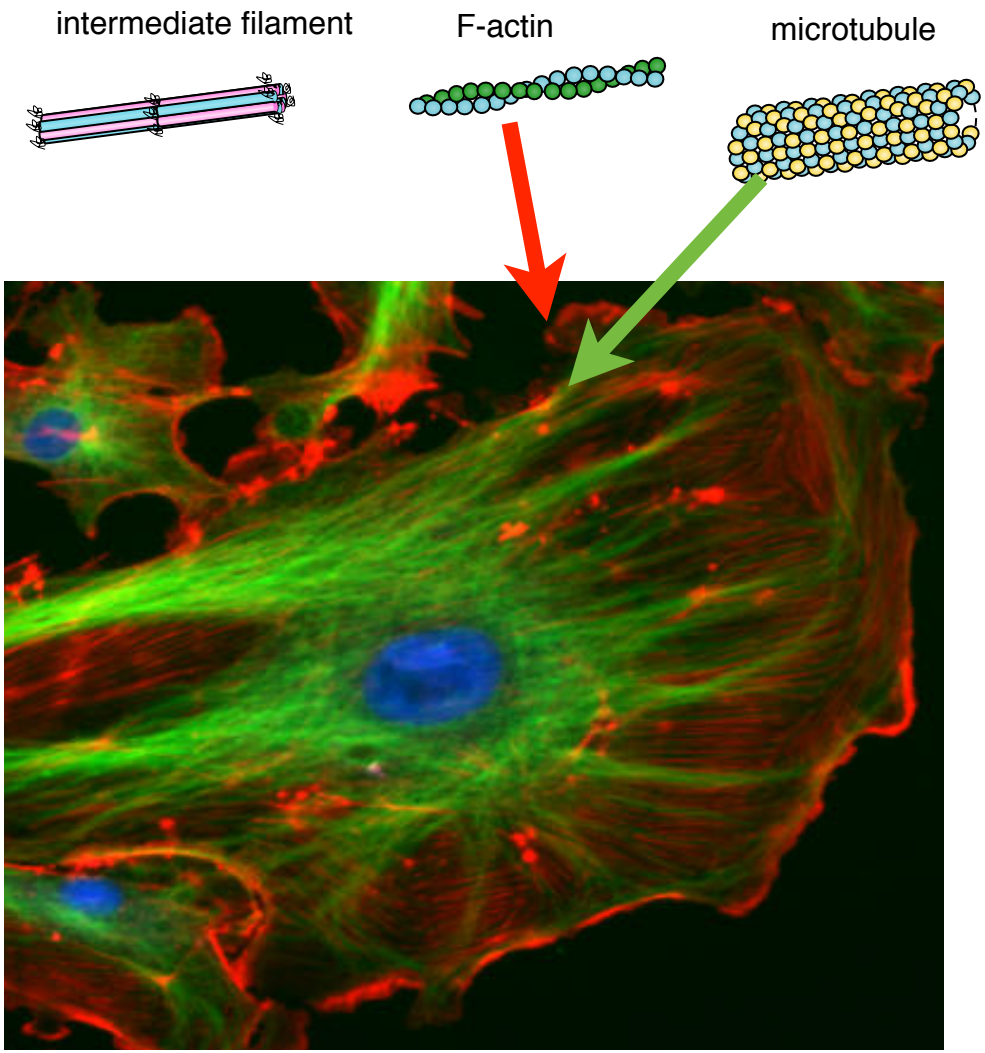
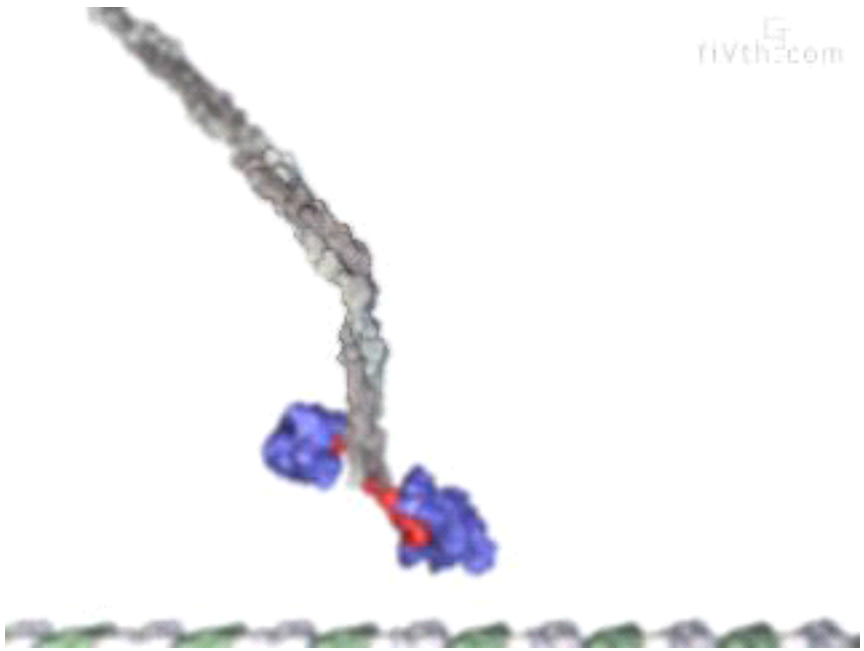
The cytoskeleton, an active *solid*

The Cell

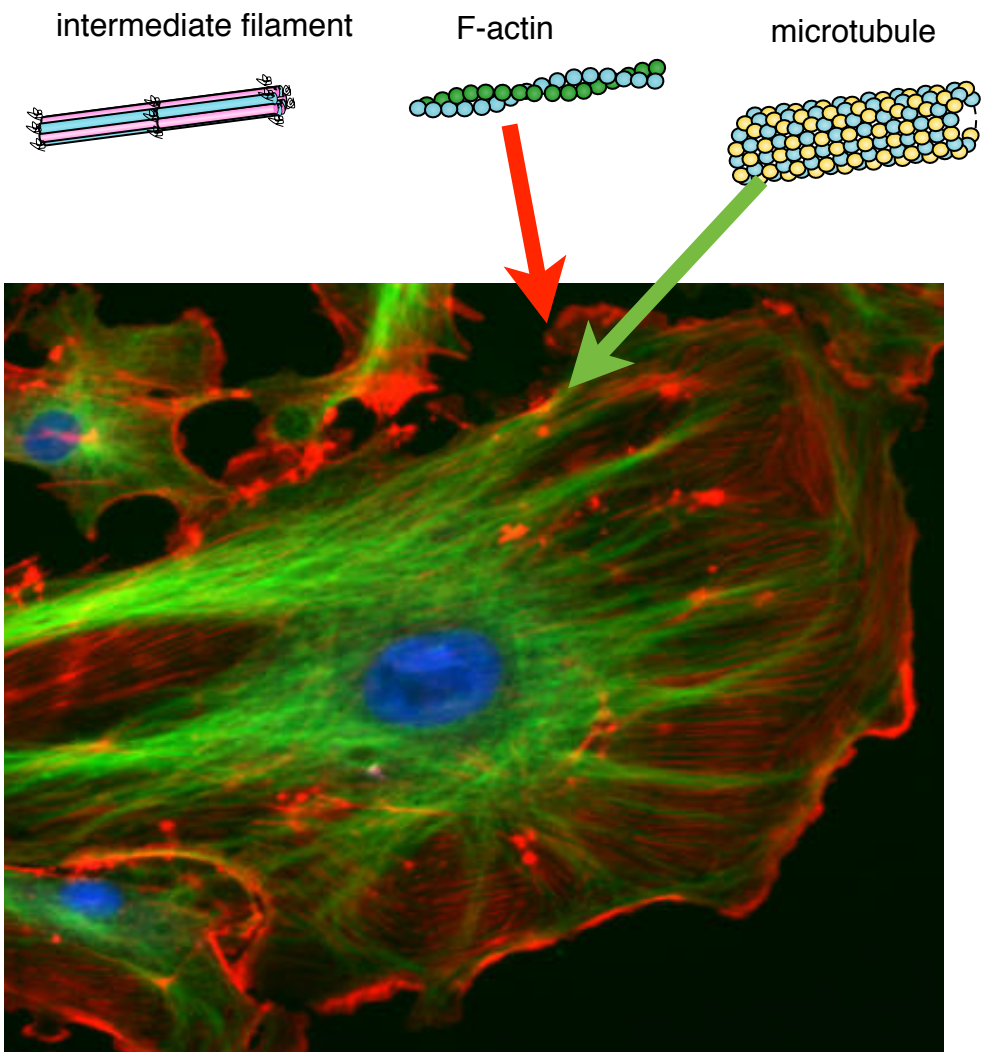


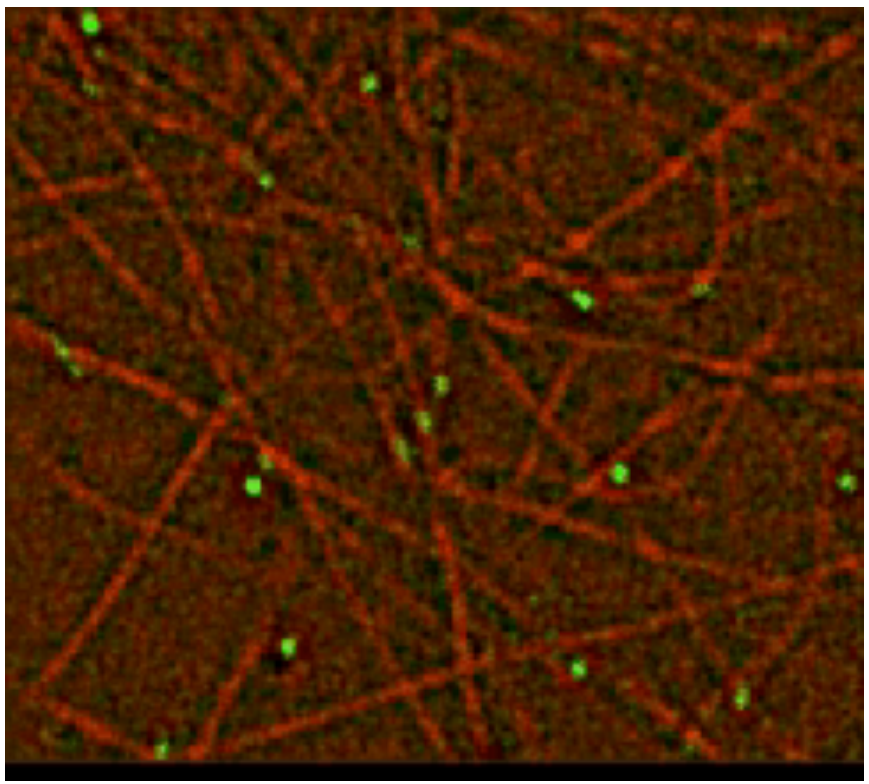


Vale lab, *UCSF*

The cytoskeleton, an active *solid*

The Cell

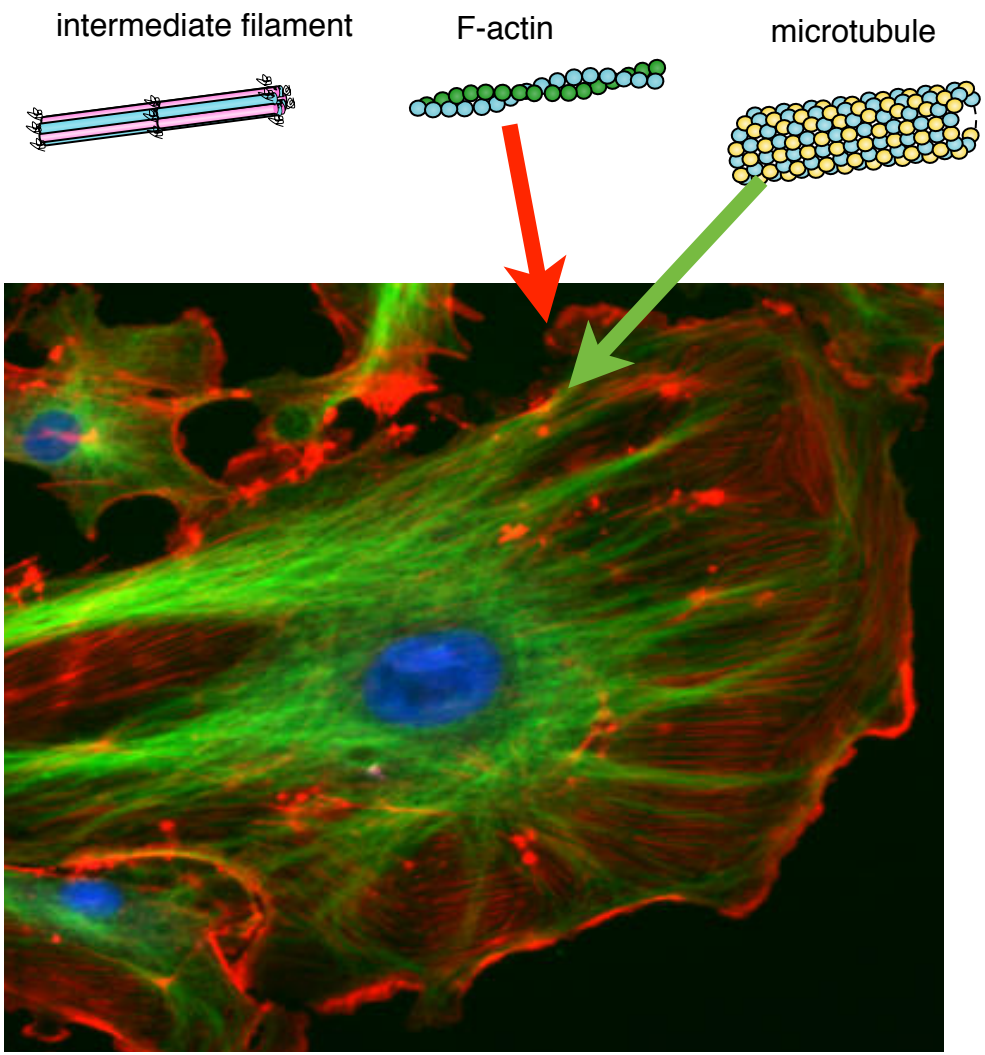


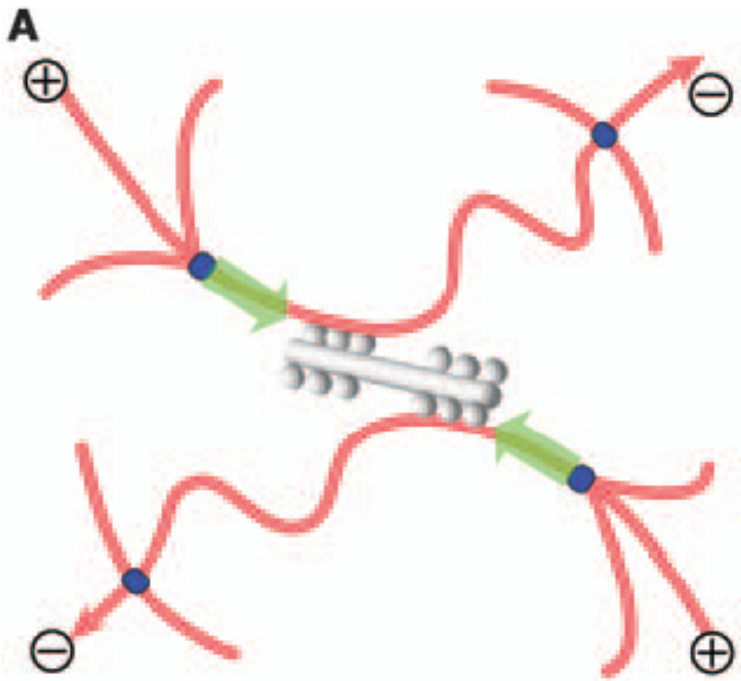


with Kapitein et al.,
Current Biol., (2010).

The cytoskeleton, an active *solid*

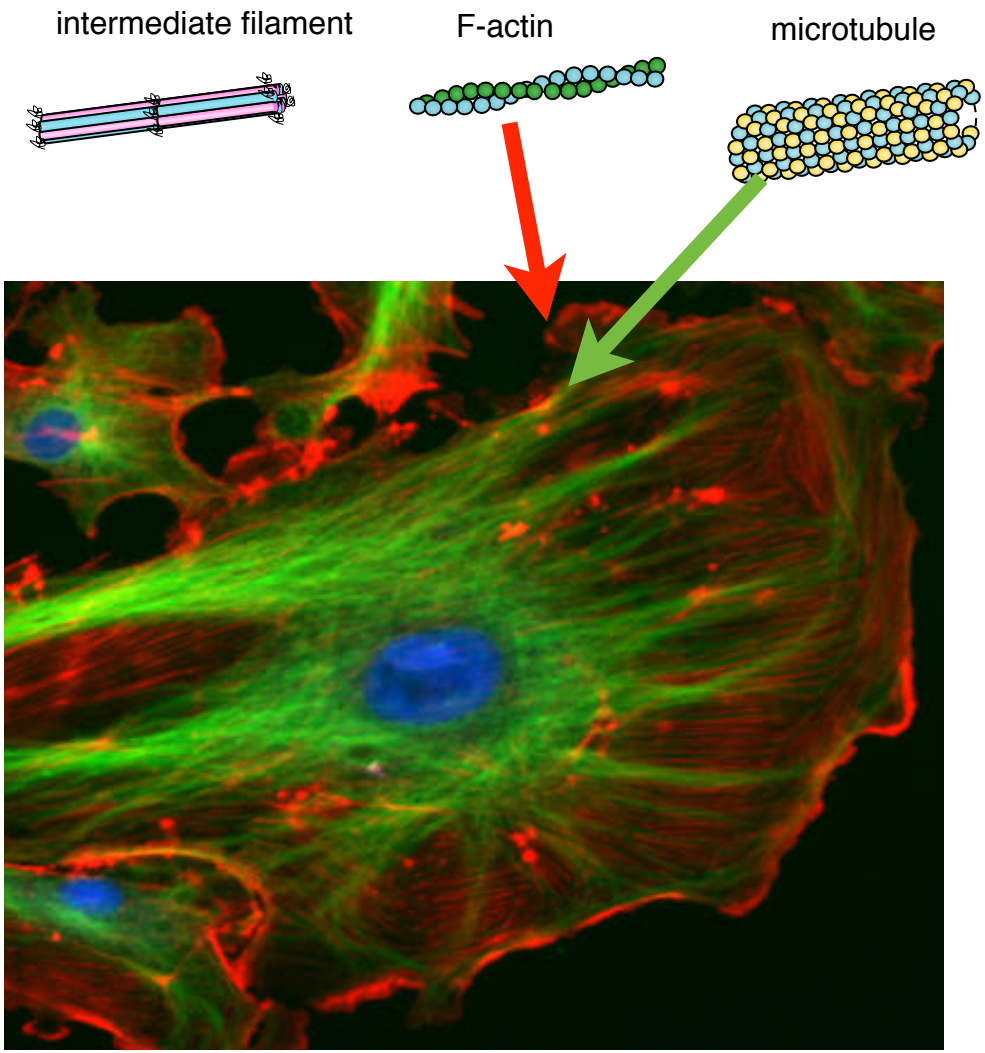
The Cell



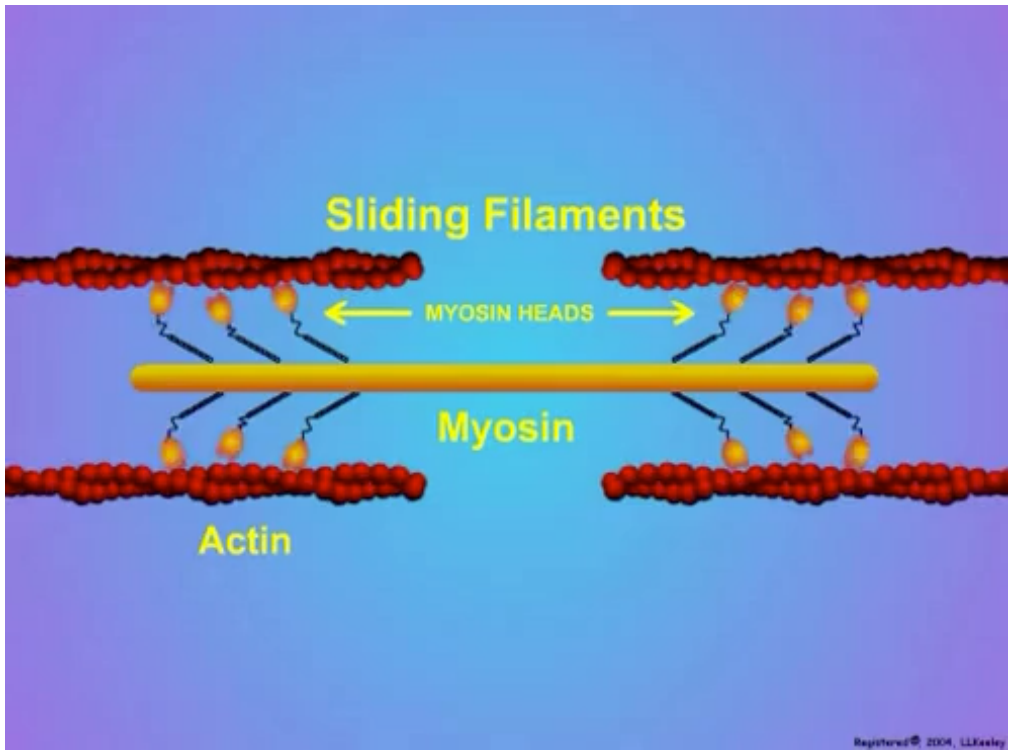


The cytoskeleton, an active *solid*

The Cell



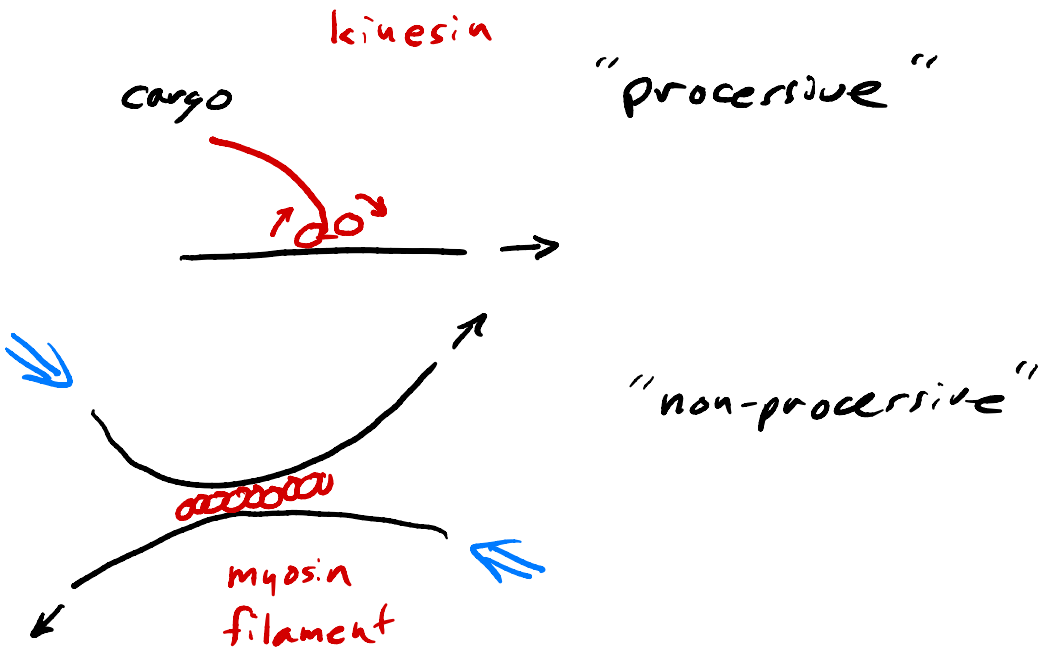
Myosin in muscle



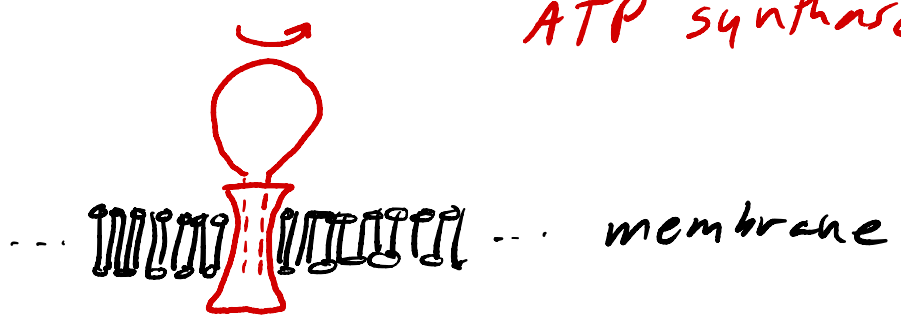
https://www.youtube.com/watch?v=zQocsLRm7_A&feature=youtu.be

Molecular motors

- Linear motors



- Rotary Motors



Biopolymers & their networks in cells

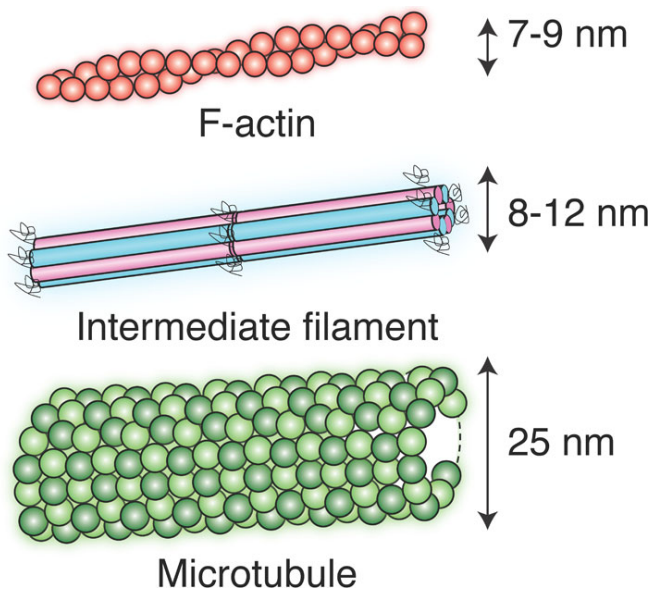


FIG. 4 (color online). The three families of cytoskeletal filaments, including F-actin, intermediate filaments, and microtubules.

see, e.g., Broedersz and FCM, Rev Mod Phys, 86: 995 (2014).

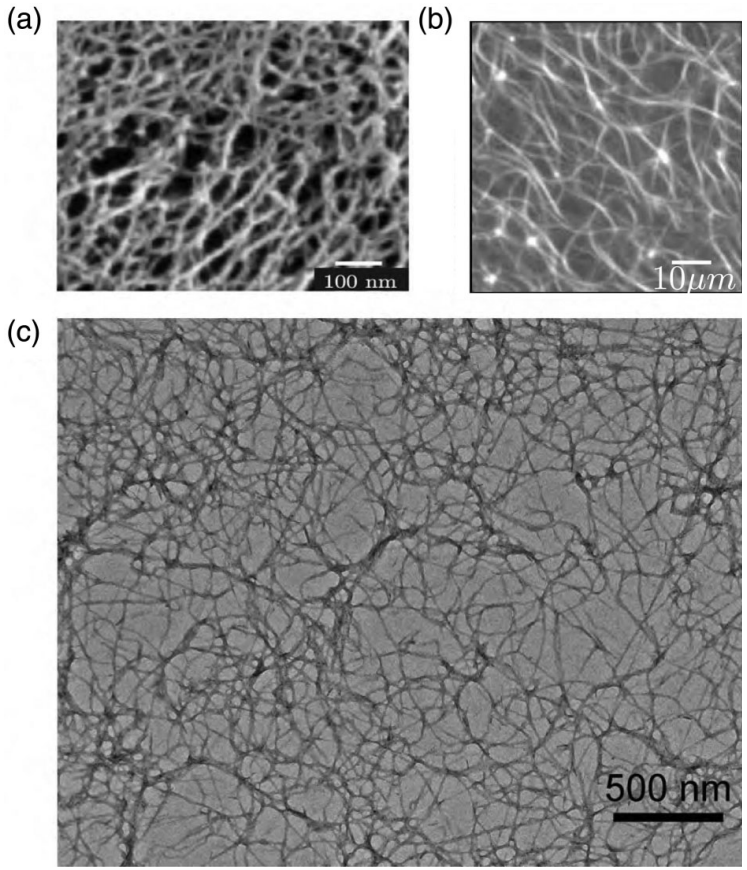
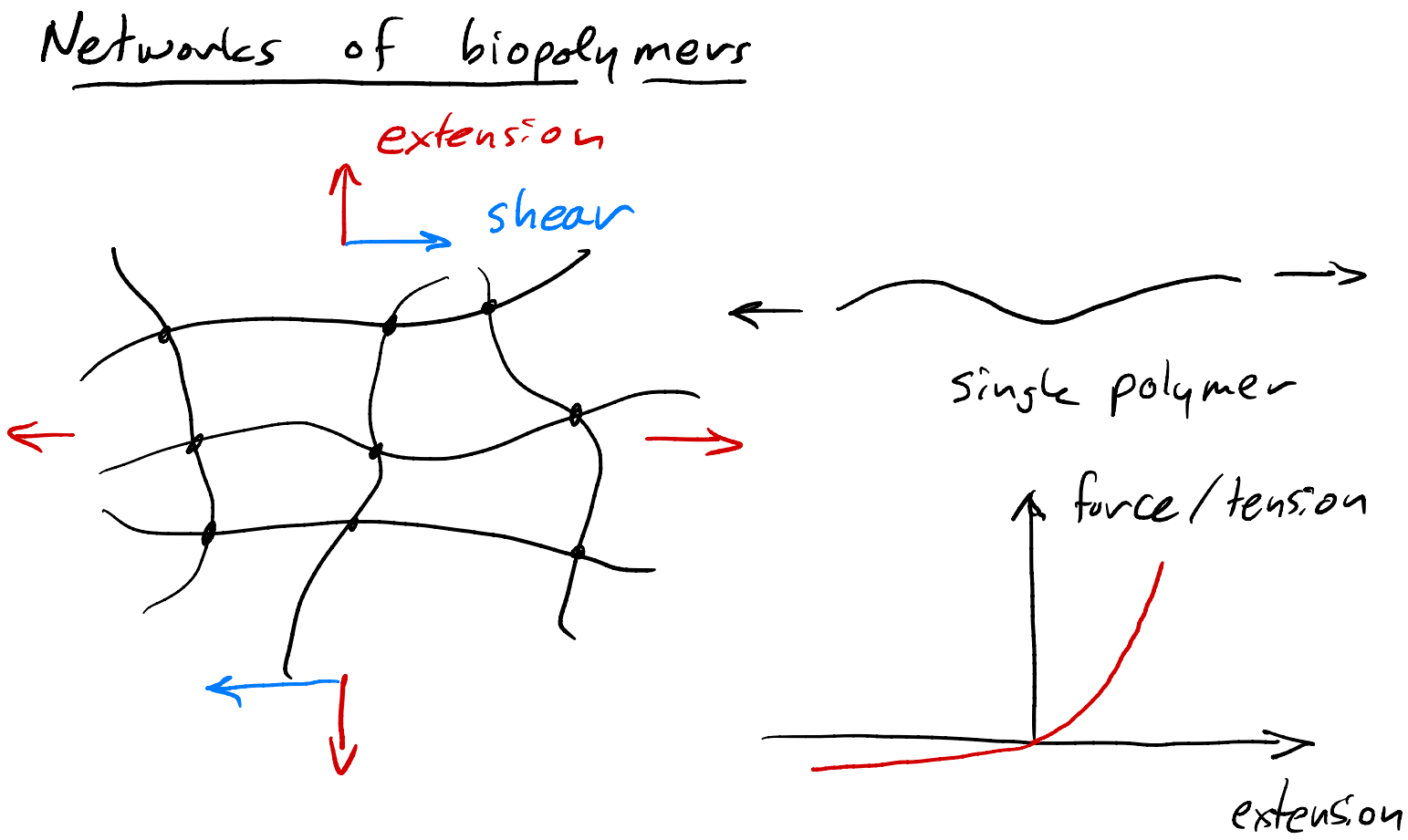


FIG. 3. (a) Electron micrograph of a fixed and rotary-shadowed filamin-F-actin network at an actin concentration 1 mg/ml, average filament length 15 μm, and a filamin:actin molar ratio of 0.005:1. From Kasza *et al.*, 2009. (b) Confocal microscopy image of a fluorescently labeled bundled filamin-F-actin network at high filamin concentrations. From Kasza *et al.*, 2010. (c) Electron micrograph of a fixed and rotary-shadowed Vimentin network. Courtesy of Y-C. Lin and D. Weitz (Harvard).

Networks stiffen under extension/deformation



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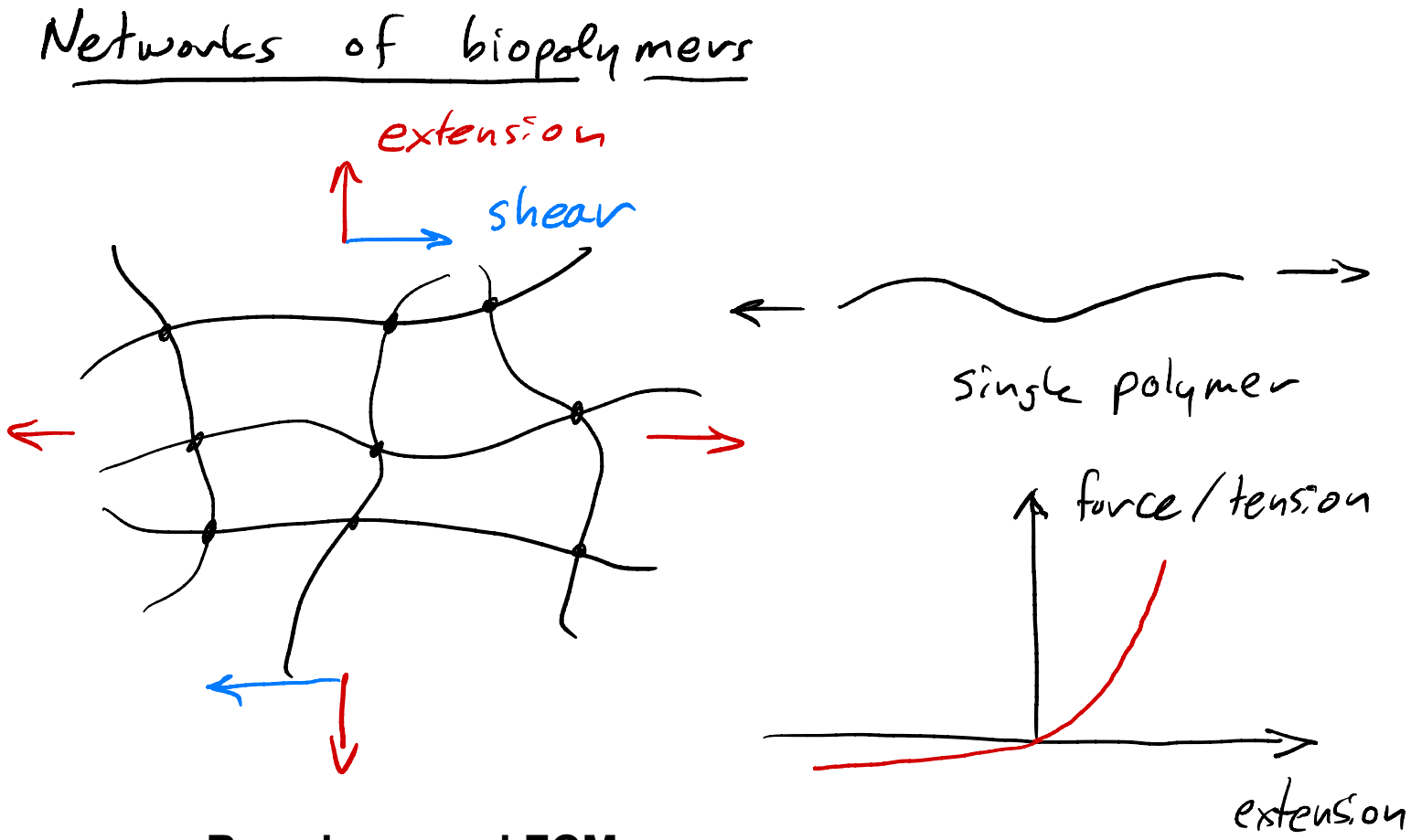
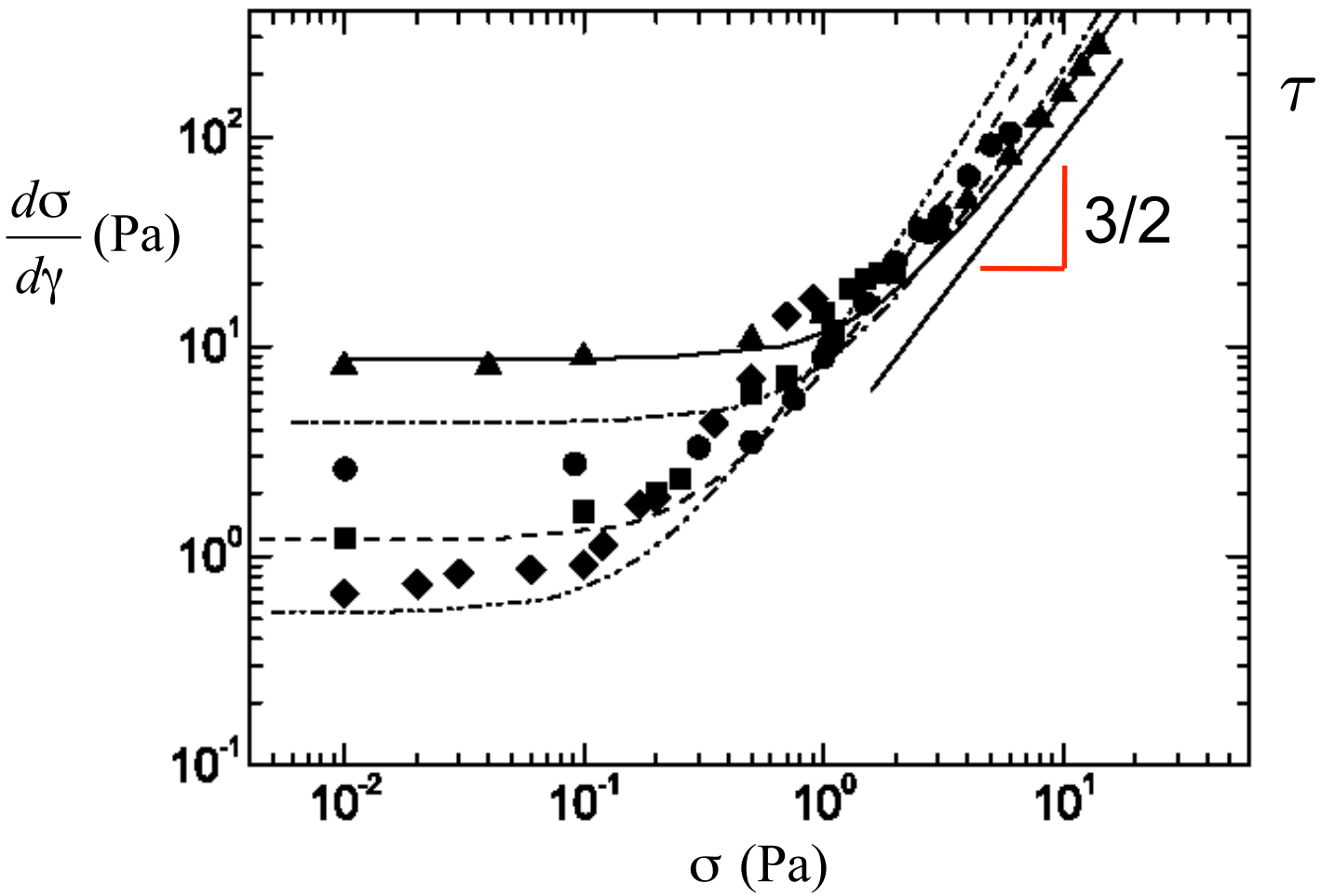
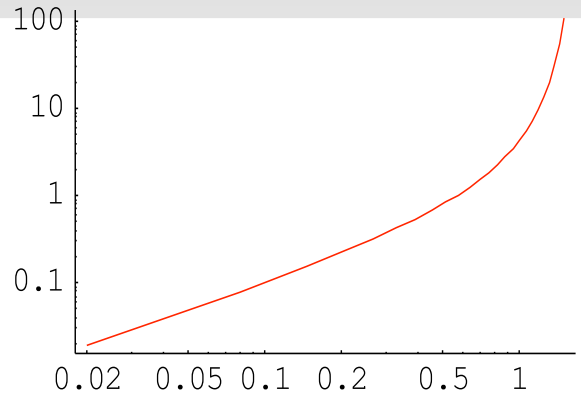


see, e.g., Broedersz and FCM,
Rev Mod Phys, 86: 995 (2014).

Scaling of Stress Stiffening





$$\tau \sim 1/\left|x_0 - x\right|^2$$

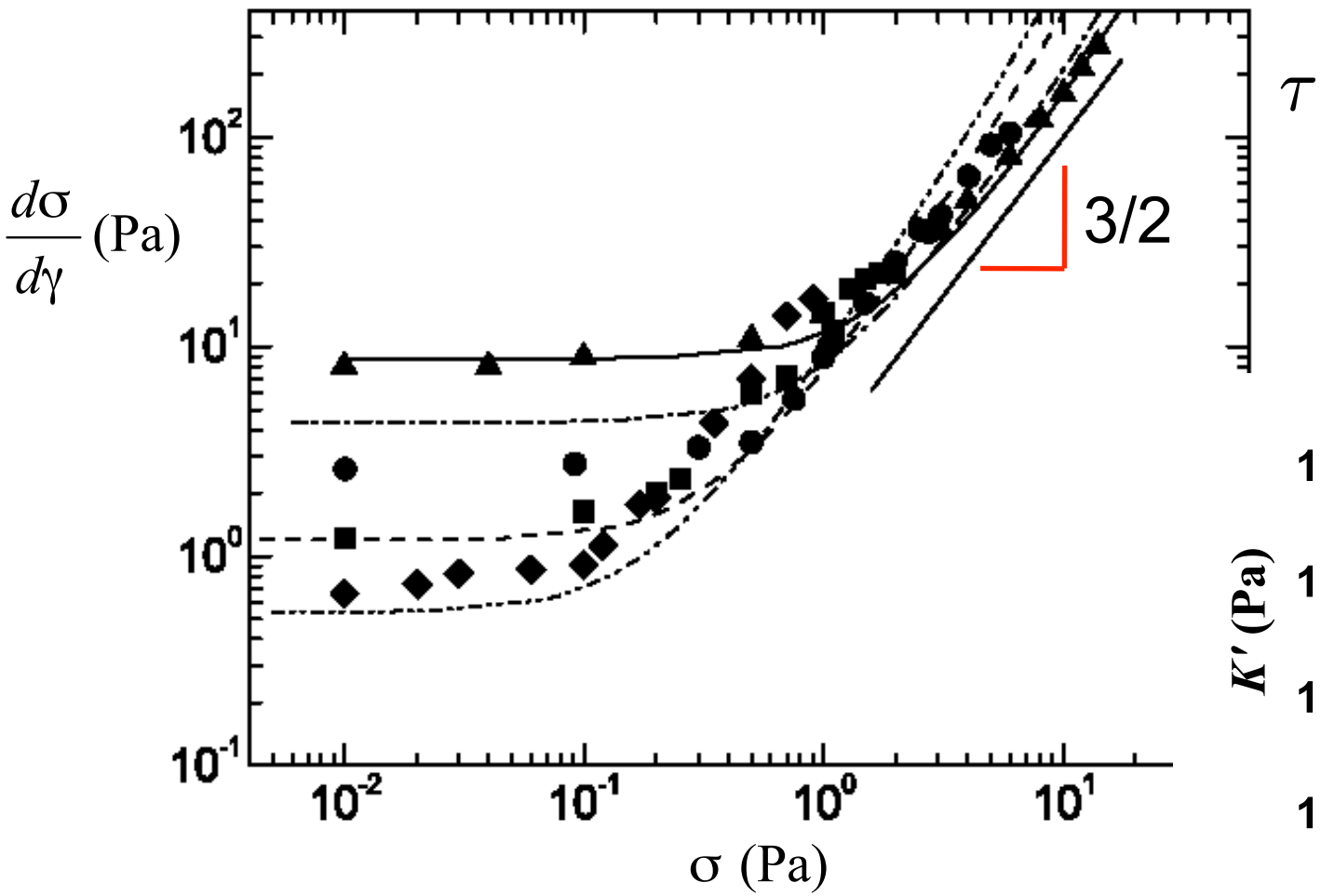
$$\sigma \sim (\gamma_0 - \gamma)^{-2}$$

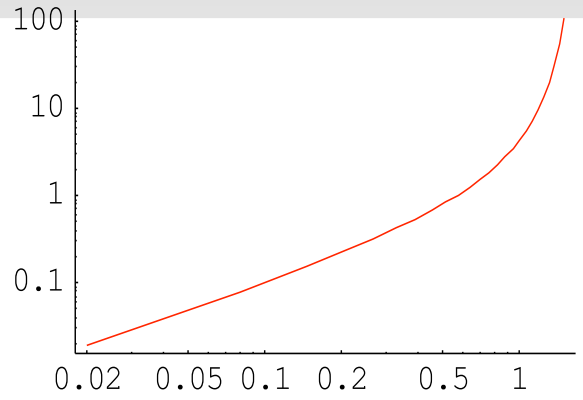
$$\frac{d\sigma}{d\gamma} \sim \sigma^{3/2}$$

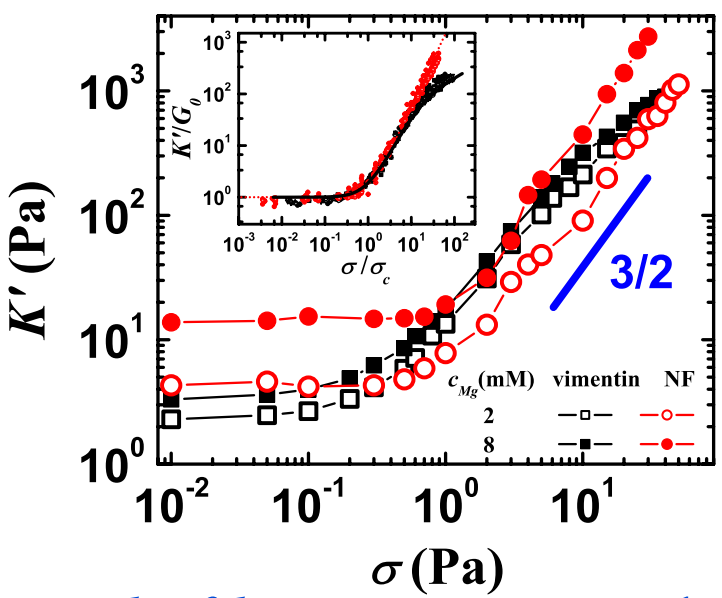
Quantitative *actin Network* elasticity from *single filament* stat. mech.

Gardel, et al., Science (2004) & PRL (2004); Lin, Yao, et al. PRL & Biophys J 2010.

Scaling of Stress Stiffening







Quantitative *actin Network* elasticity from *single filament* stat. mech.

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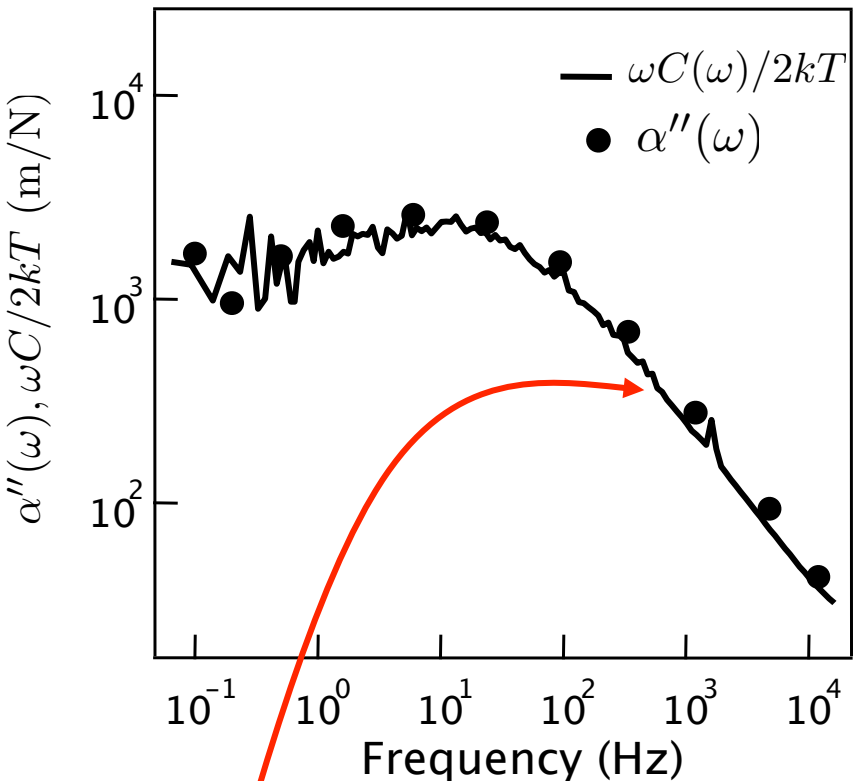
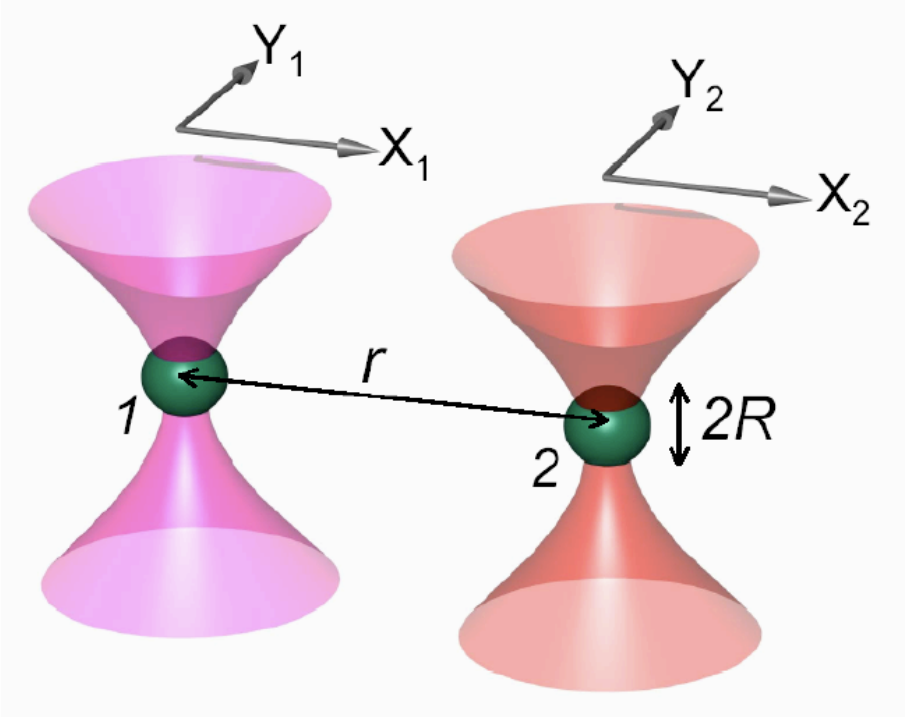
Microrheology and thermal motion

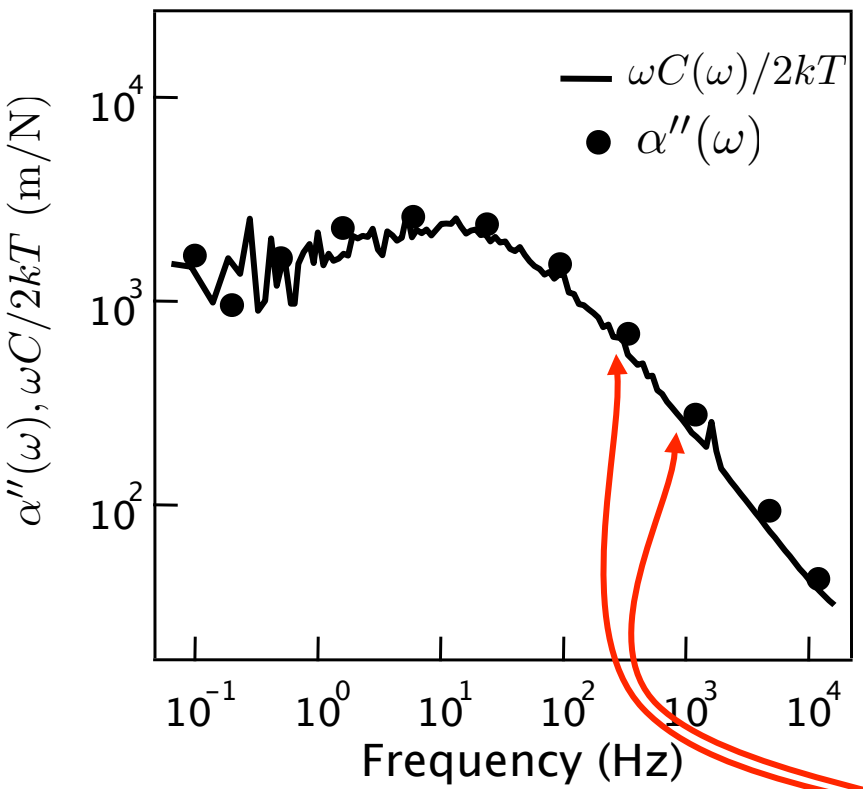


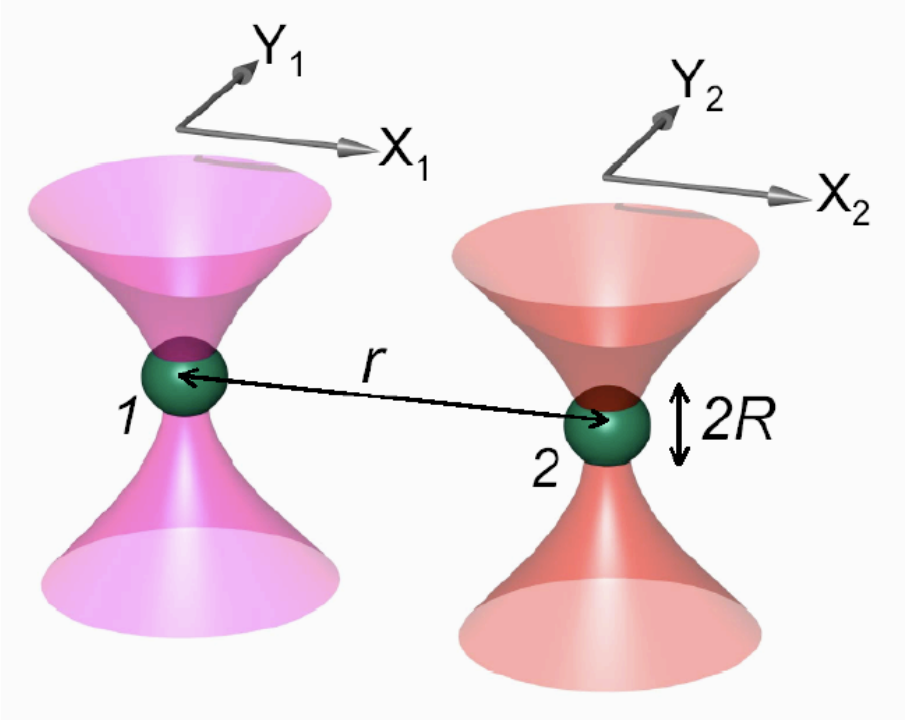


Simultaneous measurement of *passive* fluctuations and *active* response to calib. forces (Mizuno, et al. 2007)

$$C(\omega) = \int \langle x(t)x(0)\rangle e^{i\omega t} dt = \frac{2kT}{\omega}\alpha''(\omega)$$

Microrheology and thermal motion





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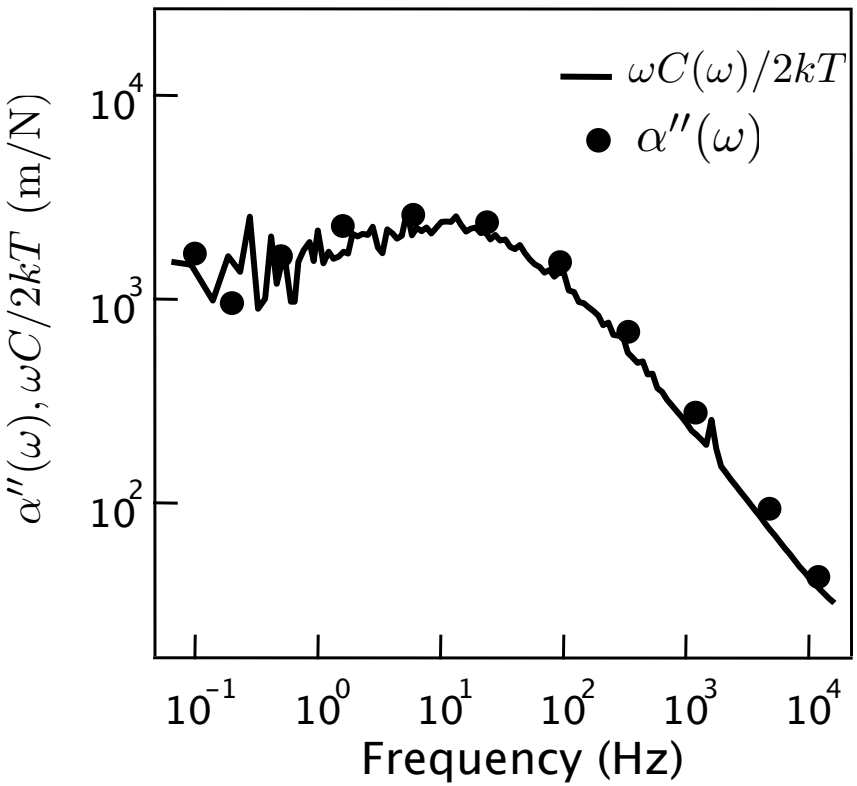
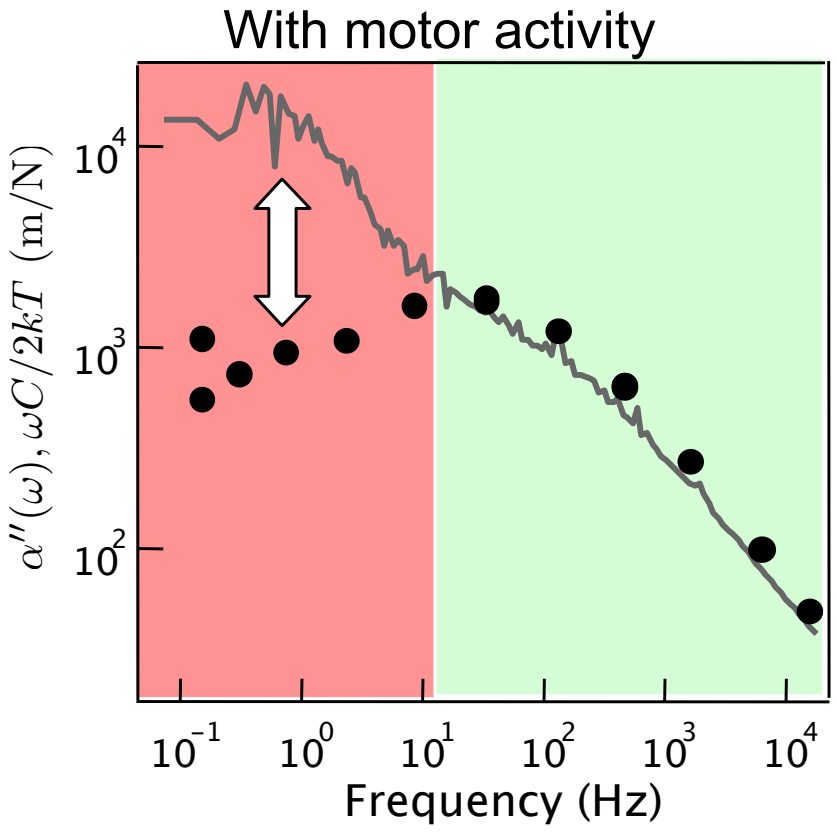
$$C(\omega) = \int \langle x(t)x(0)\rangle e^{i\omega t} dt = \frac{2kT}{\omega}\alpha''(\omega)$$

$$x_\omega = \alpha(\omega) f_\omega$$

Effect of molecular motors: *Active Gels*





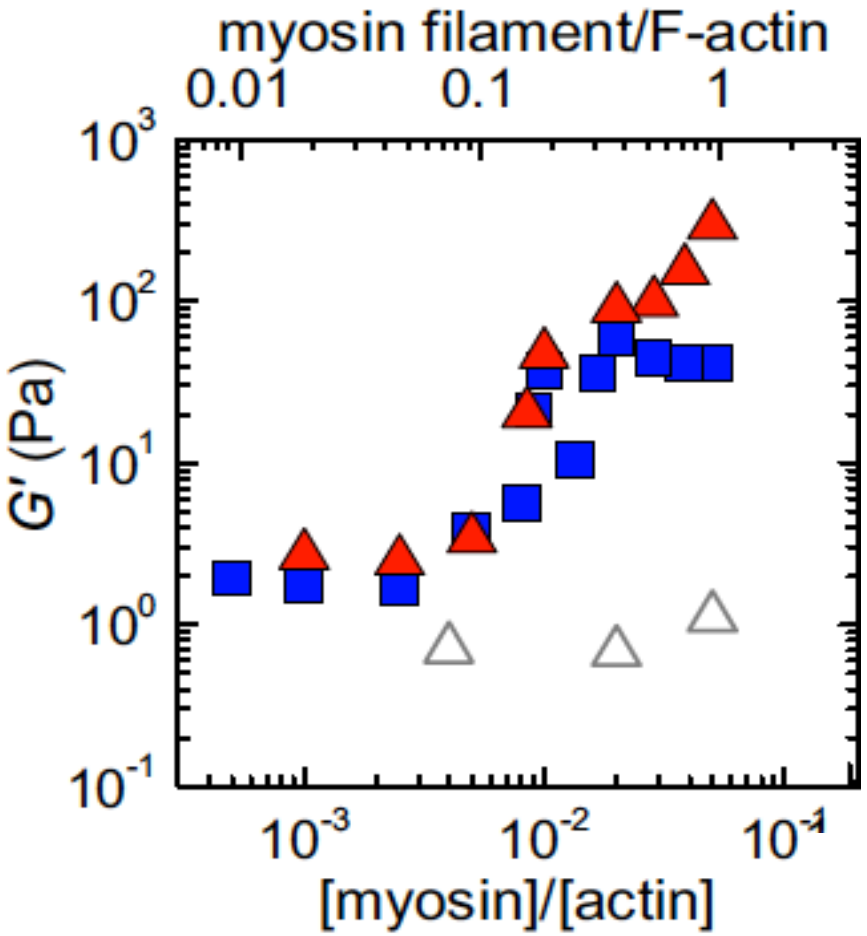
Equilib.

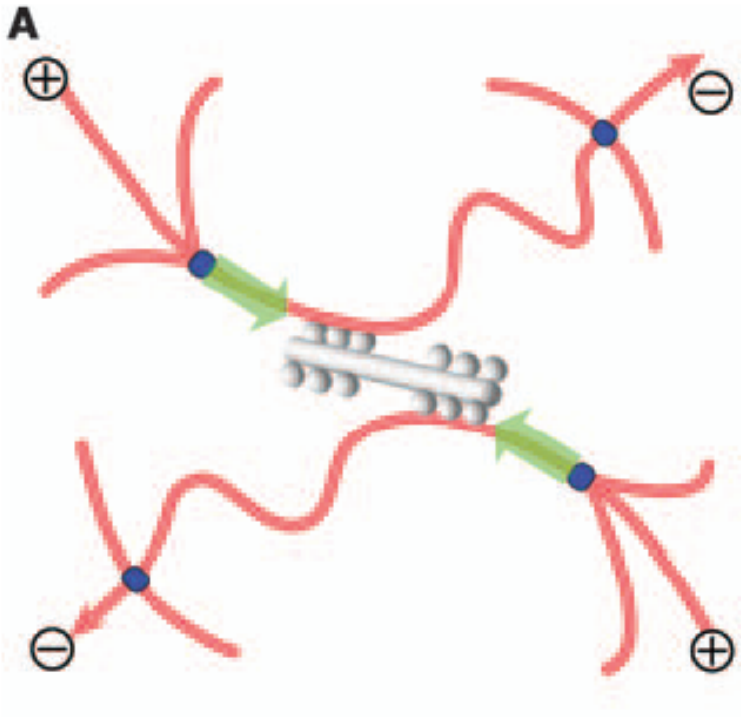
$$C(\omega) = \int \langle x(t)x(0)\rangle e^{i\omega t} dt \neq \frac{2kT}{\omega}\alpha''(\omega)$$

Mizuno, Tardin, Schmidt, FCM, *Science* 2007.

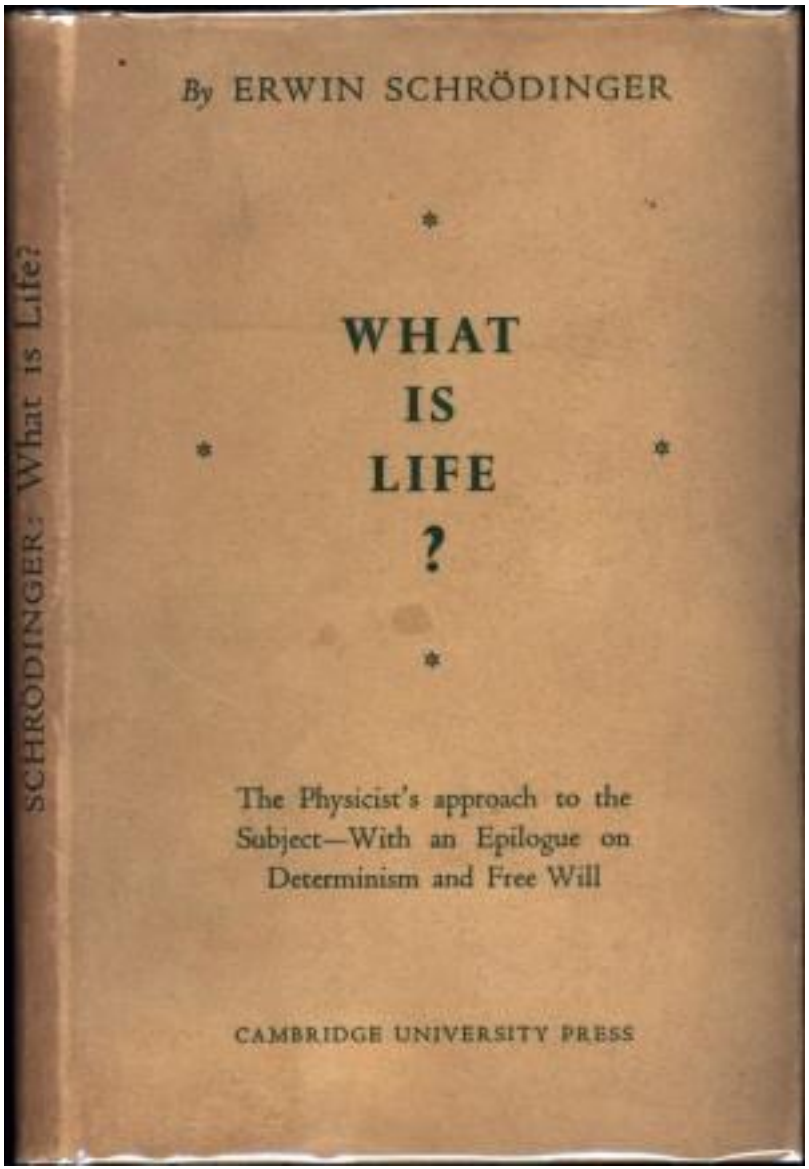
Contractile forces stiffen network

Koenderink et al.,
PNAS, **106**:15192 (2009).





Living systems must evade equilibrium (Schrödinger 1944)



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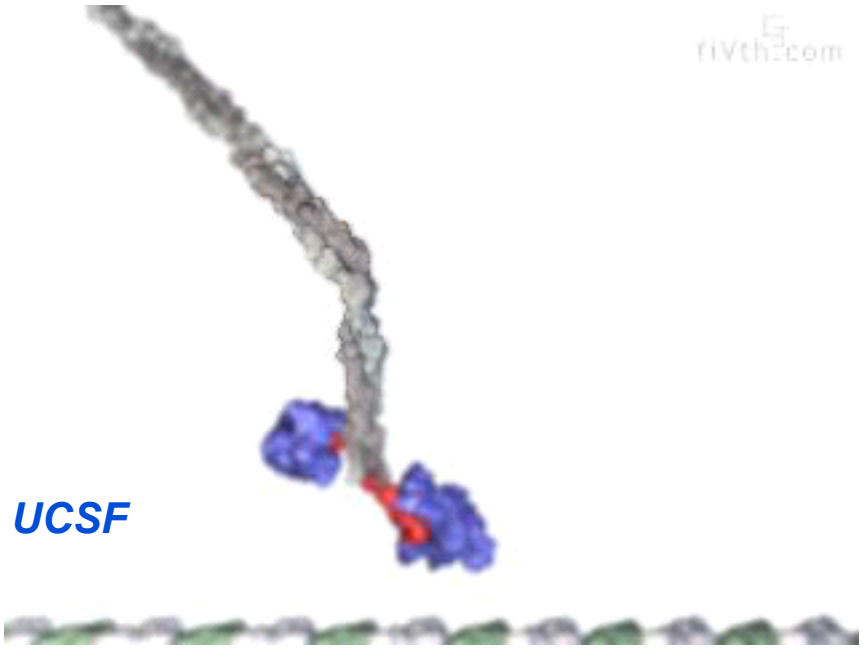
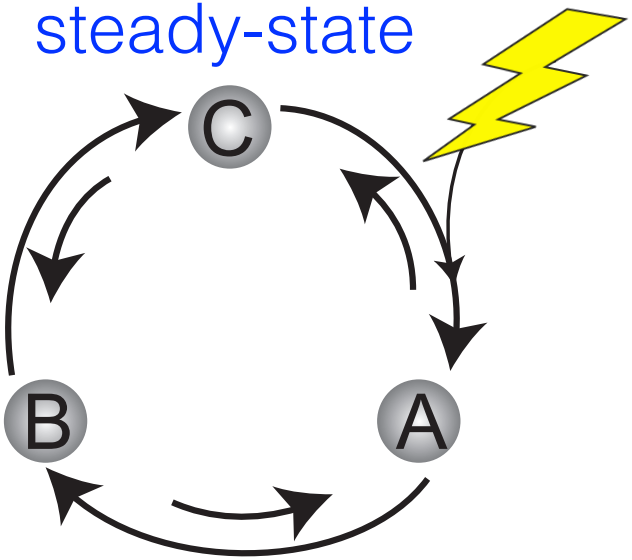


Vale lab, *UCSF*

Non-equilibrium steady-state



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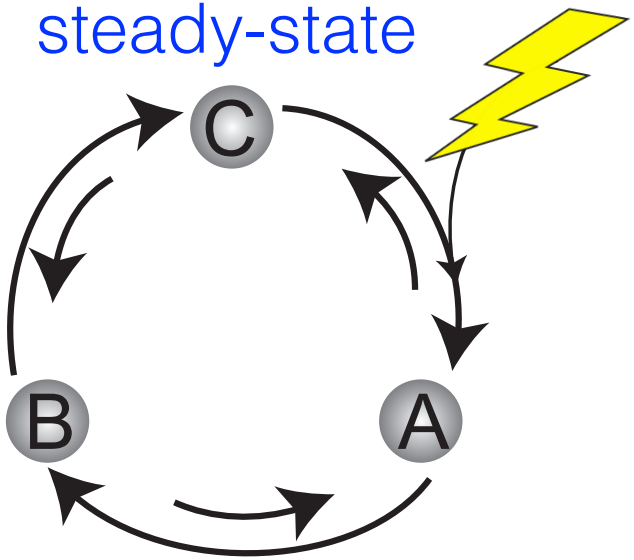
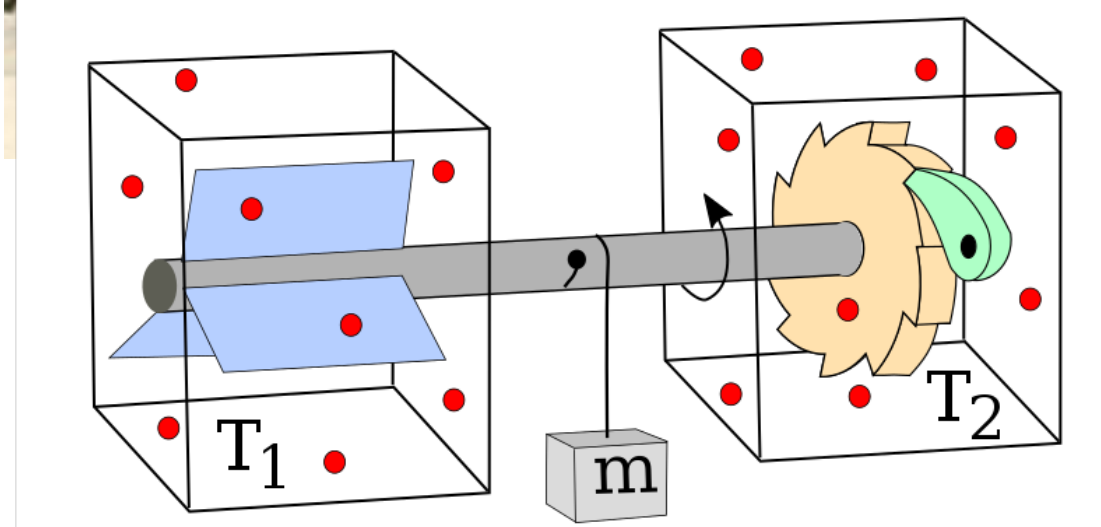
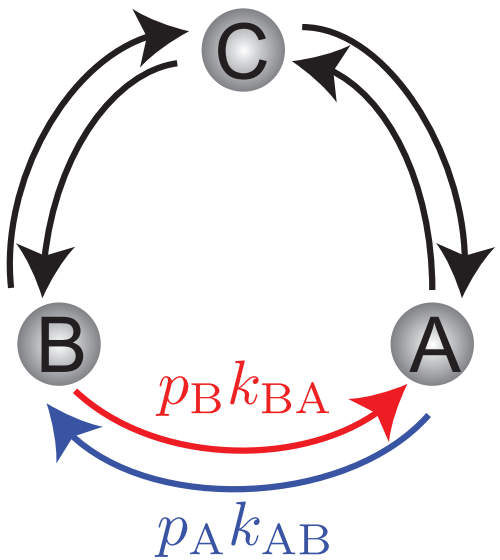




https://en.wikipedia.org/wiki/Brownian_ratchet

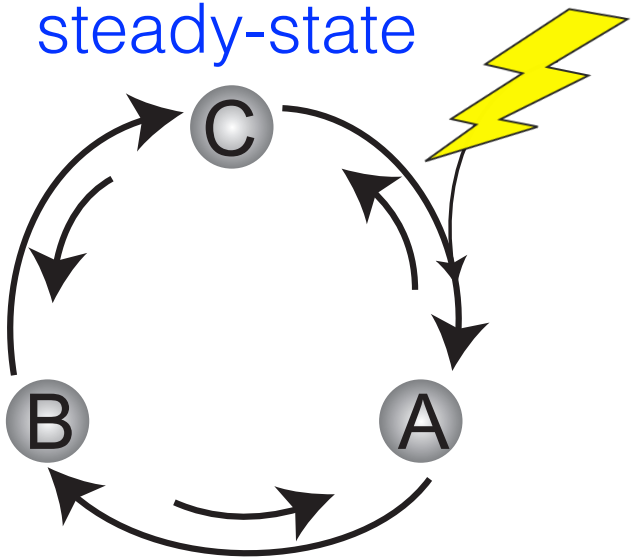
Living systems must evade equilibrium (Schrödinger 1944)

Equilibrium dynamics



Currents J and cycles forbidden in equilibirum

Non-equilibrium steady-state

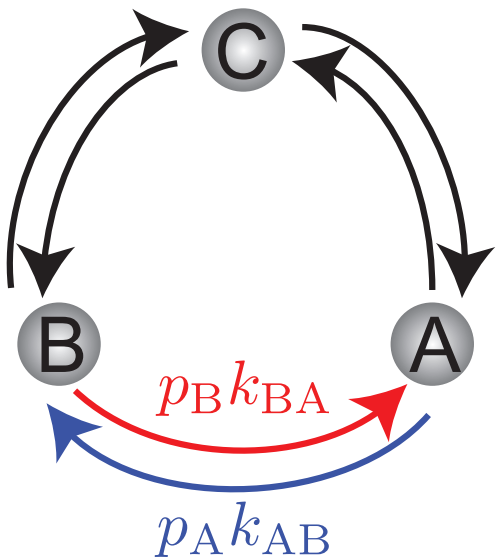


$$J_{\mathrm{AB}} = p_{\mathrm{A}} k_{AB} - p_{\mathrm{B}} k_{BA}$$

Boltzmann, Maxwell, Einstein …
Wegscheider, Onsager…

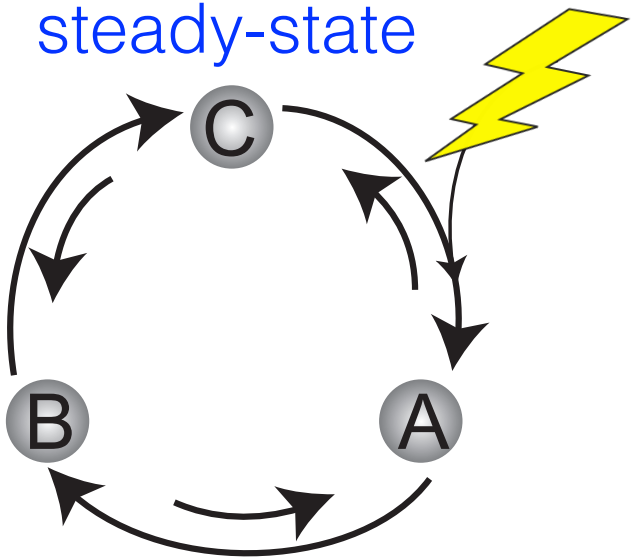
Living systems must evade equilibrium (Schrödinger 1944)

Equilibrium dynamics



Currents *J* and cycles forbidden in equilibirum

Non-equilibrium steady-state

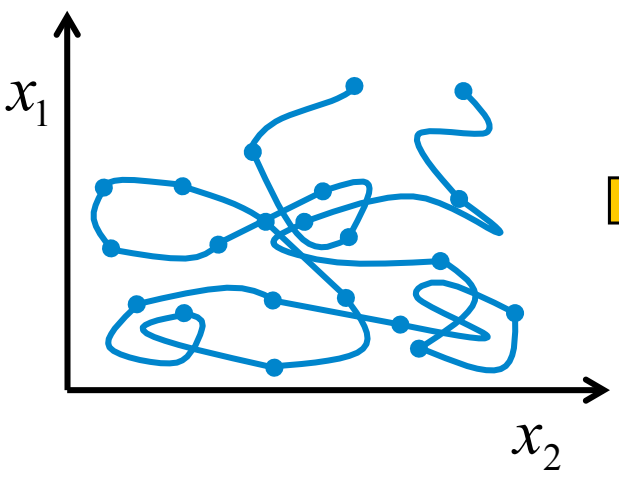


$$\frac{\partial}{\partial t}\rho = -\nabla \cdot J = 0$$

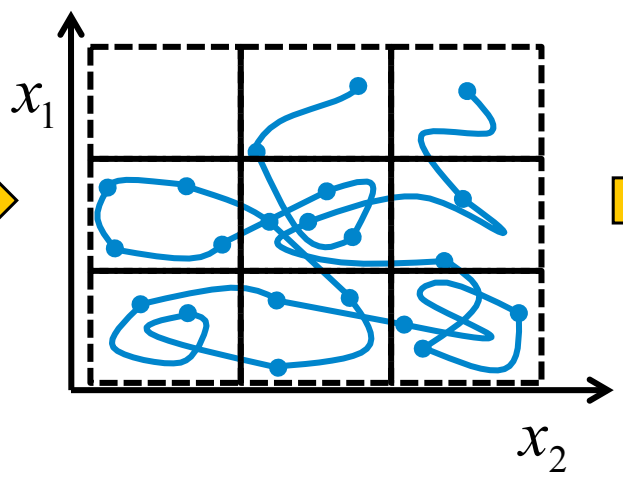
Boltzmann, Maxwell, Einstein …
Wegscheider, Onsager…

Can we see Broken Detailed Balance at macro-/meso-scale?

Trajectories in continous configurational phase space

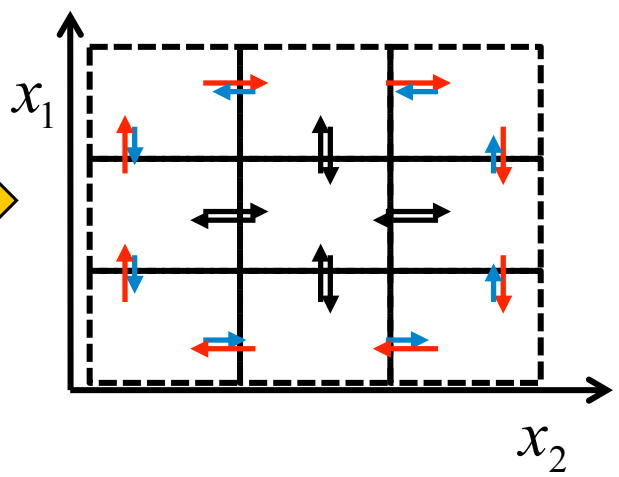


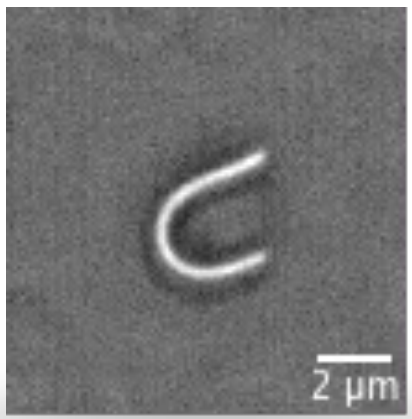
Coarse grain phase space



Probability fluxes

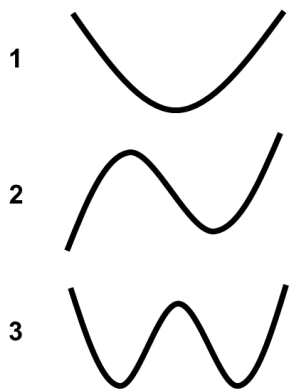
$$J_{\mathrm{AB}} = p_{\mathrm{A}} k_{AB} - p_{\mathrm{B}} k_{BA}$$





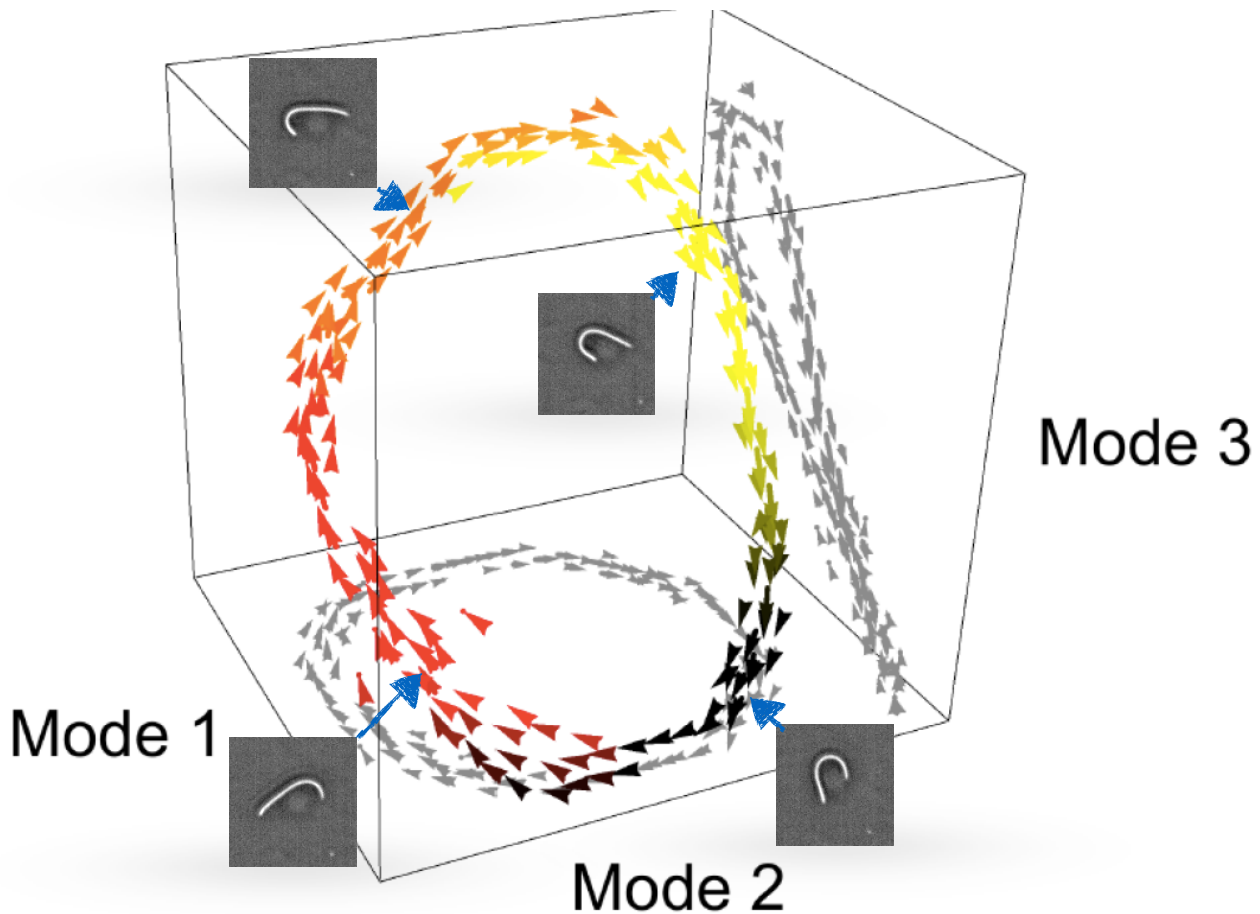
Chlamydomonas flagellum

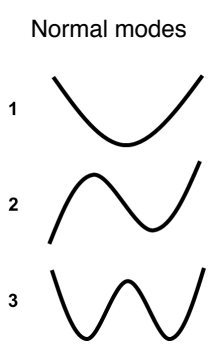
Normal modes



Battle, Broedersz, Fakhri, Geyer, Howard, Schmidt, FCM, *Science* 2016.

Projected current/flux in configurational phase space





See also:

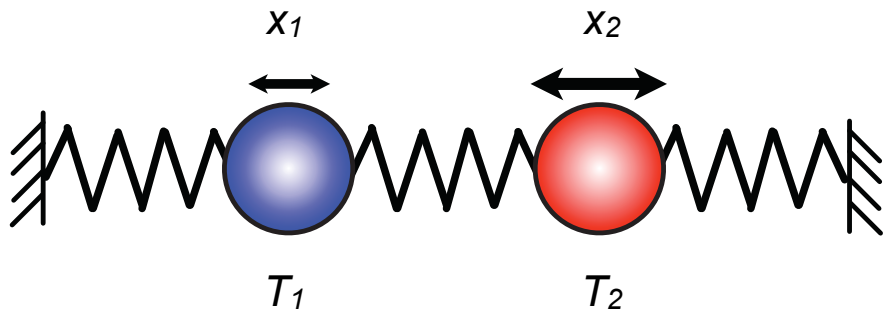
Ma, Klindt, Riedel-Kruse, Jülicher, and Friedrich, PRL **113**, 048101 (2014)
Geyer, Jülicher, Howard, and Friedrich PNAS, 110 (45), 18058(6) (2013)

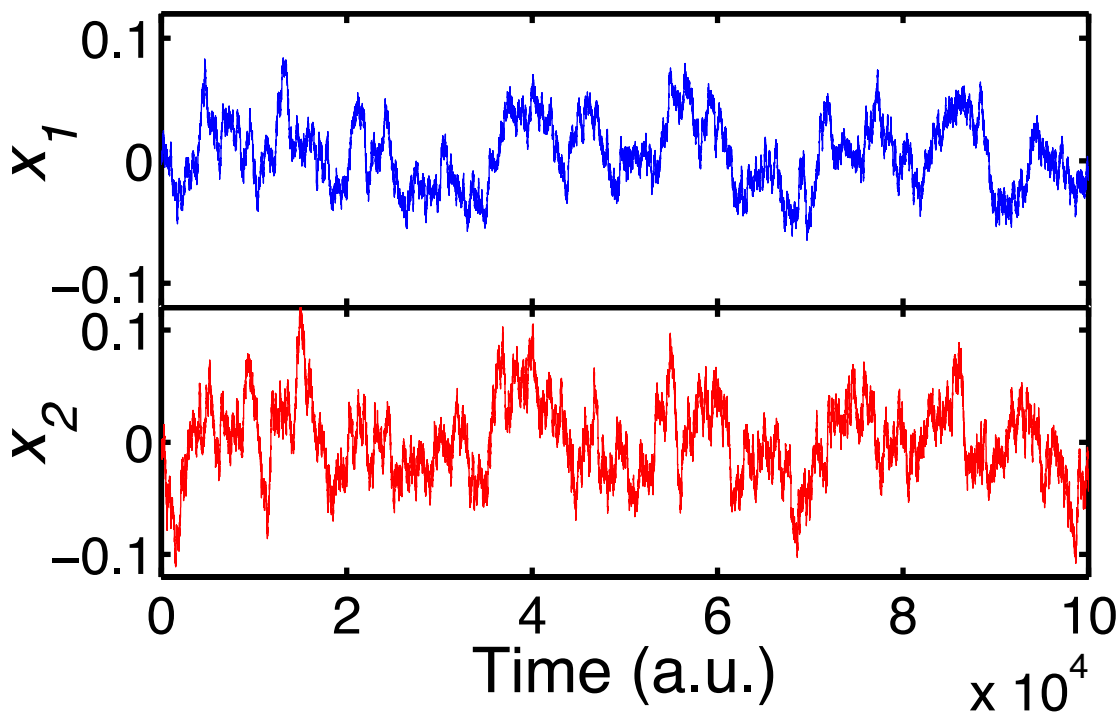
Coupled beads: A toy model

$$\frac{\mathrm{d}x_1}{\mathrm{d}t}(t) = k(x_2(t) - 2x_1(t)) + \sqrt{T_1}\xi_1(t)$$

$$\frac{\mathrm{d}x_2}{\mathrm{d}t}(t) = k(x_1(t) - 2x_2(t)) + \sqrt{T_2}\xi_2(t)$$

$$\langle \xi_i(t) \rangle = 0 \qquad \langle \xi_i(t')\xi_j(t) \rangle = 2\delta_{i,j}\delta(t - t')$$





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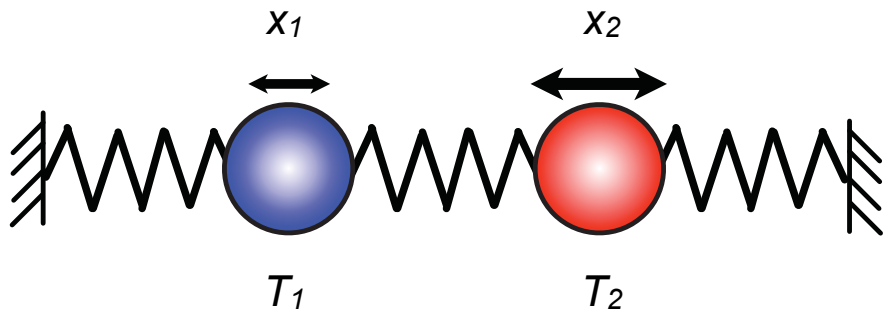
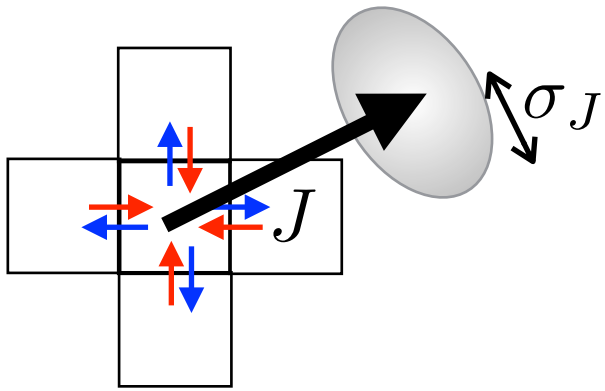
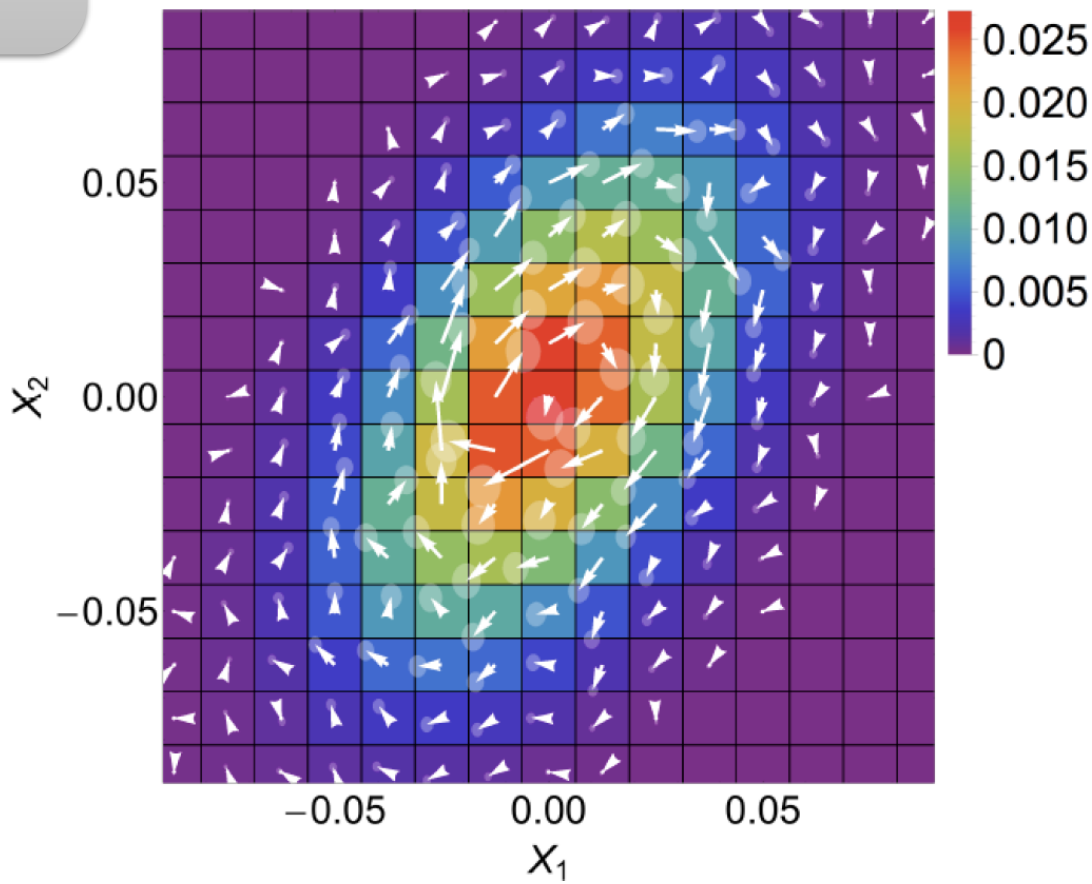
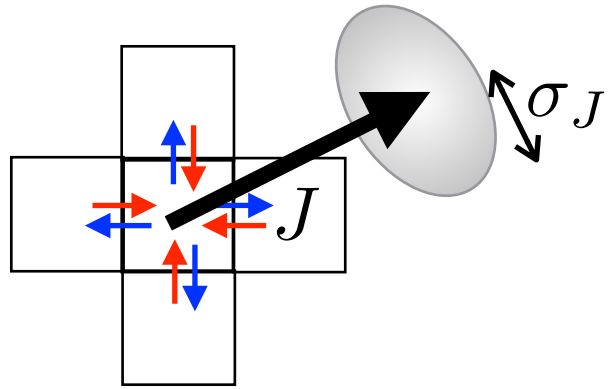


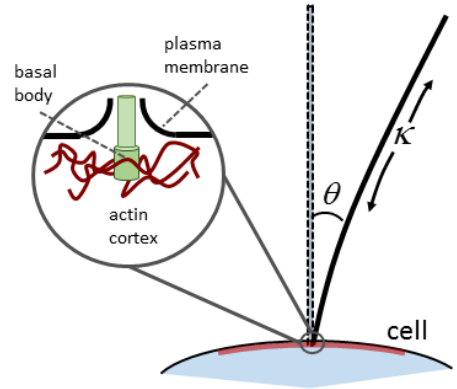


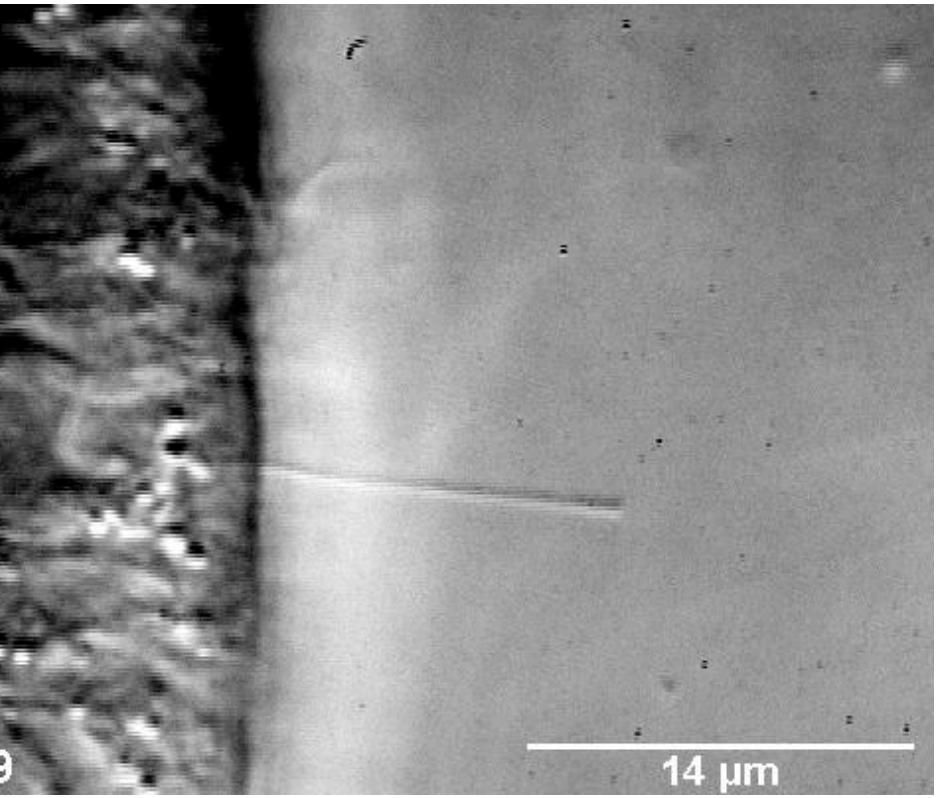


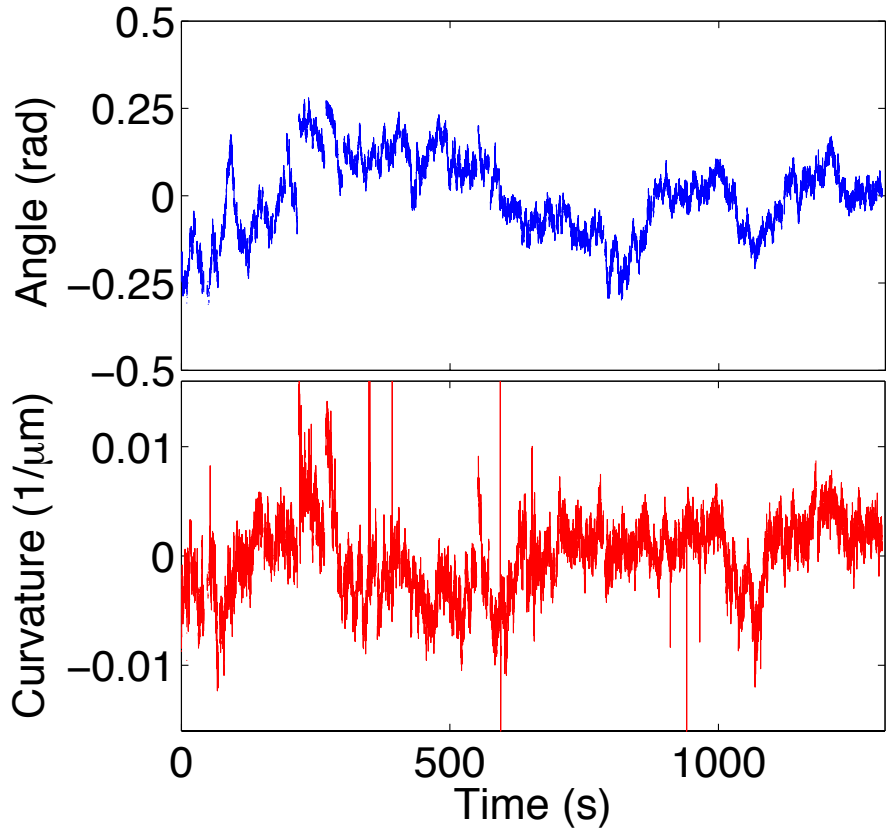
see also: Grosberg & Joanny 2015.

What drives the dynamics of the primary cilium?



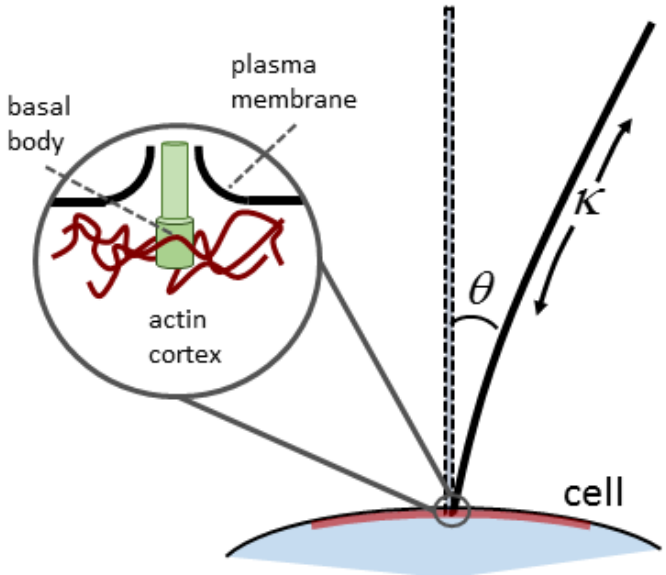


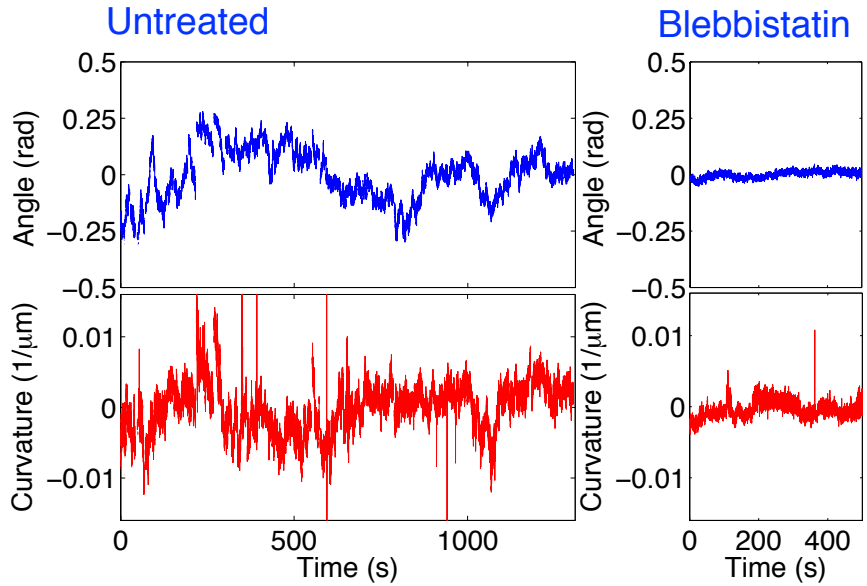




Chris Battle (University of Göttingen)

What drives the dynamics of the primary cilium?





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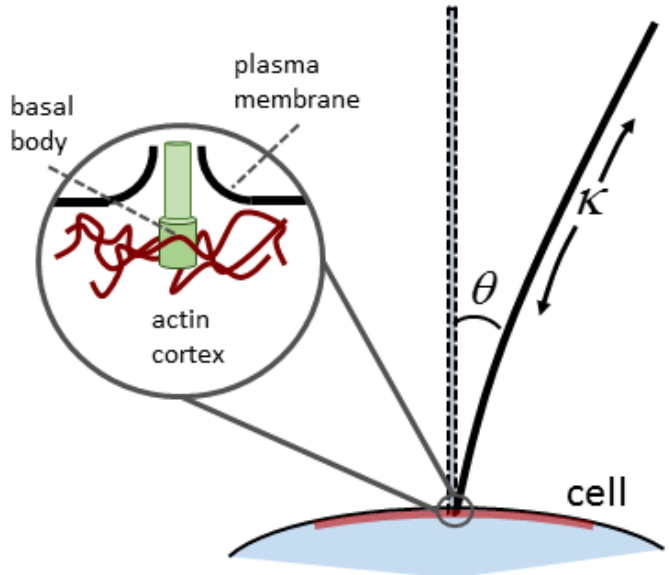
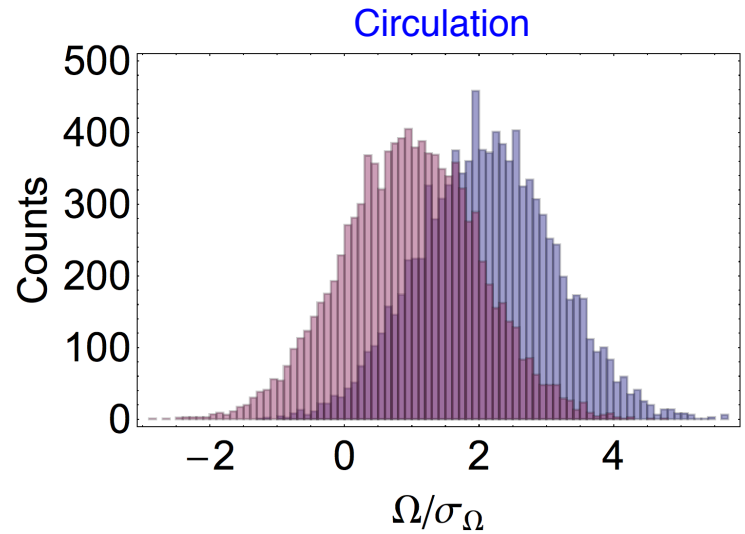
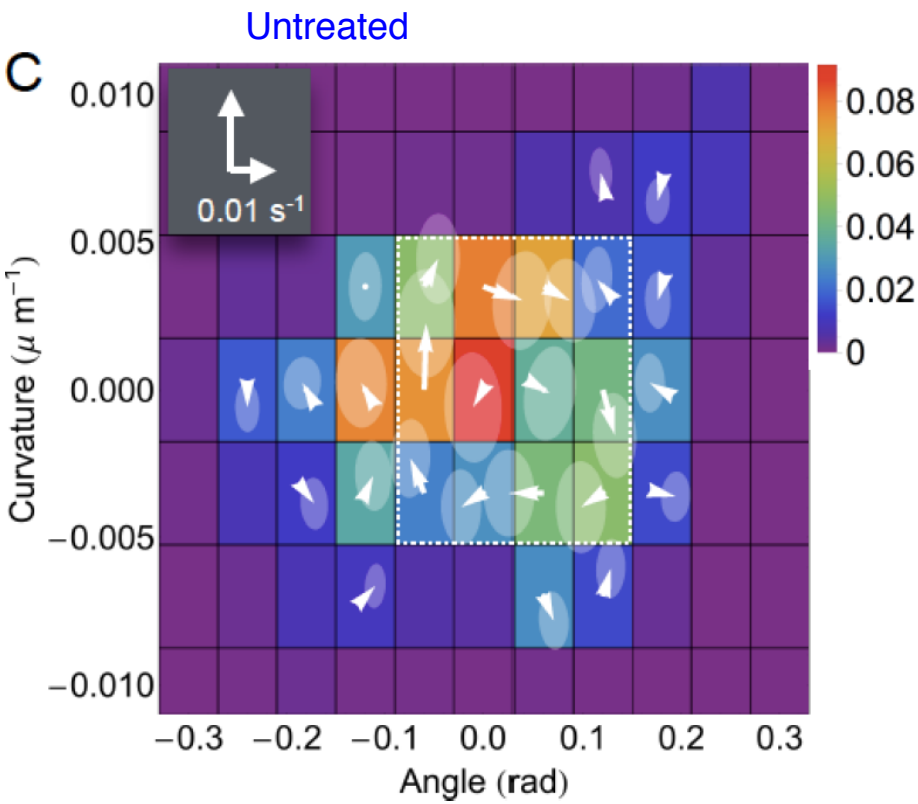
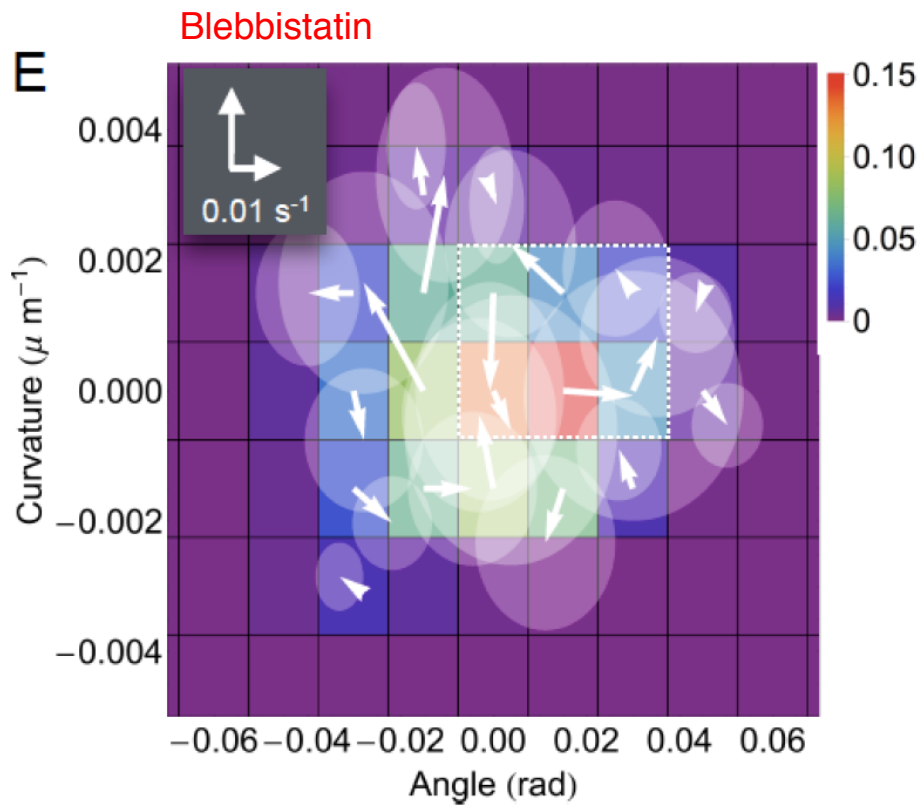
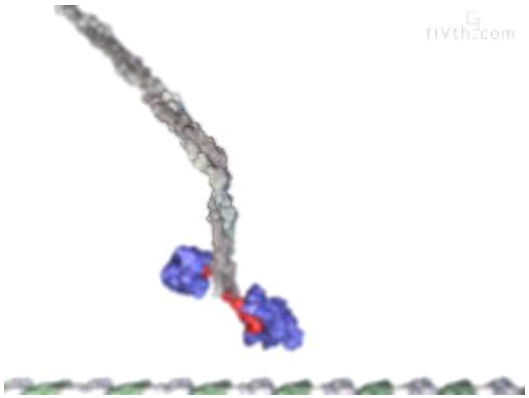






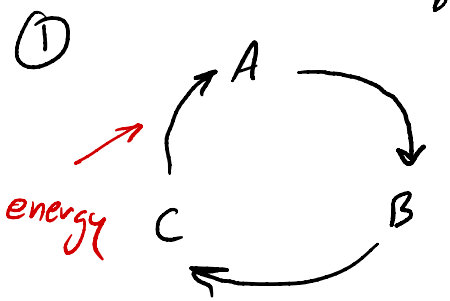


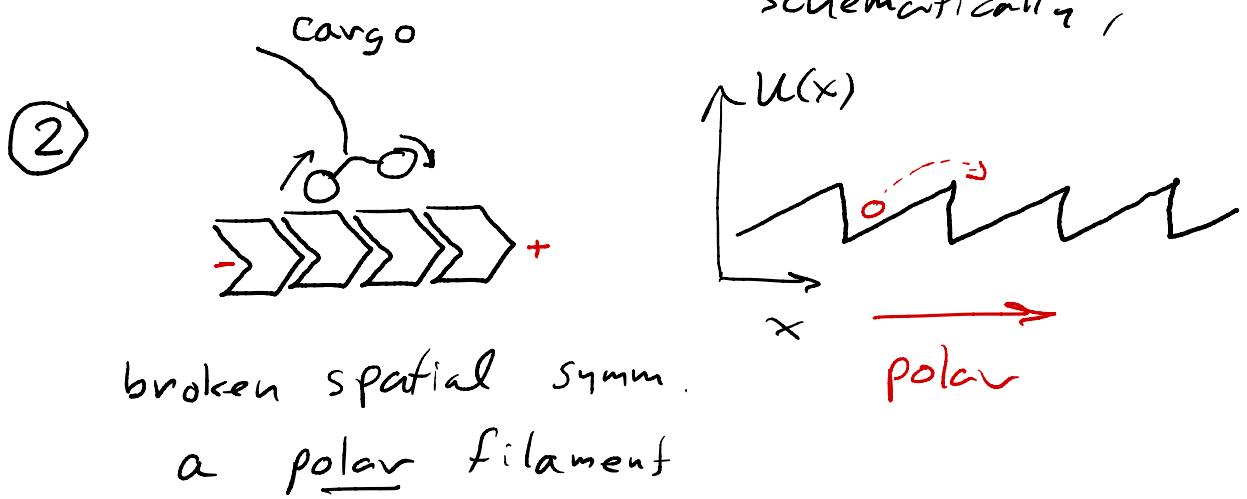
Molecular motors: minimal ingredients



Vale lab, *UCSF*

Broken Detailed Balance, or broken t-reversal symm.





see,
Magnasco, PRL 71: 1477 (1993); Prost et al. PRL 72: 2652 (1994).

All known motors operate on polar substrates

**Note that actin and microtubules are both polar,
which is essential for *myosin* and kinesis/dynein function.**

**There are no known motors on *intermediate filaments*
or *septin filaments*, which are apolar.**

But, there is evidence for contractility without acto-myosin:

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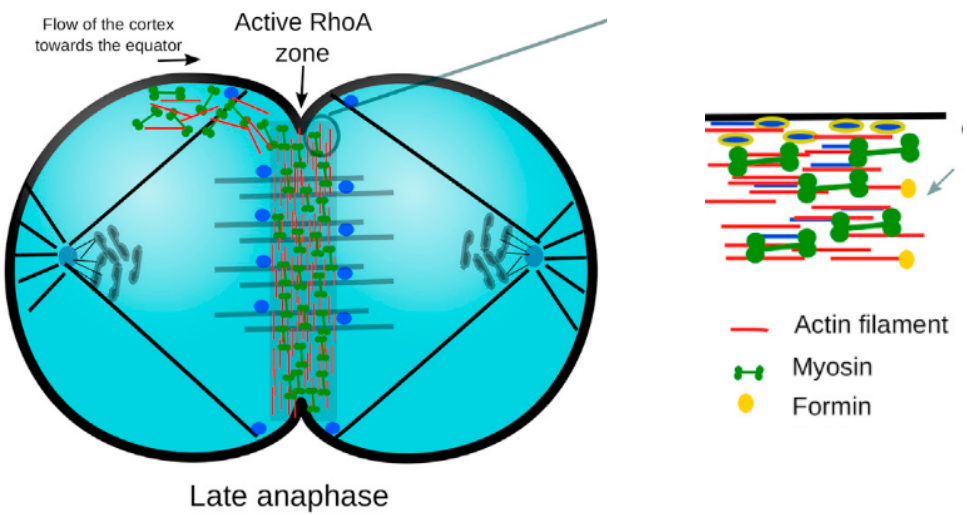

Schwayer, C. et. al. *Developmental Cell* (2016)

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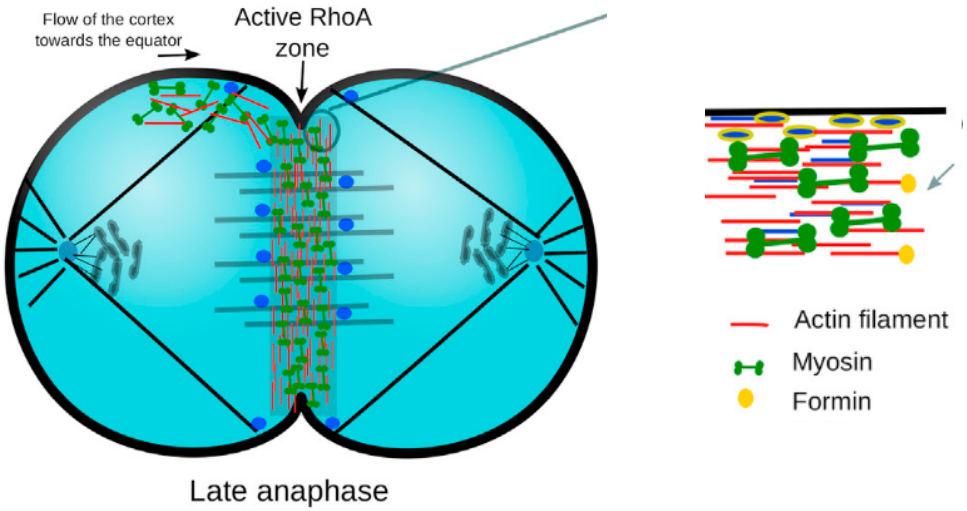

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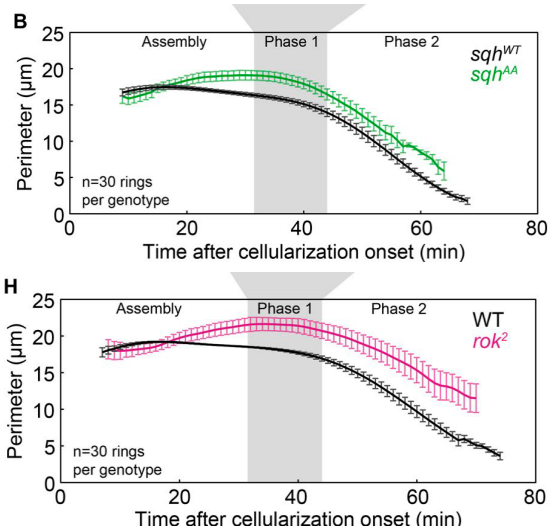
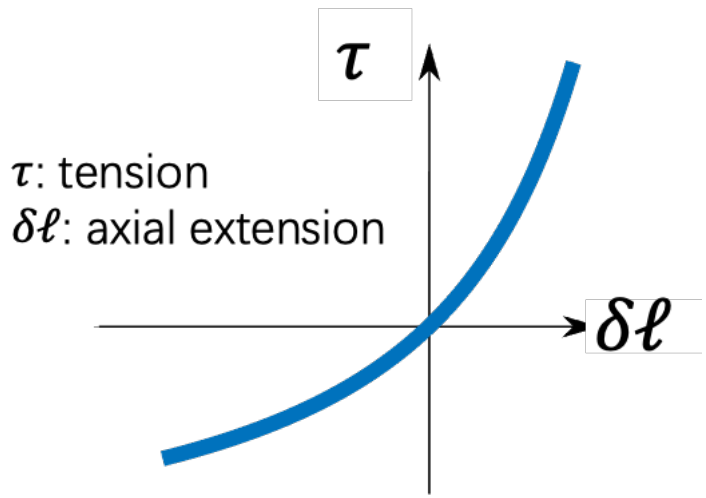


Xue, Z., & Sokac, A. M., *J Cell Biol* (2016)

Black: With Motor Activity
Red/green: Without Motor Activity

Another broken symmetry: force-extension

The nonlinear force-extension is asymmetric under extension/compression:



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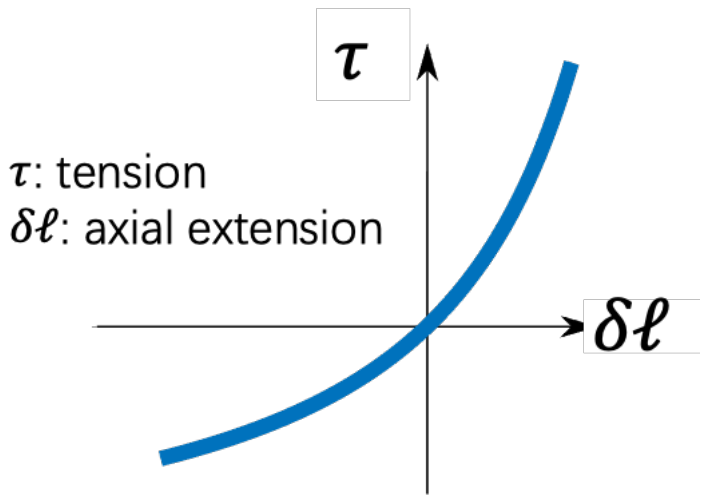

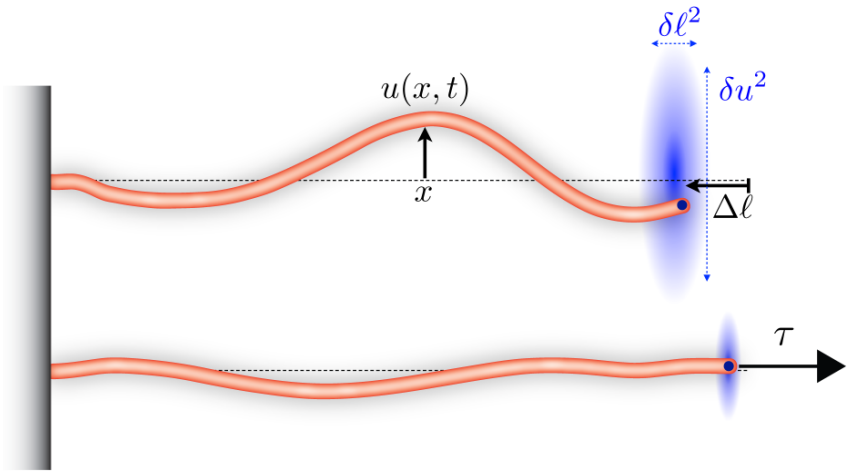

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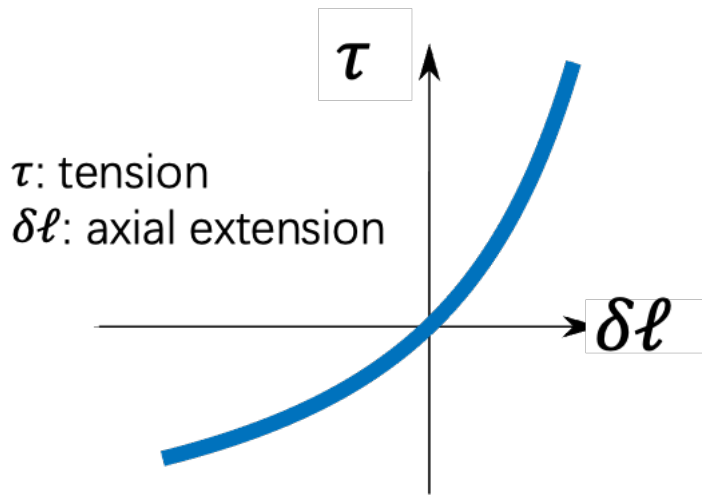

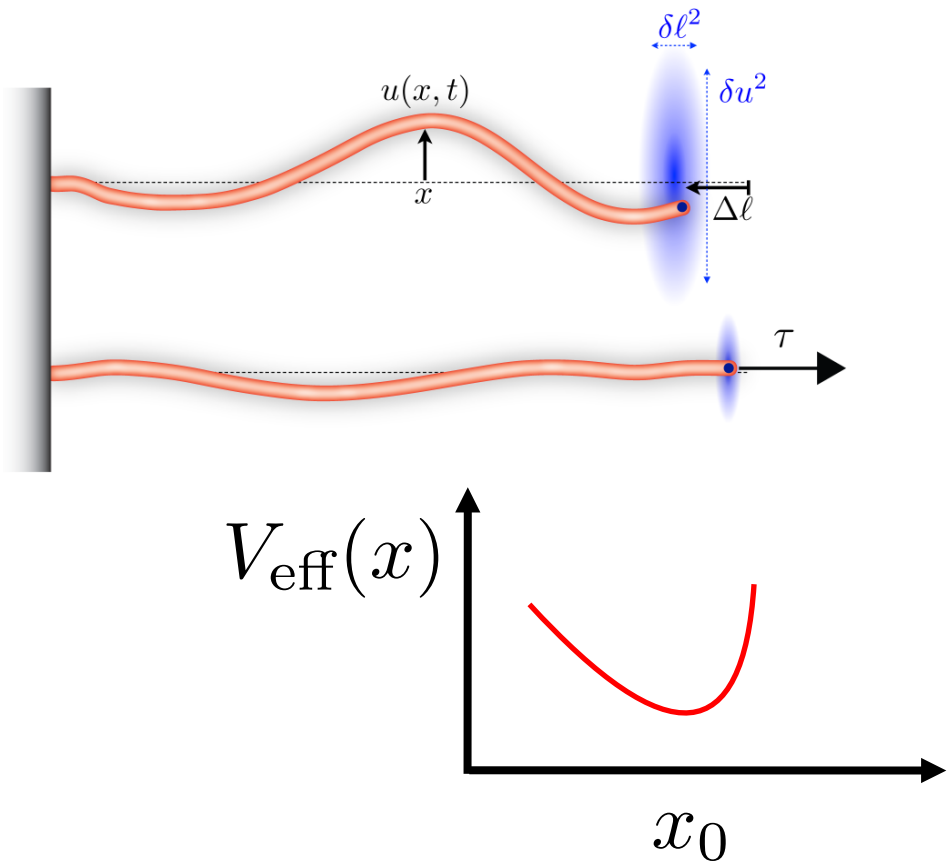

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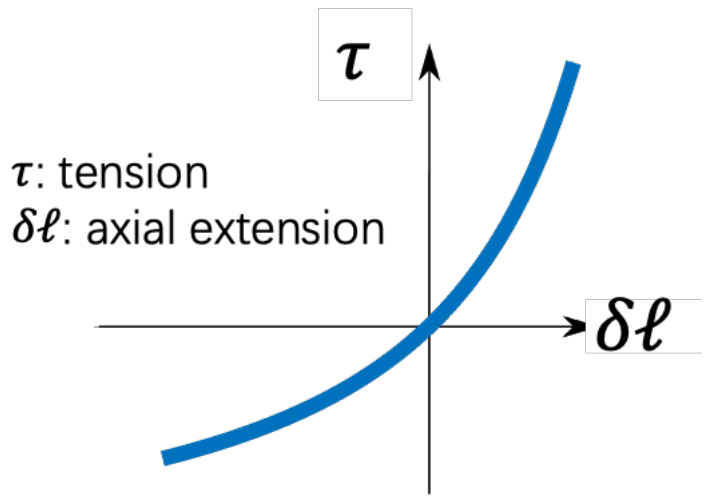

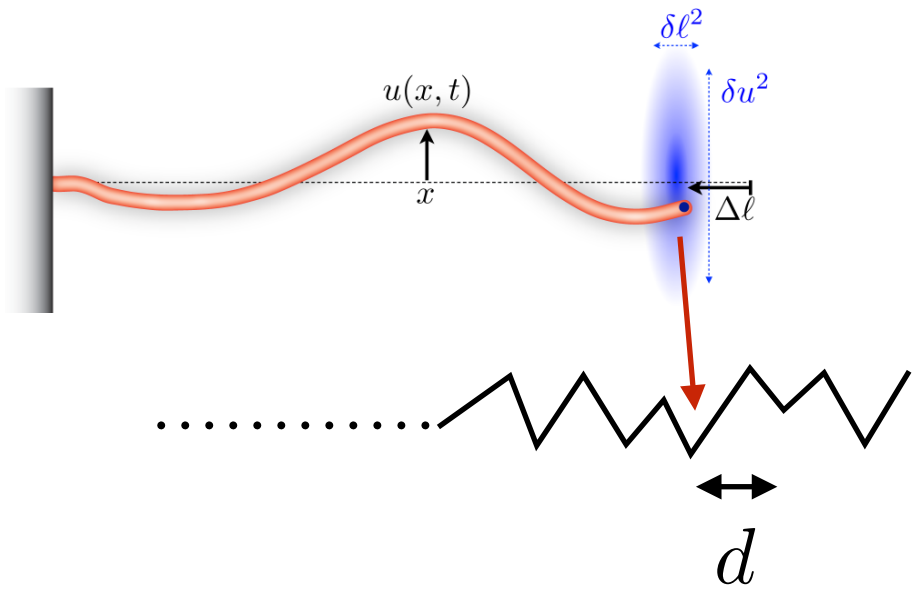

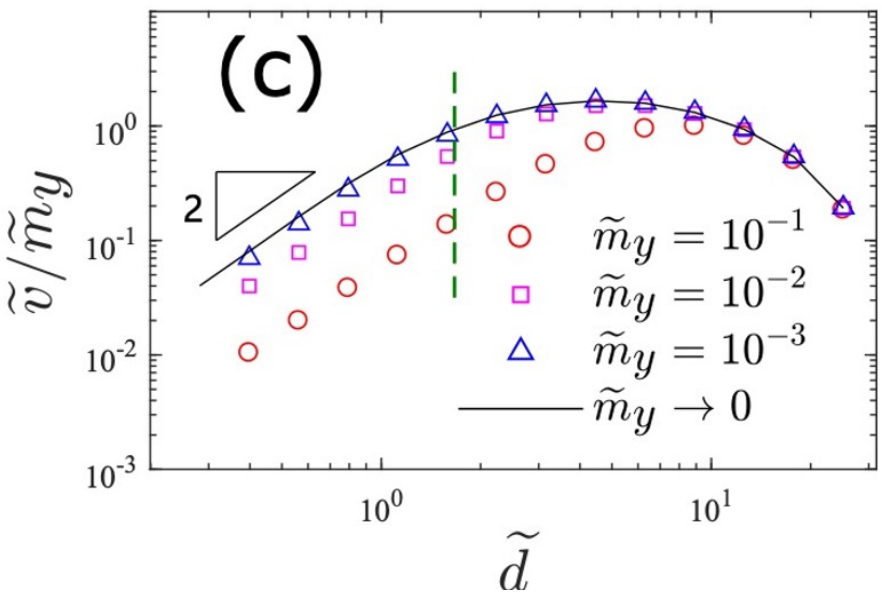

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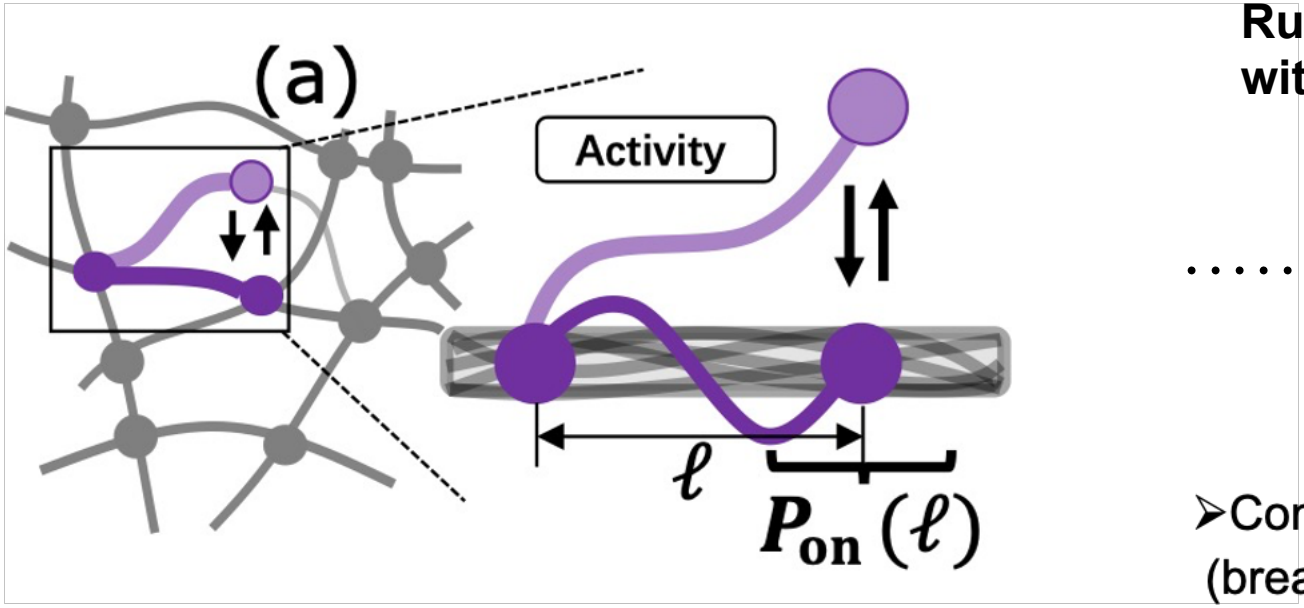
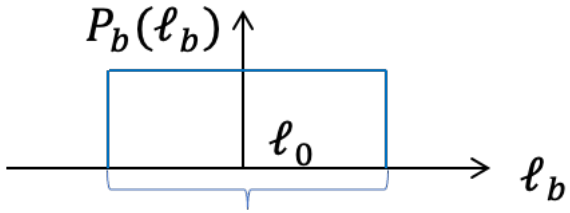
Minimal Model



Rugged binding landscape with typical spacing *d*

➢Constant Transition Rates ω_{on}, ω_{off} (breaking detailed balance)

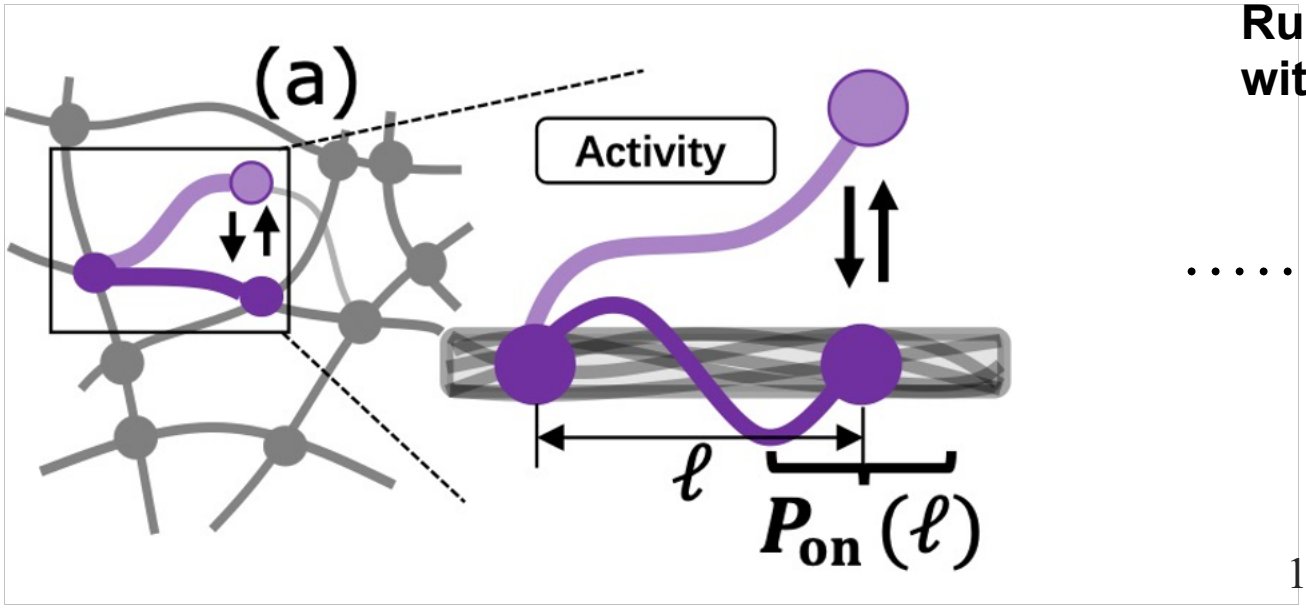
➢Two States: On and Off
➢Active Crosslinkers (Not Motors)
➢$\tau(\ell)$: Asymmetric force-extension
➢$P_{on}(\ell)$: Steady State Distribution in On state



P_b: symmetric or asymmetric
ℓ_0: rest length

Chen, Markovich & FCM *PRL* 125: 208101 (2020).

Minimal Model



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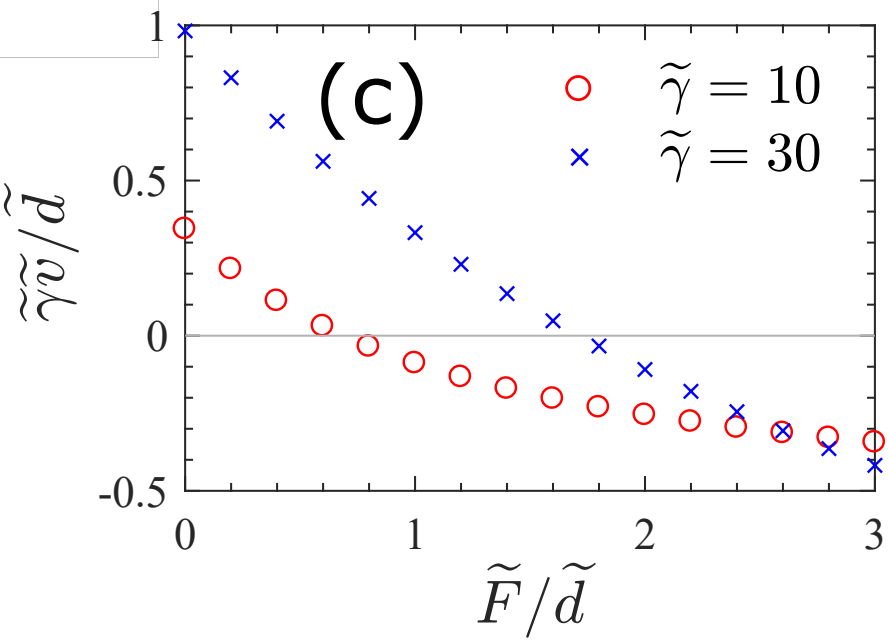

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Active fluctuations, Broken Detailed Balance & Contractile Forces

- Interest in synthetic active solids inspired by cytoskeleton
- We propose a non-motor mechanism for contractile force generation
- Also, very interesting critical/phase transition phenomena governed by contractility
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Reviews:
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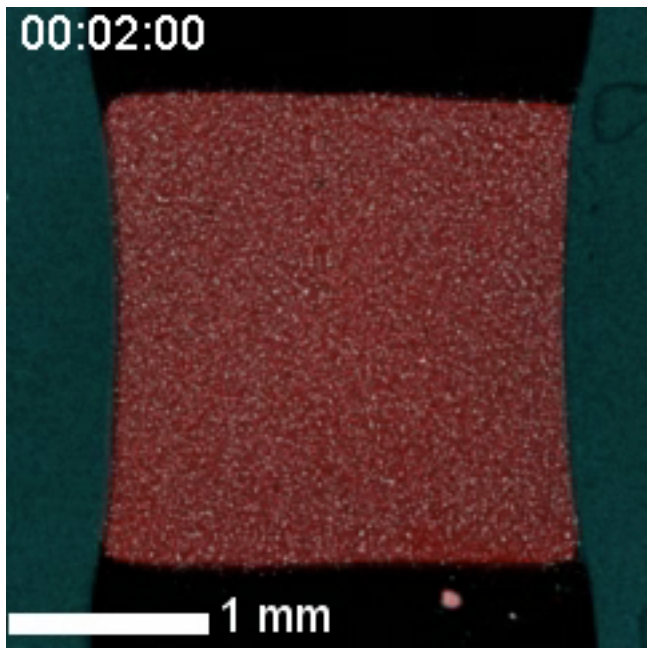

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