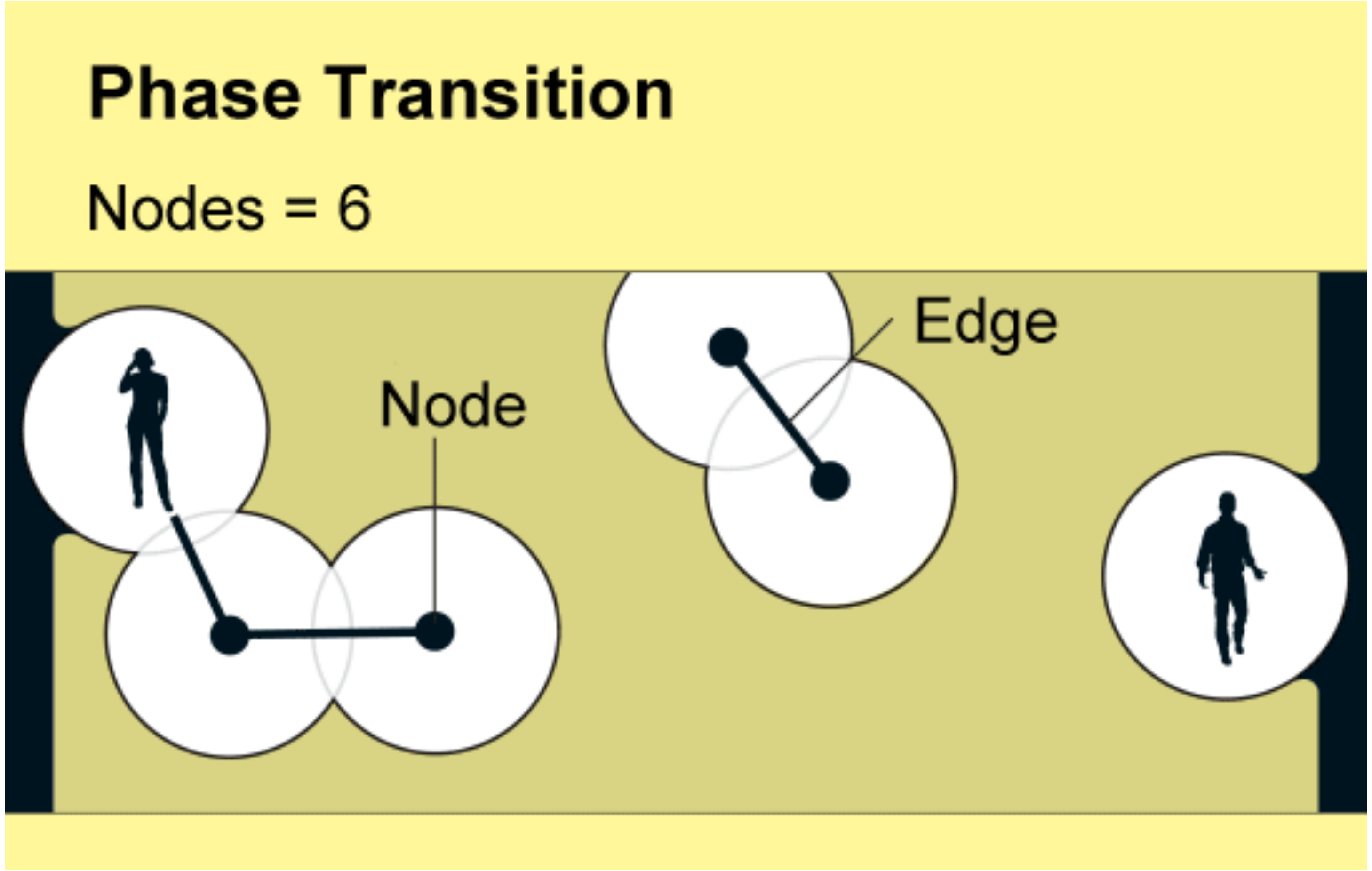
Rigidity Percolation Theory

Example of Percolation:
Connectivity percolation phase transition in cell phone networks

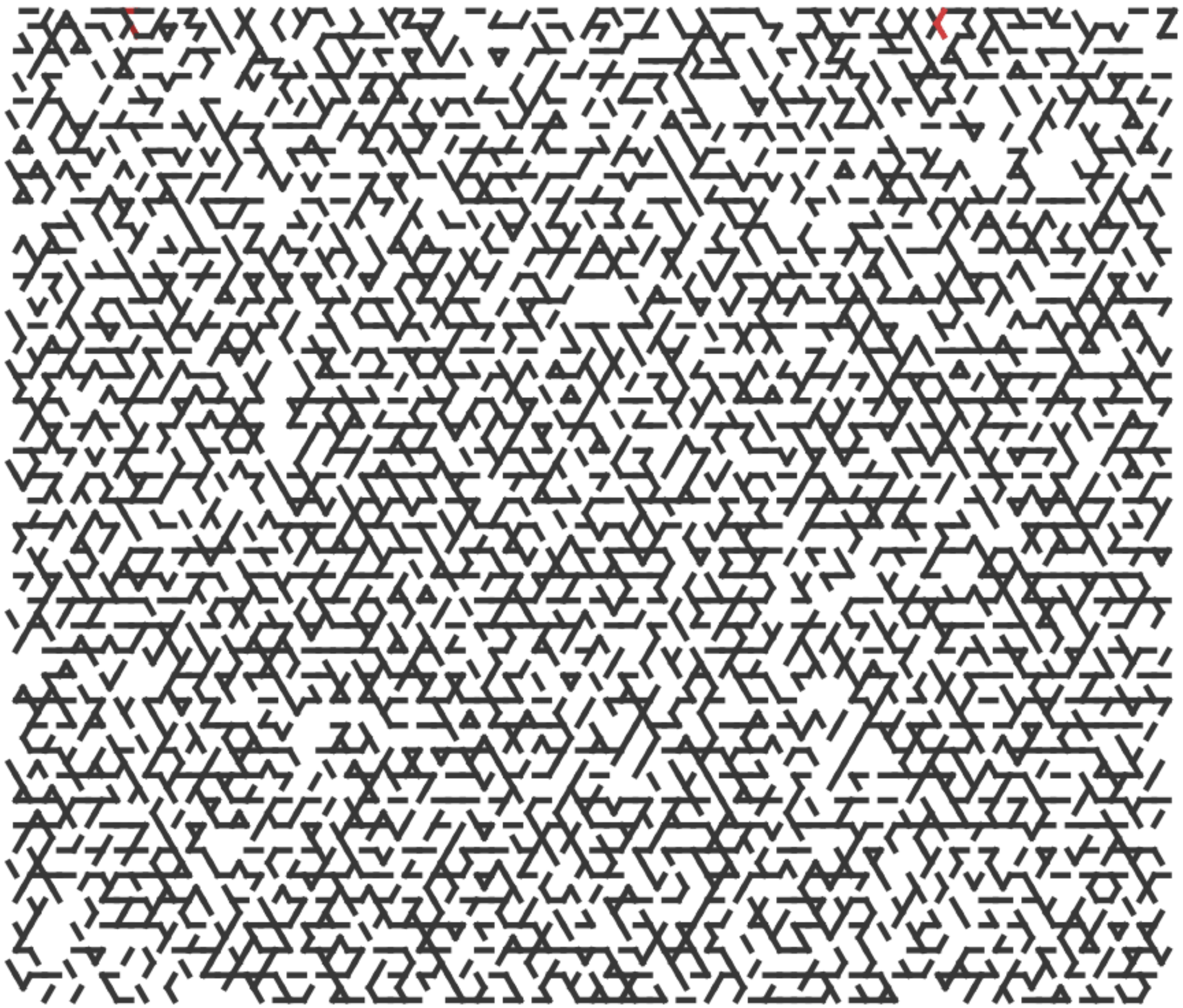


Houston-Edwards, Scientific Am. 2021

Rigidity Percolation Phase Transition

Floppy

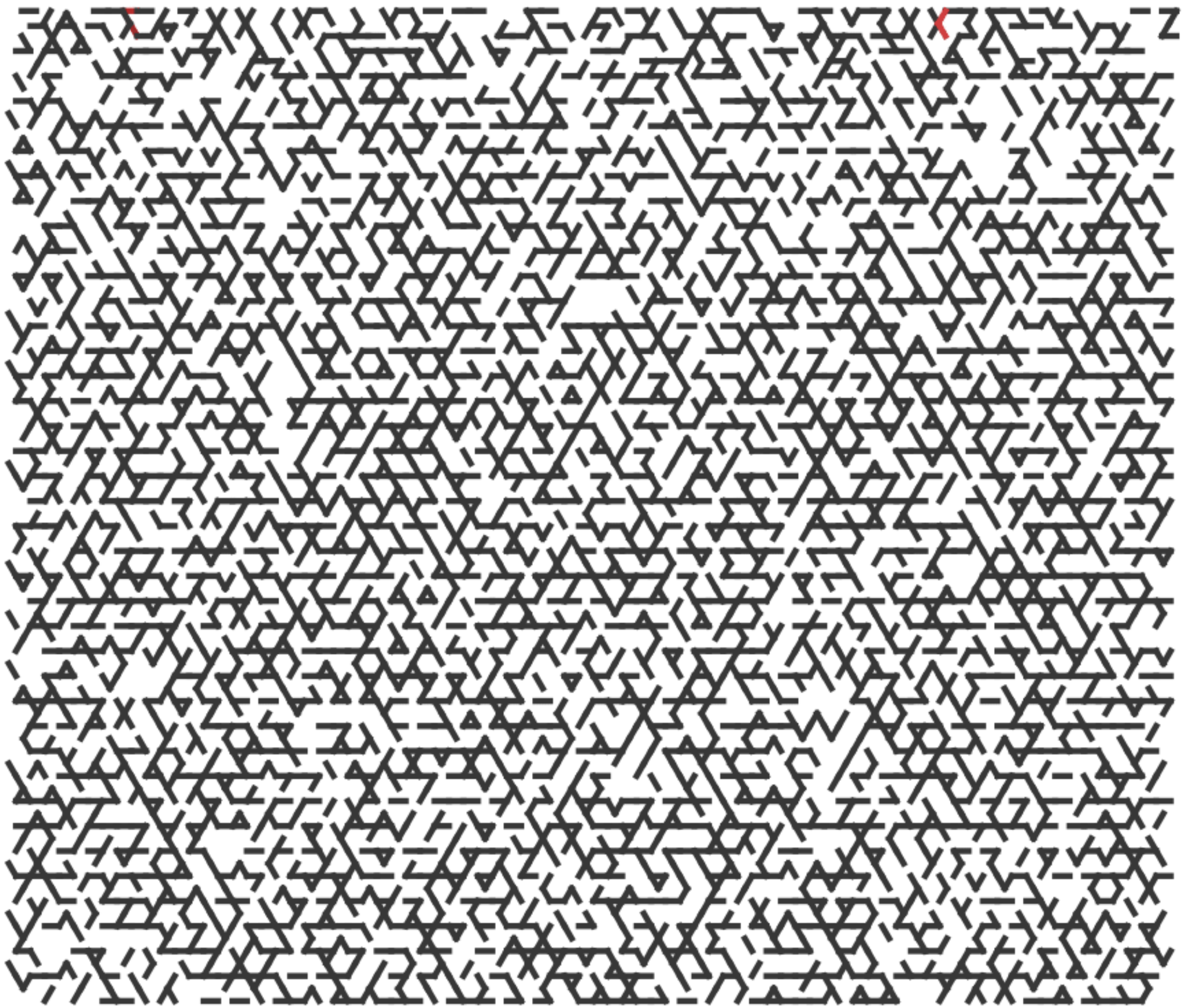
p = 0.45



Bond diluted network
on a Kagome lattice

Rigidity Percolation Phase Transition

Floppy



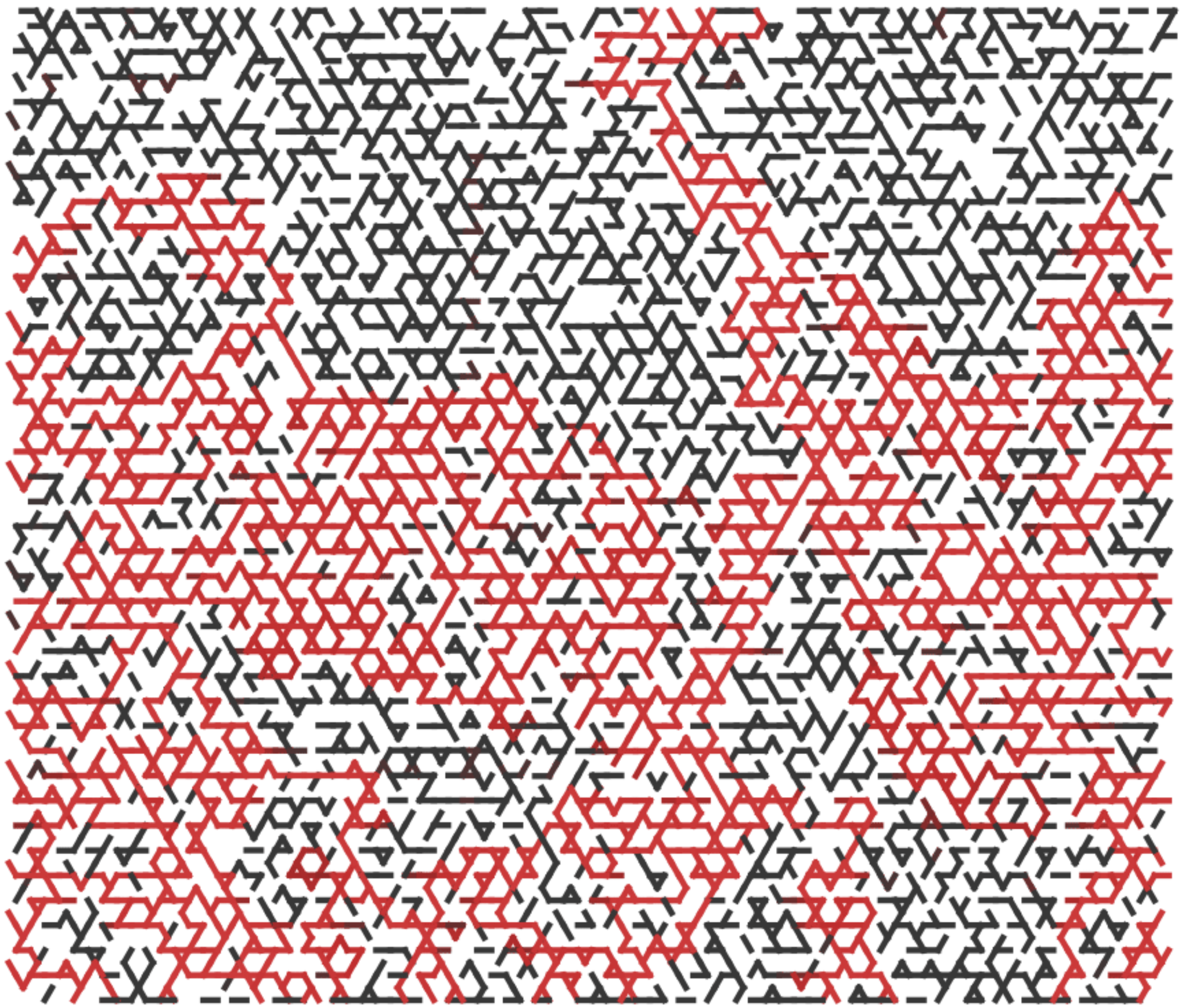
p = 0.50

Bond diluted network
on a Kagome lattice

Rigidity Percolation Phase Transition

Floppy

p = 0.55

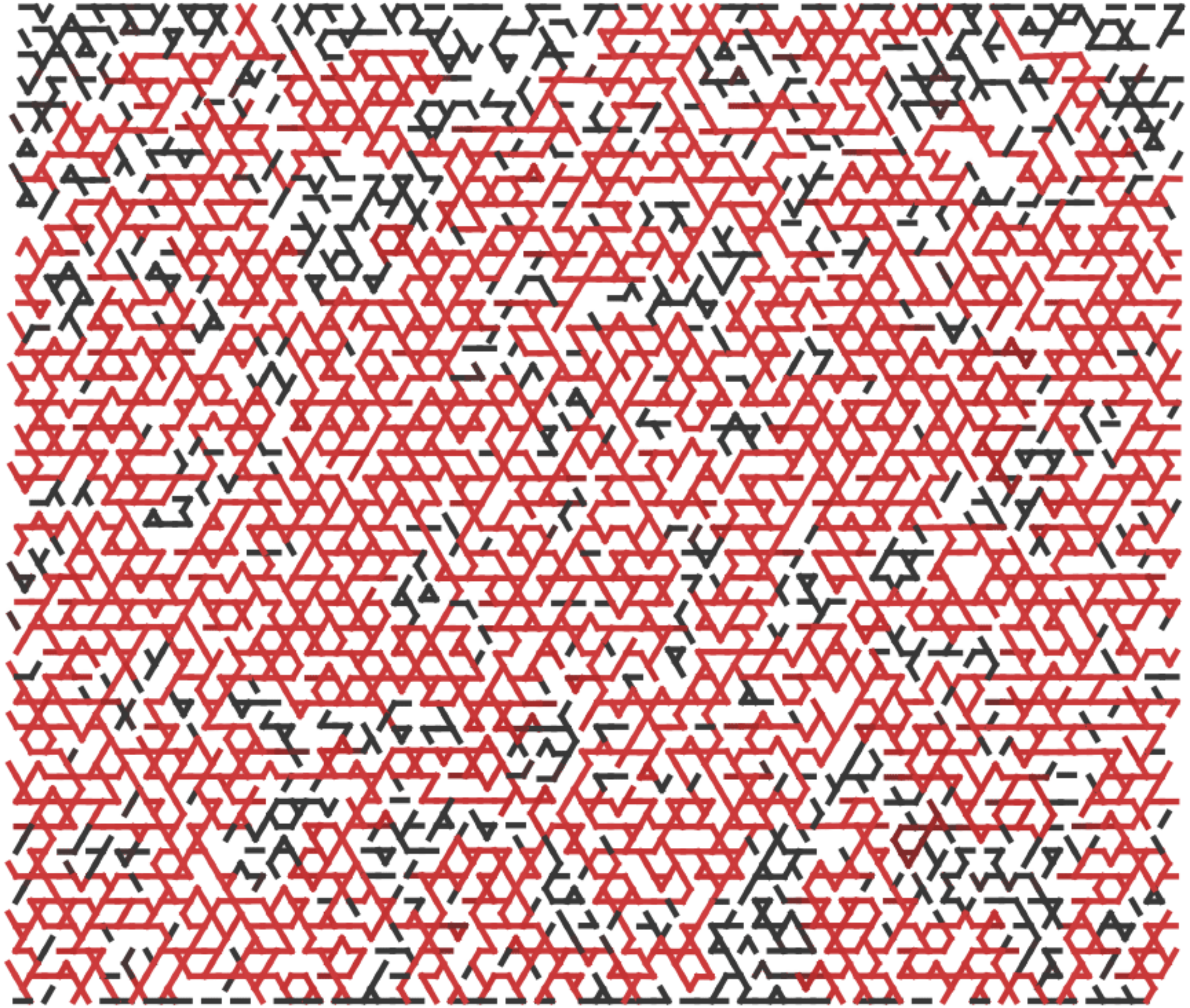


Connected cluster,
But cannot transfer forces systemwide – not rigid yet

Bond diluted network on a Kagome lattice

Rigidity Percolation Phase Transition

~~Floppy~~



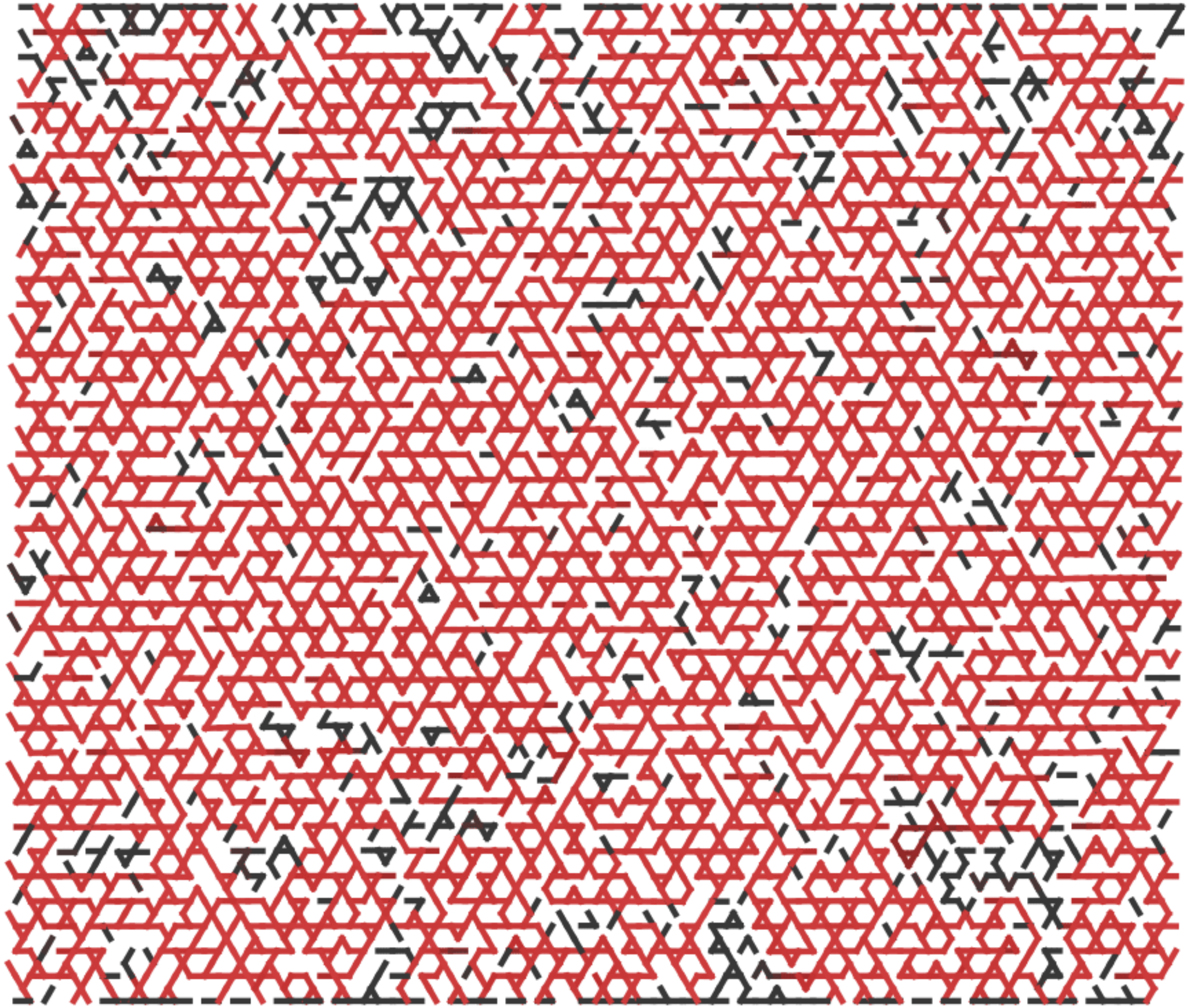
Rigid cluster which can transfer forces

p = 0.60

Bond diluted network on a Kagome lattice

Rigidity Percolation Phase Transition

~~Floppy~~



Rigid cluster which can transfer forces

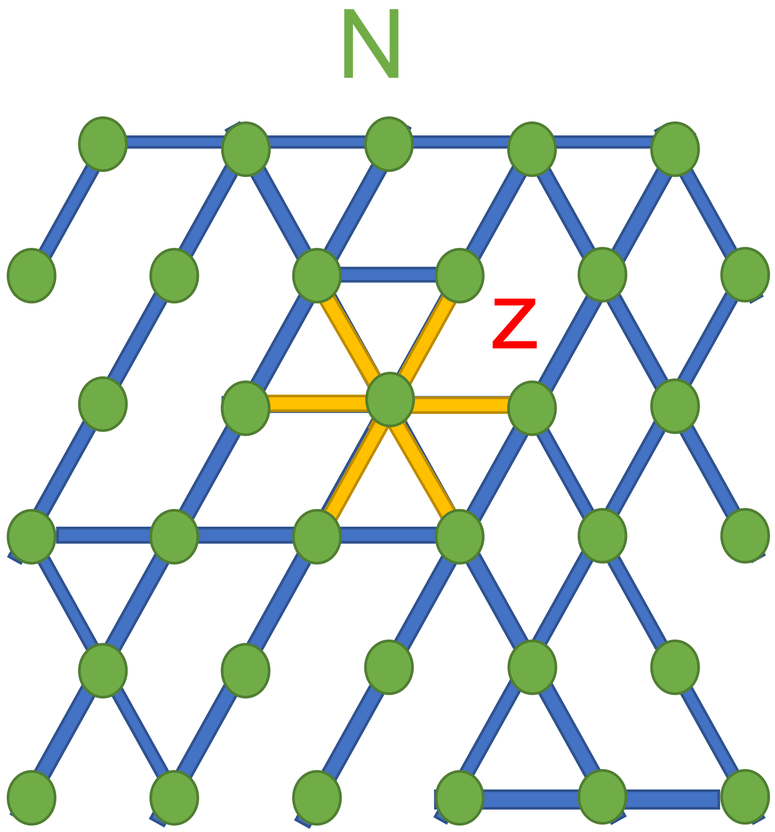
p = 0.65

Bond diluted network on a Kagome lattice

Rigidity Percolation in Spring Networks: Maxwell criterion

J. C. Maxwell, Philos. Mag., 1864

Consider a lattice of N nodes in d dimensions, z coordination number, and bond occupation probability p



# of degrees of freedom $= Nd$

constraints $= \frac{N}{2} z\, p$

Rigidity Percolation in Spring Networks: Maxwell criterion

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Consider a lattice of N nodes in d dimensions, z coordination number, and bond occupation probability p

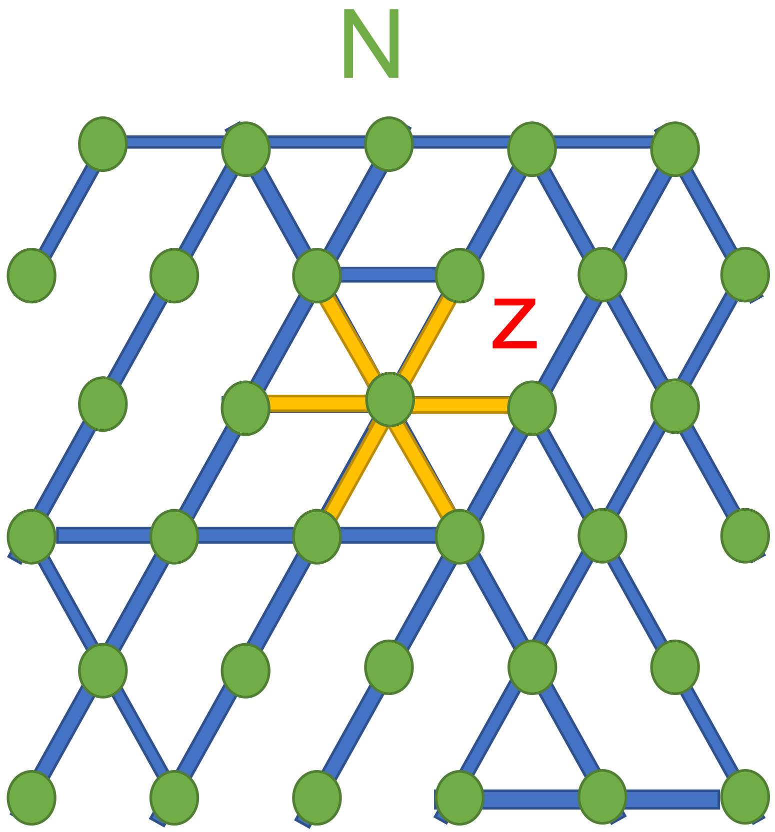
# of degrees of freedom $= Nd$

constraints $= \dfrac{N}{2} z\, p$

Maxwell criterion: Balance # constraints and # degrees of freedom

$p_c = 2d/z, \quad z_c = 2d$ Isostatic coordination

$p > p_c, z > z_c$ Condition for rigidity



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J. C. Maxwell, Philos. Mag., 1864

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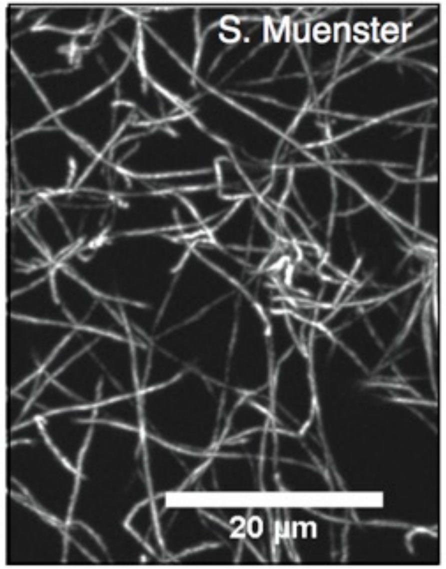
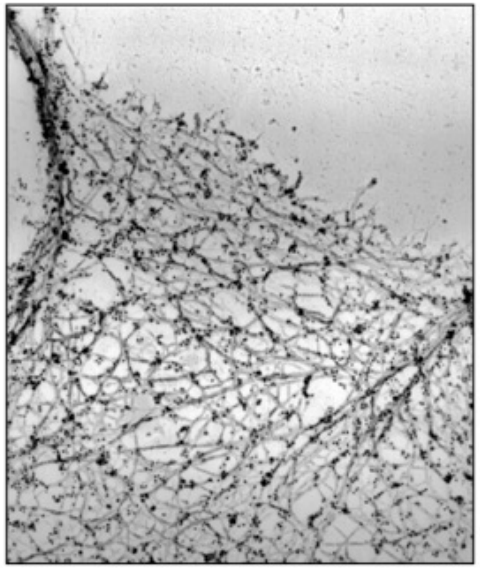
Isostatic coordination

collagen (*in vitro*)



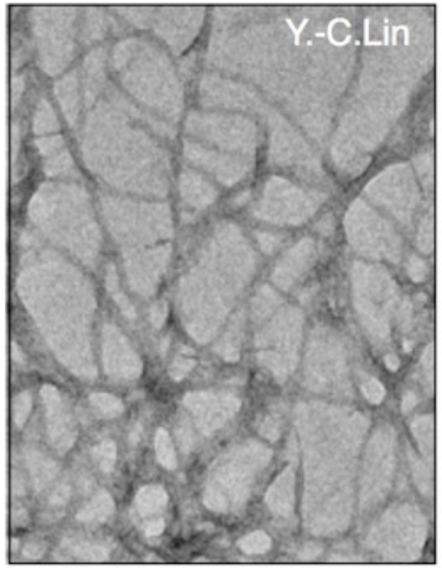
$z < z_c$

actin-cortex



$z < z_c$

vimemtin (*in vitro*)



$z < z_c$

How can these networks be rigid?

Rigidity Percolation in Spring Networks: Maxwell criterion

J. C. Maxwell, Philos. Mag., 1864

Maxwell criterion: Balance # constraints and # degrees of freedom

$$p_c = 2d/z, \quad z_c = 2d$$

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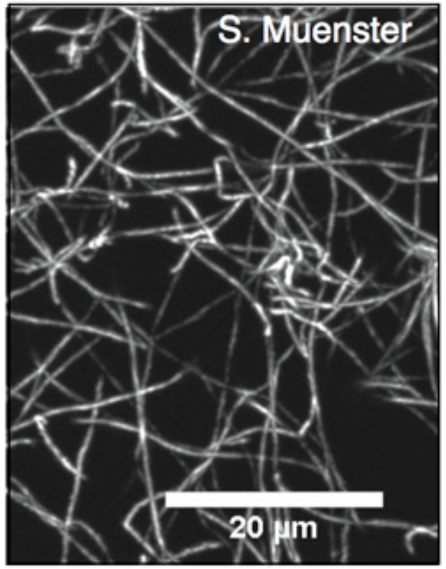
collagen (*in vitro*)



$z < z_c$

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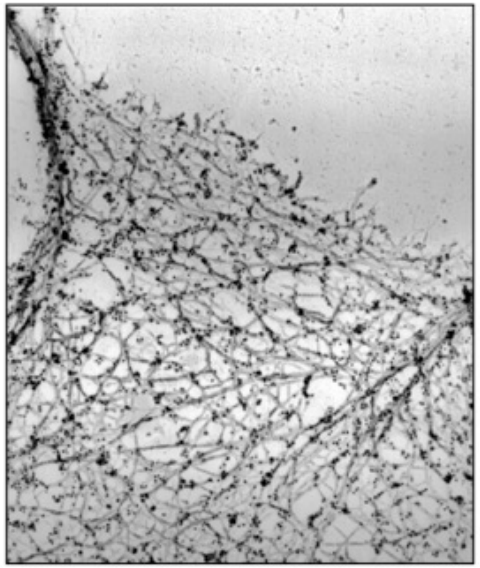
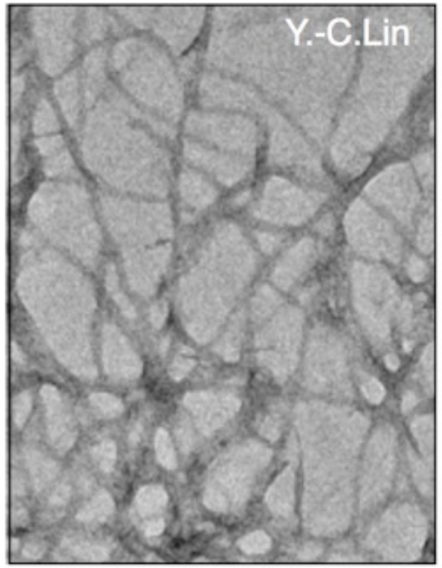


$z < z_c$

vimemtin (*in vitro*)

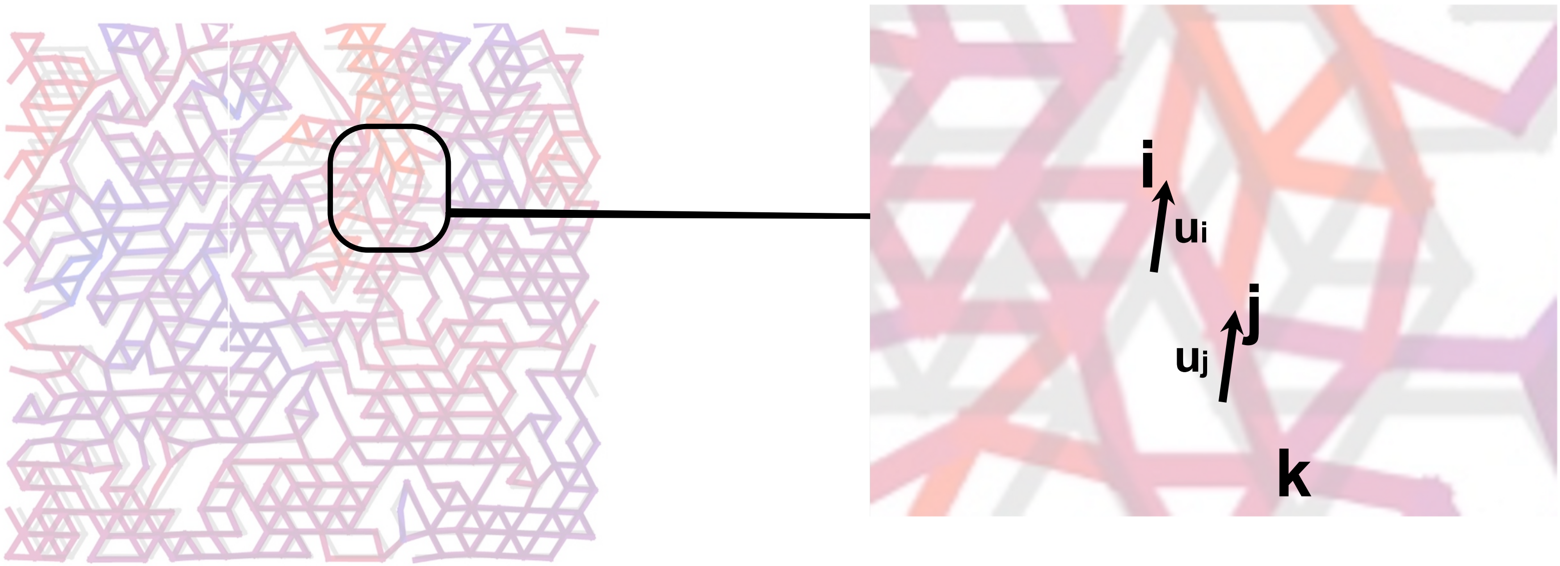


$z < z_c$

How can these networks be rigid?

Have additional constraints due to filament bending rigidity: Semiflexible Networks

Rigidity Percolation in Semiflexible Networks



$$E_{spring} = \frac{\mu}{2} \sum_{\langle ij \rangle} p_{ij} (\vec{u}_{ij} . \hat{r}_{ij})^2 \qquad E_{filament\ bending} = \frac{\kappa}{2} \sum_{\langle jik \rangle} p_{ji} p_{ik} (\theta_{jik})^2$$

$$E = E_{spring} + E_{filament\ bending}$$

Study using effective medium theory or energy minimization

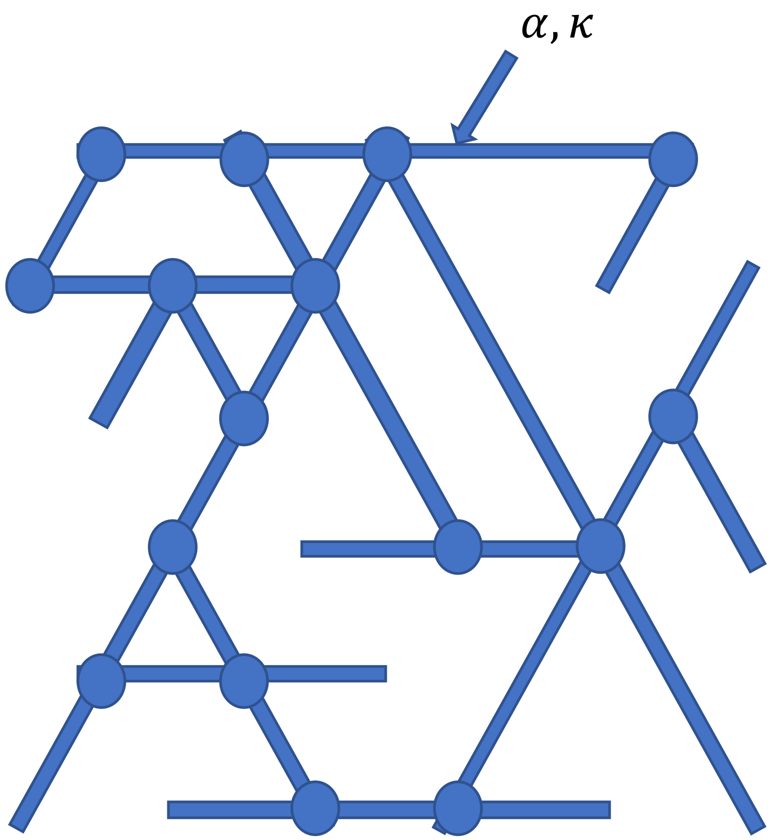
MD, MacKintosh, Levine, PRL 2007, MD, D Quint, JM Schwarz, PloS One 2012, Broedersz et al Nature Ohys 0211

Rigidity Percolation in Semiflexible Networks: Network Construction

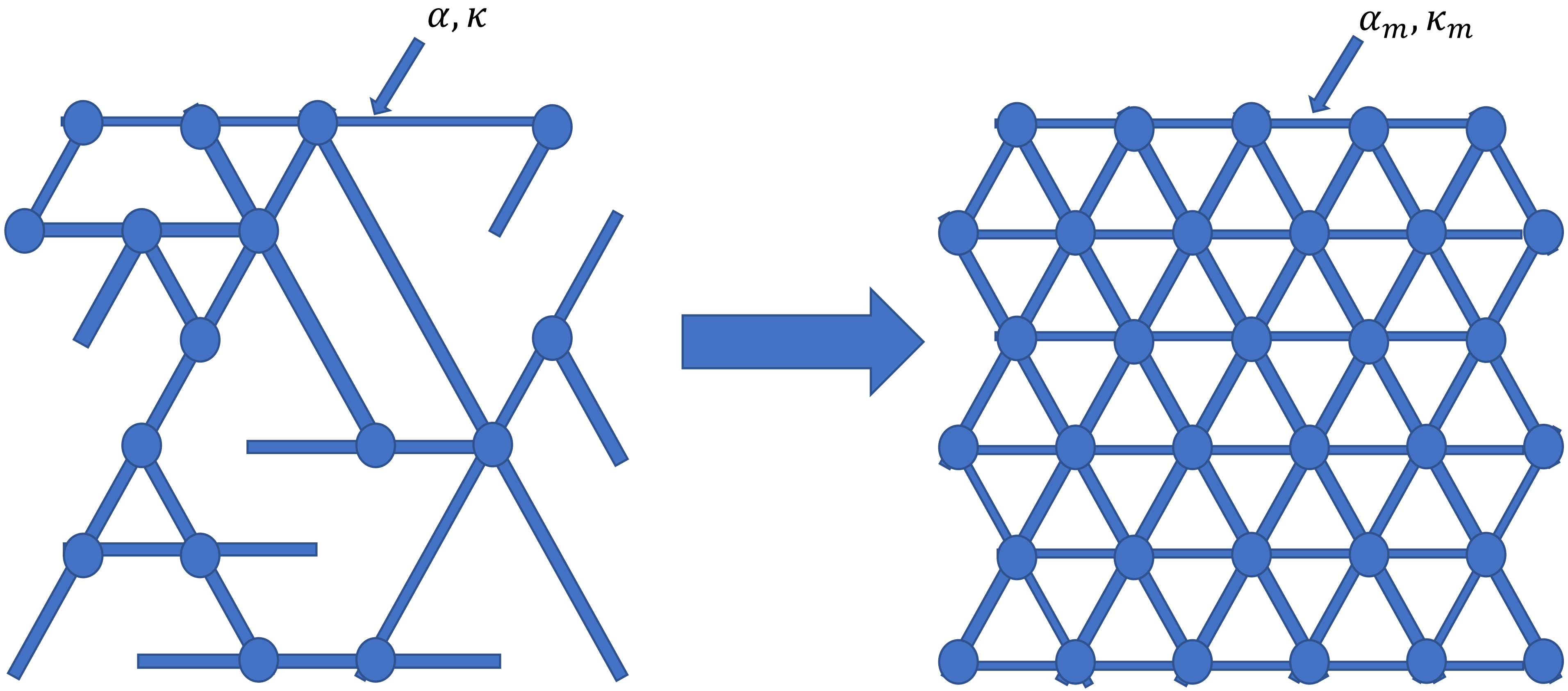
- Start with a lattice with all bonds present. Contiguous series of bonds constitutes a filament.
- Remove bonds with a probability p to create broad distribution of filament lengths.
- Distribution of the stretching and bending elasticity of bonds

$$P(\alpha') = p\delta(\alpha' - \alpha) + (1-p)\delta(\alpha')$$
$$P(\kappa') = p^2\delta(\kappa' - \kappa) + (1-p^2)\delta(\kappa')$$

- Anytime two filaments cross, we assume there is a crosslink which prevents sliding but allow free rotations

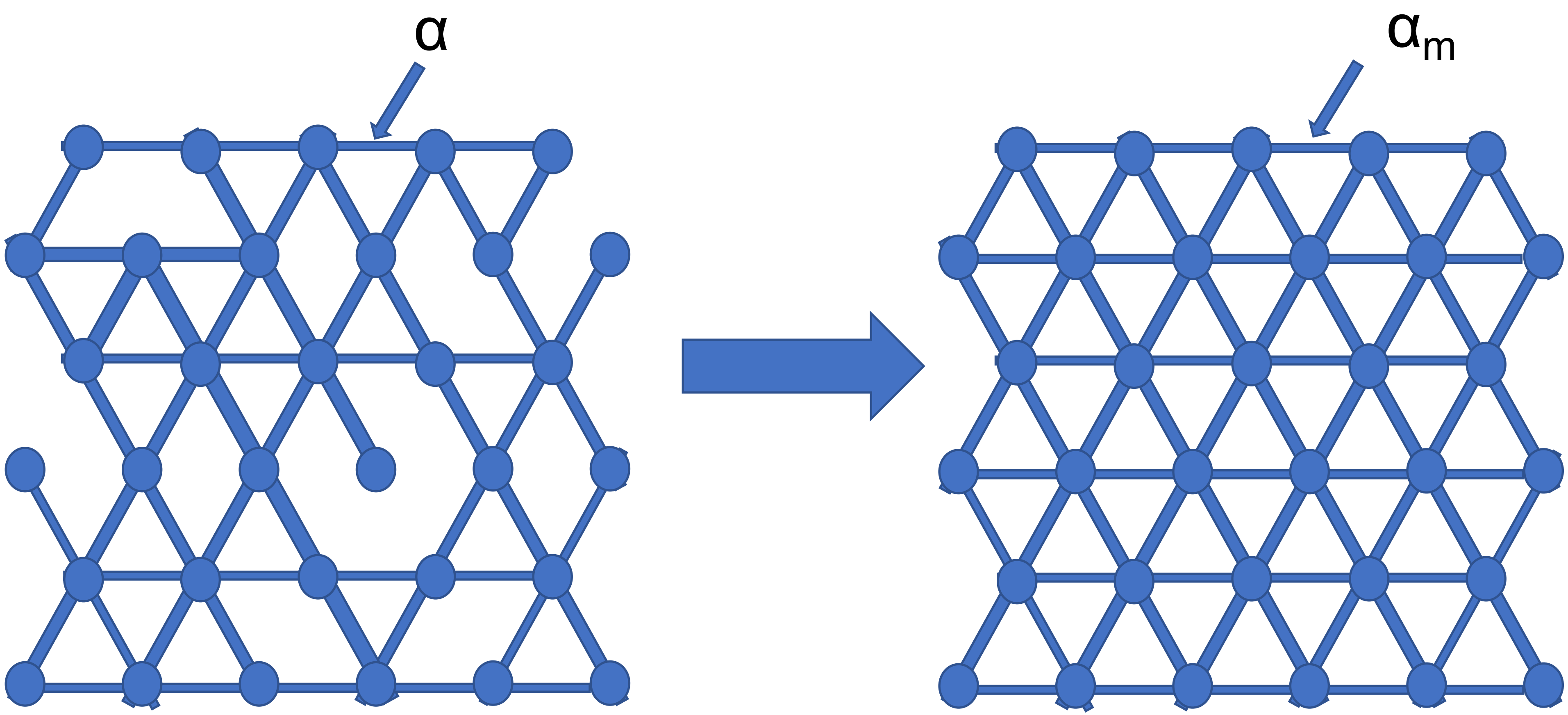


Effective Medium Theory (EMT)

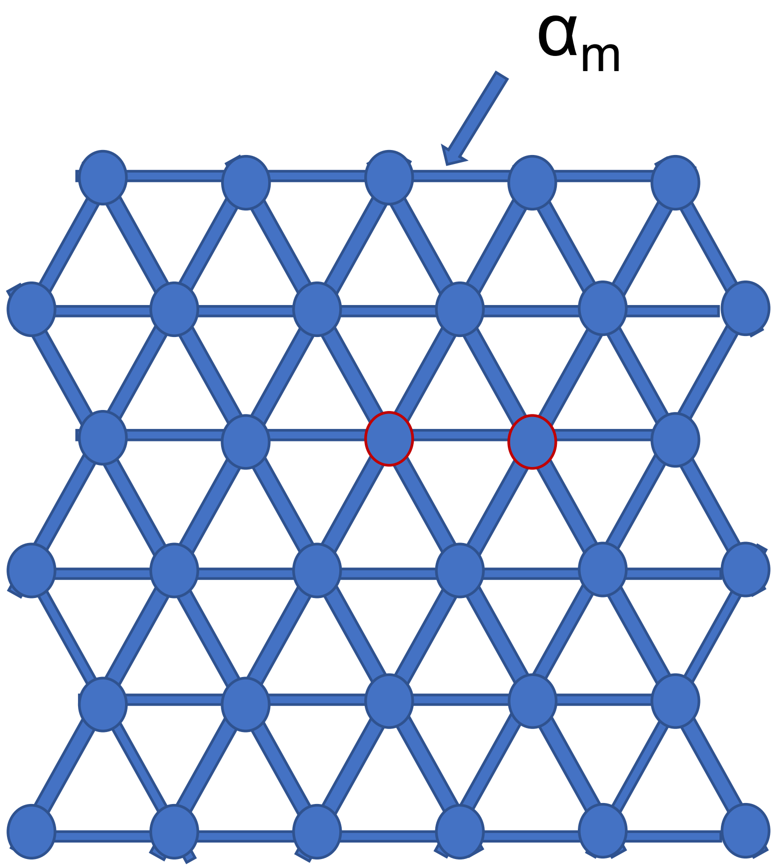


EMT for central force (spring) networks

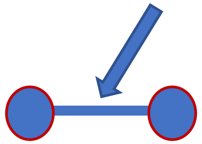
Feng, Thorpe, Garboczi, PRB 1985



Focus on one connection



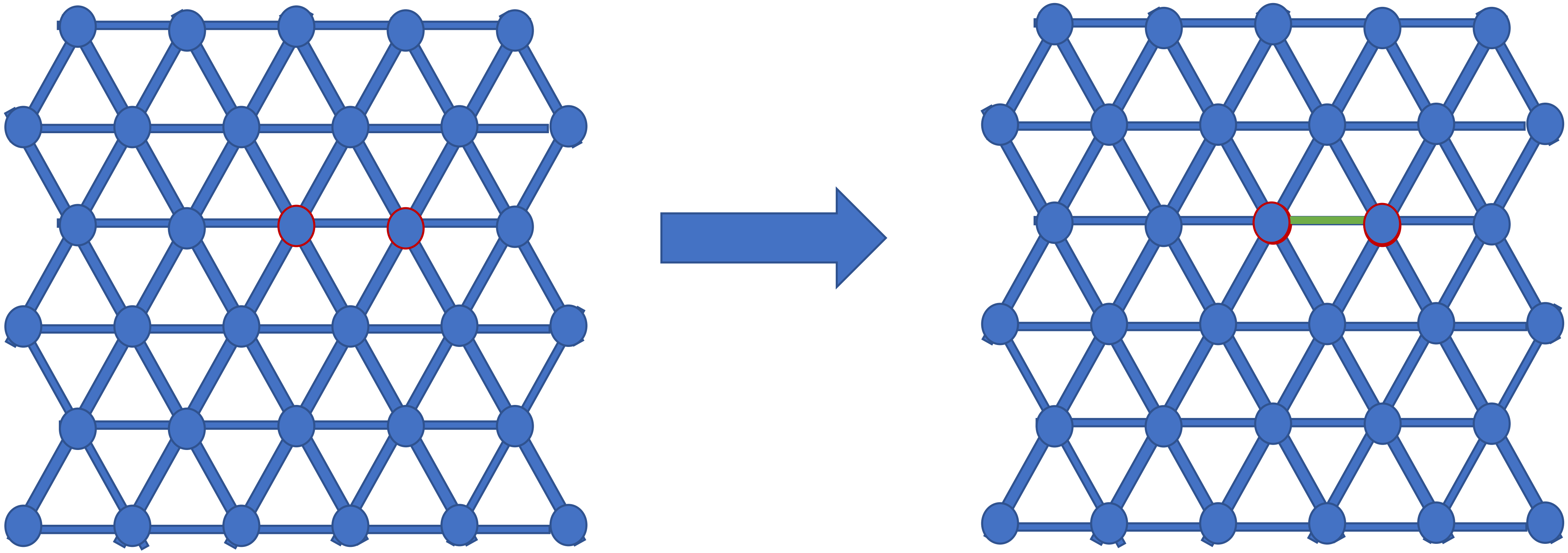
$$\alpha_{eff} = \frac{\alpha_m}{a^*}$$



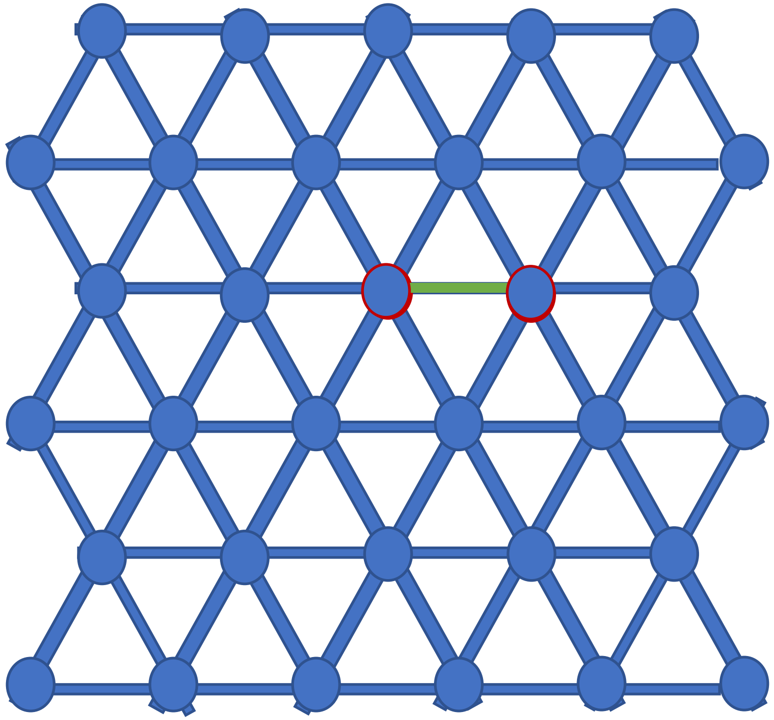
Apply Strain

- Put ordered lattice under constant strain such that every bond is deformed by δ_{um}

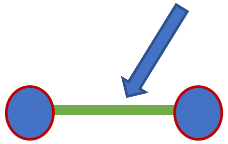
Introduce wrong bond α



Wrong bond α

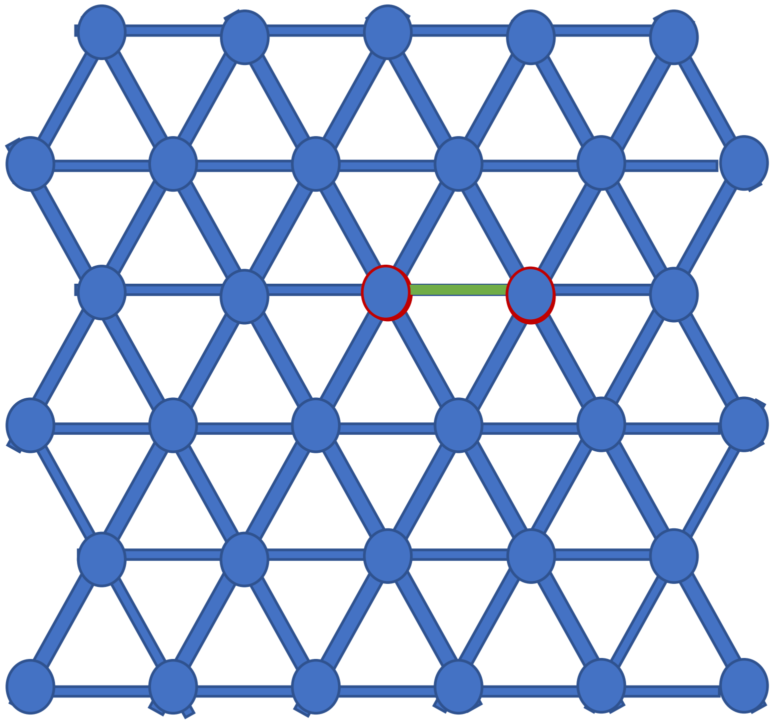


$$\alpha_{eff} = \frac{\alpha_m}{a^*} - \alpha_m + \alpha$$



What is the extra deformation δ_u of replaced bond ?

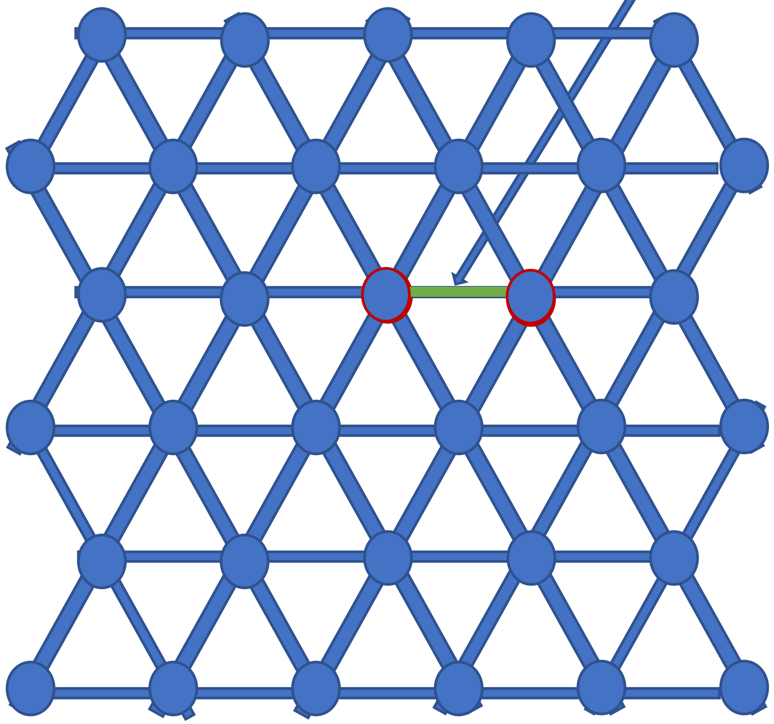
Virtual force f that can correct the extra deformation of replaced bond



$$f = \delta_{um}(\alpha_m - \alpha)$$

Apply this force f on the replaced bond

$\alpha_{eff} = \frac{\alpha_m}{\alpha^*} - \alpha_m + \alpha$

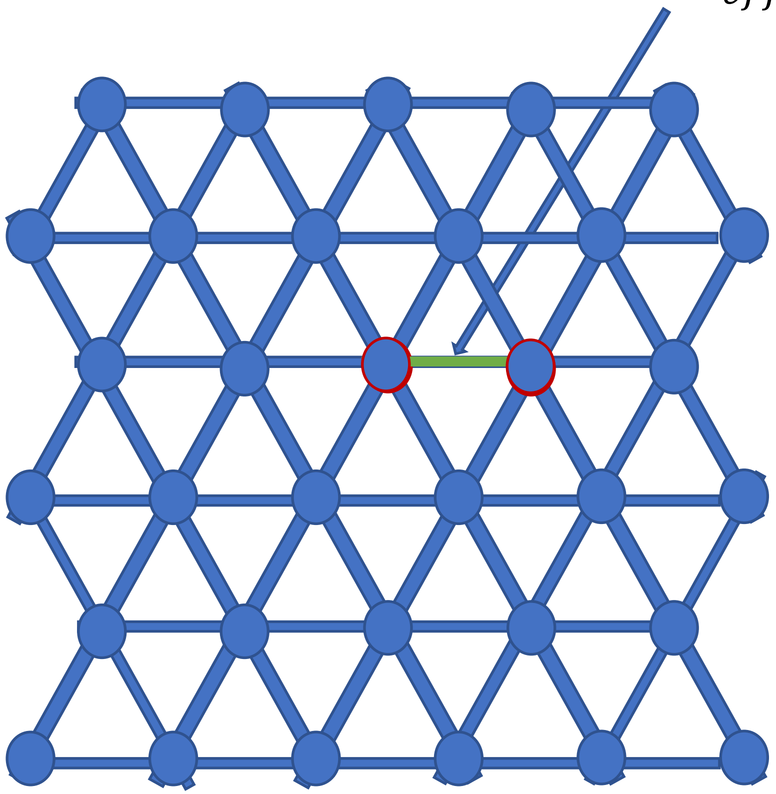


$$\delta_u = \frac{f}{\frac{\alpha_m}{\alpha^*} - \alpha_m + \alpha}$$

$$f = \delta_{um}(\alpha_m - \alpha)$$

Apply this force f on the replaced bond

$$\alpha_{eff} = \frac{\alpha_m}{\alpha^*} - \alpha_m + \alpha$$



$$\delta_u = \frac{f}{\frac{\alpha_m}{\alpha^*} - \alpha_m + \alpha}$$

$$f = \delta_{um}(\alpha_m - \alpha)$$

$$\boxed{\delta_u = \frac{\delta_{um}(\alpha_m - \alpha)}{\frac{\alpha_m}{\alpha^*} - \alpha_m + \alpha}}$$

Replacing more than one bond

When averaged over the entire system, these fluctuations should go to 0

$$\int \frac{\alpha_m - \alpha'}{\frac{\alpha_m}{a^*} - \alpha_m + \alpha'} * P(\alpha')\, d\alpha' = 0$$

Where $P(\alpha') = p\delta(\alpha' - \alpha) + (1-p)\delta(\alpha')$

$$\frac{\alpha_m}{\alpha} = \frac{p - a^*}{1 - a^*}$$

What is a^*?

- Geometric constant relating geometry of lattice to rigidity
- Evaluated in terms of Dynamical Matrix

$$a^* = \frac{1}{3} \sum_q Tr\left[\boldsymbol{D}\ (q) \cdot \boldsymbol{D}^{-1}(q)\right]$$