Modelling endocytic actin bundling

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With thanks to Kathryn Ayscough

Modelling endocytic actin bundling

- Actin bundling in endocytosis
- Program description
- Boltzmann weighting
- Results
- Next steps

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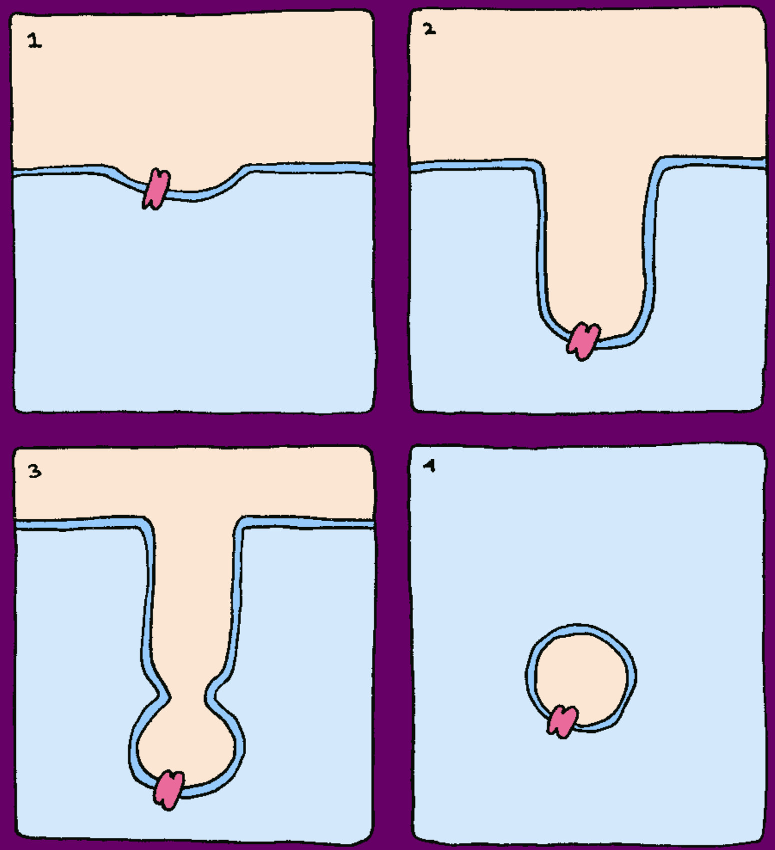
Endocytosis

The way cells take in matter from the outside

1. Pit forms
2. Pit elongates
3. Budding
4. Severing



Actin

A protein that is essential for endocytosis

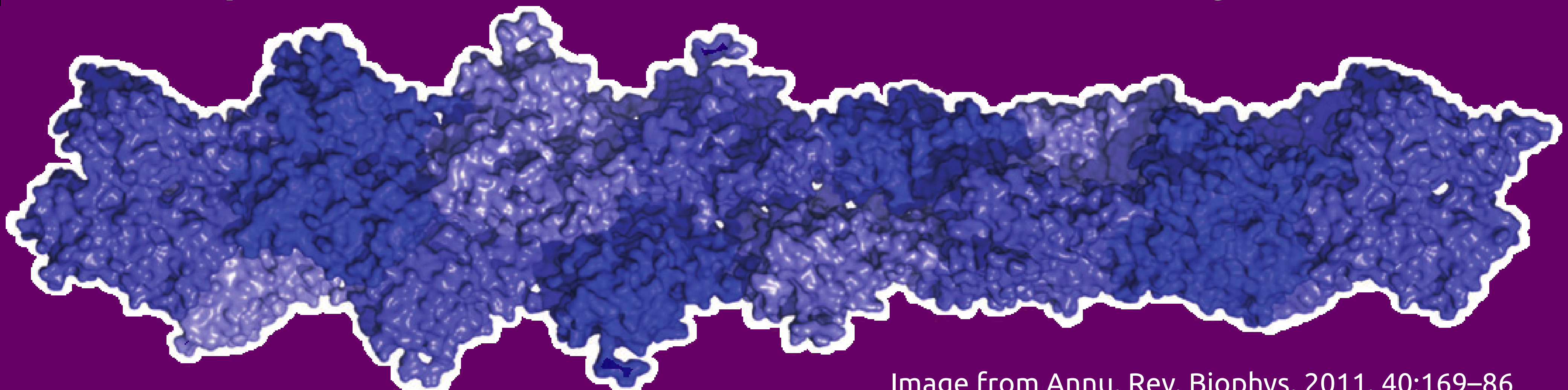
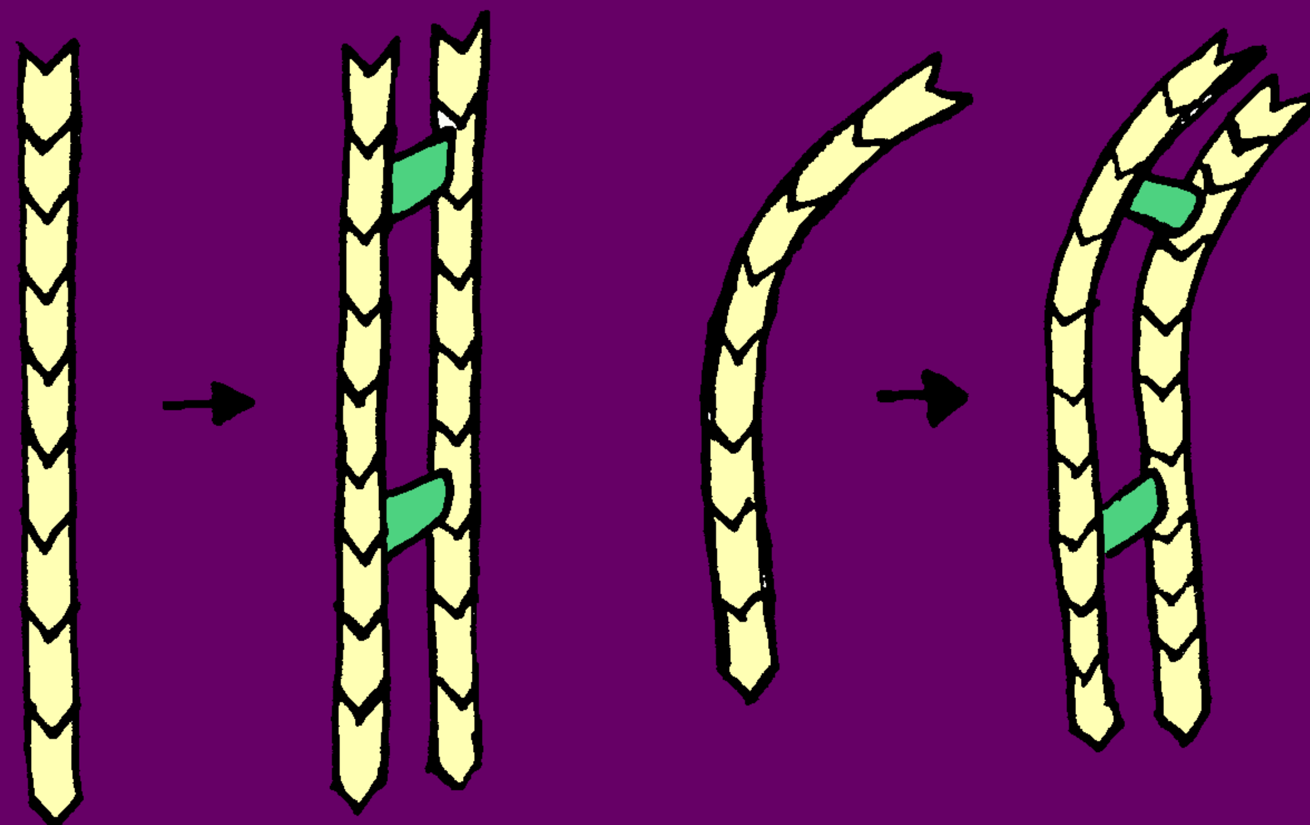


Image from Annu. Rev. Biophys. 2011. 40:169–86

- Forms long filaments
- Structurally polarised
- Actin patches at cell cortex

Fimbrin

Connects filaments together into bundles



Bundles are thicker and harder to bend

Endocytosis

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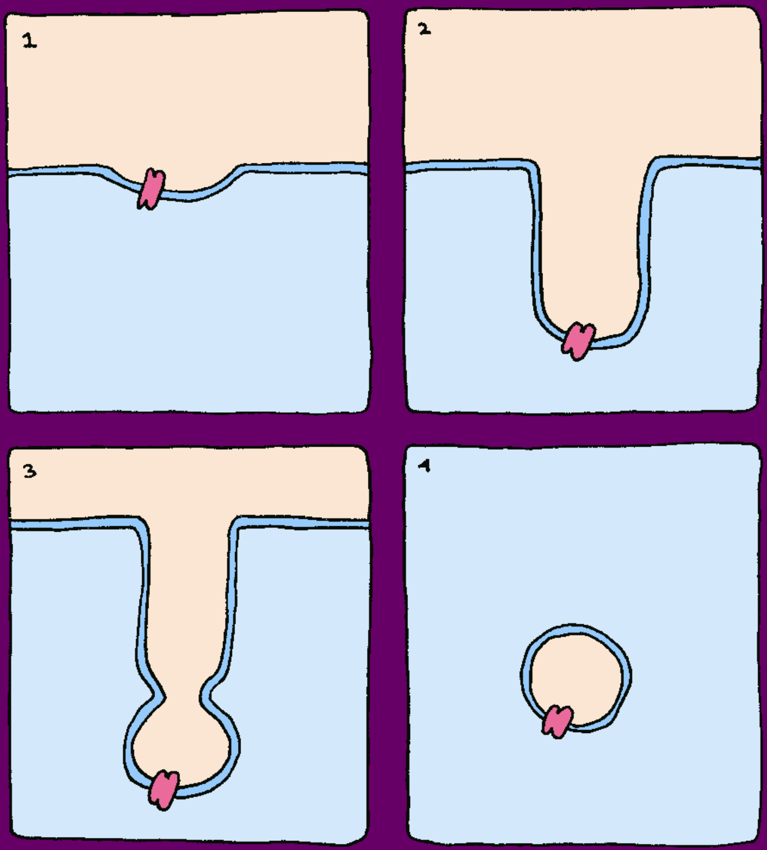
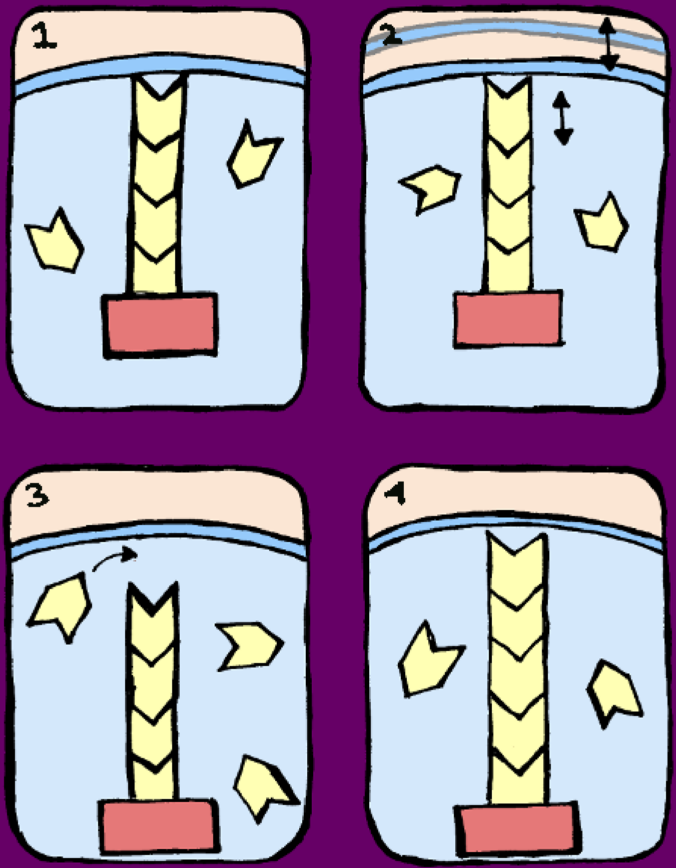


Brownian ratchet mechanism

How actin pulls the invagination tip inwards

1. Filament touches membrane
2. Heat causes movement
3. Diffusion
4. Polymerisation



How do bundling proteins affect the chances of successful endocytosis?

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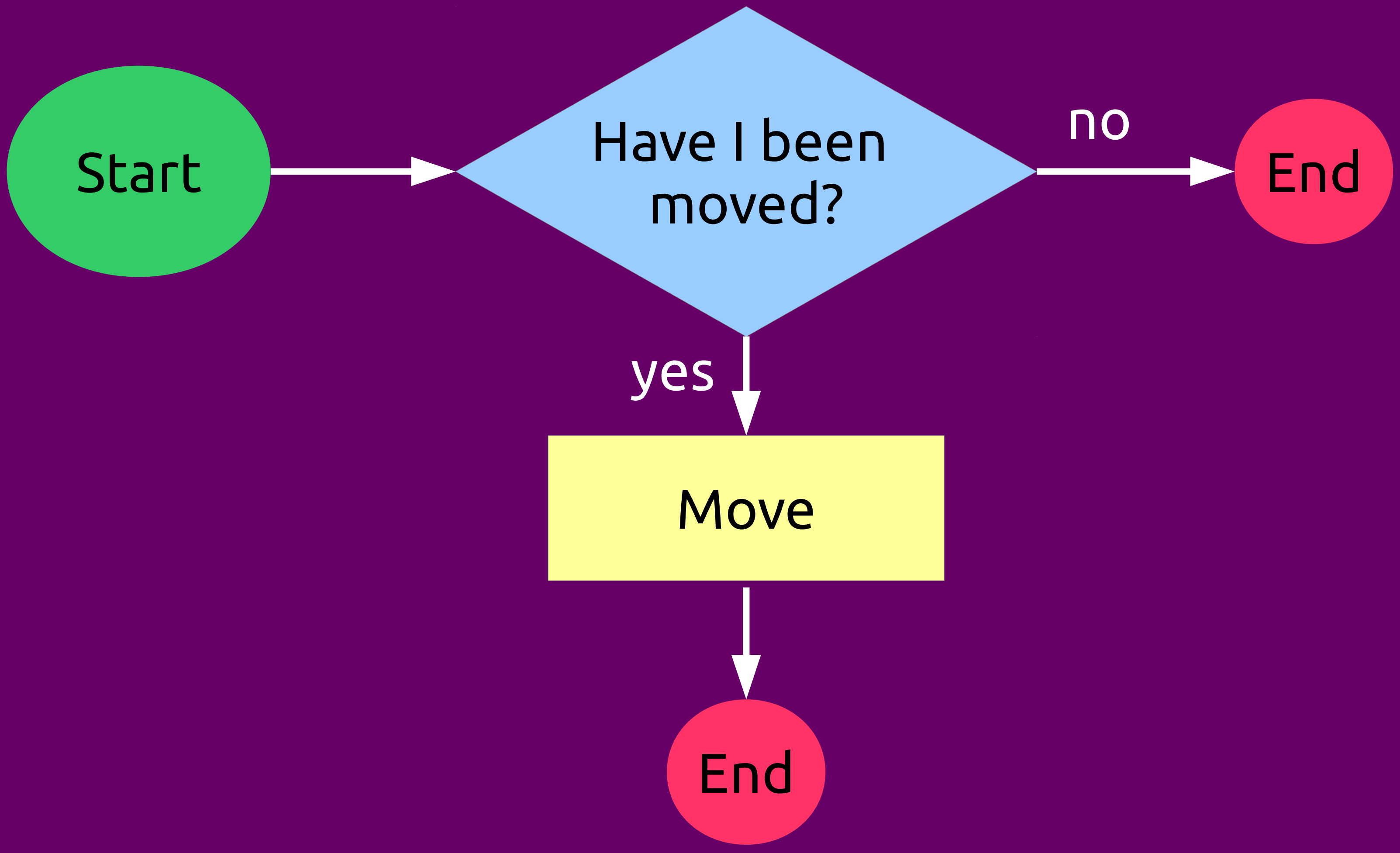
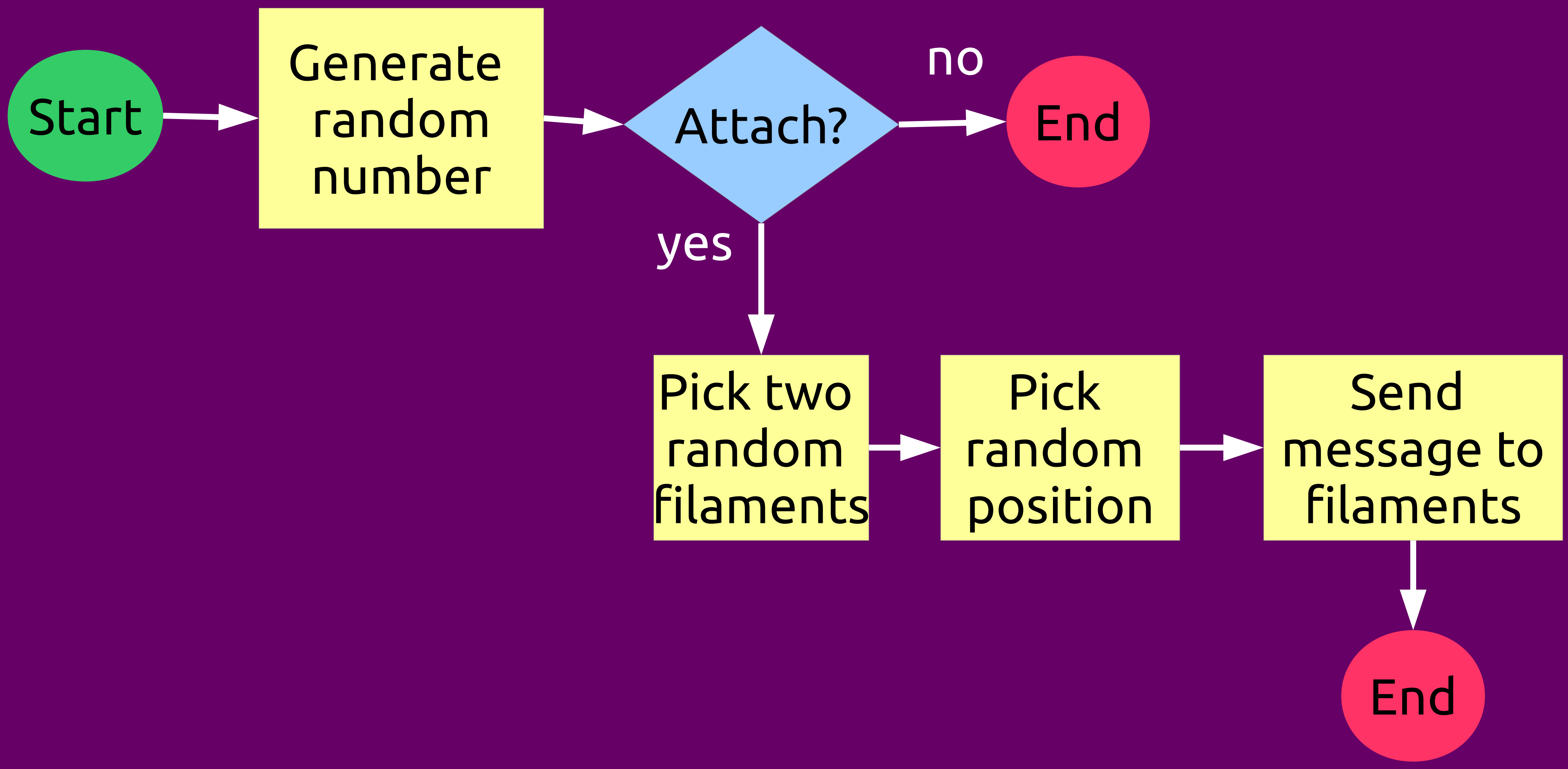
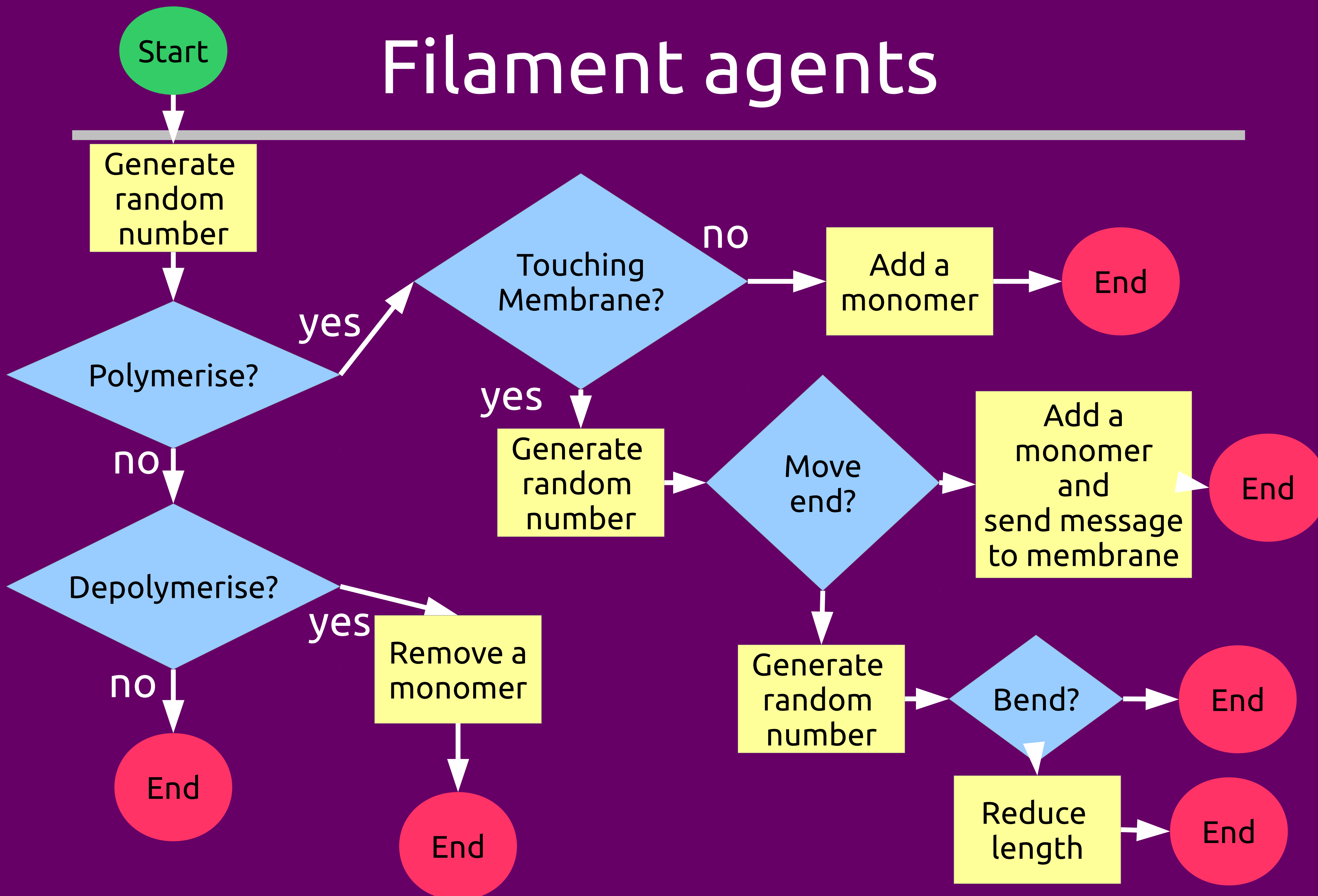
Membrane agent



Bundling protein agents



Filament agents



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Boltzmann weighting

Calculating the probabilities

$$P_i = N\, e^{\frac{-E_i}{k_B T}}$$

$$\frac{1}{N} = \int_0^{\infty} e^{\frac{-E}{k_B T}}\, dE$$

- P_i = probability of state i
- E_i = energy of state i
- $k_B T$ = thermal energy
- N = normalisation factor

Bending

$$E = Y\, l\, i\, C^2$$

$$i = \frac{\pi r^4}{4}$$

- E = energy cost
- Y = Young's modulus
- l = length
- i = moment of inertia
- C = curvature
- r = radius of bundle

Bending

$$P_{bend} = N e^{\frac{Fx - E}{k_B T}}$$

$$\frac{1}{N} = \int_0^\infty e^{\frac{Fx - E}{k_B T}} dC$$

- F = force applied by membrane
- x = distance membrane has been pushed
- E = energy cost of bending
- $k_B T$ = thermal energy

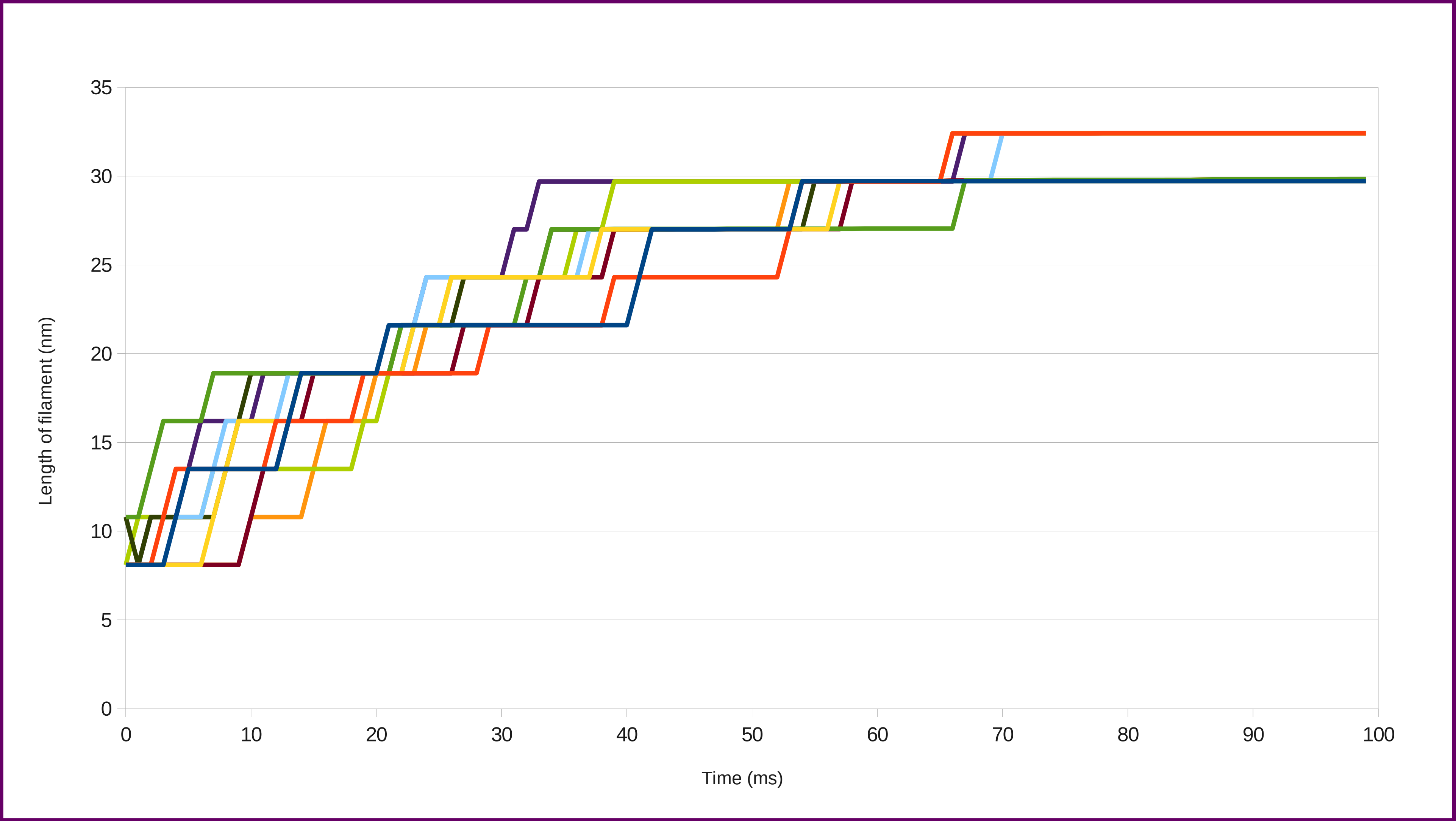
Pushing away from membrane

$$P_{push} = N e^{\frac{-\phi x^2}{k_B T}}$$

$$\frac{1}{N} = \int_0^{\infty} e^{\frac{-\phi x^2}{k_B T}} dx$$

- Φ = membrane tension
- x = distance being pushed
- $k_B T$ = thermal energy

Sample graph of simulation data



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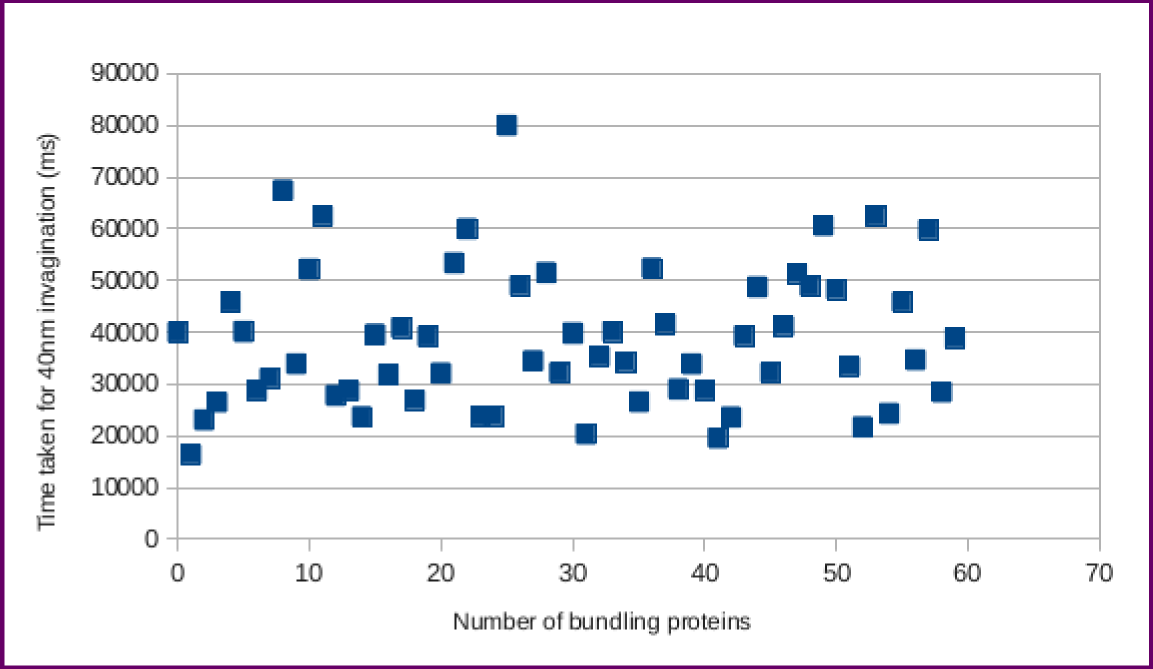
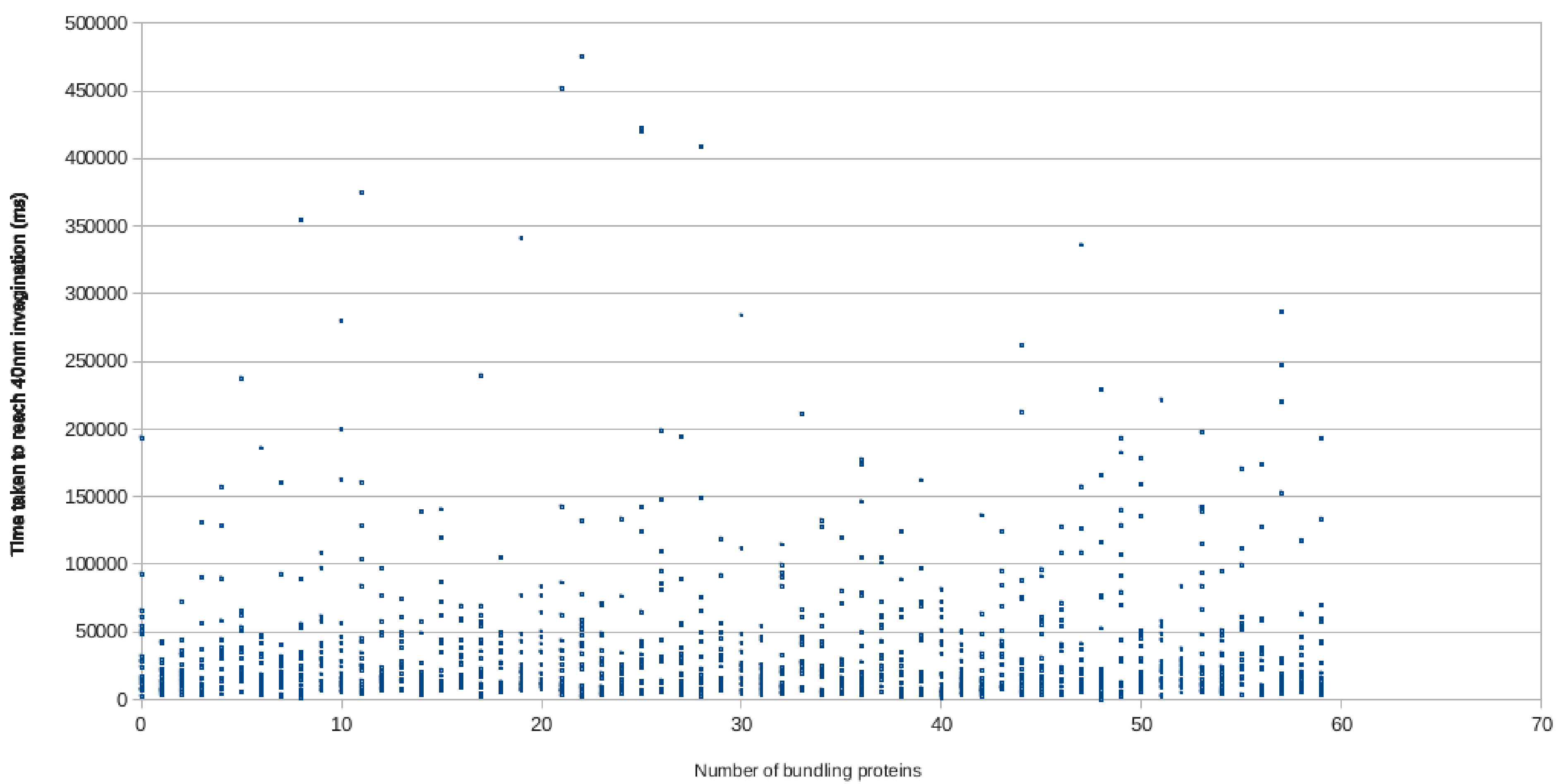
Results



90000
80000
70000
60000
50000
40000
30000
20000
10000
0
Time taken for 40nm invagination (ms)
0
10
20
30
40
50
60
70
Number of bundling proteins

Results



500000
450000
400000
350000
300000
250000
200000
150000
100000
50000
0
Time taken to reach 40nm invagination (ms)
0
10
20
30
40
50
60
70
Number of bundling proteins

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Next steps

- Order in which agents update
- Speed up simulation to allow for more iterations
- Expand simulation to two or three dimensions
- Pushing outwards or pulling inwards?
- Investigate severing, capping and branching

Conclusion

- Agent based model
- Filaments growing against a barrier
- Bundling proteins modify bending
- Wide range of results