# Simulating Contraction of Disordered Actomyosin Networks

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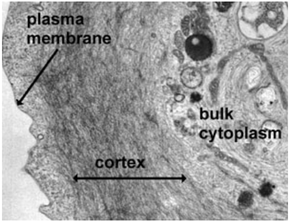
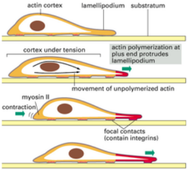
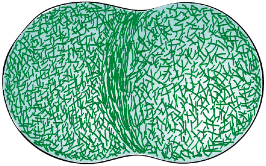
# Motivation: Cell Cortex

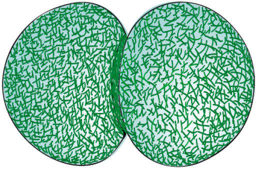
- Thin layer of proteins on the inside of the cell membrane




- Cortex deformation controls cell motility and division
- Movement of **actin** and **myosin** deforms the cortex

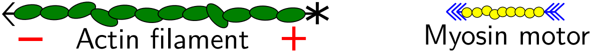


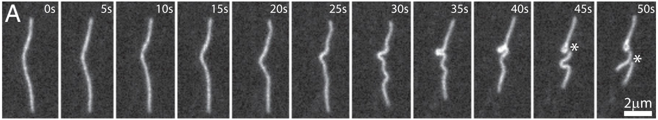



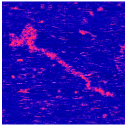


# Actin and Myosin

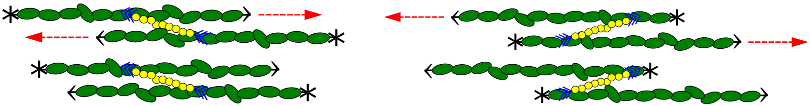
- **Actin** molecules form polarised filaments ($\sim 1\,\mu$m)
- **Myosin** forms molecular motors that bind to filaments
  - Hydrolyse ATP and move towards actin filament plus ends



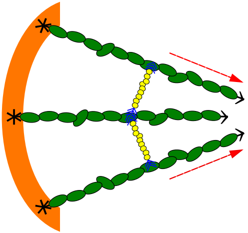
- Actin–myosin interactions can generate contraction/expansion

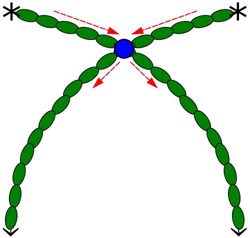


- In the cortex, filaments have random positions and orientations
- Research question: **Why do disordered networks contract?**

# Actomyosin Contraction

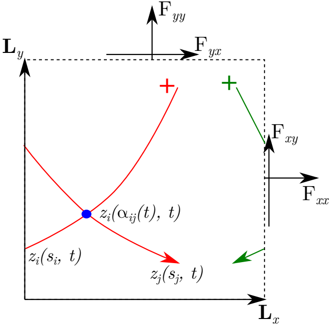
- Hypothesised contraction mechanisms for disordered networks:
  - Structural asymmetry
    - Actin filament ‘zippering’
    - Actin network architecture/anchoring
    - Actin filament ‘treadmilling’
    - Myosin motor differentiation
  - Force asymmetry
    - **Actin filament bending/buckling**
    - Position-dependent myosin stall force

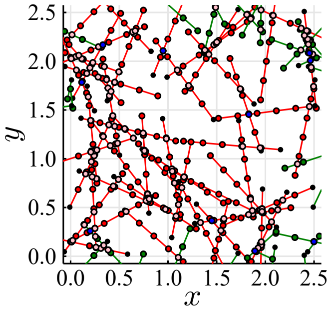




# 2D Agent-Based Model

- Simulate evolution of network model DOF:
  - Filament positions: $z_i(s,t)$, represented as nodes
  - Motor relative positions: $m_{ik}(t)$
- Motors attach at random intersections, detach at force-dependent rate
- Protein friction acts at filament intersections without a motor
  - Implemented as point-wise drag restricting relative motion



# Energy Method

$$E_{network} = \sum_{\substack{filaments\ i,j \\ motors\ k}} E_{a,bend} + E_{a,spring} + E_{a,drag} + E_{a,pf} + E_{m,spring} + E_{m,a}$$

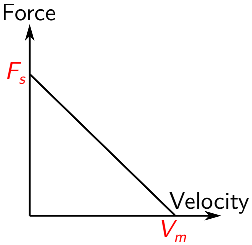
- Energy terms depend on parameters and DOF

$$E_{a,spring} = \int_0^{L_i} \frac{k_a}{2} \left(|z_i'| - 1\right)^2 \, \mathrm{d}s, \qquad E_{m,spring} = \frac{k_m}{2} \left| z_i(m_{ik}) - z_j(m_{jk}) \right|^2$$

$$E_{a,bend} = \int_0^{L_i} \frac{\kappa_a}{2} \left| z_i'' \right|^2 \, \mathrm{d}s$$

$$E_{a,drag} = \int_0^{L_i} \frac{\lambda_a}{2\Delta t} \left| z_i - \boldsymbol{F} z_i^n \right|^2 \, \mathrm{d}s$$

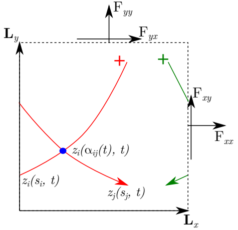
$$E_{a,pf} = \frac{\lambda_{pf}}{2\Delta t} \left| z_i(\alpha_{ij}) - z_j(\alpha_{ji}) \right|^2$$




$$E_{m,a} = \frac{F_s}{V_m} \frac{\left(s_{ik} - s_{ik}^n\right)^2}{2\Delta t} - F_s \left(s_{ik} - s_{ik}^n\right)$$

# Numerical Method

- Energy minimisation yields a time-implicit scheme
- Quasi-Newton optimisation performed using `Optim.jl`
  - LBFGS with automatic differentiation (`ForwardDiff.jl`)




- Force components are Lagrange multipliers that constrain domain size and shape

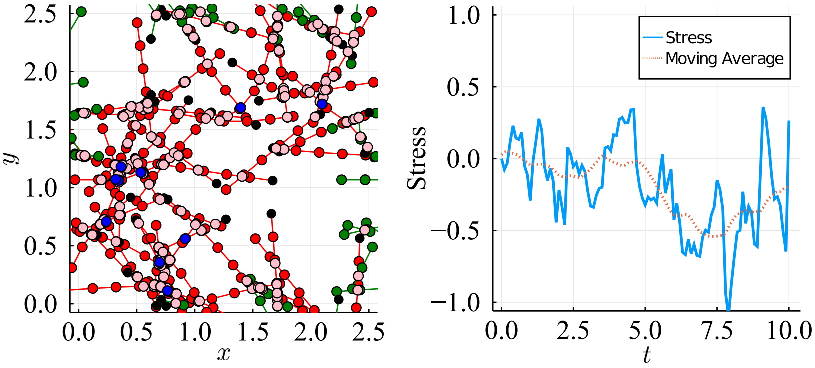
$$E_{total} = E_{network} + \boldsymbol{F}_x \cdot \boldsymbol{L}_x + \boldsymbol{F}_y \cdot \boldsymbol{L}_y$$

- Numerical method enables exact calculation of force and stress

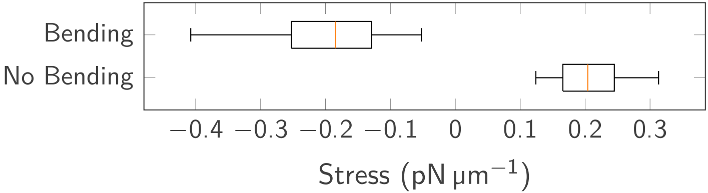
$$F_{xx} = -\frac{\partial E_{network}}{\partial L_x}, \quad F_{yy} = -\frac{\partial E_{network}}{\partial L_y}$$

$$\bar{\sigma} = \frac{1}{2}\left(\frac{F_{xx}}{L_{xx}} + \frac{F_{yy}}{L_{yy}}\right)$$

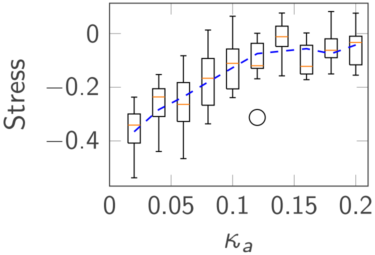
# Example Simulation

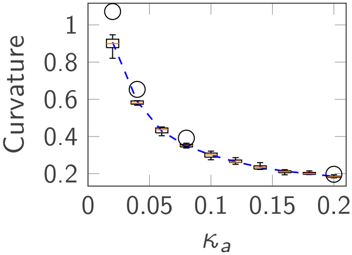


# Actin Bending Generates Contractile Bias



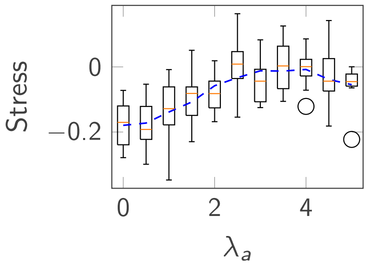

- Stress and curvature depend on actin flexural rigidity

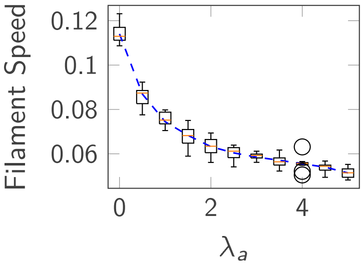


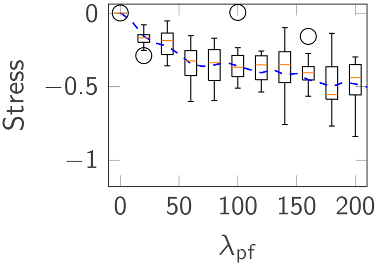
# Effect of Drag on Contraction

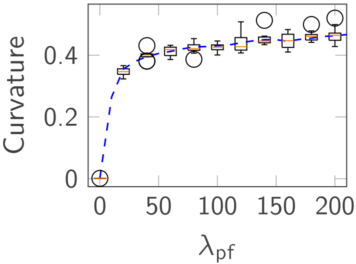
- Viscous drag inhibits contraction by slowing filaments



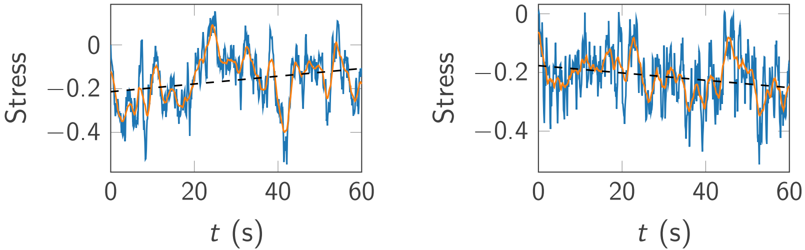

- Protein friction enhances contraction by increasing bending



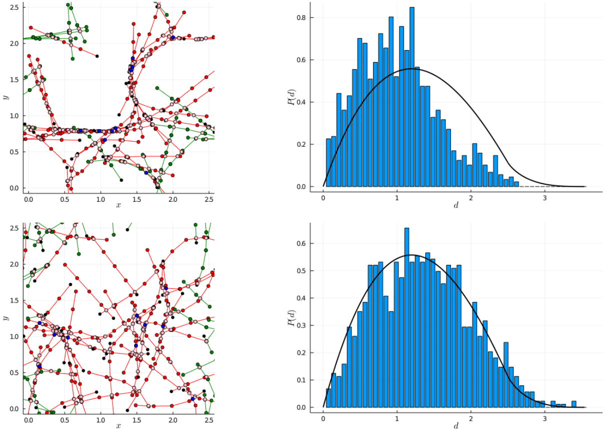
# Filament Turnover Enables Persistent Contraction

- **Turnover**: random exchange of filaments between network and background
  - Model by removing filaments and replacing them with rate $k_{\text{off},a}$
- No turnover ($k_{\text{off},a} = 0$): network loses contractility over time
- Fast turnover ($k_{\text{off},a} = 0.2\,\text{s}^{-1}$): network sustains contractility



# Turnover Prevents Pattern Formation

- Aggregation/pattern formation causes loss of contractility without turnover



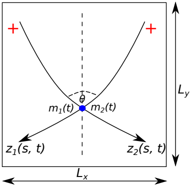

- Actin stress fibres are aggregates that persist with turnover
- New research question: How do stress fibres self-organise?

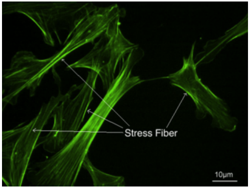
# Summary

- Actomyosin contraction enables cell motility and division
- Actin bending and protein friction generate contraction in disordered networks

Ongoing Work:

- Exact solutions for two filaments
- Self-organisation of stress fibres





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