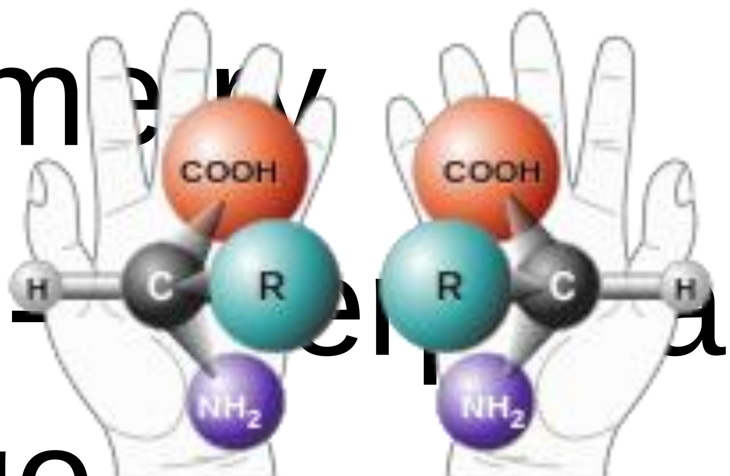
Active torque generation in a disordered actomyosin network

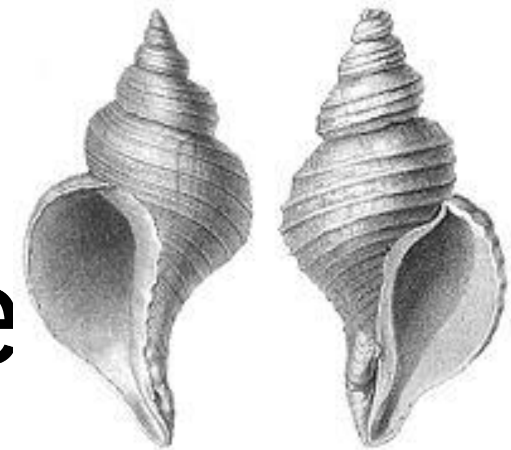
Outline

- Chiral/Left-right symmetry breaking in organisms
- Cellular scale - Actomyosin cortex
- Experiment: Chiral flows in the cell cortex during embryogenesis
- Active torque generation in a disordered actomyosin network
- - single, pair and multiple filaments
- Twist-stretch coupling in a chiral filament
- Microtubule self-organization – pair to bundle formation

Chirality

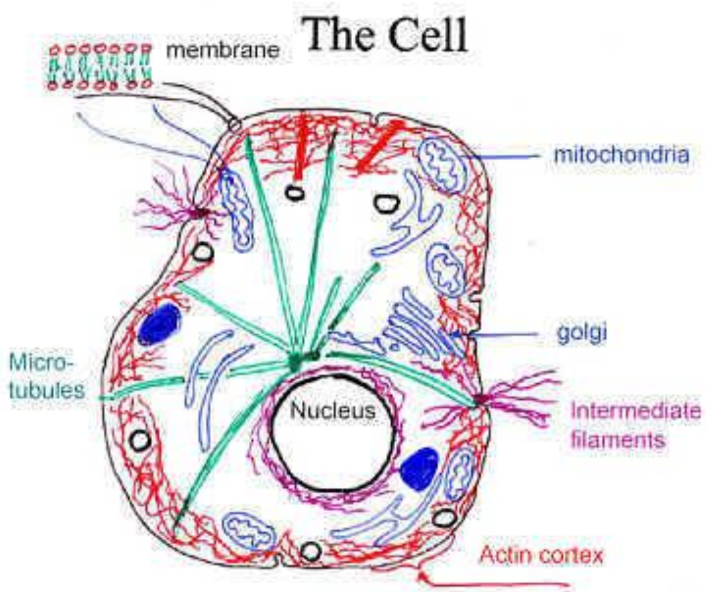
- Absence of left-right symmetry
- Non-superimposable image

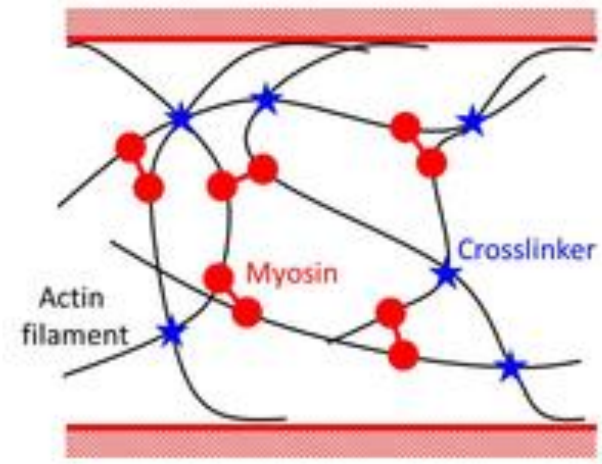




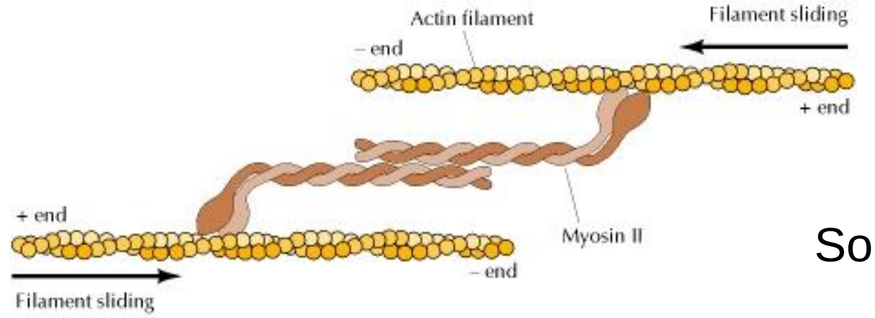
Courtesy: Wikipedia

Cell cortex - Actomyosin network





Lee, Pruessner, PRE (2016)



Source: Google images

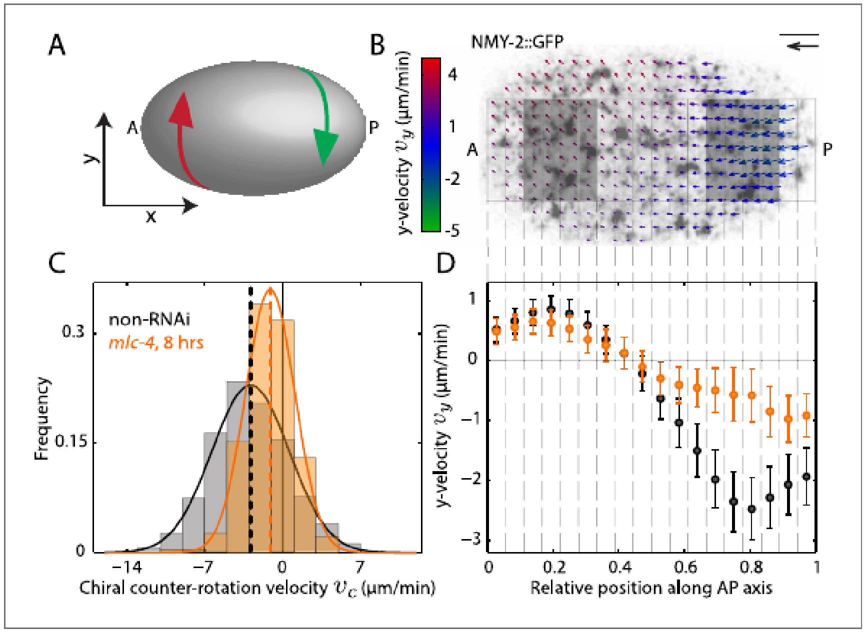
- Network of actin filaments, myosin motors and crosslinkers
- Controls cell shape, key in cell migration, embryogenesis
- Myosin motors provide both sliding and twisting forces on the filaments

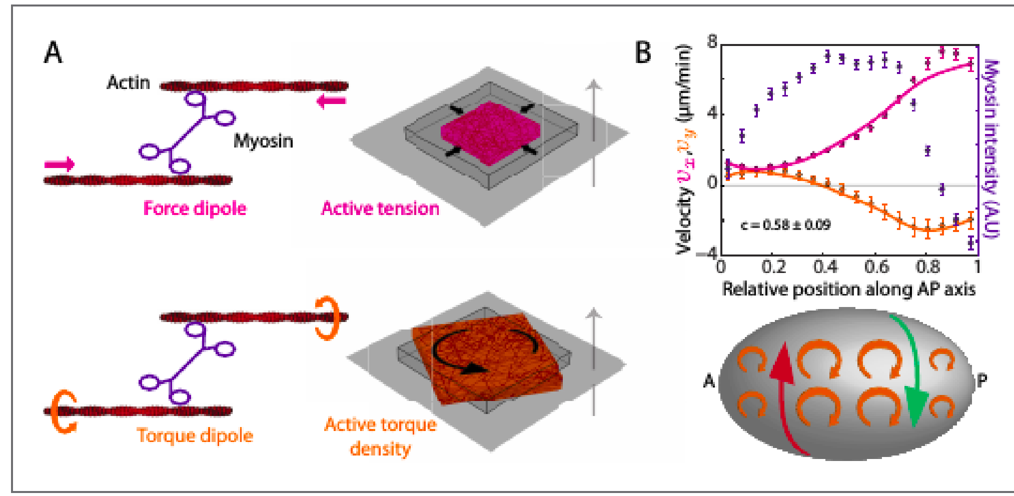
Chiral flow – single cell *C. elegans* embryo

- Counter-rotating flows during Anterior-Posterior (AP) polarization, breaks chiral symmetry
- Inhibition of myosin activity (RNAi), reduces both AP and chiral flow velocity

Naganathan et al. eLife 2014;3:e04165

Chiral flows in the actomyosin cortex during embryogenesis





- Cortical flow: at the cellular scale, large scale hydrodynamic flow. Driven by actomyosin
- contractility. Myosin activity dependent.

- Flow primarily along anterior-posterior (AP) axis.

- Chiral flow: orthogonal to AP flow. Counter-rotating in the AP half.
- Myosin activity dependent

Naganathan et al. eLife 2014;3:e04165

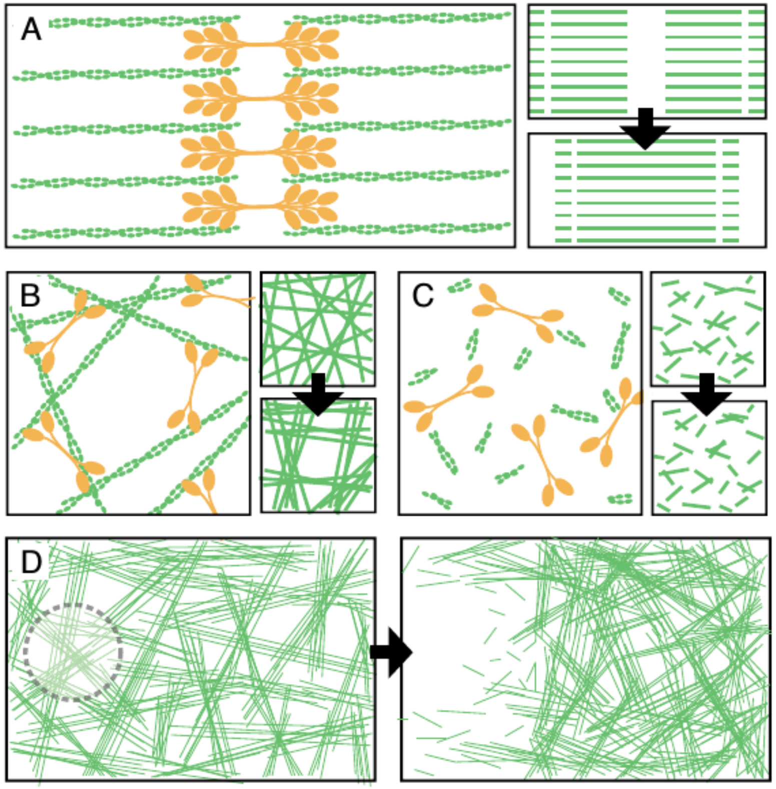
Disordered actomyosin mesh – contractile

- Ordered network (eg., Sarcomere) known
- mechanism of contraction

- Disordered networks are largely contractile
- as well

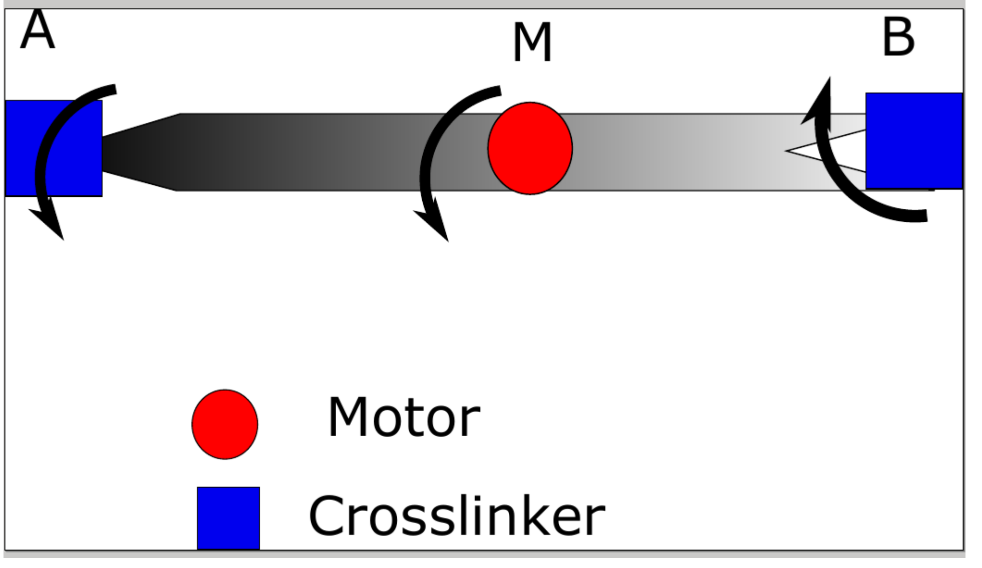
- Microscopic origins of symmetry breaking
- between contractile and extensile stress:
- M. Lenz, Phys. Rev. X (2014)

- Point motor - position dependent stall-force, finite-size motor (motion towards barbed-end), buckling of filaments



Cowan, Hyman (2007)

Single filament mechanics - I



From torque balance condition: $$\tau_0 = \tau_A + \tau_B$$

Torque - Twist angle $$\tau_0 = GJ\frac{d\theta(x)}{dx}$$

From the continuity of the twist angle, and clamped boundary conditions :

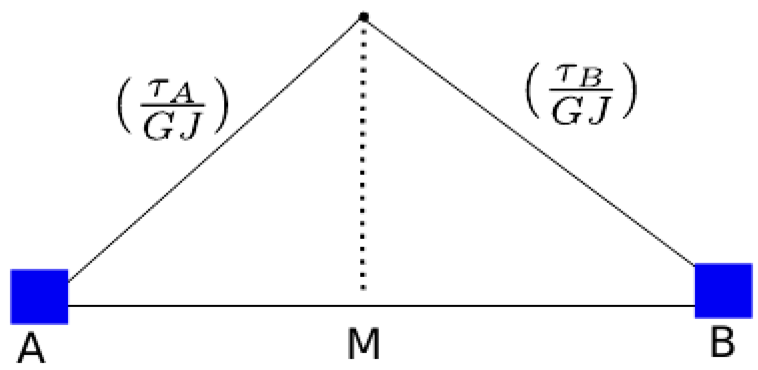
$$\tau_A = \tau_0 \frac{L_{MB}}{L}$$

$$\tau_B = \tau_0 \frac{L_{AM}}{L}.$$

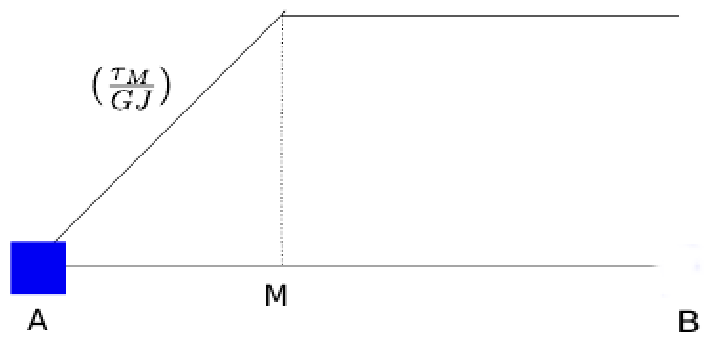
Single filament mechanics - II

Twist angle profiles

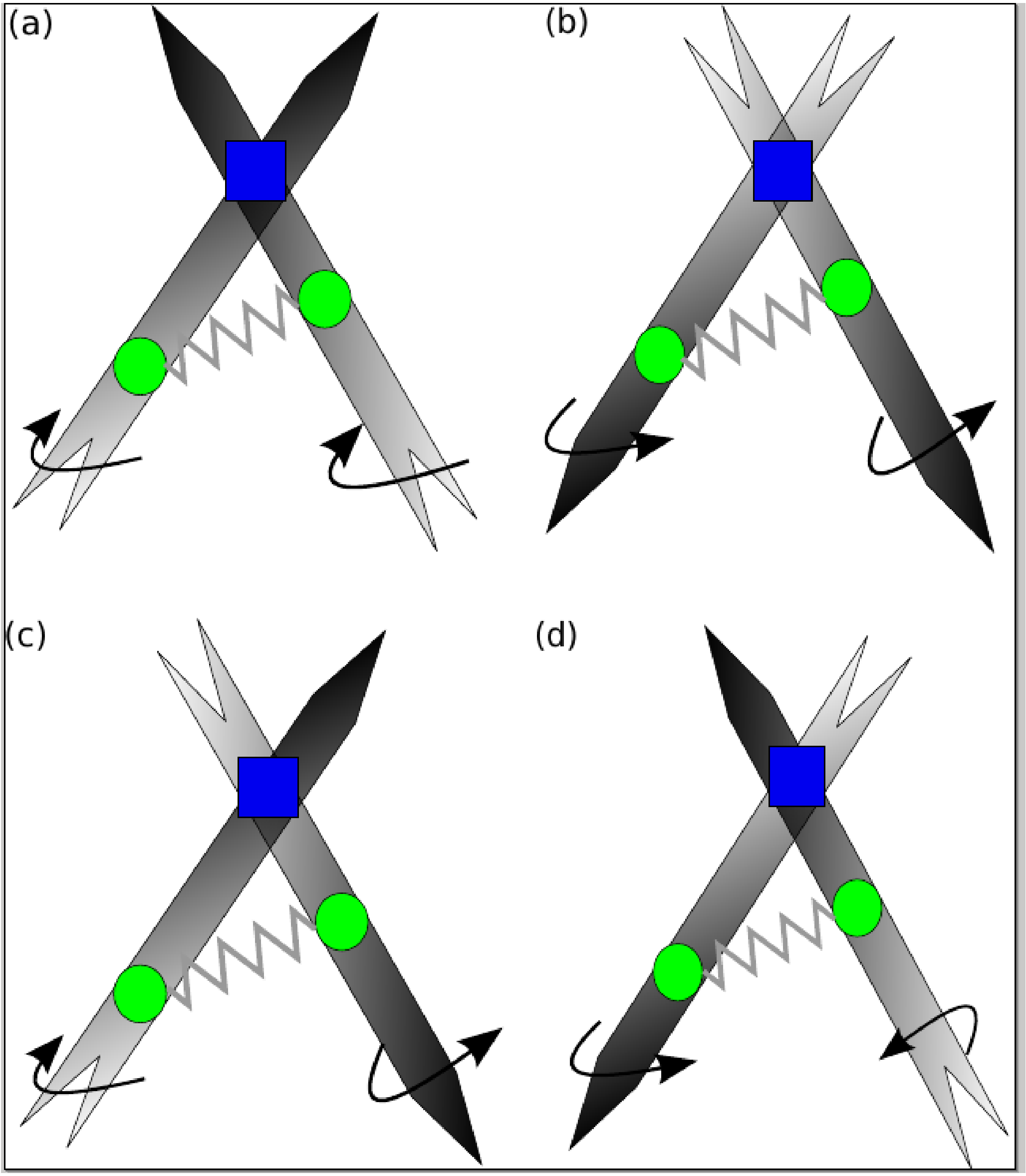
Both ends clamped



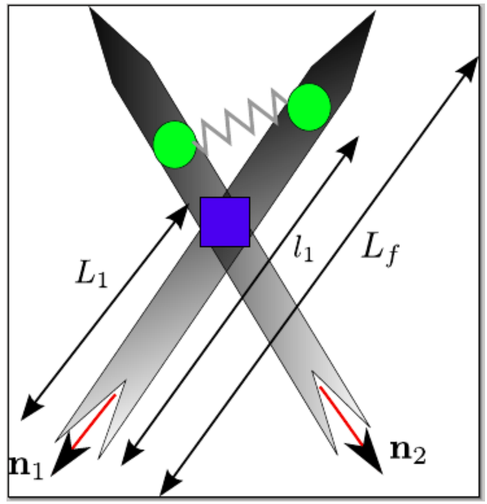
One end free

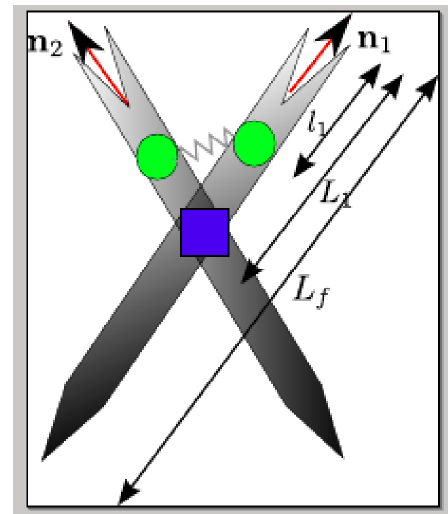


Elementary unit of two crosslinked filaments



Two filaments – analytical results





For a bare constant torque due to the motor heads, net average torque is zero

Introduce a position dependent torque : $\tau(l) = \tau_0(1 - e^{-l/d})$

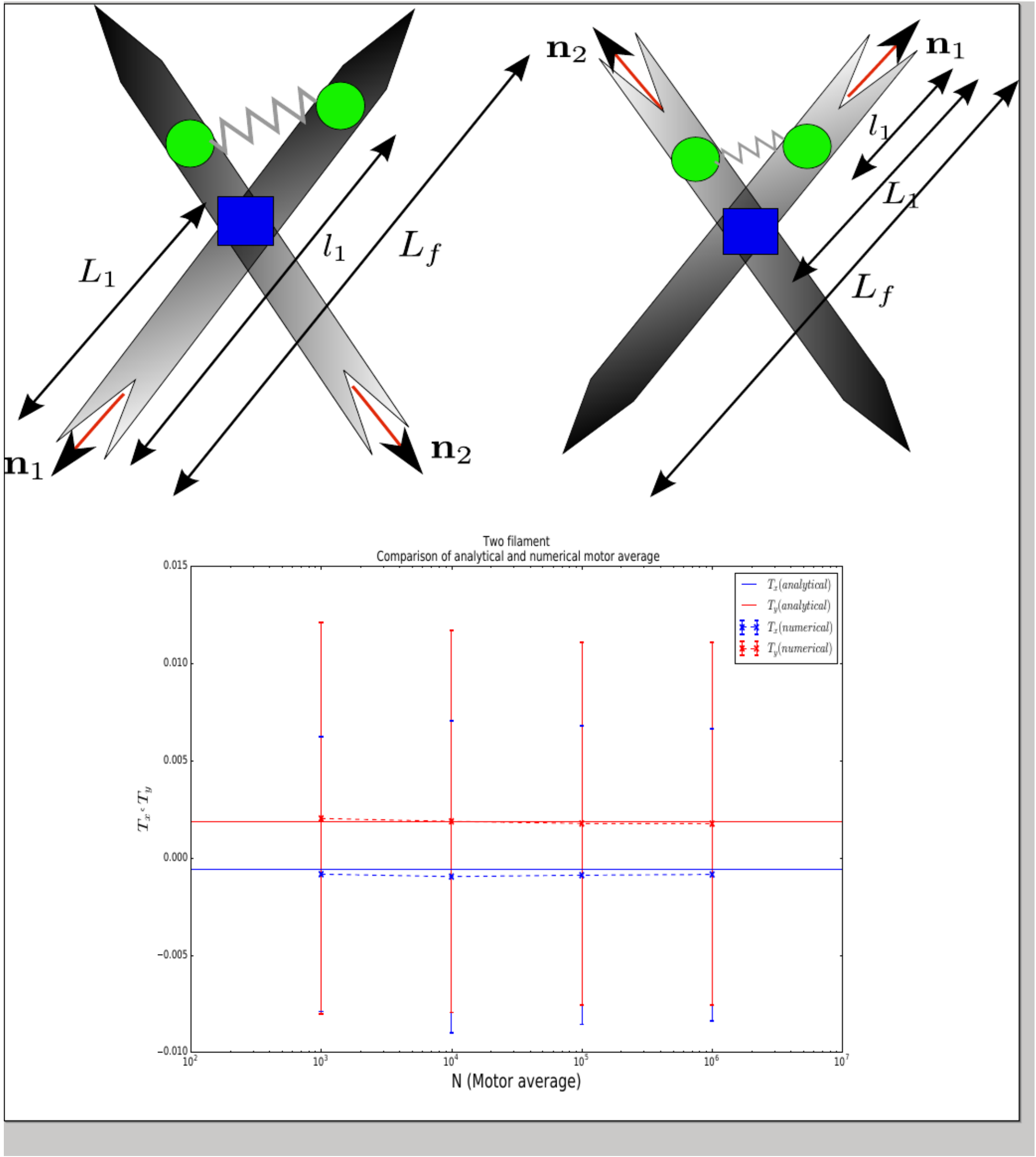
Average over motor, crosslinker positions and polarity reversal of filaments :

$$\langle \boldsymbol{\tau}_a \rangle_{average} = \tau_0 \left[\frac{\epsilon}{L_f} + \frac{d}{L_f} \ln(\frac{L_f}{\epsilon})(1 + e^{-L_f/d}) + \frac{d}{L_f} \left(e^{-L_f/d} \int_{\epsilon/d}^{L_f/d} \frac{e^y}{y} dy - \int_{\epsilon/d}^{L_f/d} \frac{e^{-y}}{y} dy \right) \right] \mathbf{n_1} \quad + \tau_0(...)\mathbf{n_2}.$$

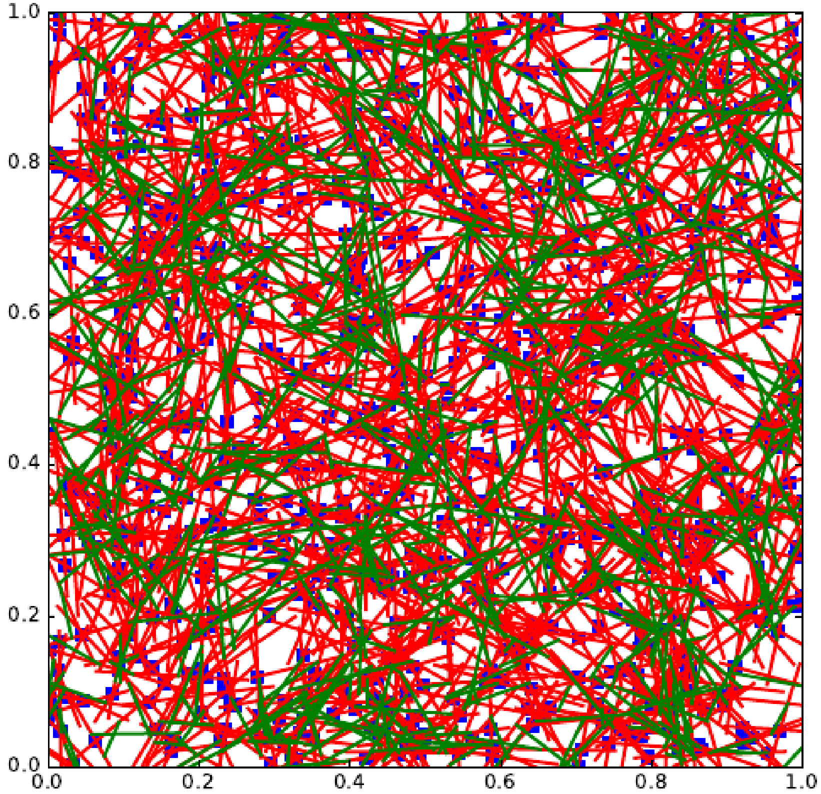
Further average over filament orientations: $\langle \tau \rangle = \frac{\tau_0}{2} f(\frac{\epsilon}{d}, \frac{L_f}{d}) \mathbf{n_1} + \frac{2}{\pi} \frac{\tau_0}{2} f(\frac{\epsilon}{d}, \frac{L_f}{d}) \hat{\mathbf{k}}$

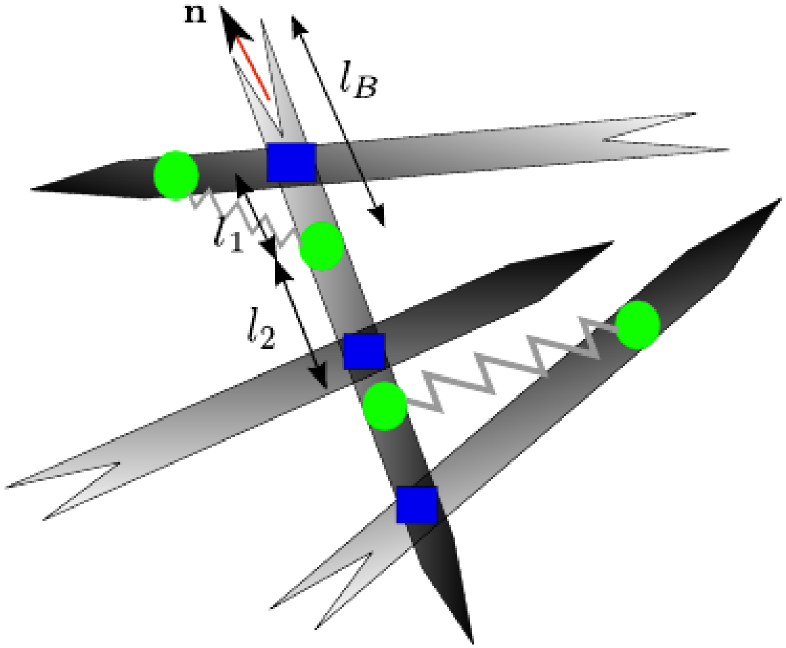
Net average torque possible!

Comparative plot for motor average



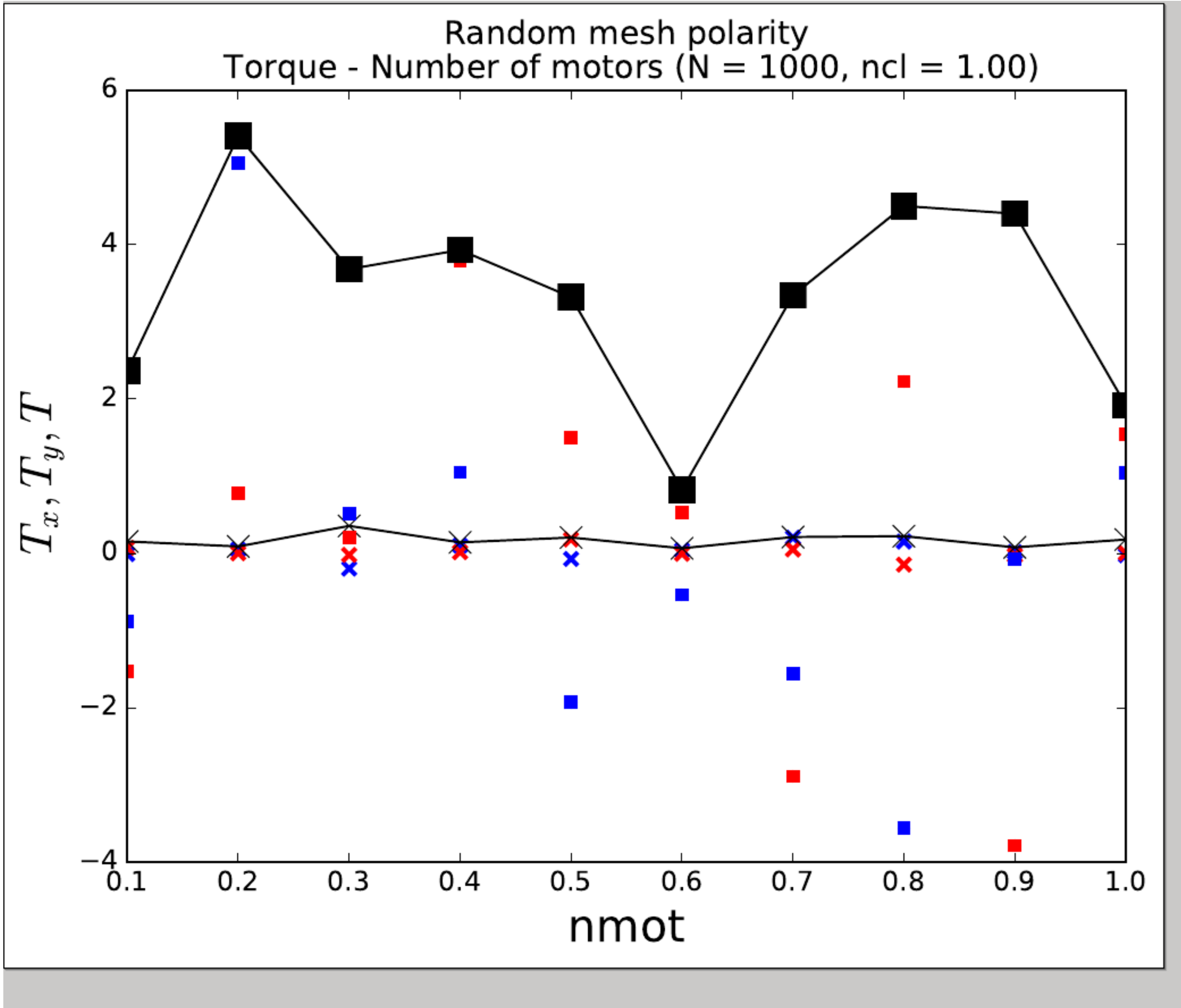
Disordered Actomyosin meshwork



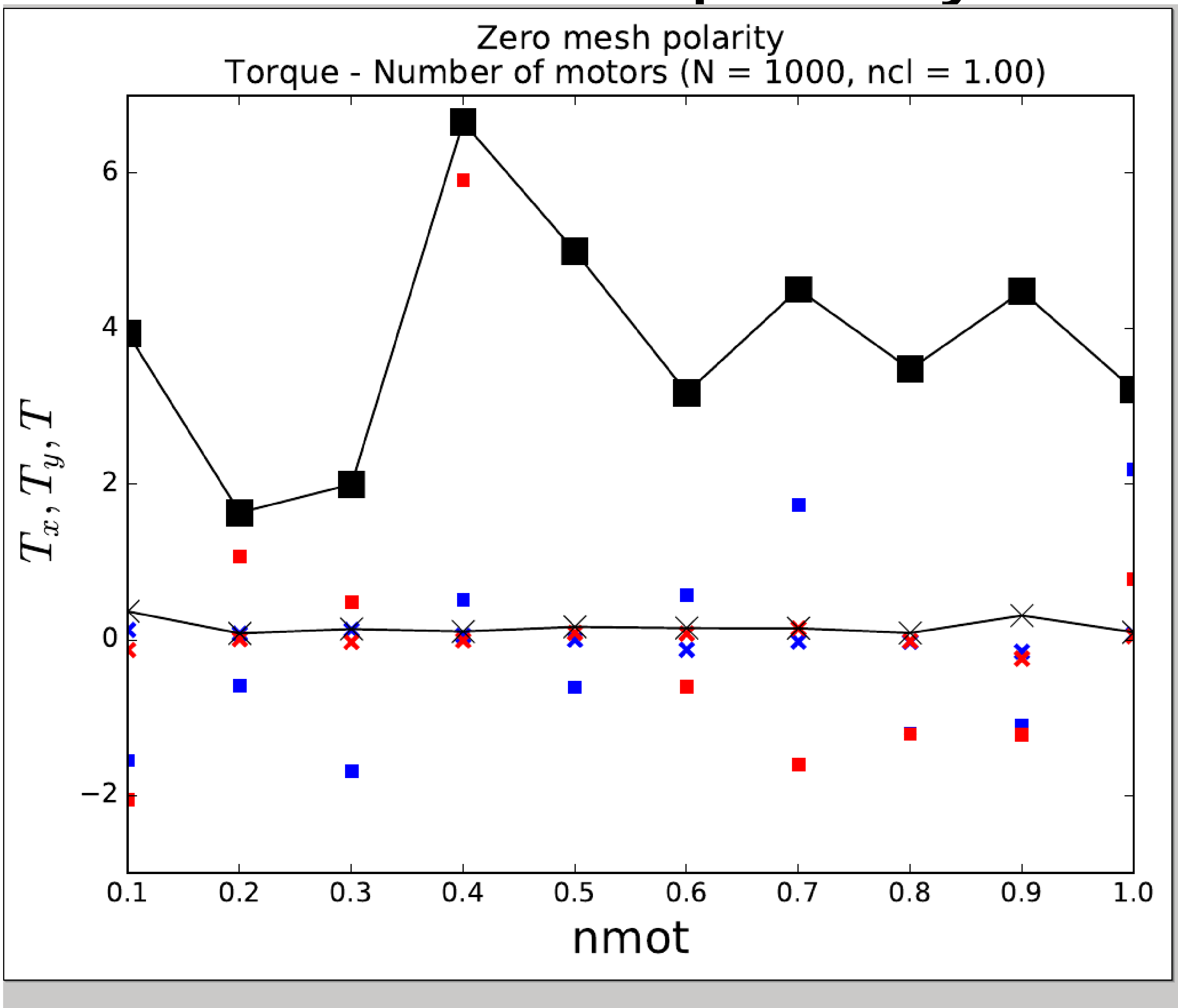


For a given mesh, with fixed number of crosslinks...Net torque is average of many motor c

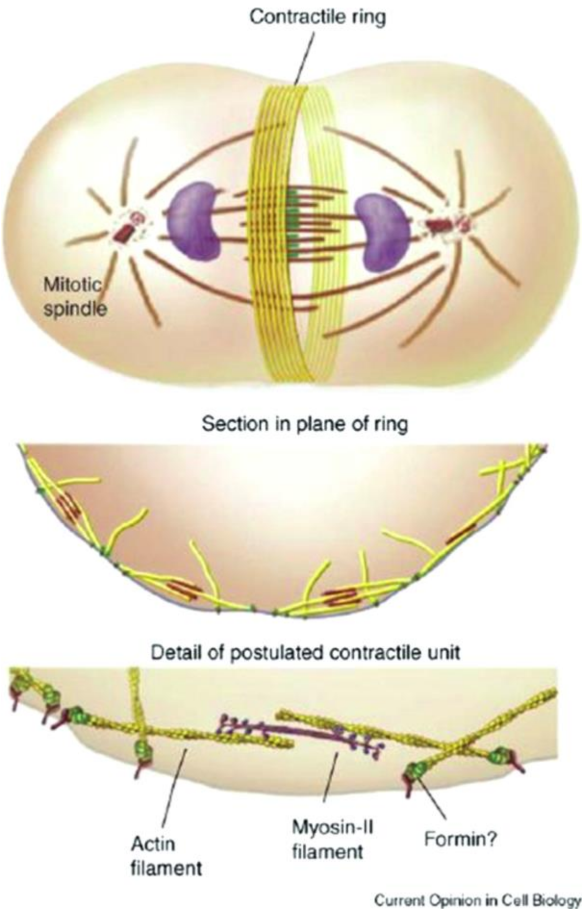
Random mesh polarity

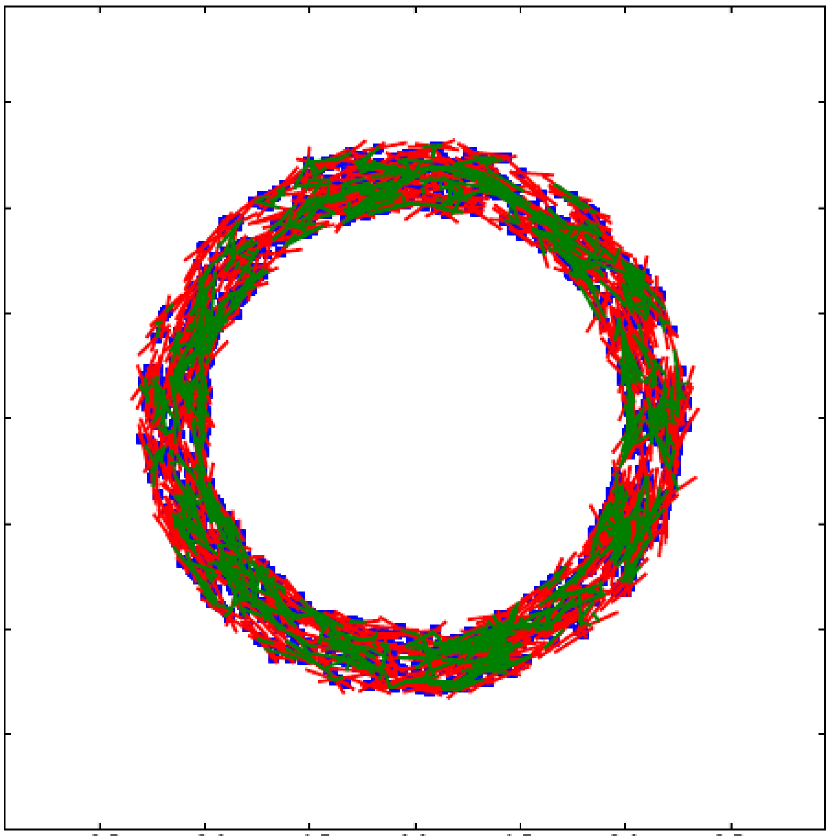


Zero mesh polarity



Contractile Ring geometry



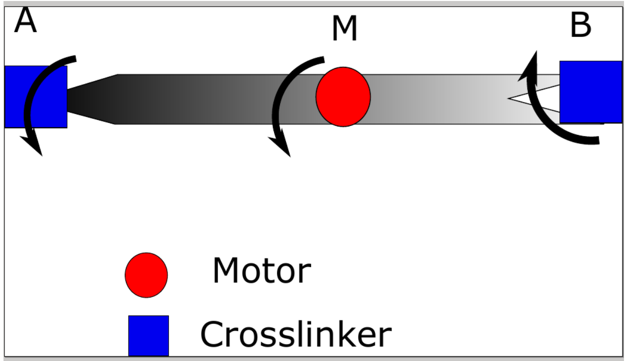


Effect of net polarity of the filaments, and varying densities of crosslinkers/motors

Implications of chiral behavior during cell division?

Twist-stretch coupling

- Actin filament is a right-handed helix
- Longitudinal and angular strains
- would be coupled



Free energy: $$F = \frac{1}{2}k_\epsilon \epsilon^2 + \frac{1}{2}k_\phi \phi^2 + k_c \epsilon\phi - f\epsilon - \tau\phi$$

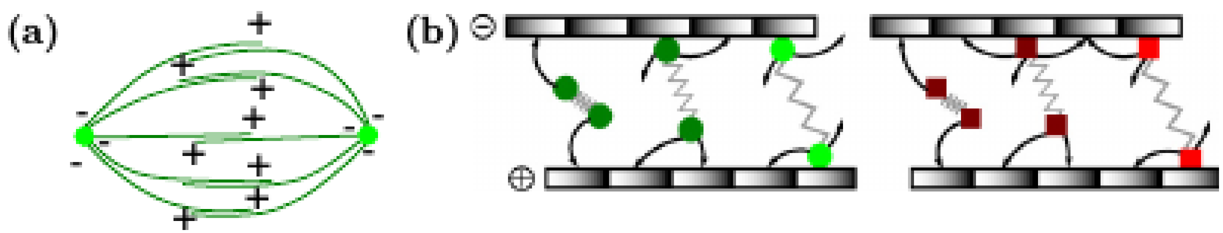
Equations for the linear and angular displacement fields: $\frac{d}{dx}(dF/d\phi) = 0$, $\frac{d}{dx}(dF/d\epsilon) = 0$

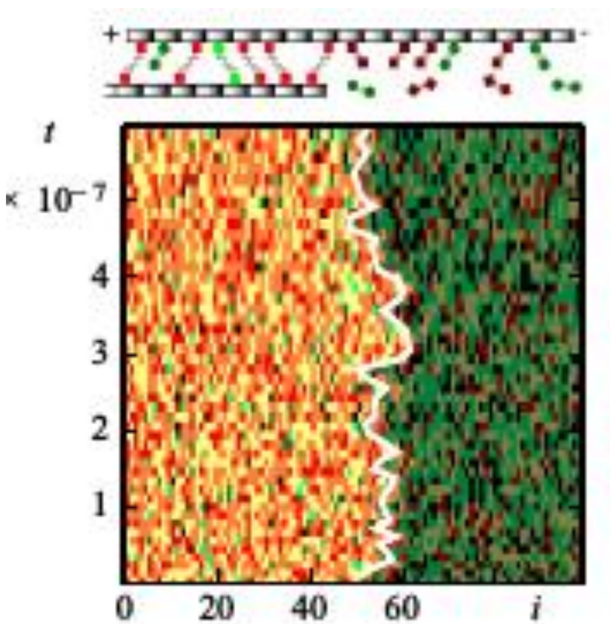
$$\begin{aligned}
f(x) &= k_\epsilon \frac{(k_\phi f_m - k_c \tau_m)}{({k_c}^2 - k_\epsilon k_\phi)} \frac{L - x_0}{L}, \quad x < x_0, \\
&= -k_\epsilon \frac{(k_\phi f_m - k_c \tau_m)}{({k_c}^2 - k_\epsilon k_\phi)} \frac{x_0}{L}, \quad x > x_0. \\
\tau(x) &= k_\phi \frac{(k_\epsilon \tau_m - k_c f_m)}{({k_c}^2 - k_\epsilon k_\phi)} \frac{L - x_0}{L}, \quad x < x_0, \\
&= -k_\phi \frac{(k_\epsilon \tau_m - k_c f_m)}{({k_c}^2 - k_\epsilon k_\phi)} \frac{x_0}{L}, \quad x > x_0.
\end{aligned}$$

Outstanding questions

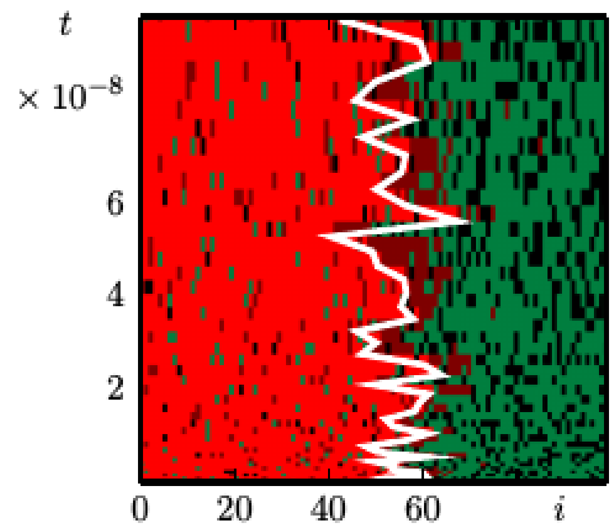
- Phase diagram with varying motor and crosslinker densities
- Mean-field theory
- Are contractile and chiral features simultaneous?
- Effect of net polarity of the system on forces and torques
- Inclusion of dynamics

Self-organization of a pair of microtubules





Stable overlap without steric interaction



Overlap with steric, but non-crosslinking motors

Phys. Rev. E. 93, 062415 (2016)

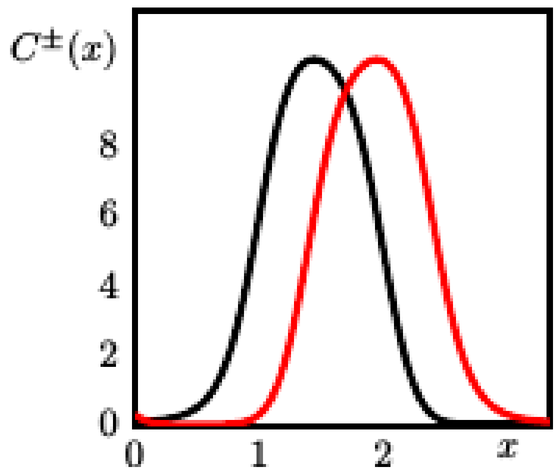
MT self-organization – bipolar bundle formation

- Consider an effectively 1D bundle interacting with passive crosslinkers and motors

$$\partial_t c^+ = D\partial_x^2 c^+ - \partial_x \left(J^{++} + J^{+-}\right)$$
$$\partial_t c^- = D\partial_x^2 c^- - \partial_x \left(J^{--} + J^{-+}\right)$$

- The currents depend on the force-velocity relation of the species.

- Linear stability analysis, about a constant homogeneous number density



Phys. Rev. E. 93, 062415 (2016)

Open questions

- Effect of dynamic filaments on the stability of overlaps
- Extension of the effective 1D bundle theory to
- higher dimensions

Acknowledgments

Vijay Krishnamurthy, Madan Rao

Physical Biology group at ICTS, NCBS

Karsten Kruse (Uni. Geneva)