Jan 11

An idea to test anti-gravity: Ask for an excersize (maybe in excel) to understand Actin comet tail code more intuitevely by writing out a couple of iterations by hand . I can give professor Tom use AI by hand a Google sheets for as an example for better context of what I'm looking for, if i can get my hands on one that is free.

Jan 13

Wossner 2025

↳ local monomer depletion as negative feedback

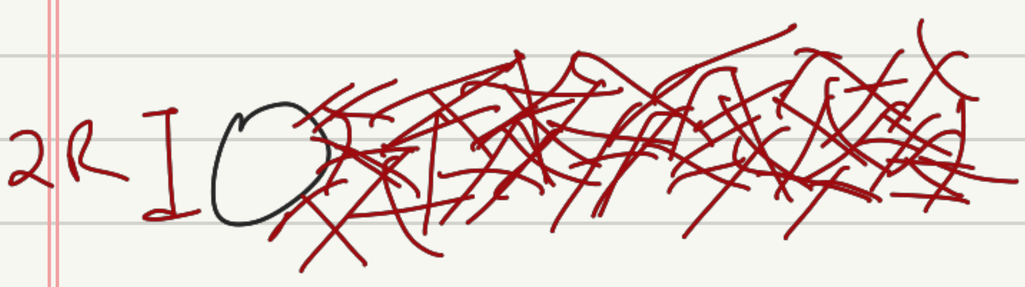
II Model

A. Molecular mechanisms and

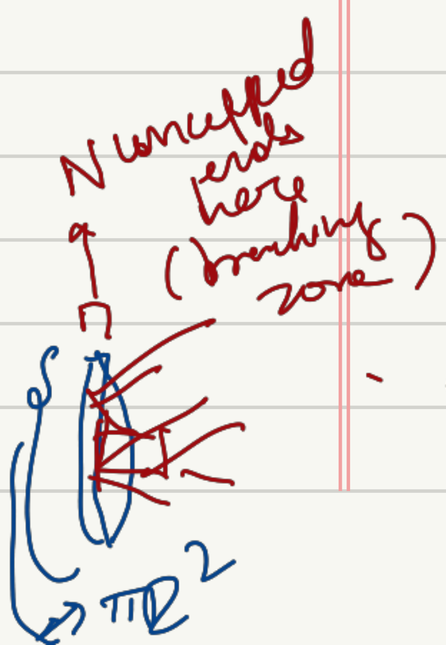
Fast monomer consumption (more monomer depletion)
↓
locally dense networks.
↓
system's growth becomes diffusion-limited.

ADF/cofilin depletion can lead to positive feedback.
↓
possible increase the network length.

B. Growth eqn



assuming network is a cylinder with same radius as the bead (ignoring curvature of the bead in the network's shape))



- N: all uncapped barbed filament ends within the branching region.
- $n = \frac{N}{\pi R^2}$ area density of uncapped filaments in the branching zone.

eqn (1)

$$\dot{n} = ([NPF][Arp]\, k_{branch}\, g(n) - [cap]\, k_{cap})\, n$$

- [NPF] → surface density of NPFs
- [Arp] → vol. density of Arp2/3 & capping proteins
- g(n) → conc^n of actin monomers in the branching zone.

two steady states from this eqn:

for $n = 0$

$\dot{n} = 0$

for $g(n) = \dfrac{[cap]\, k_{cap}}{[NPF][Arp]\, k_{branch}}$

$\Rightarrow \dot{n} = 0$

∴ Local monomer depletion as negative feedback.

- Local :⟶ the branching zone

1. Monomer depletion rate depends on actin polymerisation rate

⇒ total # of monomers getting polymerized by the growing network (per second)

$$\pi R^2 k_{poly}\, g(n)\, n$$

2. Monomer replenishment depends on diffusion of monomers to the branching region (from all directions)

the diffusion can be described by the following equations:

eq.(2a) $$\frac{D}{r^2}\frac{\partial}{\partial r}\left[r^2\frac{\partial}{\partial r}g(n,r)\right] = 0$$

- no source term (use eqn (2b) instead for monomer conc^n)

eq(2b) $$\int_V g(n,r)\,dv = G(n)$$

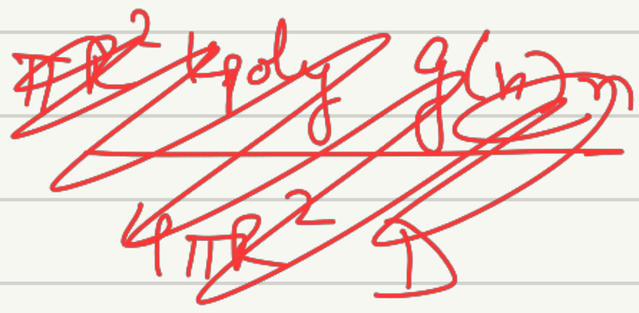
dv: volume of the n-well

$G(n)$: total # of available monomers in the n-well.

eq(2c) $$\text{or} \quad g(n,R) = \frac{k_{poly}\, n}{4D}\, g(n,R)$$

the Boundary cond^n.

↳ comes from equating the total monomer consumption to the diffusive replenishment in the branching zone.



- monomer consumption rate = diffusive replenishment (flux)

$$\rightarrow \pi R^2 k_{poly}\, g(n,R)\, n = 4\pi R^2 \cdot D \cdot \frac{\partial}{\partial r} g(n,r)$$

$g(n,R)$ ↓ at the boundary ($r=R$)

$$\rightarrow \boxed{\text{eqn (2c)}}$$

analytic solution of (2a), (2b) & (2c) gives the total monomer concentration at $r = R$:

eq(3)

$$g(n) = \frac{6(n)}{\sqrt{\left[1 + \frac{R \cdot k_{poly} \cdot n}{4D}(1-\Delta)\right]}}$$

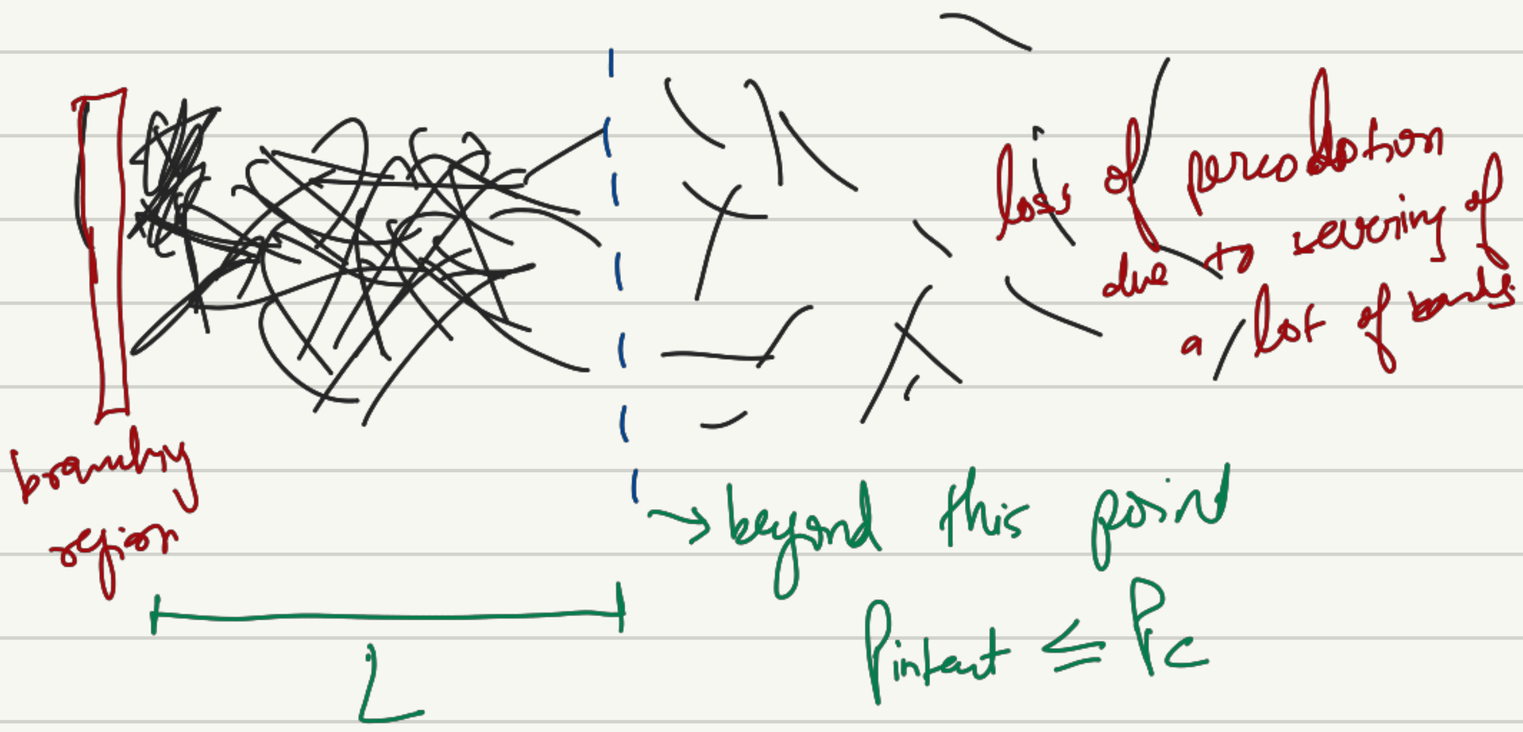
Δ : dimensionless geometrical factor

$g(n) \sim \frac{1}{(1+n)}$ (which matches Banerjee & Bowyer's result (2022))

D. Loss of percolation determines network length.

p_c : critical bond fraction characterizing loss of percolation in the network.

p_{intact} : fraction of intact bonds in the network



* severing rate $\propto$ length of filaments. (severing can take place at any point on the filament)

$\propto \xi$ (mesh size)

some effective base rate per unit length.

$\therefore$ total severing rate $\approx K_{sev}\,\xi$

$P_{intact}(t) = \exp\left[-K_{sev}\,\xi\,t\right]$

frac. of intact filaments after time 't'

with $t = \frac{l}{V}$; l → dist. from branching zone; V → velocity of network growth

eq (4) $$P_{intact}(l) = \exp\left(-\frac{K_{sev}\,\xi\,l}{V}\right)$$

eq (5) Network length: $$L = \frac{V}{K_{sev}\,\xi}\ln\left(\frac{1}{P_c}\right)$$

↳ from simulation by Michalski & Carlsson.

- K_{sev} is not very well known (b/c the molecular details are not very well measured ADF/ cofilin ...)

- P_c is not known (i.e. precise value is not available in the literature)
  ↳ set equal to the value for simple cubic lattice and choose two effective sets of branching & severing as DOF

* velocity of network growth as a fn of polymerization velocity:

eq (6)

$$V = \phi V_{poly} = \begin{cases} 0 & , \quad n = 0 \\ \phi \, k_{poly} \, g(n) \, d_0 & , \quad n > 0 \end{cases}$$

ϕ → $\cos(35^\circ) \approx 0.82$ for low load force against polymerization

d_0 → half-size of actin monomers.

also,

$$\xi = \frac{1}{\sqrt{n}}$$

mesh size, corresponds to avg. filament spacing.

n →
- density of uncapped barbed ends in the branching zone.
- Same as the filament density (1 barbed end = 1 filament)

$$F = \text{branching zone area} \times \int_0^L \text{filament density} \; \frac{}{d_0 \phi}$$

L → integration over network length.

F → total # of actin monomers in the network

$d_0 \phi$ → to convert the numerator to # of monomers.

$$F = \pi R^2 \cdot \frac{1}{d_0 \phi} \int_0^L n \cdot P_{\text{linker}}(l) \, dl$$

$P_{\text{linker}}(l)$ → filament density (exponential decay as it moves away from the seed)

using expr. of [redacted] Pinduct/l) & 'L'

eq.(8) $$F(n) = \frac{\pi R^2 K_{poly} (1-P_c)}{l K_{sen}} g(n) n^{3/2}$$

now,

for 1 bead in a u-well : $G(n) = A_{tot} - F(n)$

eq (9) for N beads in a u-well : $G(n_1, \ldots, n_N) = A_{tot} - \sum_{i=1}^{N} F_i(n_1, \ldots n_N)$

A_{tot} → total monomers in u-well known from experiments.

i → bead index

plugging in eq(3) ($g(n)$) & eq(8) ($F(n)$):

eq(10) $$G(n_1, \ldots n_N) = \frac{A_{total}}{1 + \sum_{i=1}^{N} \frac{\pi R^2 K_{poly} (1-P_c) n_i^{3/2}}{\sqrt{K_{sen}} \left[1 + \frac{R K_{poly} n_i (1-D)}{4D}\right]}}$$

global monomer conc^n when there's multiple beads in the u-well

to make Eqn (1) dimensionless:

Scale n by: $\left[\frac{V K_{sev}}{\pi R^2 K_{poly}(1-\rho_c)}\right]^{2/3}$

and time by: $\frac{1}{[cap]\, K_{cap}}$

eq(11)

$$\dot{x}_i = \left[\frac{A_i}{1+\sum_{j=1}^{N}\frac{x_j^{3/2}}{1+\beta x_j}}\cdot\frac{1}{1+\beta x_i} - 1\right] x_i$$

x_i ← dimensionless filament density.

main result

↳ dynamics of dimensionless filament densities

#Jan 14

eq(12a) effective branching parameter: $A_i = \frac{A_{tot}\,[NPF]_i\,[Arp]\,k_{branch}}{V\,[cap]\,k_{cap}}$

* A_i ~ $\frac{\text{branching}}{\text{capping}}$

↳ different for different beads ($[NPF]_i$)

eq(12b) effective depletion parameter: $\beta = \left(\frac{l_{poly}}{R}\right)^{1/3}\left(\frac{V K_{sev}}{\pi(1-\rho_c)}\right)^{2/3}\frac{1-\delta}{l_D}$

* $B \propto \frac{1}{D}$ (inversely propto D, affects local monomer conc^n)

$D \to \infty$, $B \to 0$ (all depletion vanishes)

III Results

A. Single network & parameter estimates

for single bead, eq^n (11) becomes

eq(13) $$x^{3/2} + Bx + 1 - A = 0$$

$x > 0$ (non-zero solutions only)

* Bifurcation point in all the graph correspond to onset of network formation.

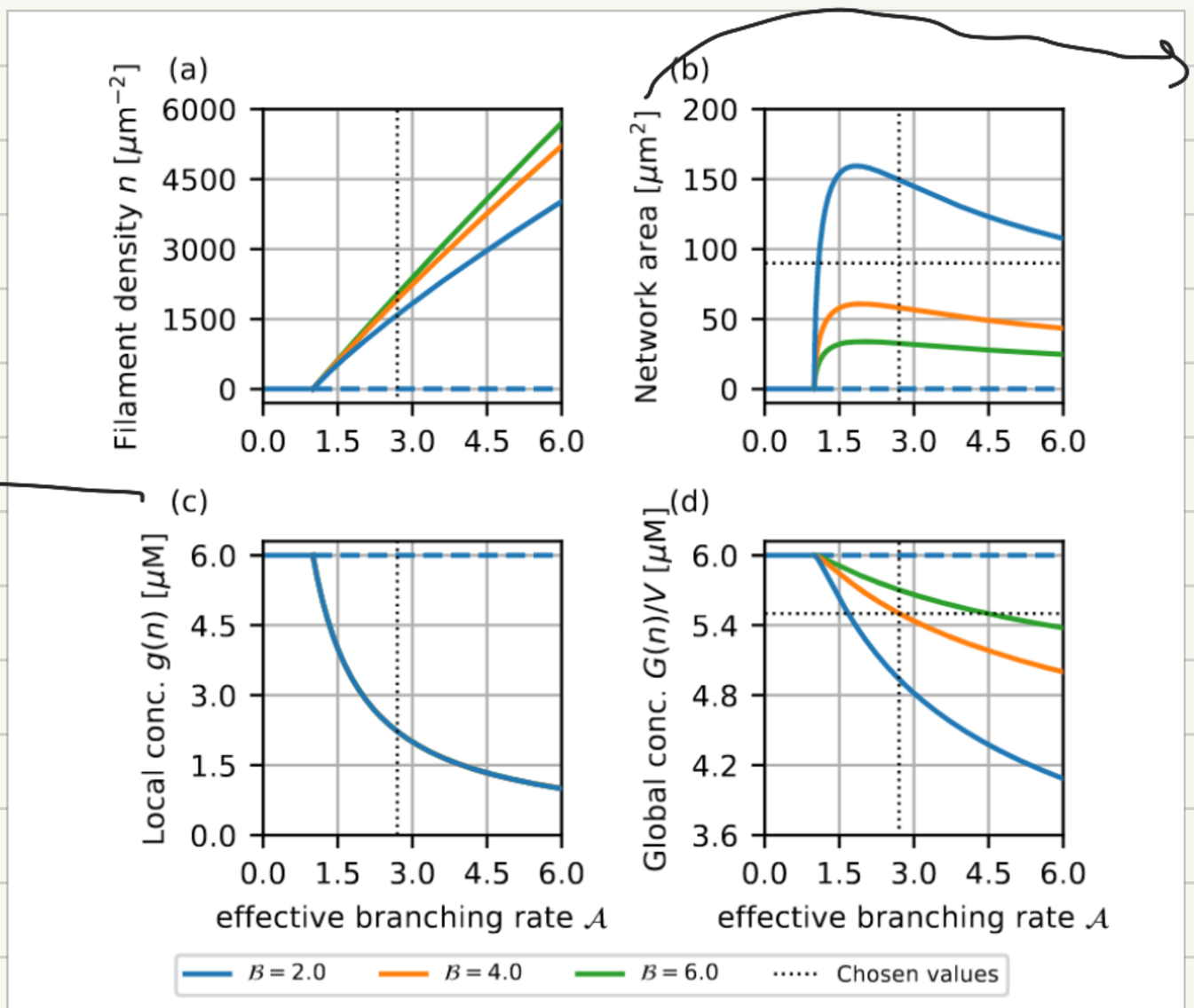


FIG. 3. Bifurcation diagram for a single network obtained by numerical continuation. (a) Filament density n of the network in the branching zone as a function of effective branching rate $\mathcal{A}$ for different values of the depletion parameter $\mathcal{B}$. The dimensionless parameters $\mathcal{A}$ and $\mathcal{B}$ correspond to the rates k_{branch} and k_{sev}, respectively. (b) Projected area of the network given by $2R$ times the network length L. (c) Local concentration $g(n)$ of actin monomers in solution inside the branching zone, independent of $\mathcal{B}$. (d) Global actin monomer concentration as average over the whole microwell.

Area = $2RL$

remember the eqn (5) for network length derived from percolation arguments & lattice models

$g(n) \propto \mathcal{A}^{-1}$

$\Rightarrow$ $g(n) \propto k_{branch}^{-1}$

(irrespective of value of $\mathcal{B}$)

- exactly as expected.

Estimating $\mathcal{A}$ & $\mathcal{B}$

choose $\mathcal{A} = 2.7$

from (12a) $k_{branch} \approx 7.26 \times 10^{-11}$

$\mathcal{B} = 4.0$ to match $G(n) = 5.5$ from Guérin et al. (2022)

$\Rightarrow$ $L = 13\,\mu m$

$\therefore A = 2RL \approx 60\,\mu m^2$

within same order of magnitude as measured in Guérin et al.

B. Competition b/w identical networks

$A_i \equiv A$ (i can be dropped b/c same NPf surface density for all the seeds)

eq(15) $x_i = x_j \quad \forall\, i,j \in \{1, \ldots, N\}$

⋮

~~Summation eqn~~

filament density eqn becomes.

eq(16) $N x^{3/2} + Bx + 1 - A = 0$

$K_{sev}^{slow\ turn.} = K_{sev}^{fast\ turn.}$

FFT C. Coexistence of dense & sparse networks.

$A_{week} = \frac{1}{2} A_{strong}$.

* competition strength can be controlled by α: $\frac{[NPF]_{weak}}{[NPF]_{strong}}$.

$\delta(C)$: $V_{week} \sim g_{week} \sim \frac{1}{[NPF]}$

Fig 7

is dashed line : steady state value obtained by equation (3) (eqn of $g(n)$) obtained by not considering the source term from sensing & assembly.