Growing actin networks

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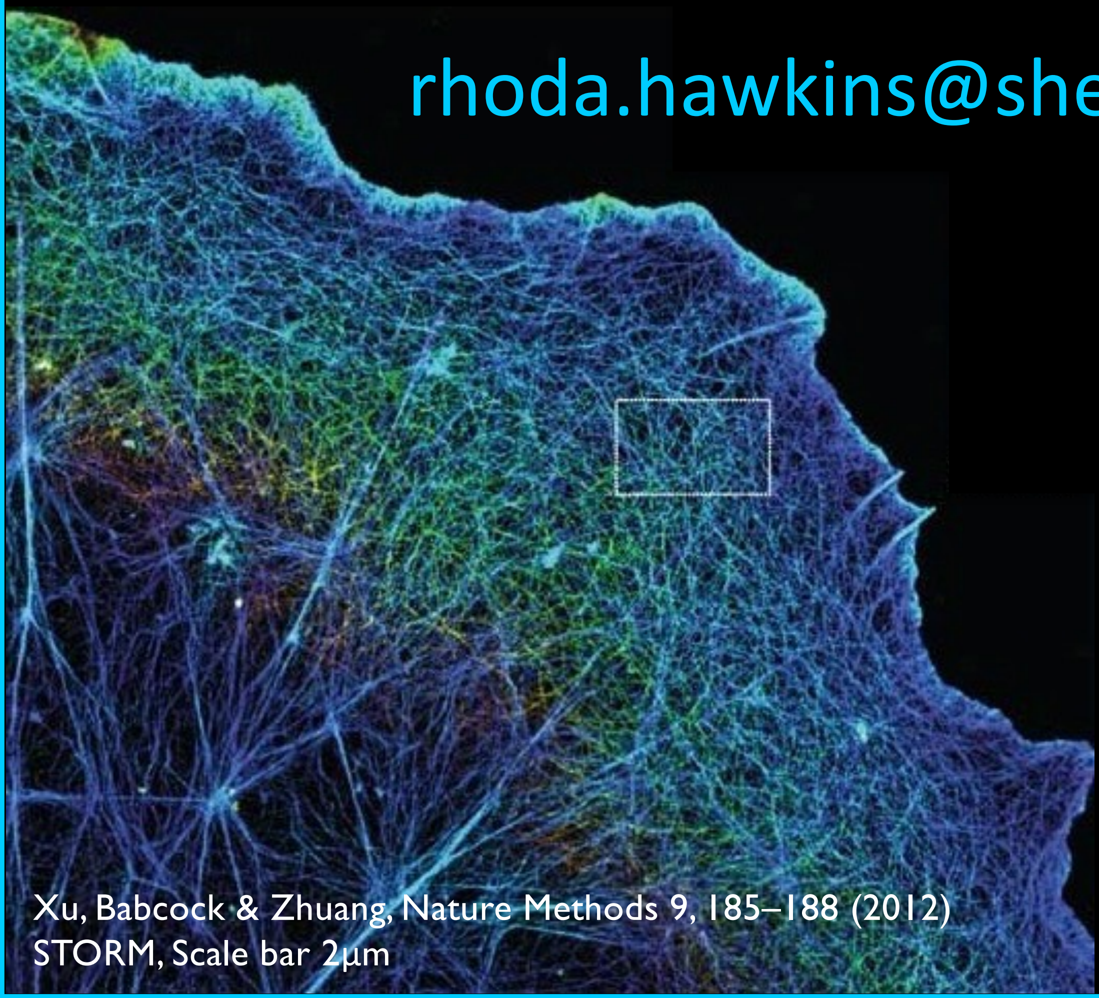


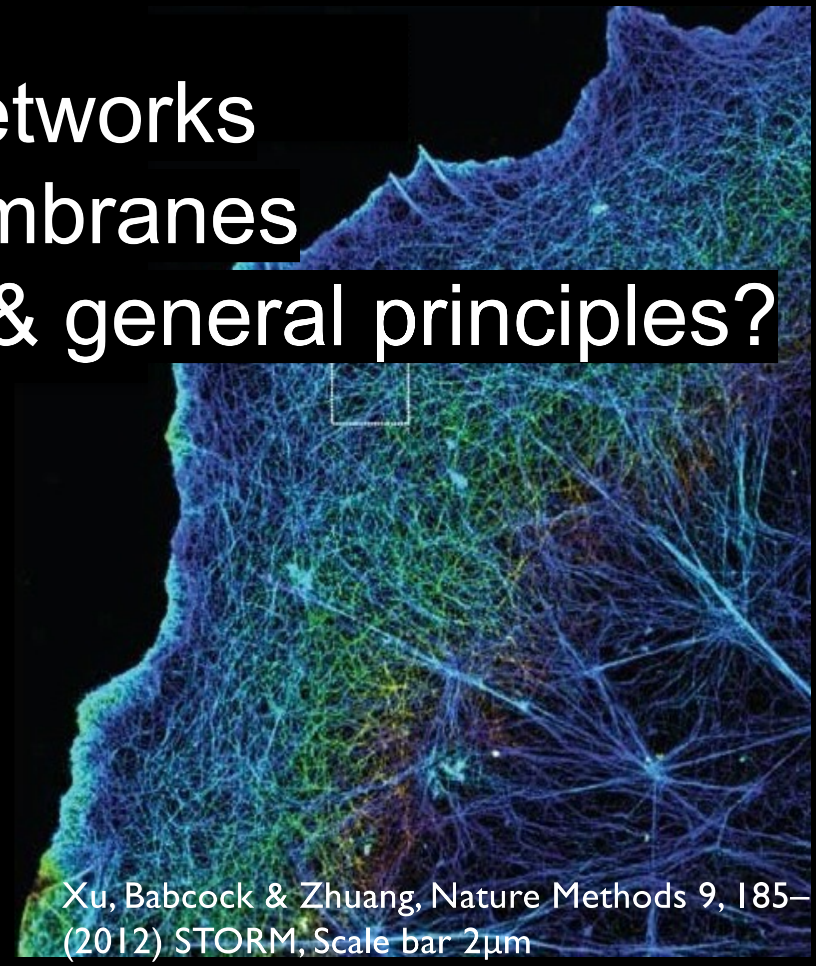
Xu, Babcock & Zhuang, Nature Methods 9, 185–188 (2012)
STORM, Scale bar 2μm

The University Of Sheffield.

Growing actin networks

Talk outline

- Introduction
- Polymerisation of actin networks
- Actin growth pushing membranes
- Universal characteristics & general principles?
- Conclusion



Xu, Babcock & Zhuang, Nature Methods 9, 185–
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James Bradford
Natasha Cowley
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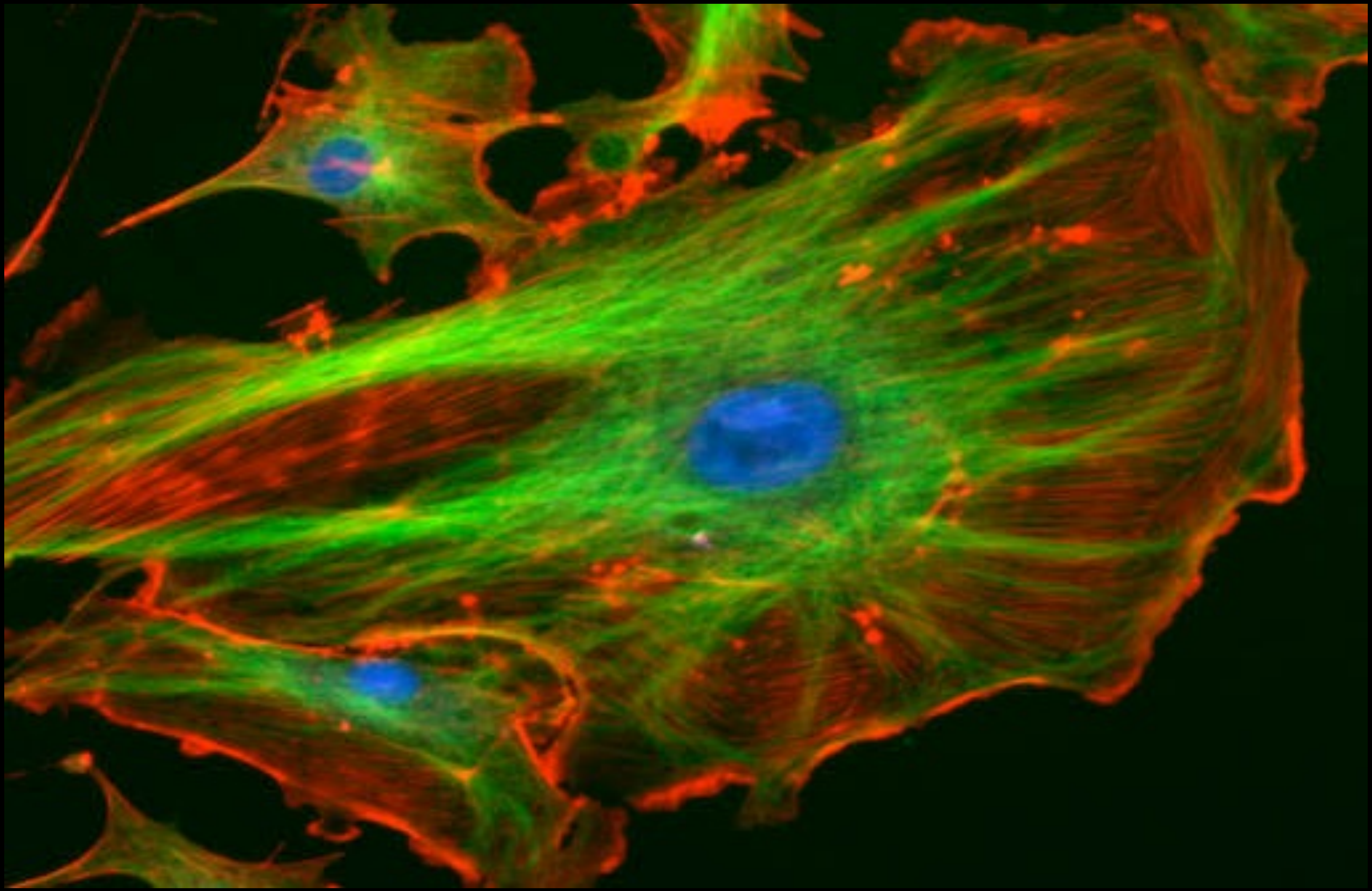
Ellen Allwood, John Palmer, Kathryn Ayscough

EPSRC Engineering and Physical Sciences Research Council
BBSRC bioscience for the future
The University Of Sheffield.

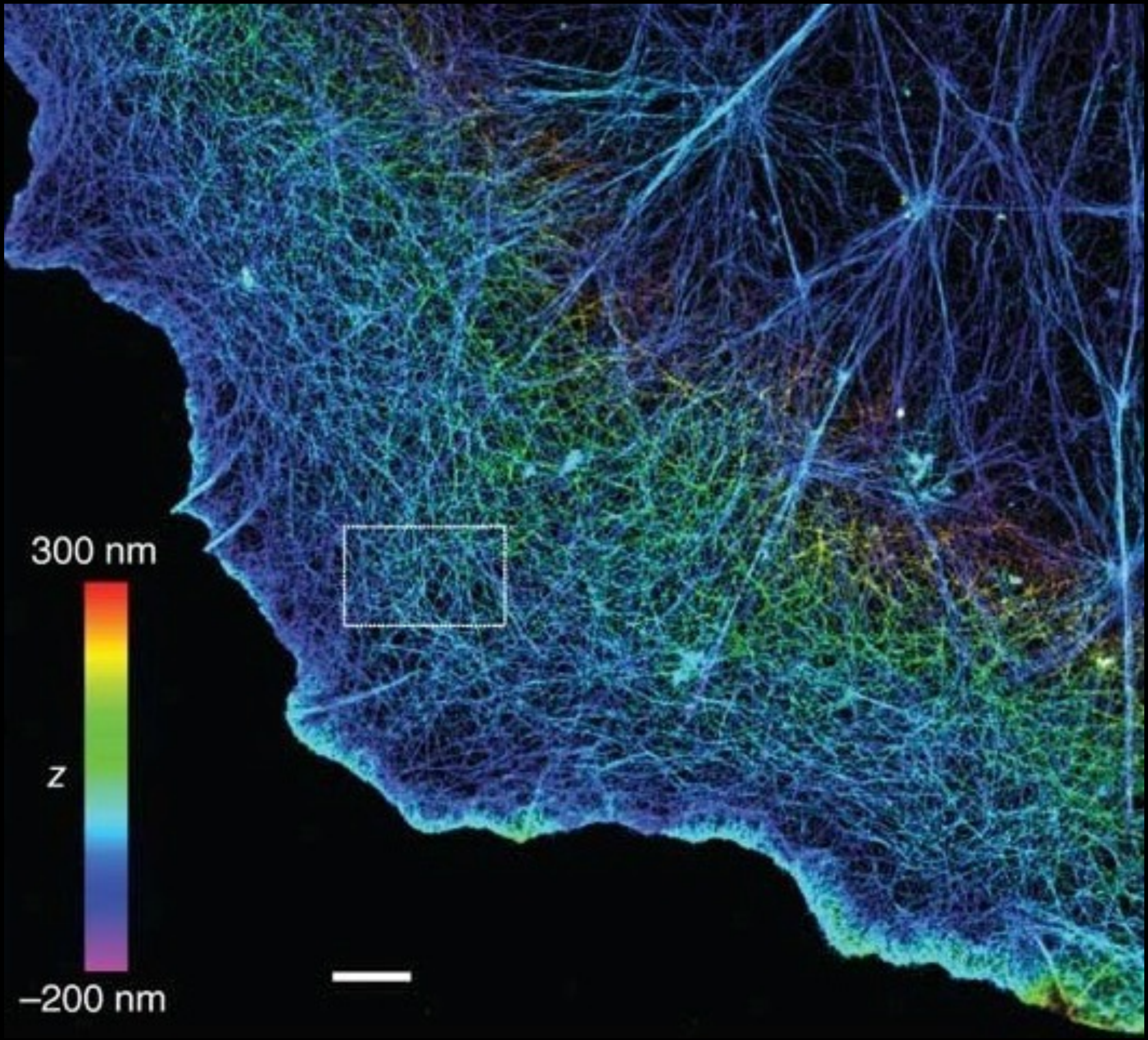
Cytoskeleton



Cytoskeleton polymers: microtubules + actin

Soft, Active Matter

Actin



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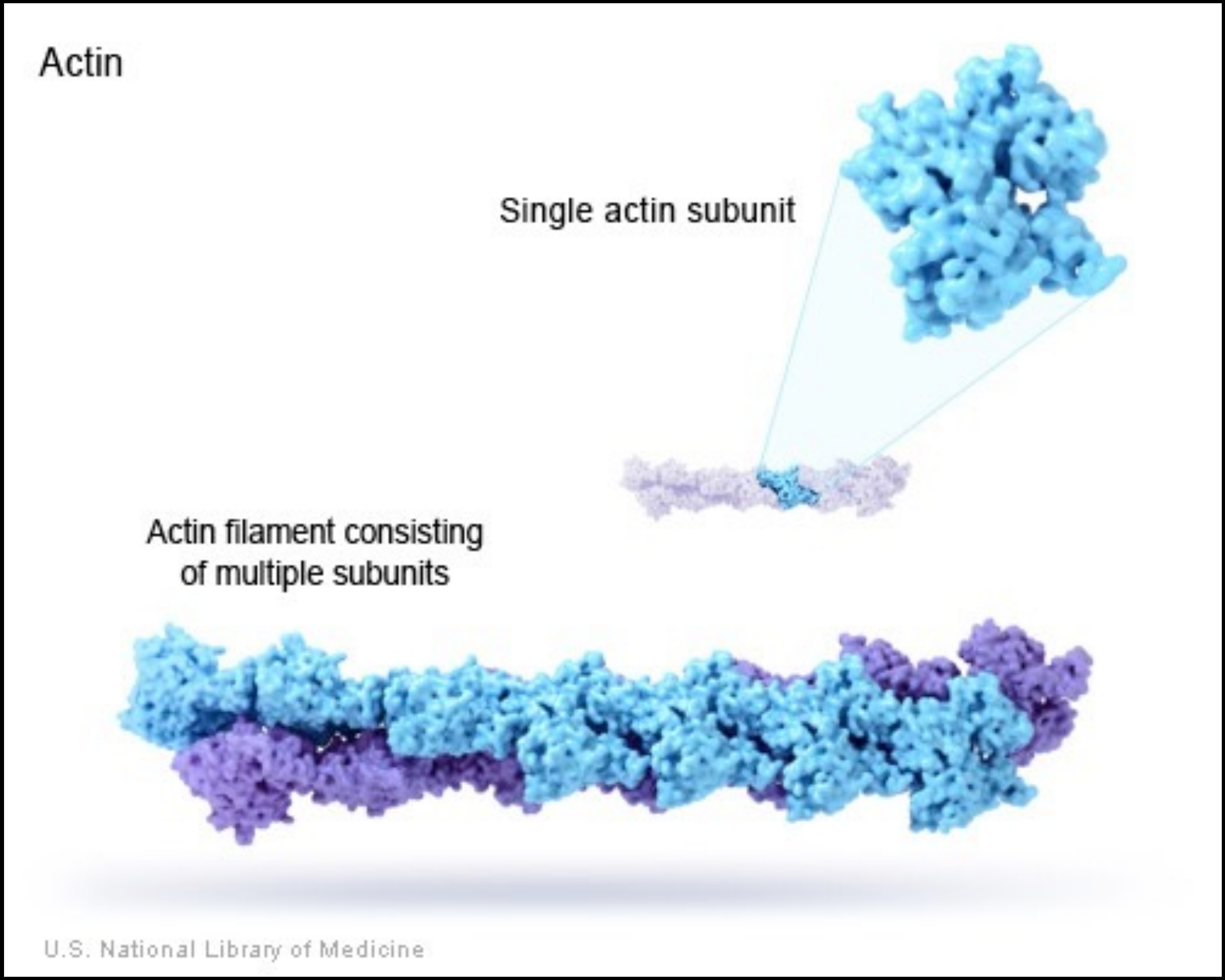
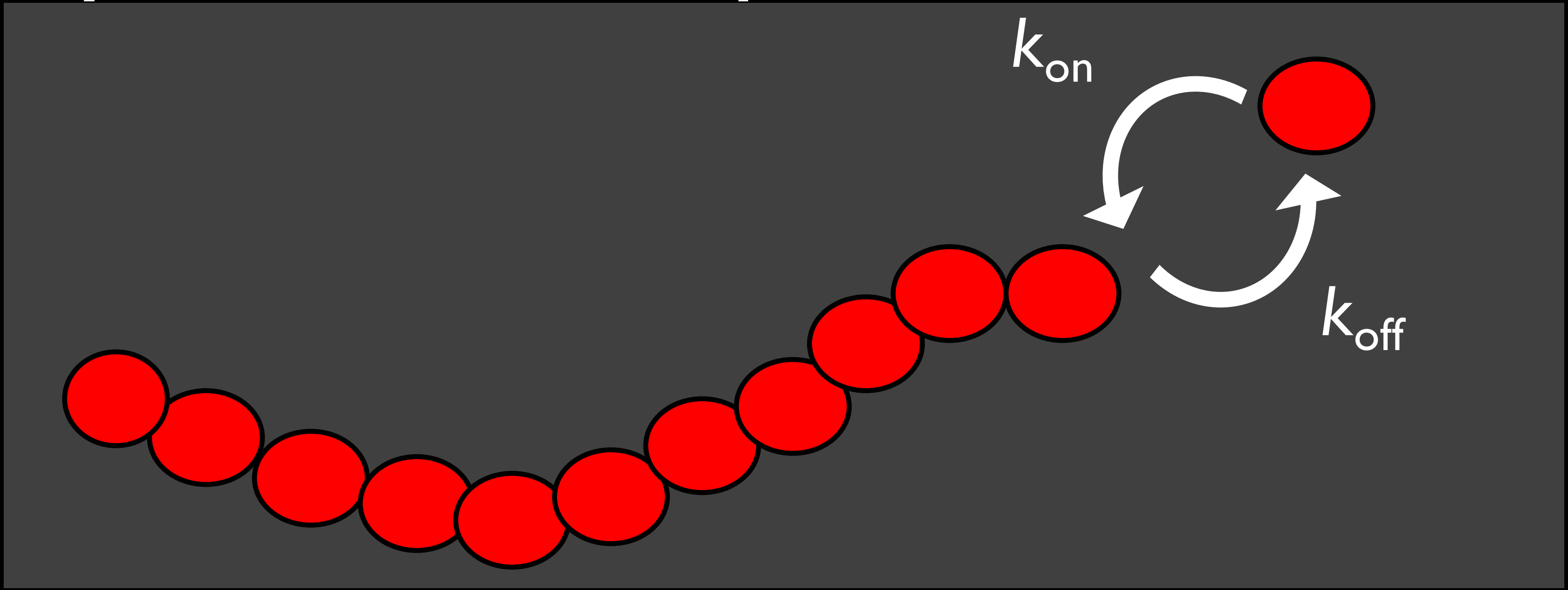
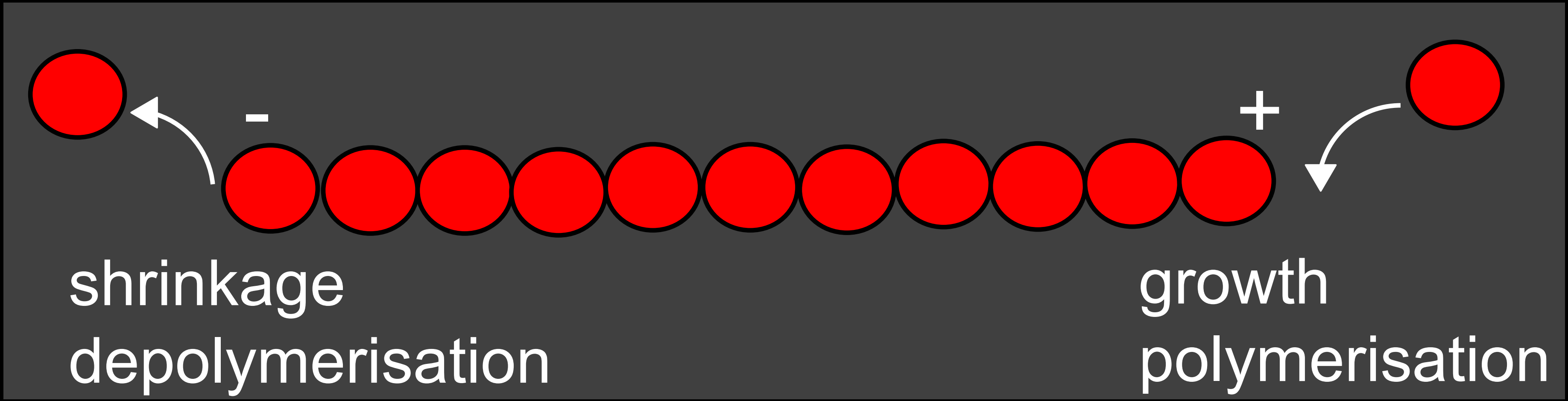
Actin monomers and filaments



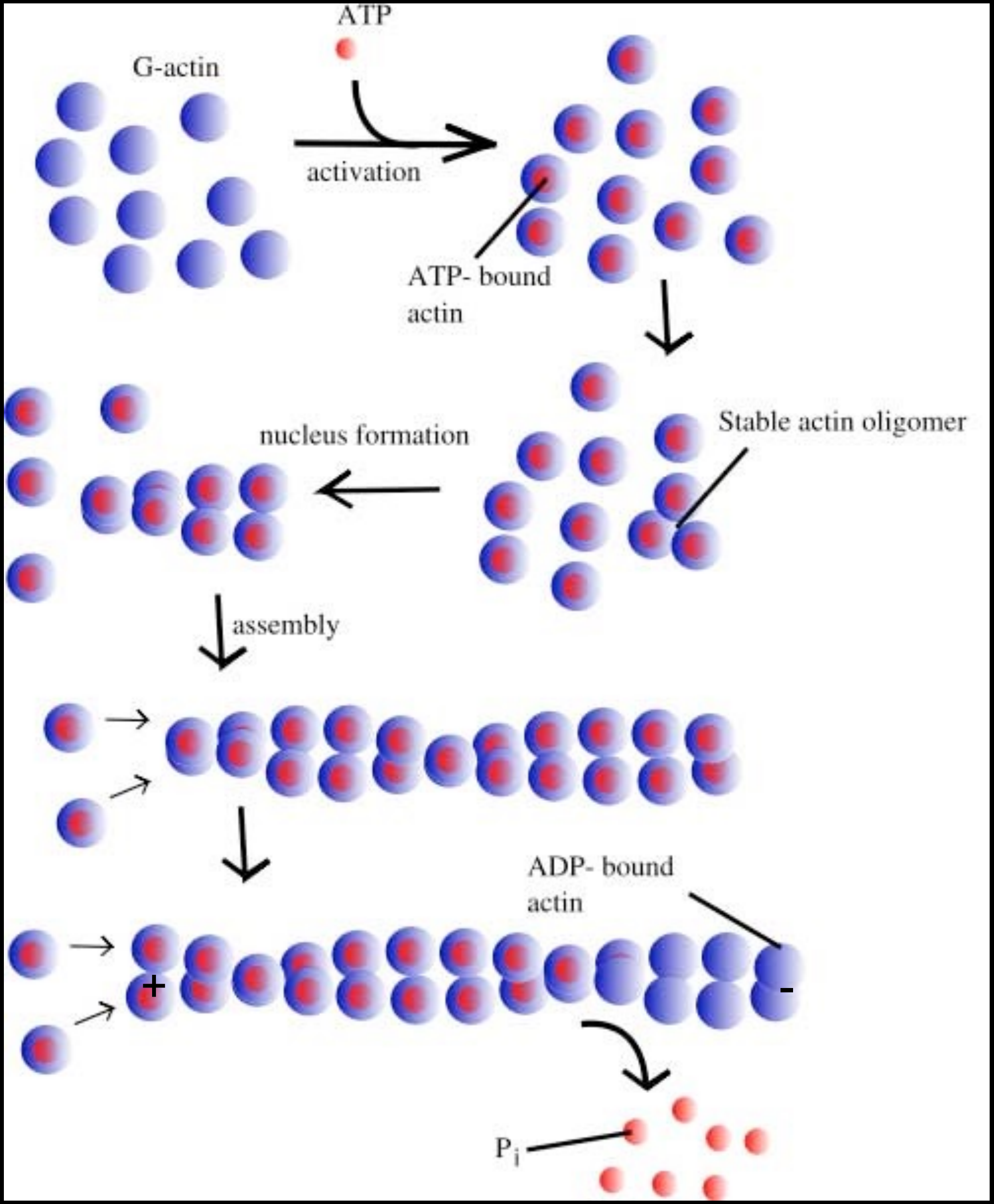
Polymerisation of protein filaments



Actin treadmilling:



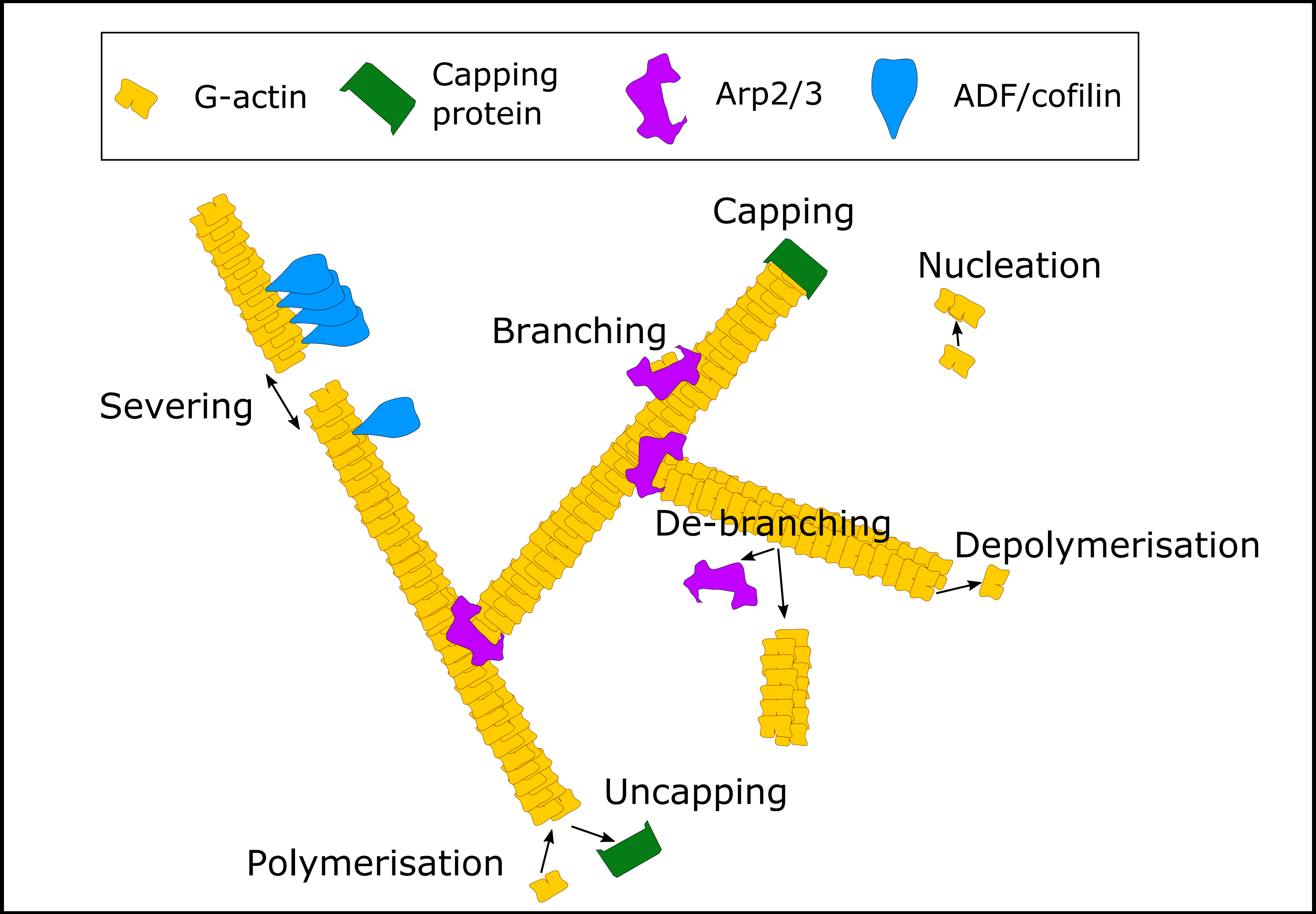
Actin polymerisation & depolymerisation



barbed/plus end

pointed/minus end

Actin binding proteins



Actin polymerisation: analytical calculations

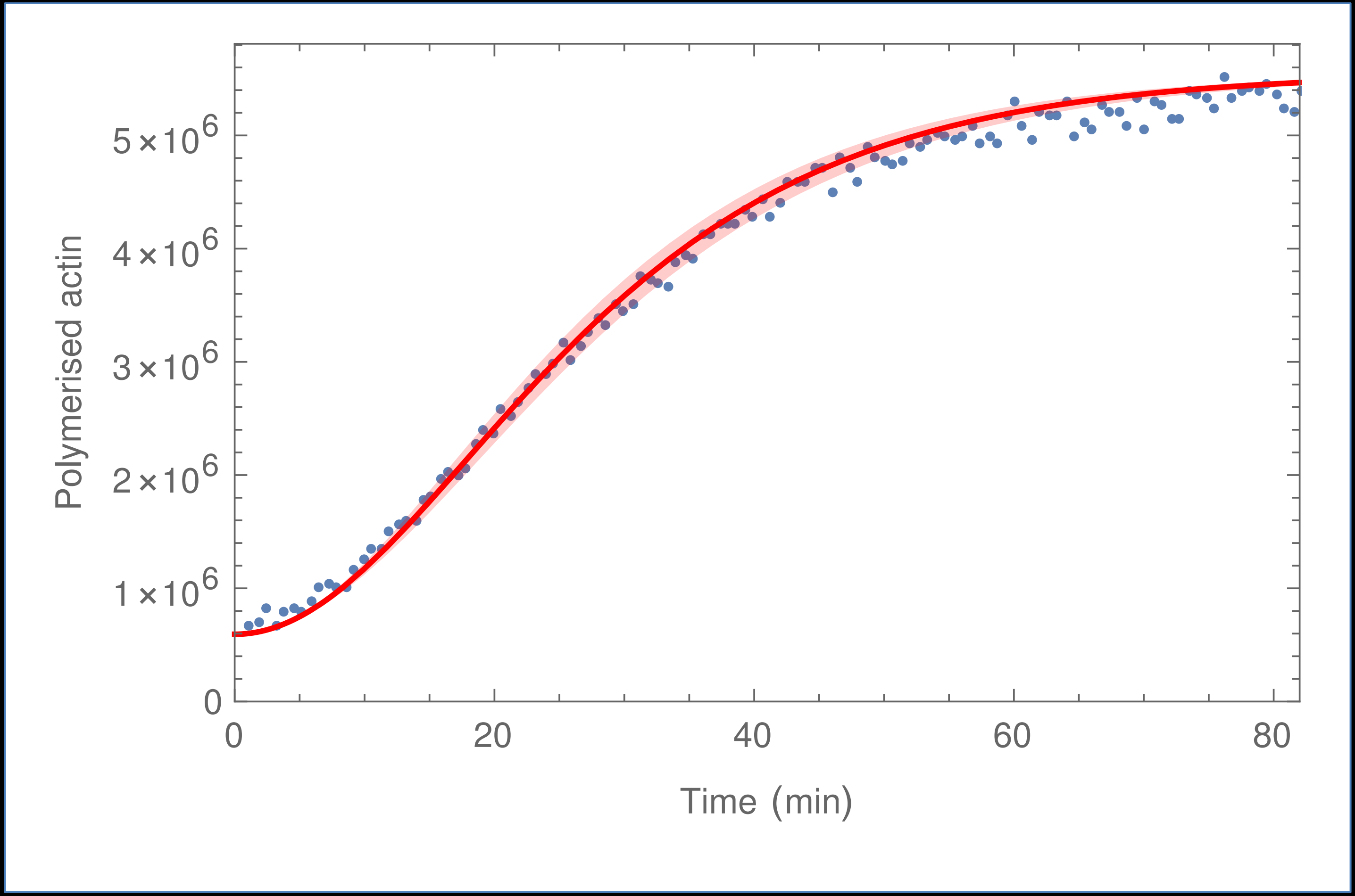
$$\dot{c}_1 = k_d c_f - k_p c_1 c_f - \beta k_n c_1^\beta,$$

$$\dot{c}_p = -k_d c_f + k_p c_1 c_f + \beta k_n c_1^\beta = -\dot{c}_1,$$

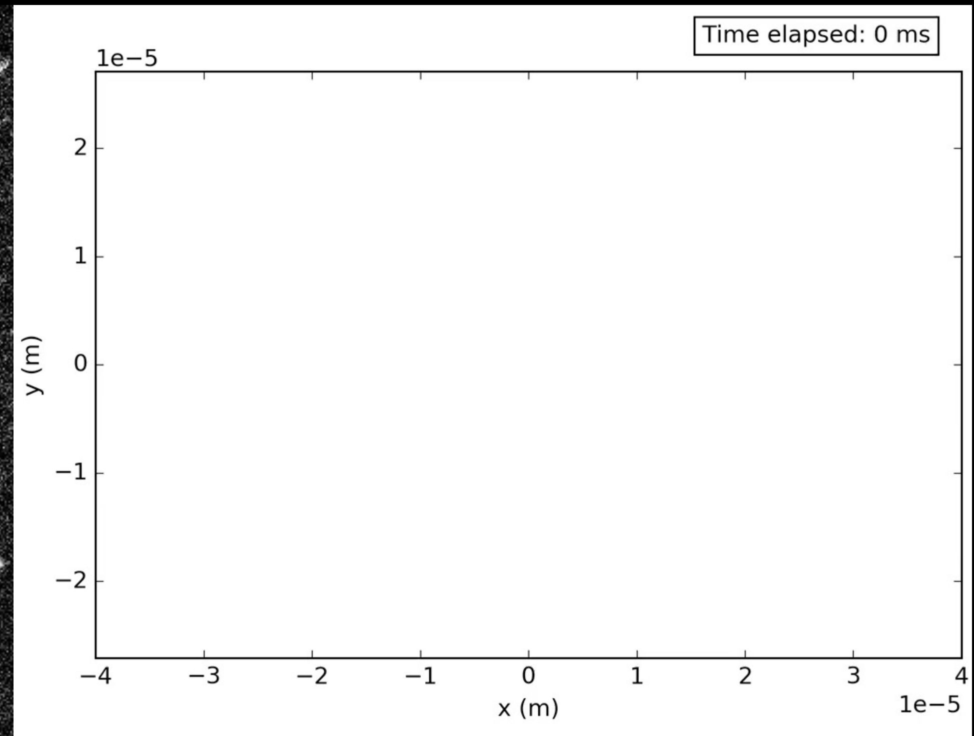
$$\dot{c}_f = k_n c_1^\beta.$$

- free monomers c_1 , polymerised c_p , filaments c_f
- (de)polymerisation rate $k_{d,}\, k_p$
- nucleation rate k_n and order β
- Neglect dissociation of filaments
- Coupled nonlinear differential equations solved numerically

Fit to pyrene assay polymerisation experiments



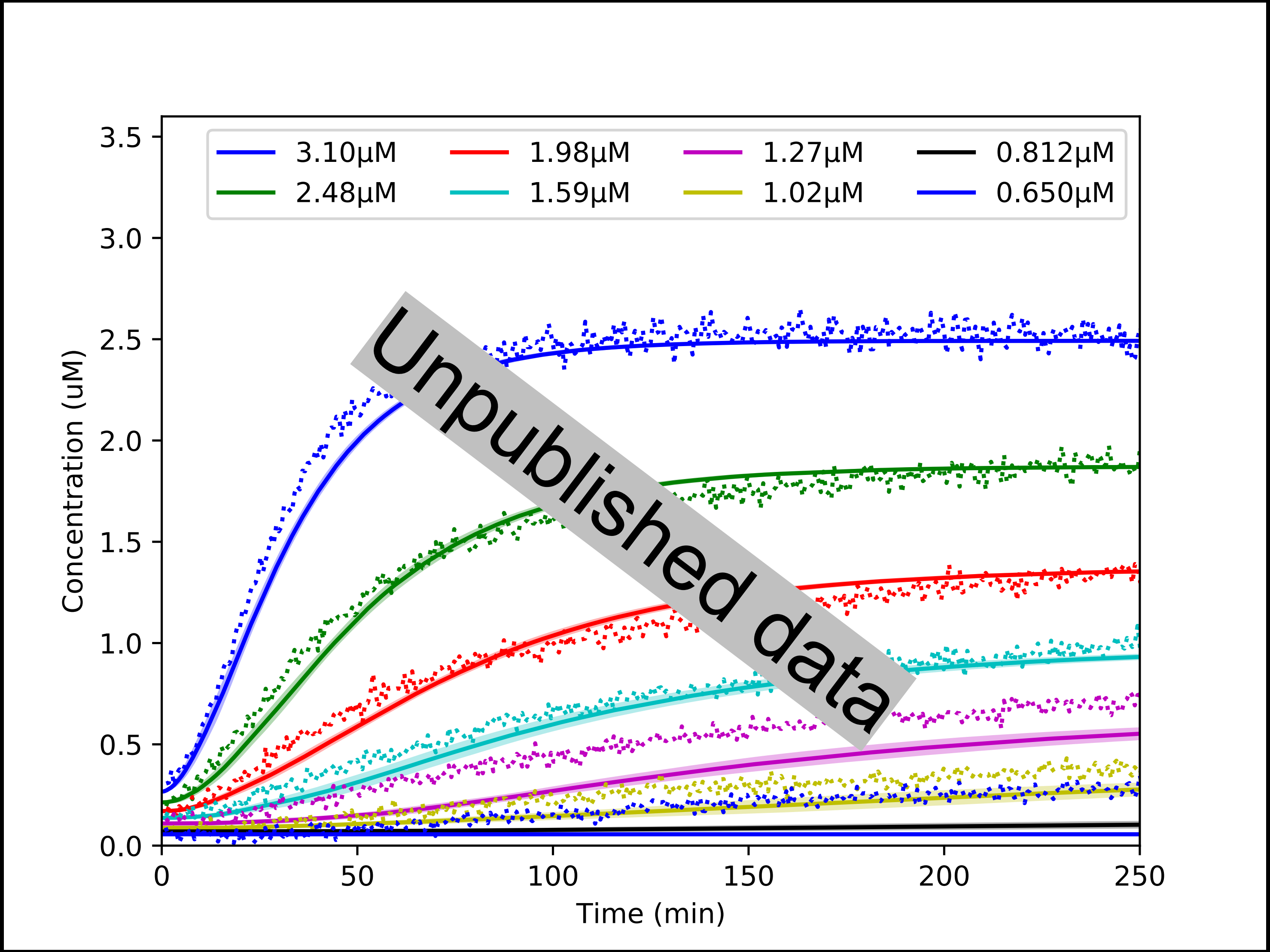
Actin polymerisation TIRF & simulation



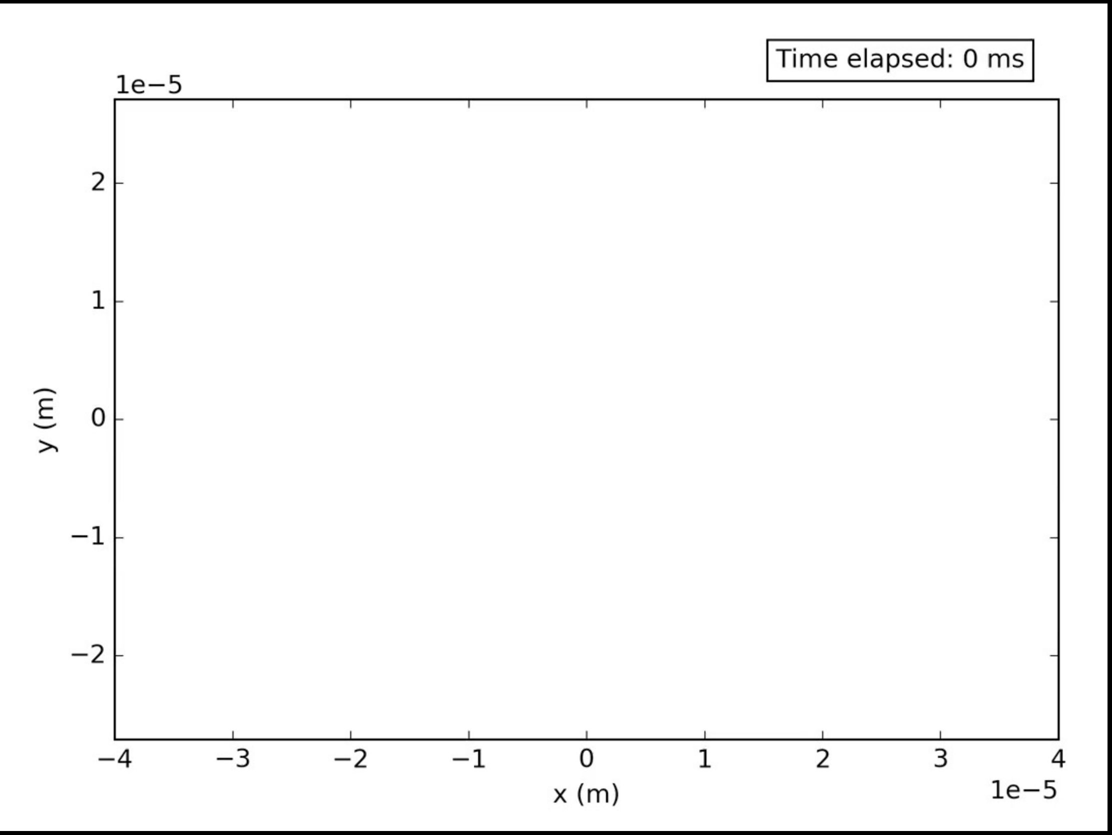
Brownian Dynamics
& Monte Carlo methods

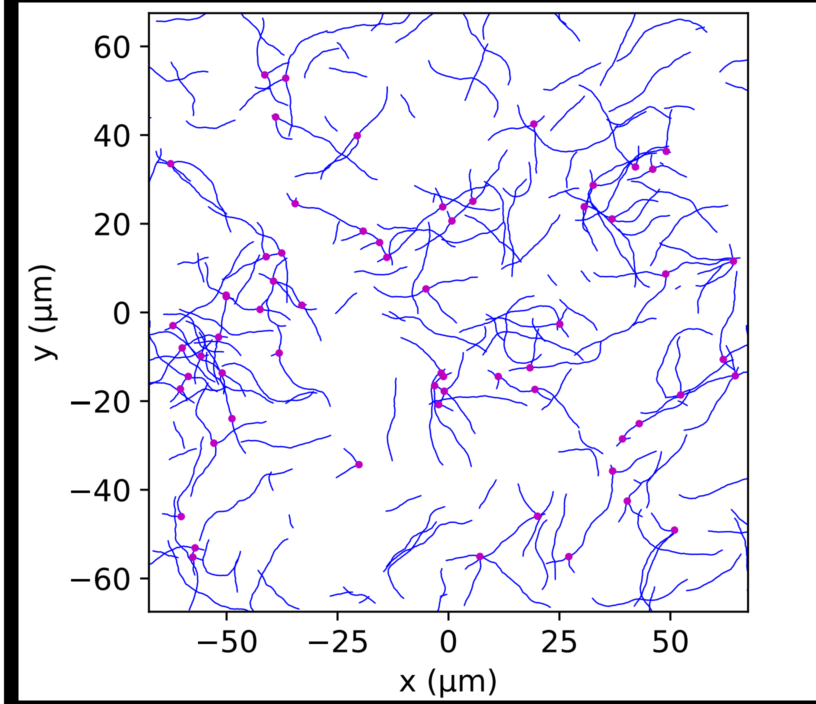
Including: Nucleation, Diffusion, Polymerisation, Bending & Tethering
Can also include branching (Arp2/3), capping etc

Actin polymerisation pyrene assay & simulation

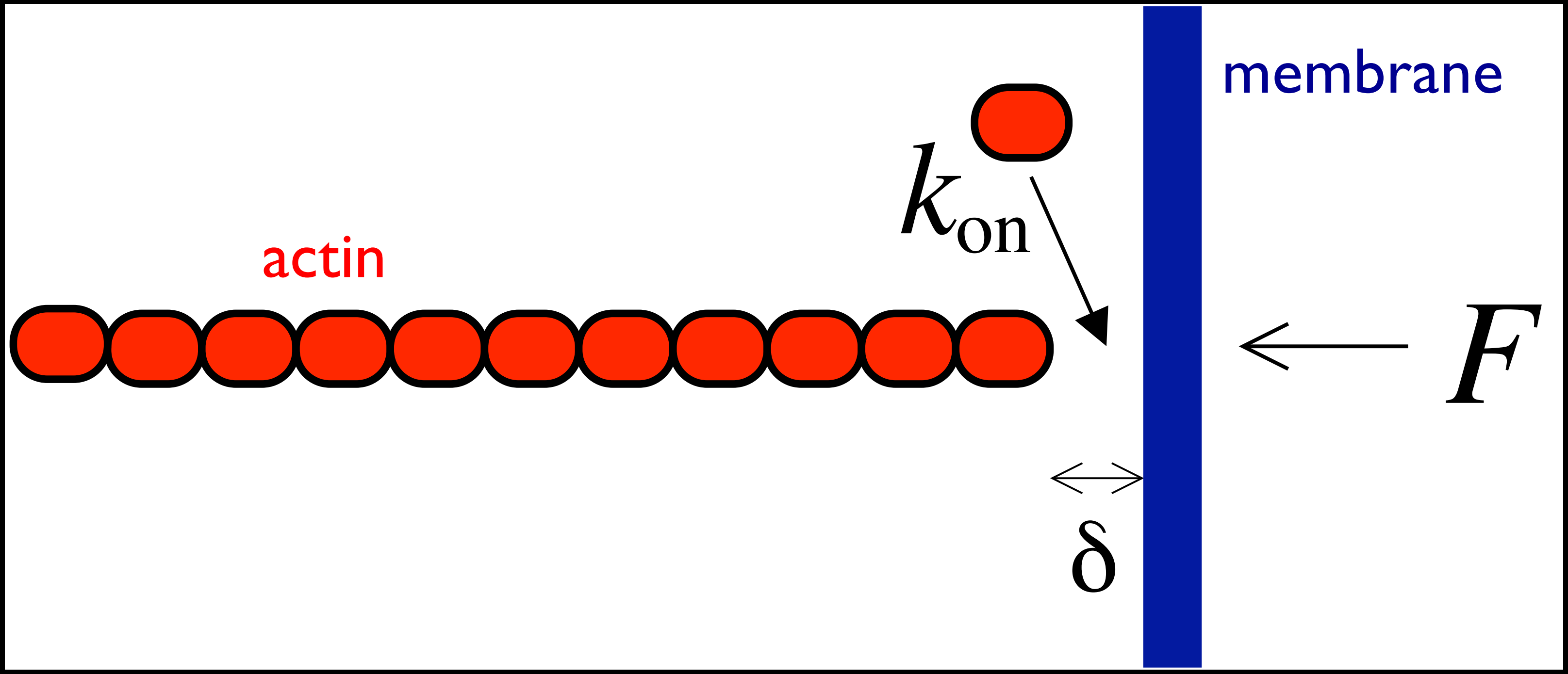


Branching (with Arp2/3)

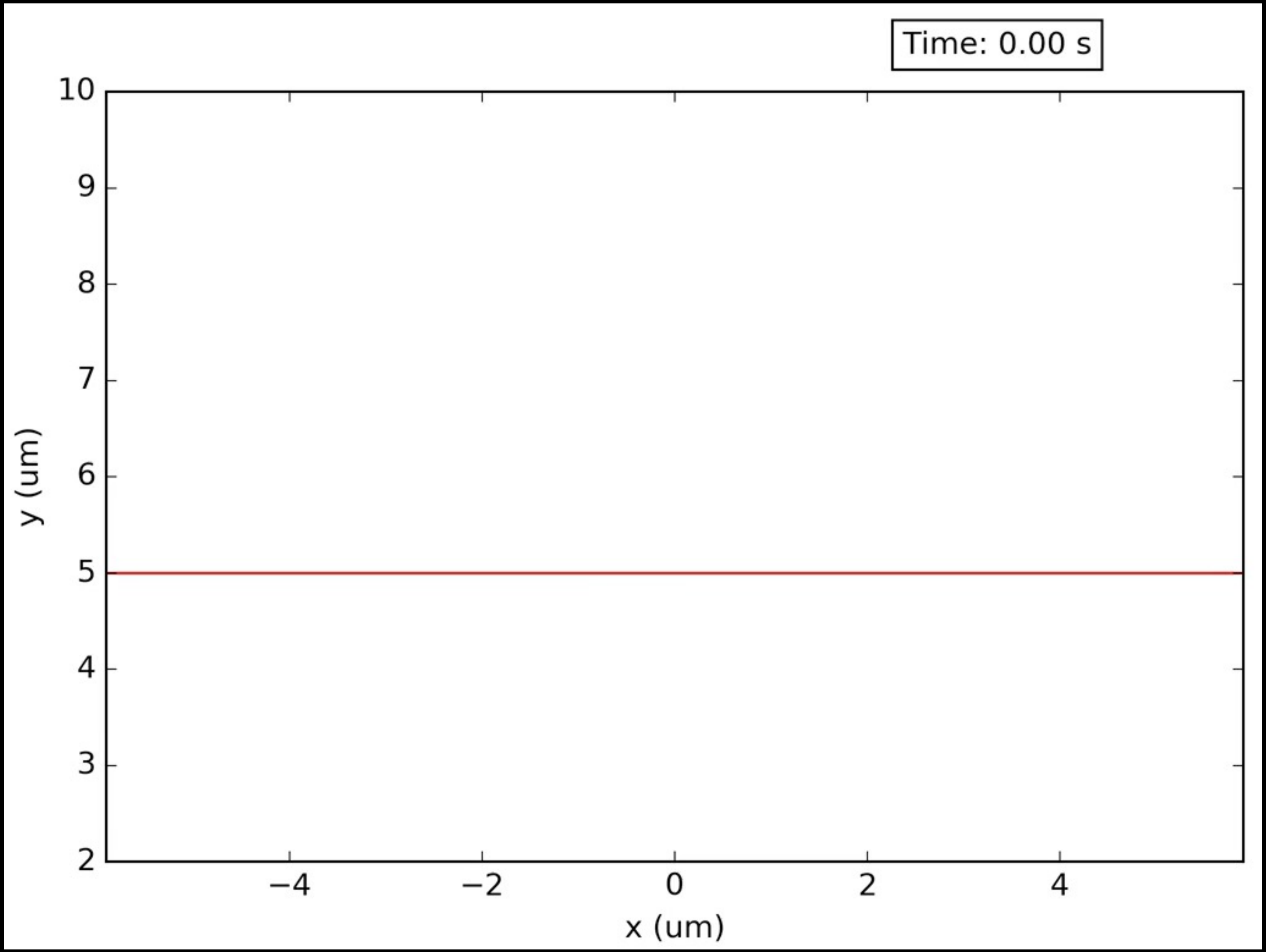




Polymerisation generating a force
Brownian ratchet model

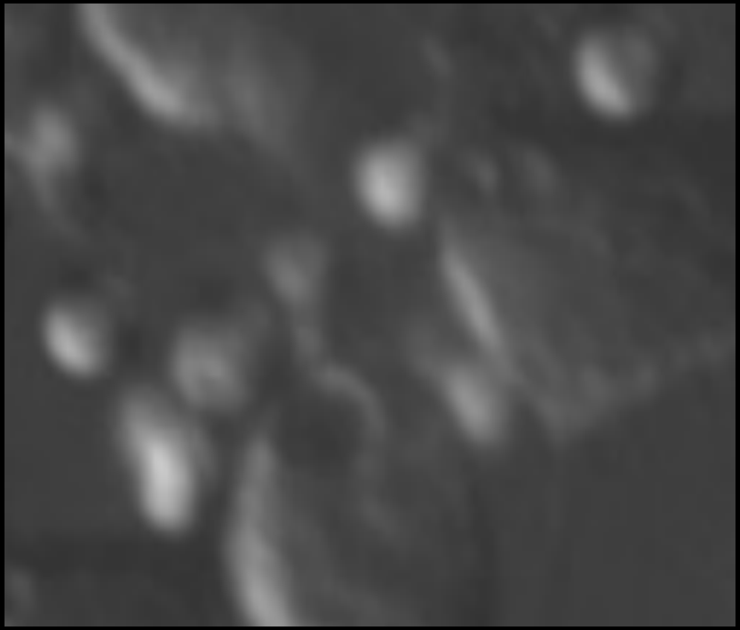


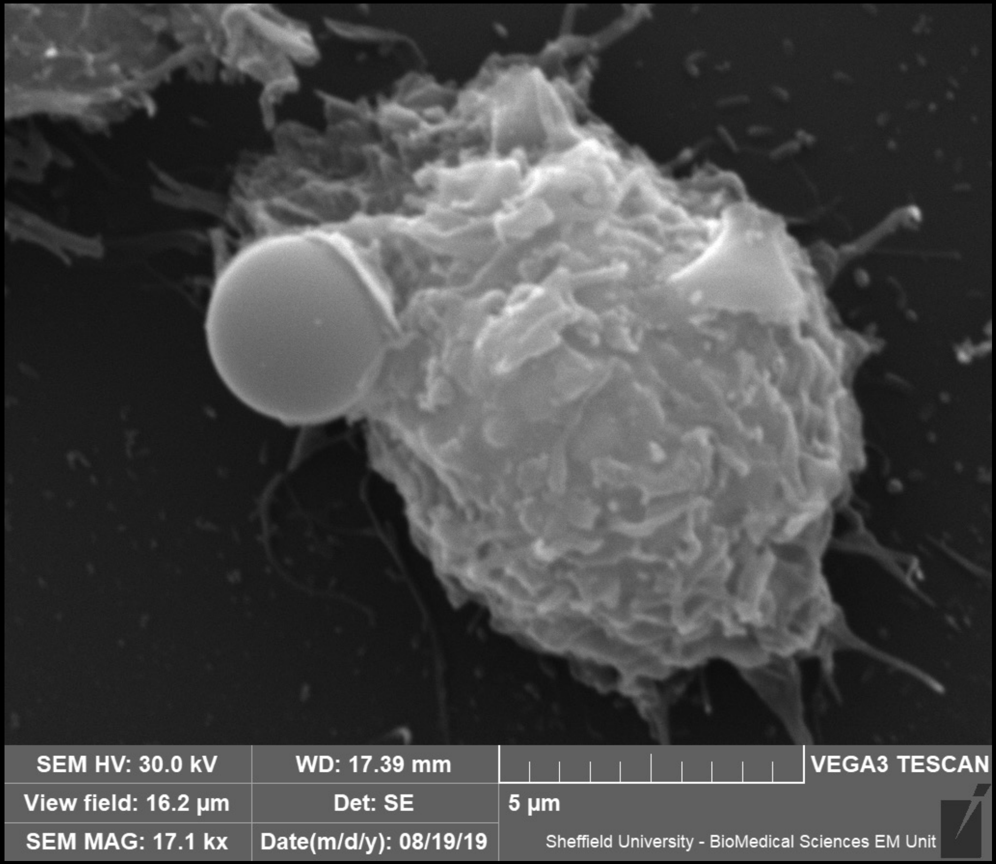
Simulation of actin polymerisation pushing Brownian ratchet mechanism



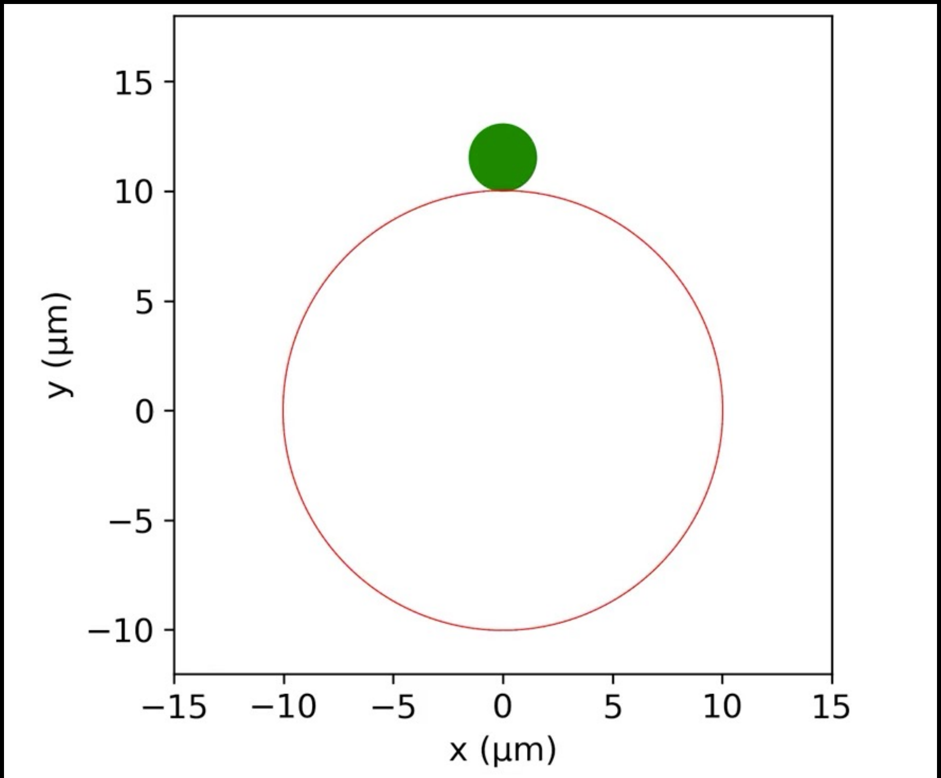
Phagocytosis

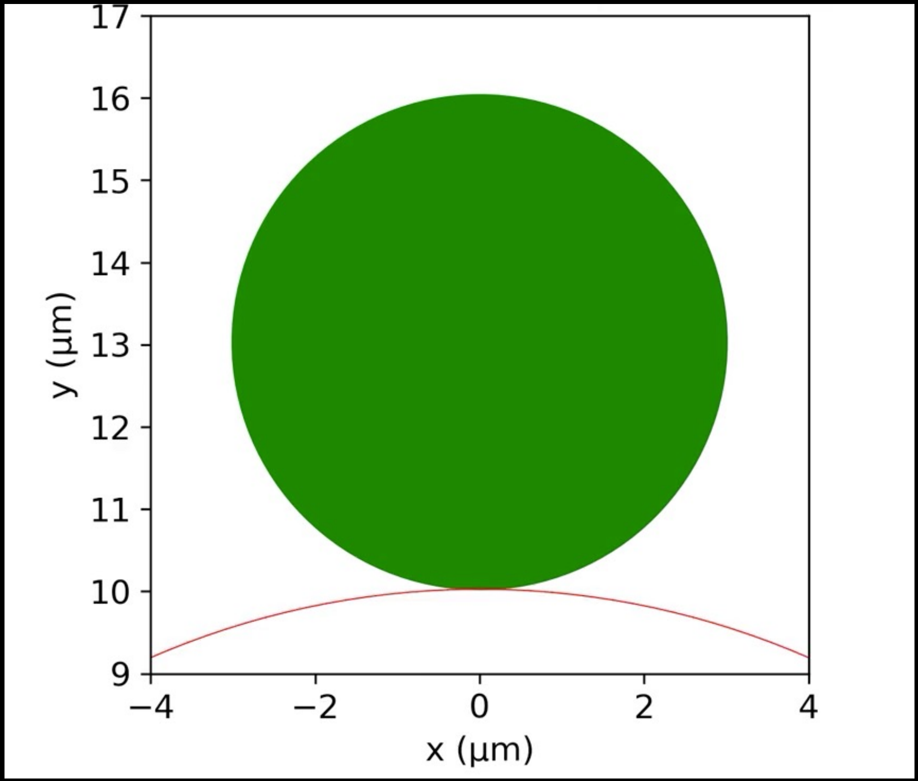
Cryptococcus ingested by macrophage





Phagocytosis simulations



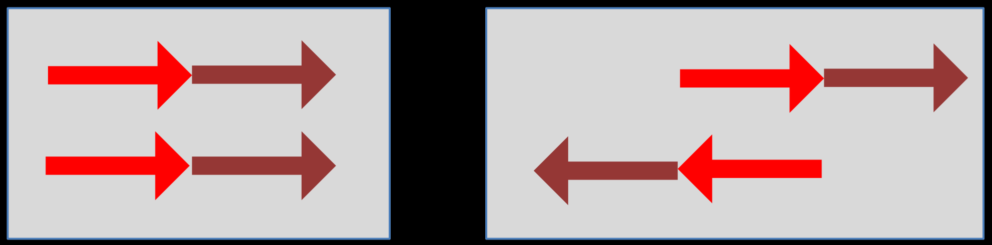


Relate to continuum hydrodynamic models
Kruse et al,…

- Extensile active gel model i.e. $\zeta > 0$

$$\sigma_{\alpha\beta} = \underbrace{2\eta u_{\alpha\beta}}_{\text{viscous stress}} + \underbrace{\frac{\nu}{2}(p_\alpha h_\beta + p_\beta h_\alpha) - \frac{1}{2}(p_\alpha h_\beta - p_\beta h_\alpha)}_{\text{distortion stress}} \underbrace{- \zeta \Delta\mu (p_\alpha p_\beta - \frac{\delta_{\alpha\beta}}{d})}_{\text{active stress}}$$

- Growing filaments exert extensile stress on network
- Nematic or polar?

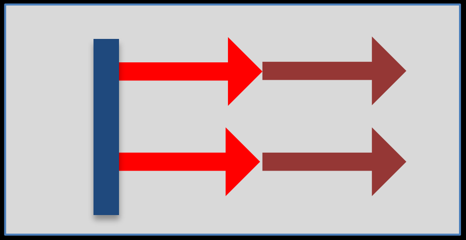


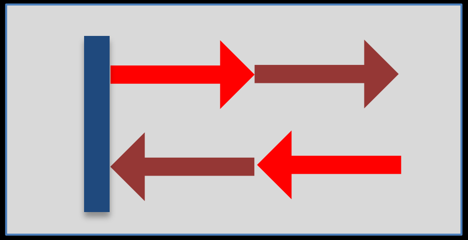
Relate to flocking models
Vicsek, Toner&Tu,…

- Self propelled particles

$$\partial_t \rho = \underbrace{D\nabla^2\rho}_{\text{diffusion}} \underbrace{- \nabla \cdot (\boldsymbol{v}\rho)}_{\text{advection by self propulsion velocity}}$$

- Growing filaments polymerisation velocity
- Nematic or polar?

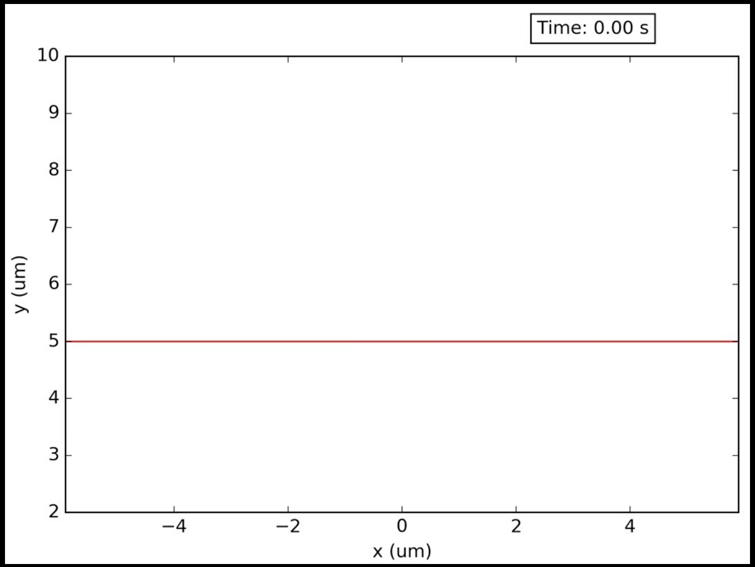


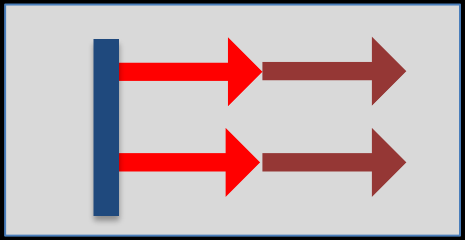


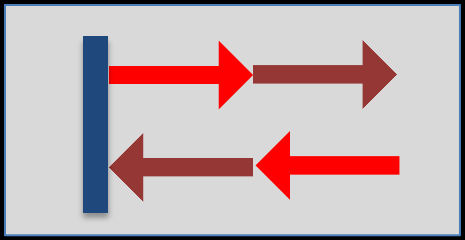
- Treadmilling vs filament growth

Boundaries matter

- Source term for fluid flow
- Pushing against barriers
- Retrograde flow/protrusions at cell boundary



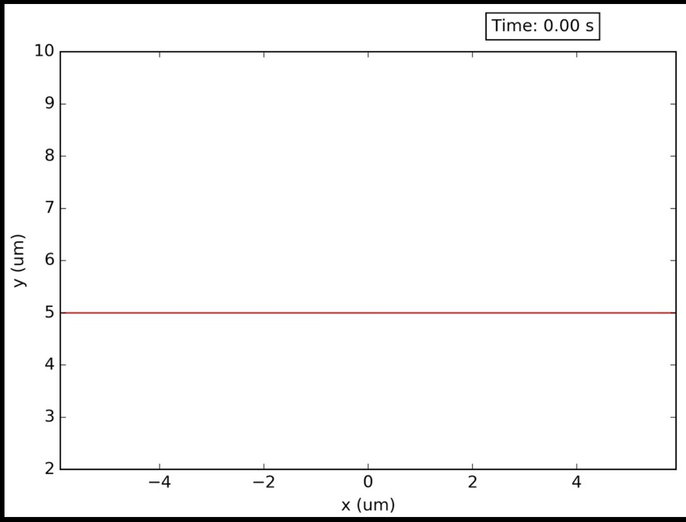




Conclusions & future work

- Polymerising actin networks are an example of growing active matter
- Simulations reproduce Brownian ratchet mechanism for force generation

- Continuum modelling of growing actin networks including extensivity and self propulsion



Title "Growing actin networks”

Abstract:

When driven out of equilibrium by the consumption of biochemical energy, cytoskeletal protein filaments alone and in combination with molecular motors are able to generate sufficient forces to deform and move cells. In particular the protein actin can polymerise into filamentous networks. Continued growth of actin filaments contributes to cell motility and deformation.
First I will discuss our work on polymerising branched actin, comparing in vitro data with simulations and analytical calculations. Then I will present stochastic simulations of polymerising branched actin exerting force to deform a model membrane in the context of phagocytosis, which is a process by which immune cells engulf pathogens.
I will conclude with some discussion of potential universal characteristics and general principles of growing active matter from the perspective of growing actin networks.