How to convert the chemical free energy to mechanical work?

What is the simplest molecular robot that can move?

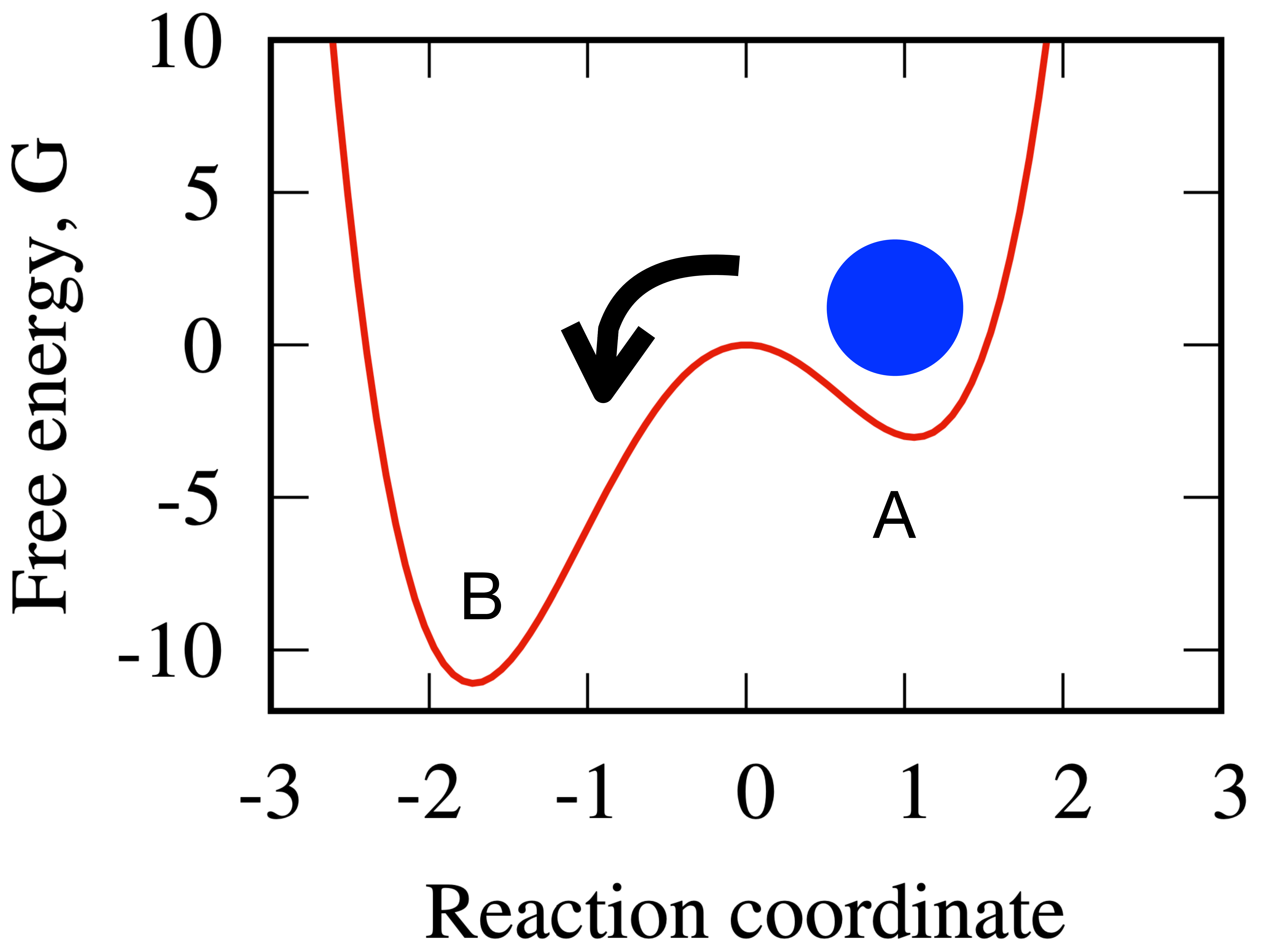
Energy transducer

The free energy gain

$$A \rightleftharpoons B$$

$$\Delta G = \Delta G^0 + k_B T \ln\left(\frac{[B]}{[A]}\right)$$

$$\Delta G^0 = -k_B T \ln\left(\frac{[B]_{eq}}{[A]_{eq}}\right)$$



This is chemical energy. How to convert to mechanical work?

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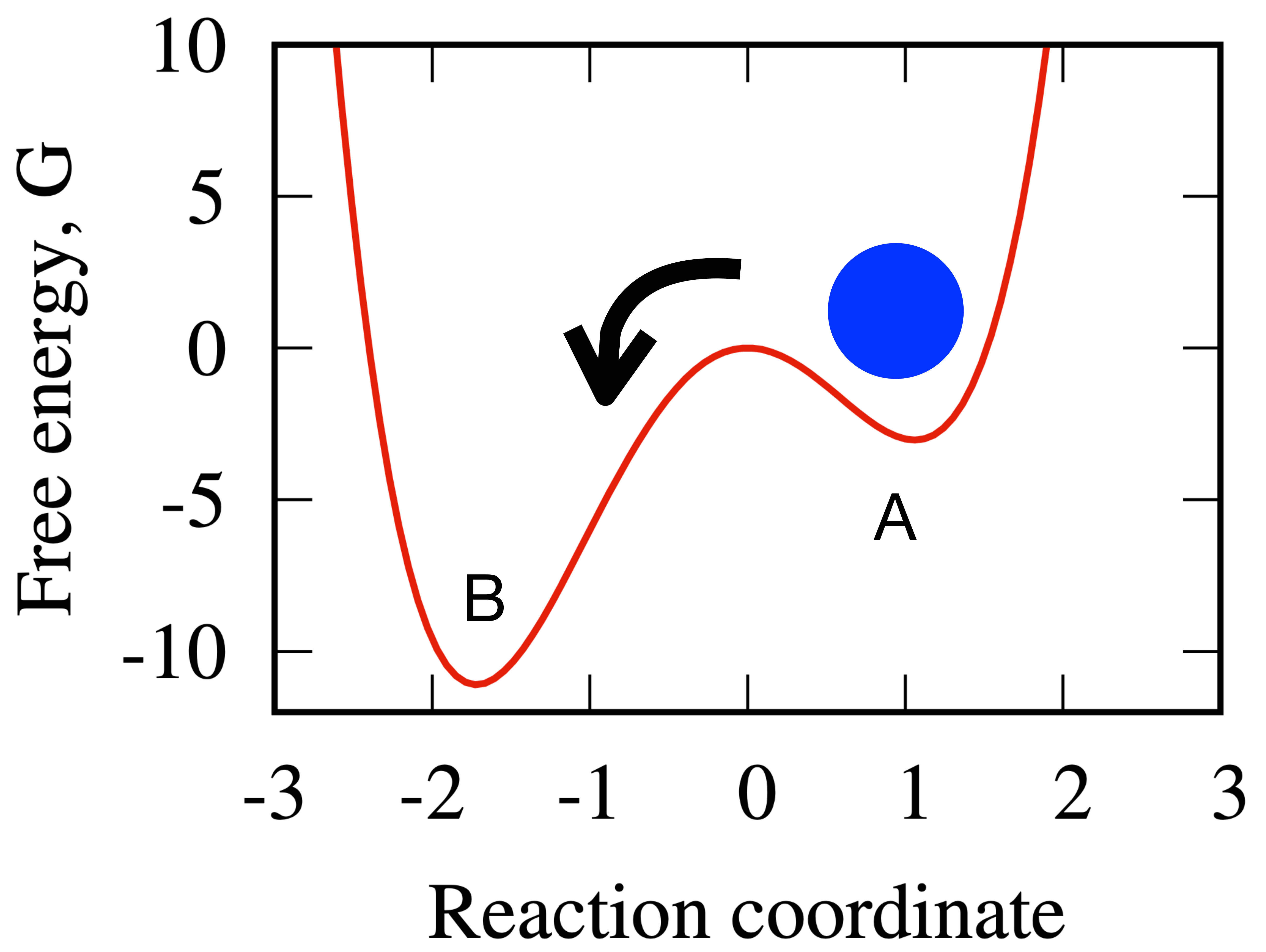
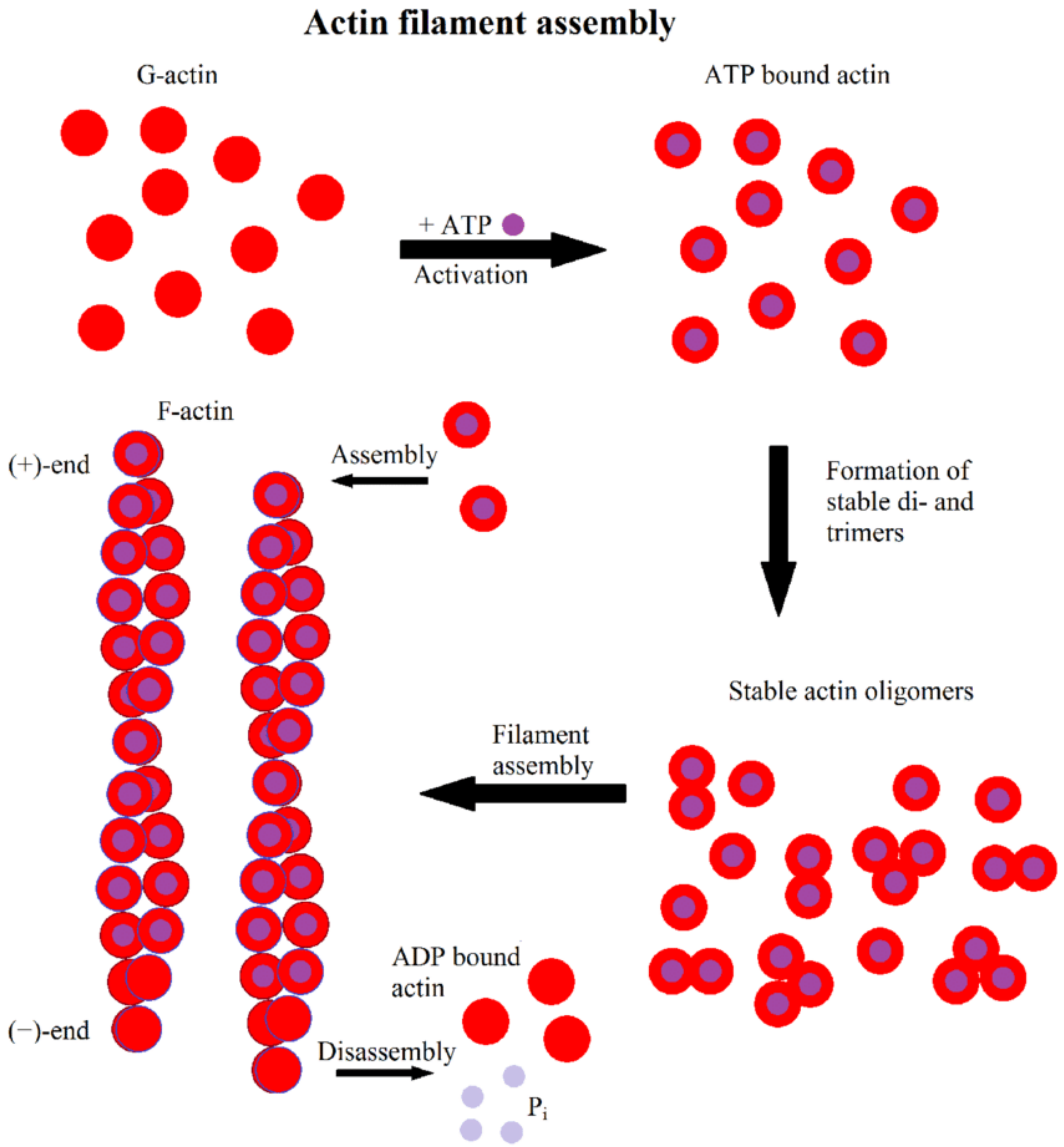


Actin is probably the simplest machine

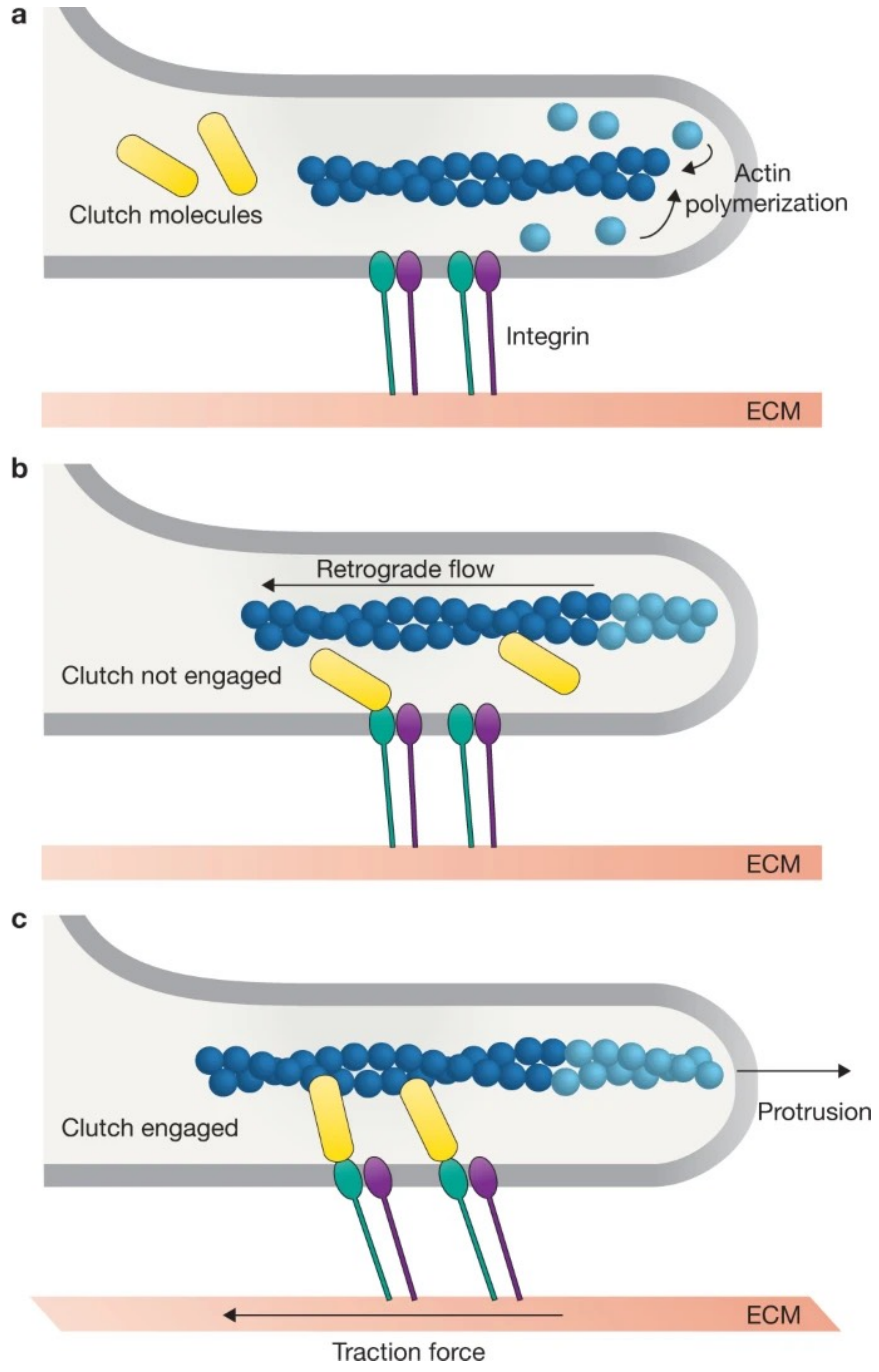


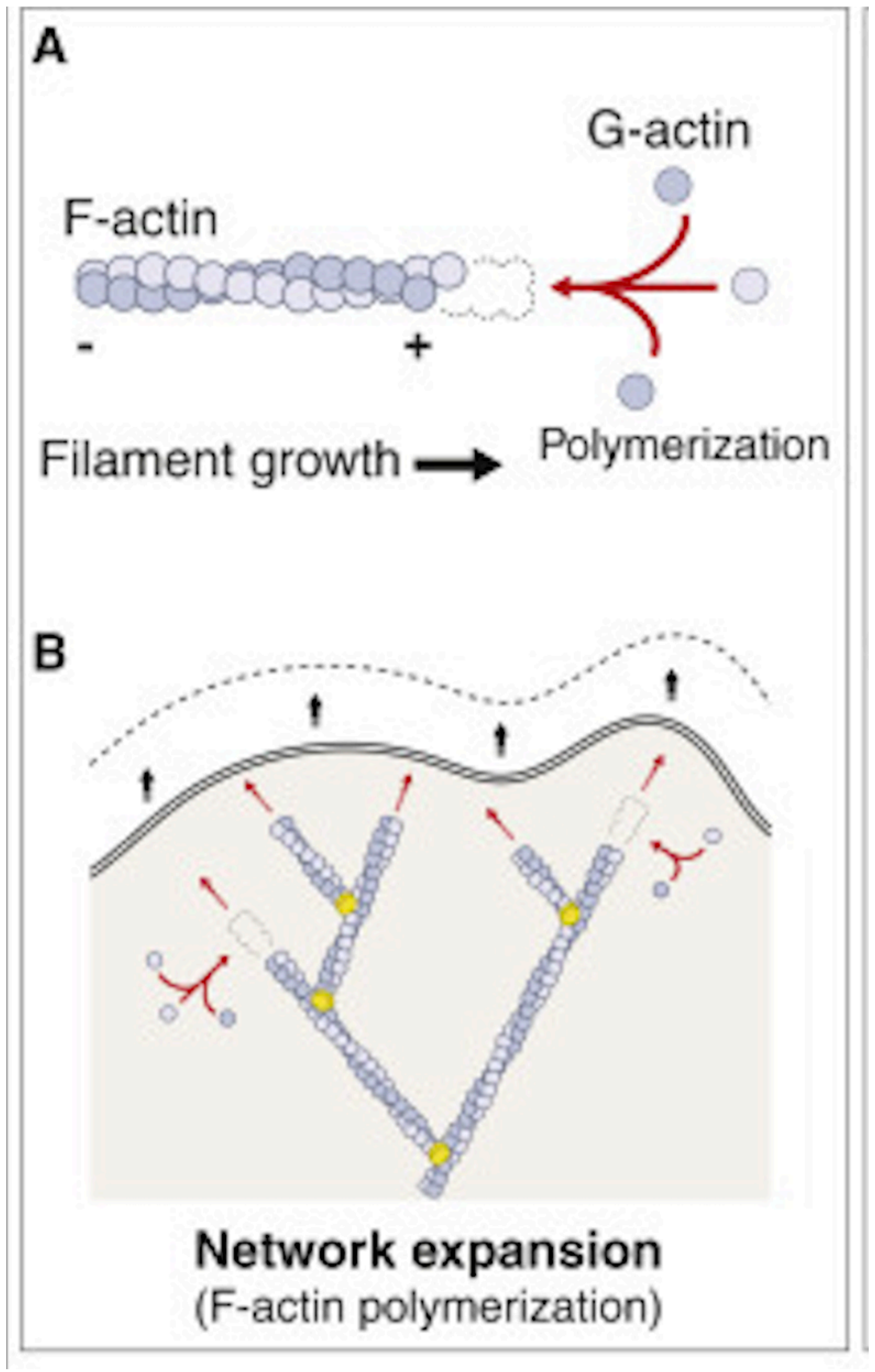
Actin is a protein

Many actin monomers self-assemble and form long filaments

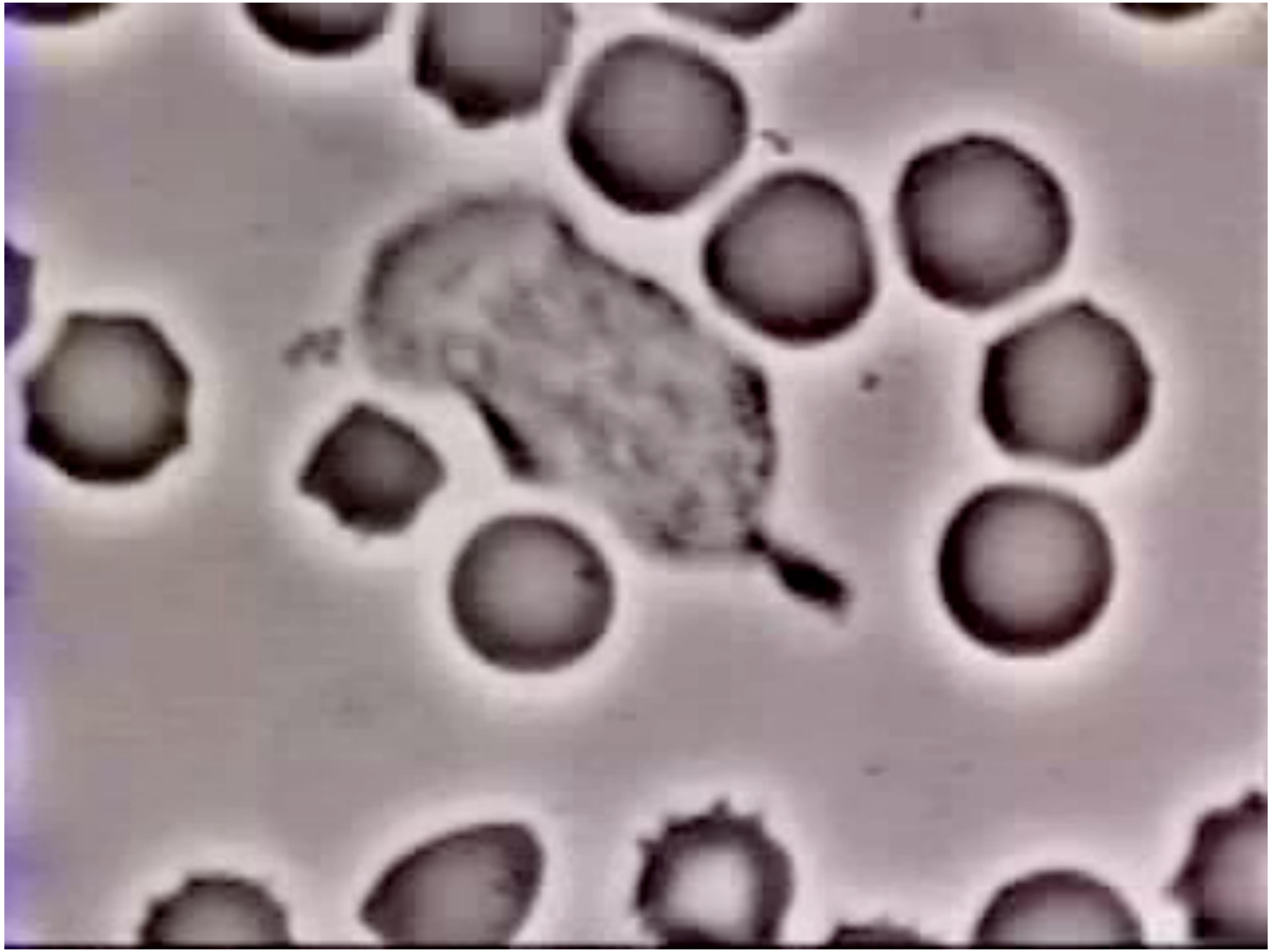
These filaments generate force

Actin polymerisation can push cell membrane





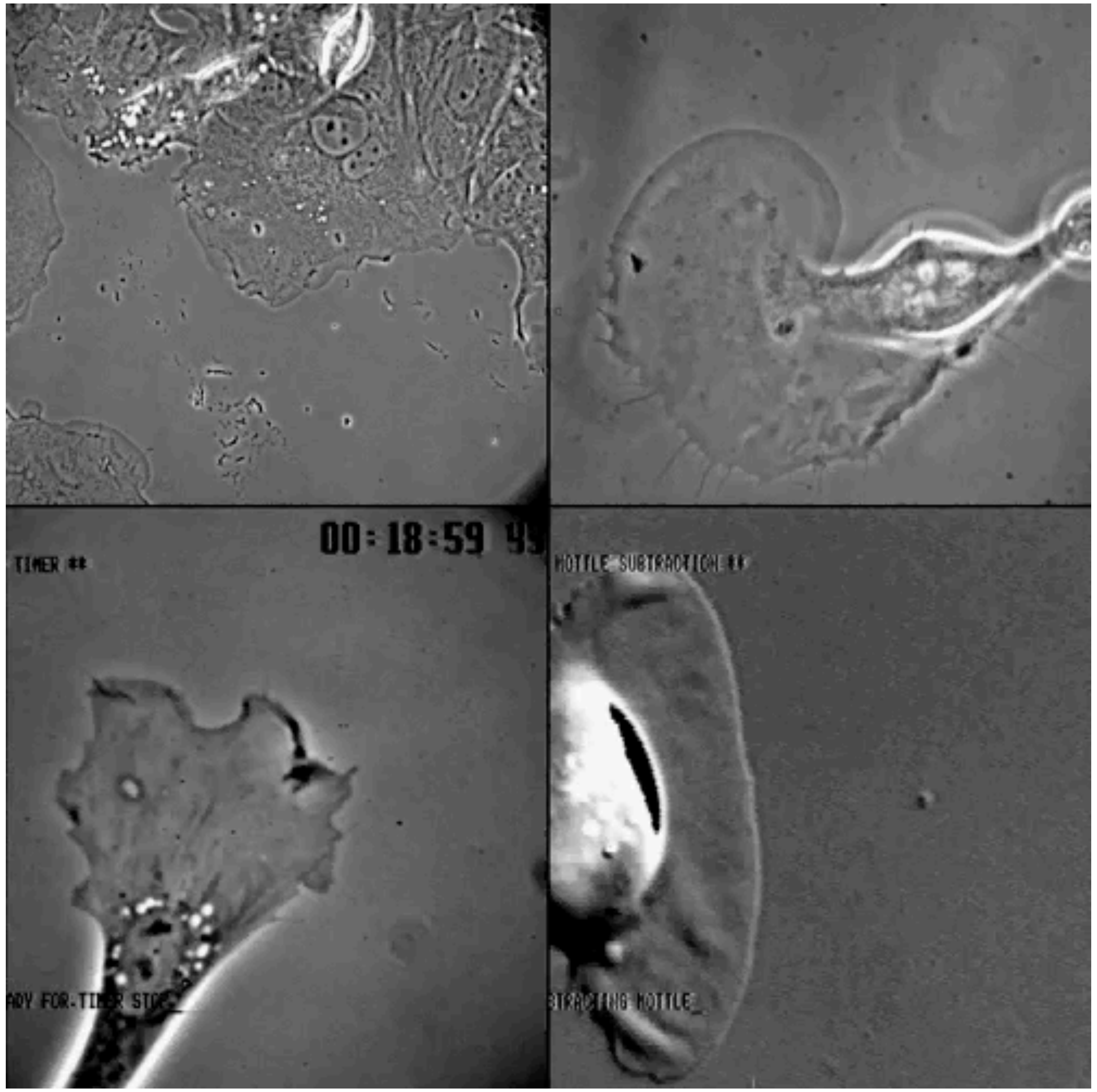
White blood cell chasing bacteria



Cells can generate force and move

Mouse fibroblasts:
Wound healing

Mouse melanoma
cell



Chick fibroblast

Trout epidermal
keratocyte

http://cellix.imba.oeaw.ac.at

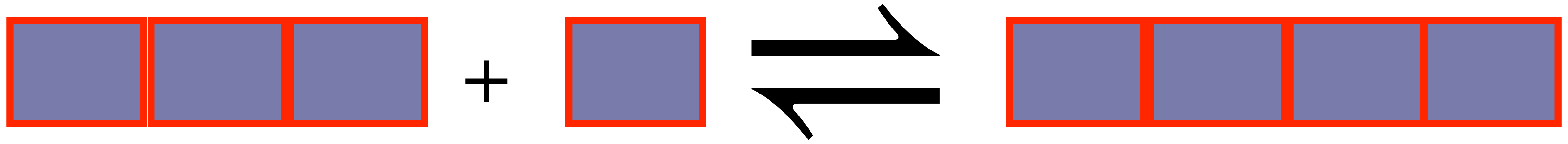
When actin polymerises how is chemical energy getting converted to mechanical energy?

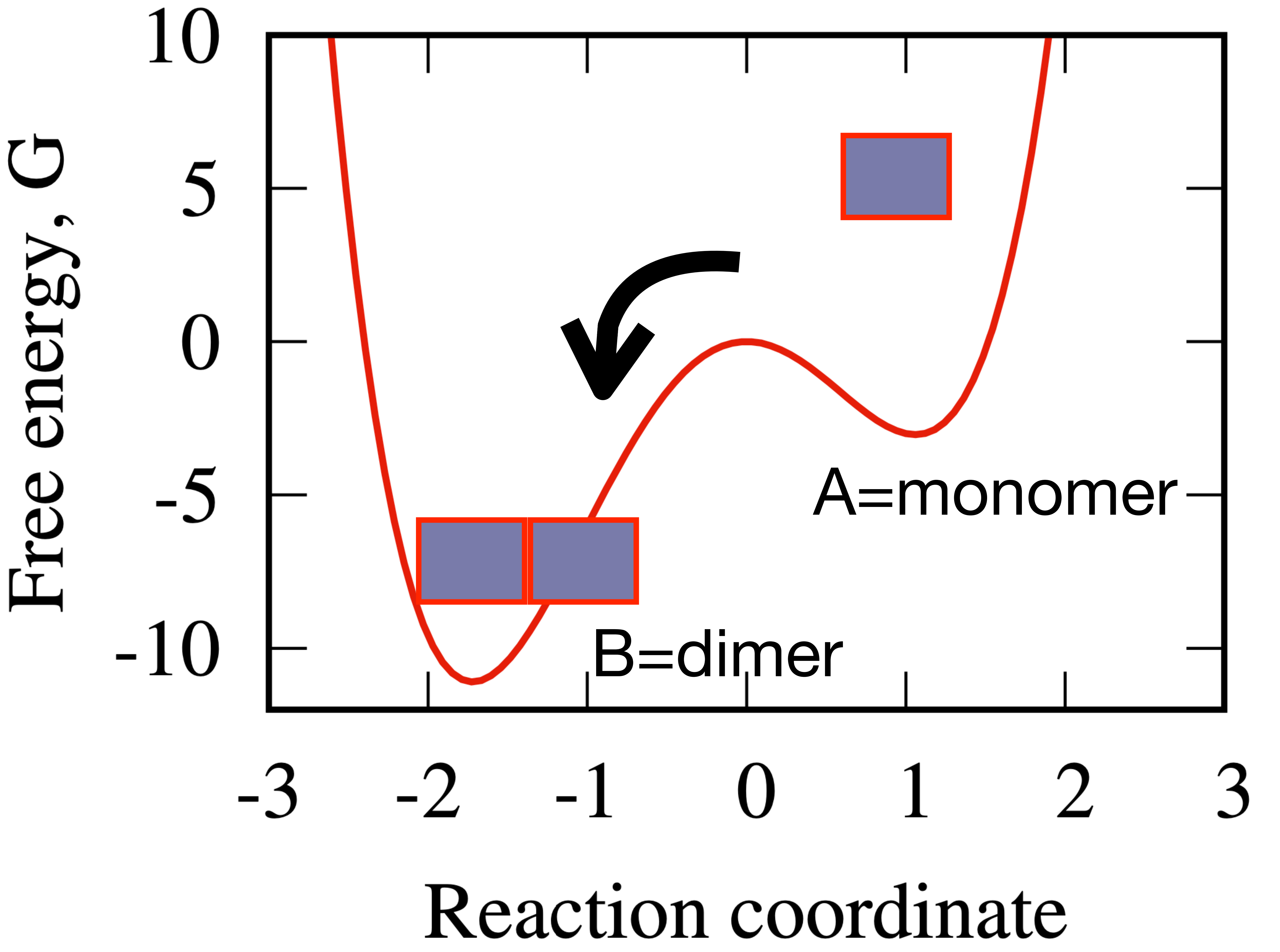
Polymerisation

Monomer $\rightleftharpoons$ Dimer

kmer $\rightleftharpoons$ (k + 1)mer

Consider the following reaction





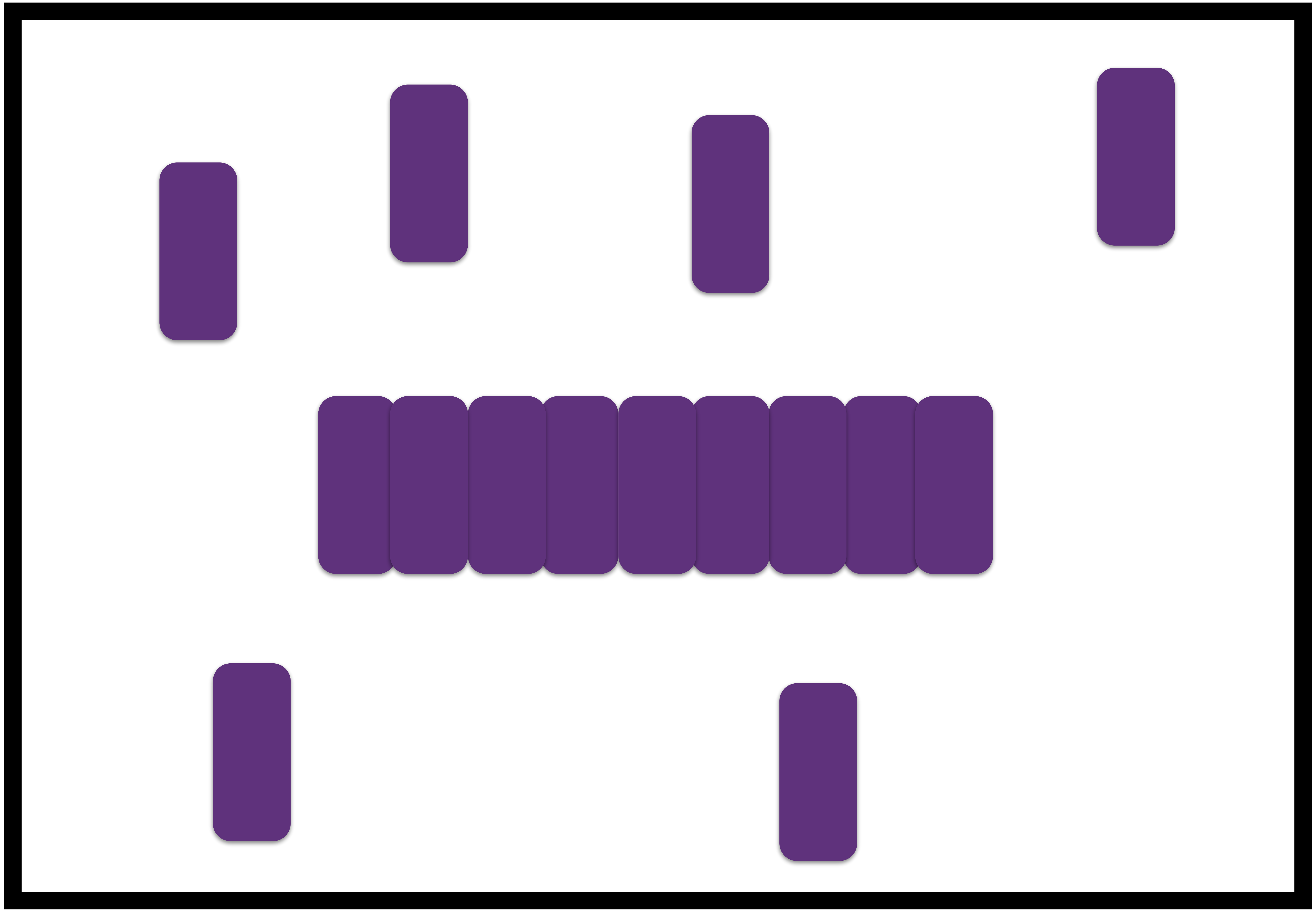
Imagine you put a bunch of monomers into a beaker

What will happen?

Imagine you put a bunch of monomers into a beaker

What will happen?

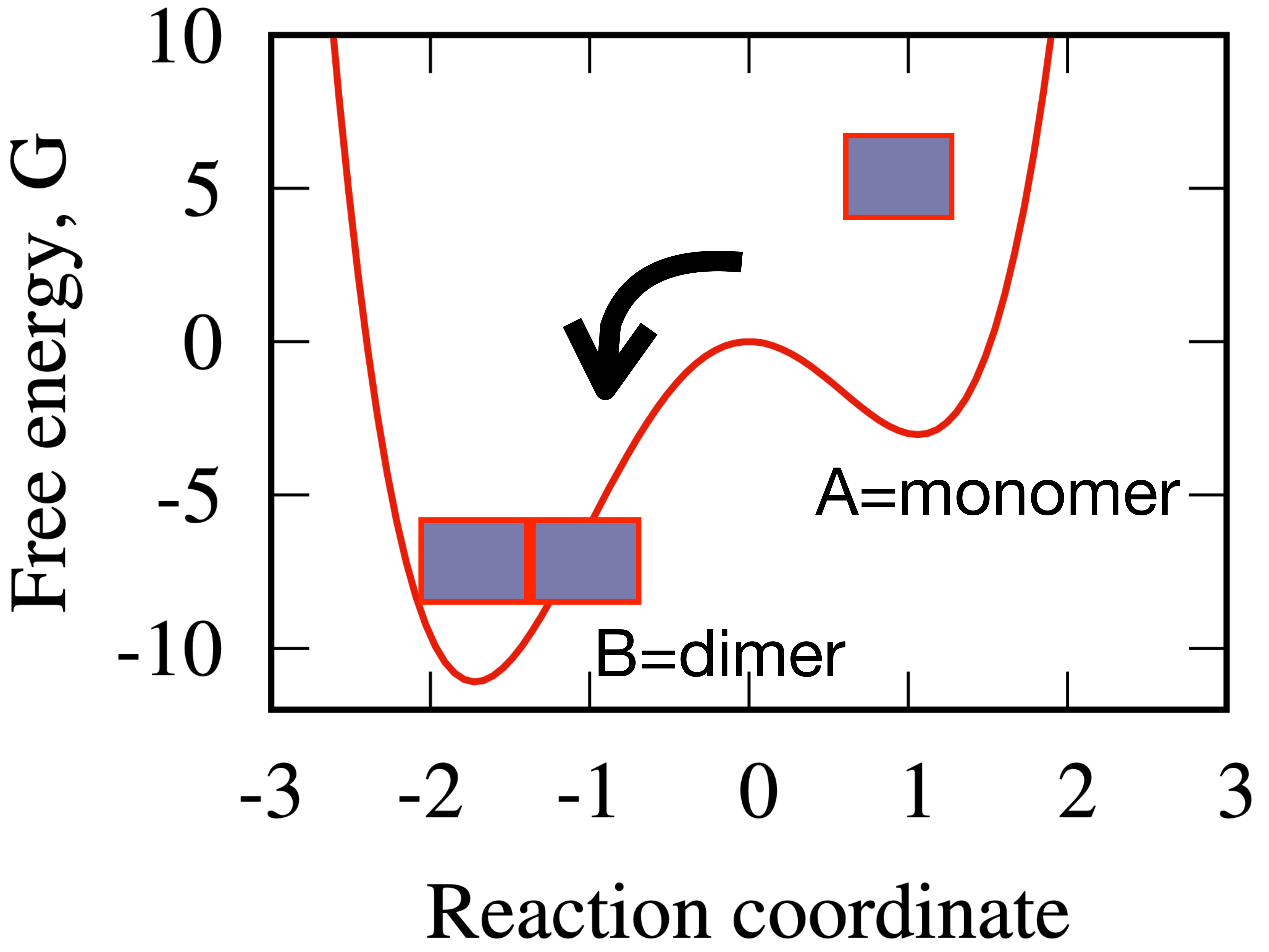
They will polymerise



Imagine length vs time of the polymer, and plot

Rate of polymerisation

$$k_{\text{on}} = k_0[c]$$



Rate of polymerisation

$$k_{\mathrm{on}} = k_0[c]$$

Rate of de-polymerisation

$$k_{\mathrm{off}}$$

As concentration of monomers decrease, rate of polymerisation will decrease, and will be equal to rate of depolymerisation

$$k_0[c] = k_{\text{off}}$$

$$\text{When,} \quad [c] = \frac{k_{\text{off}}}{k_0}$$

Critical concentration. At this [c], there is no average growth. Filament will just fluctuate around a constant length.

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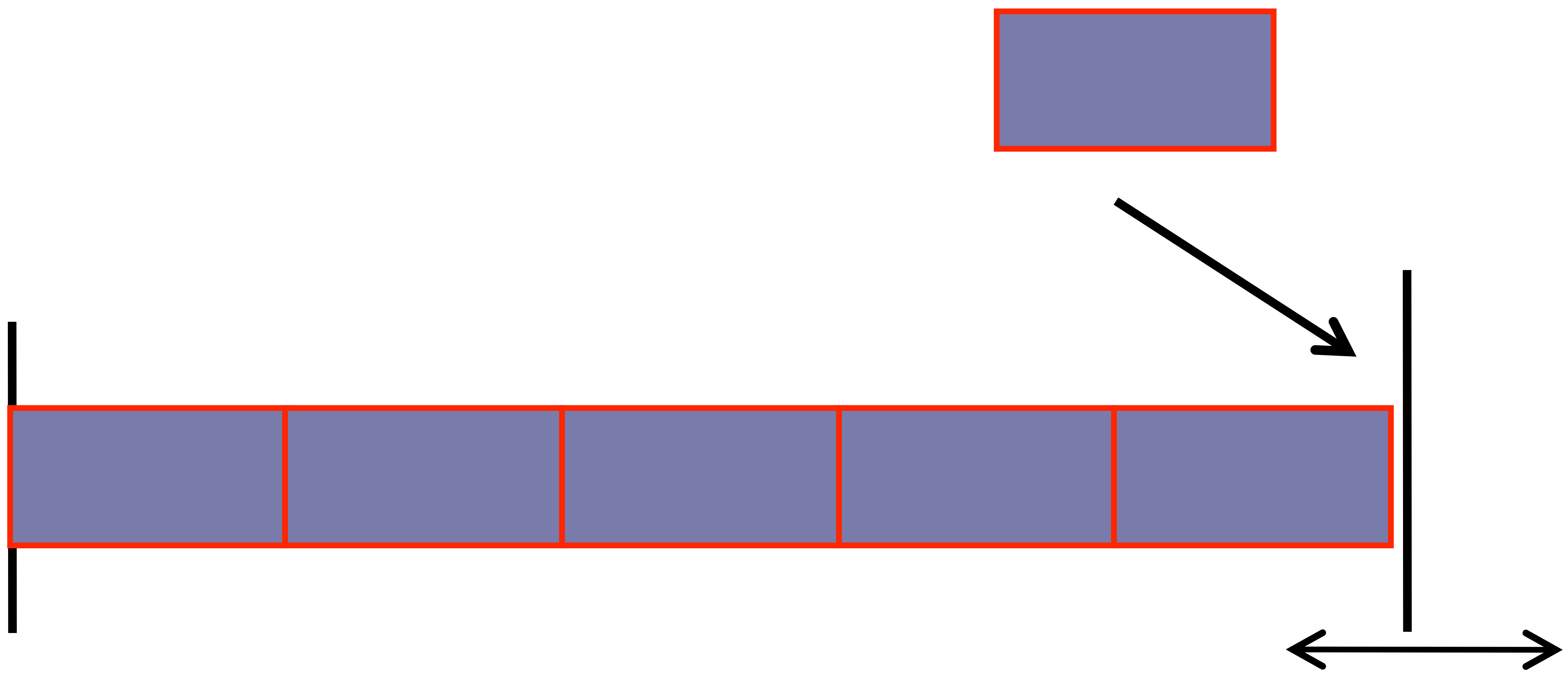
Critical concentration. At this [c], there is no average growth. Filament will just fluctuate around a constant length.

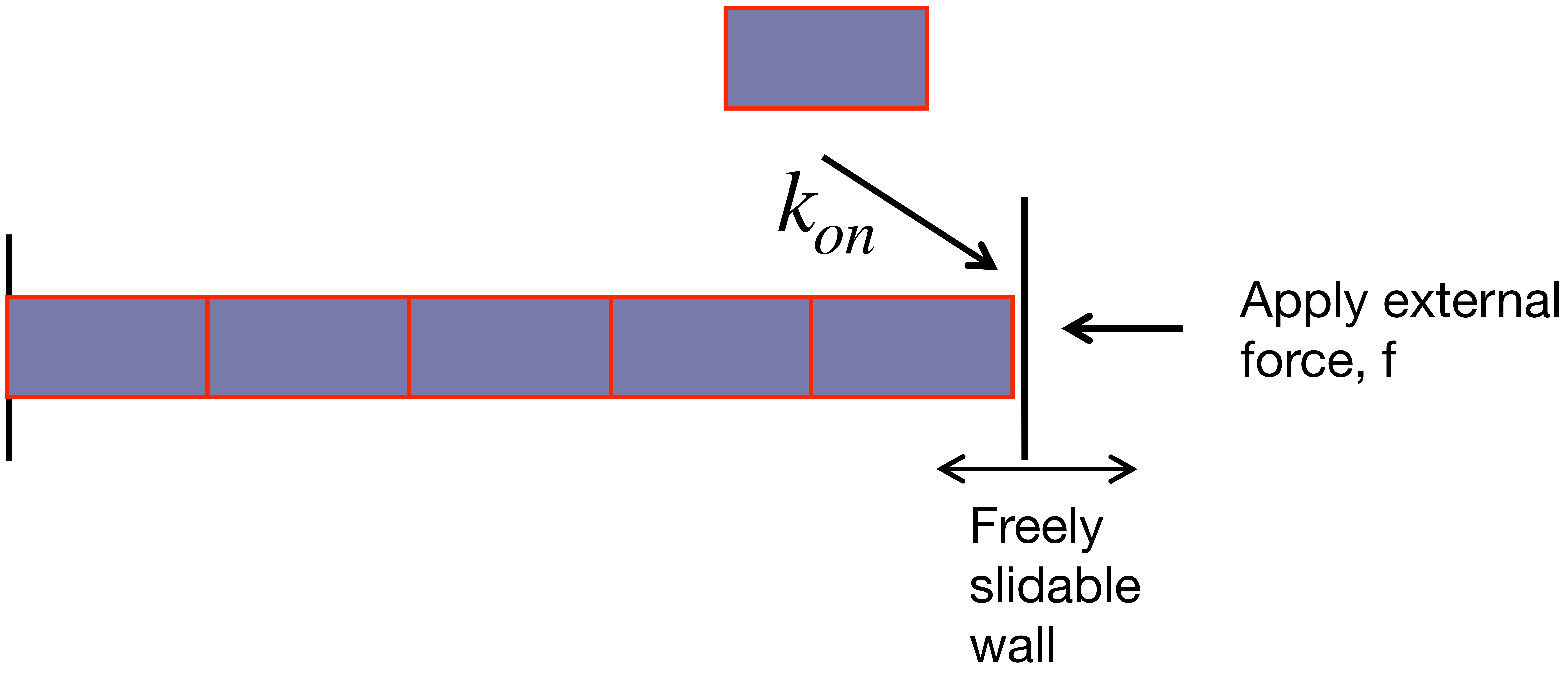
$$\text{Actin, } k_0 \approx 12\ \mu M^{-1} s^{-1}$$

$$\text{Actin, } k_{off} \approx 2\ s^{-1}$$

Polymerization can push against a wall = generate force

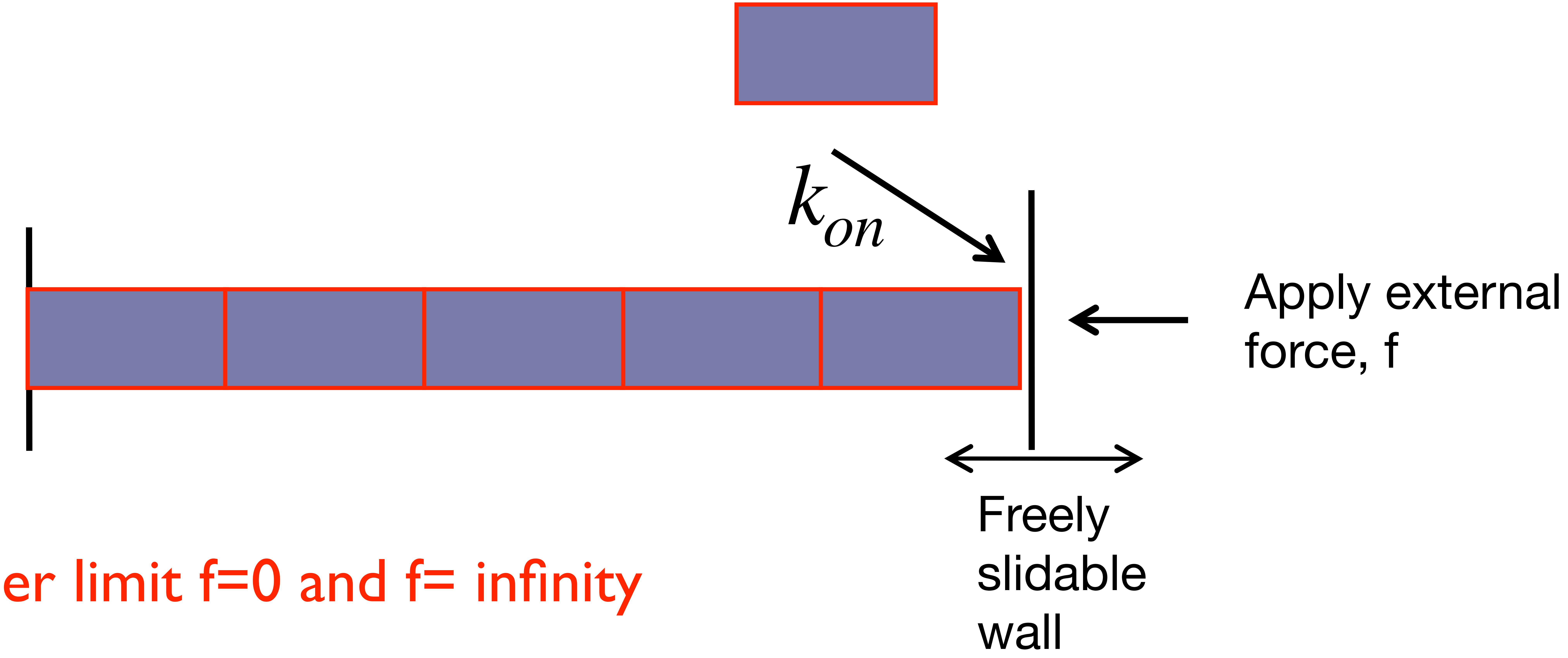


Imagine an experimental setup where you apply an external force, f, against a polymerising actin



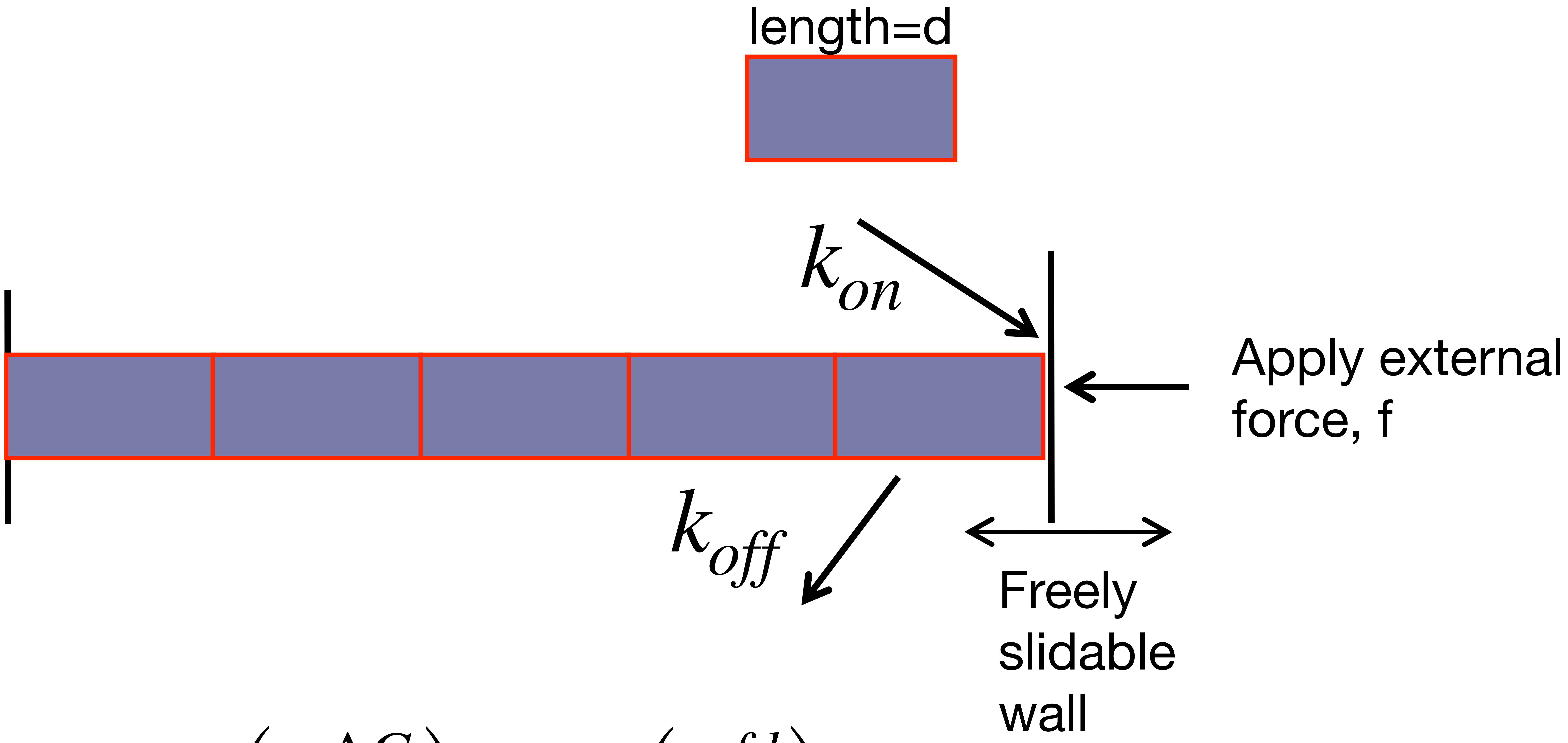
If the external force is high, what happens to the polymerisation rate?

Can you think of a functional form using which polymerisation force will decrease.



Consider limit f=0 and f= infinity

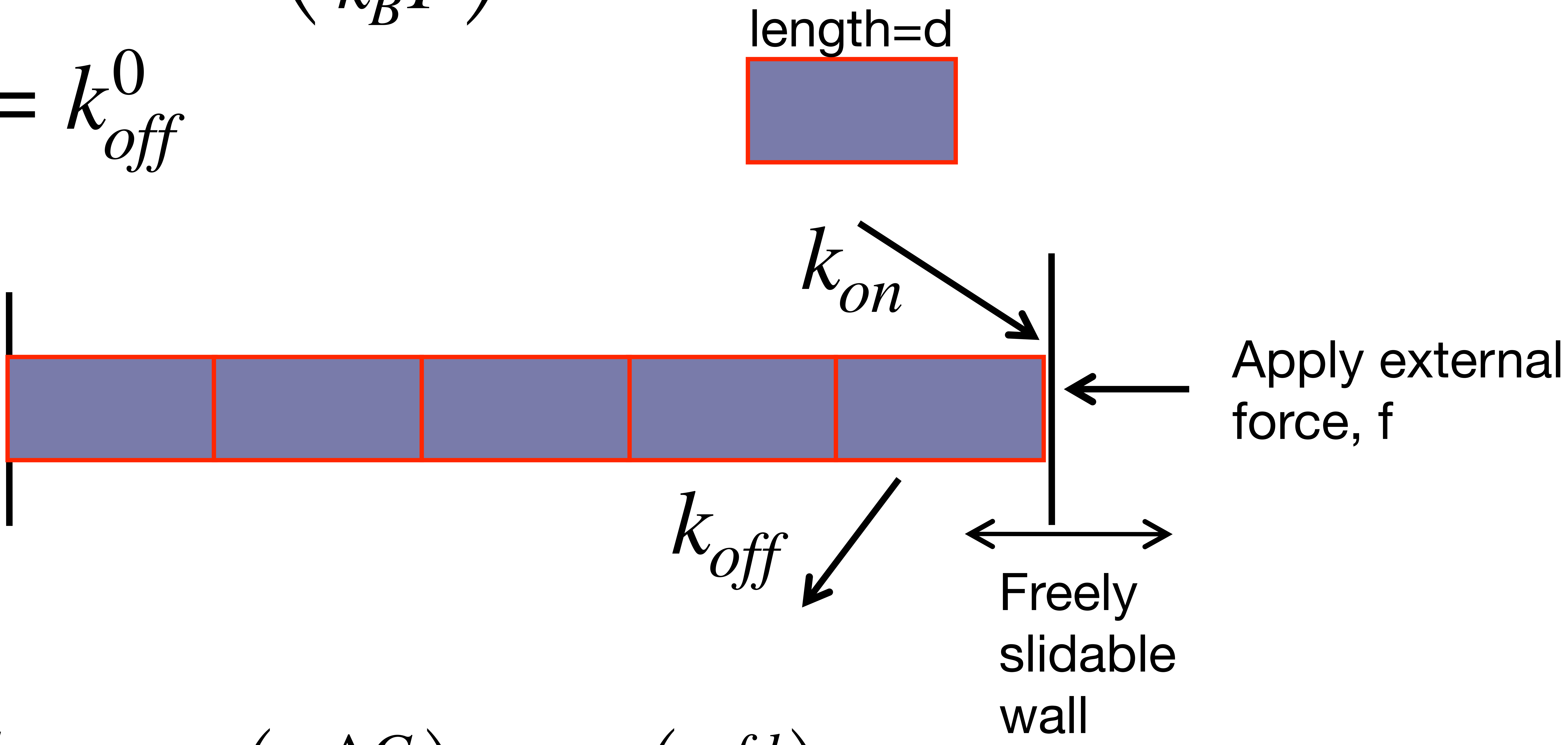
Can you think of a functional form using which polymerisation force will decrease.



$$\frac{k_{on}}{k_{off}} = \exp\left(\frac{-\Delta G}{k_B T}\right) \propto \exp\left(\frac{-fd}{k_B T}\right)$$

$$k_{on} = k_0[c]\exp\left(\frac{-fd}{k_BT}\right)$$

$$k_{off} = k_{off}^0$$



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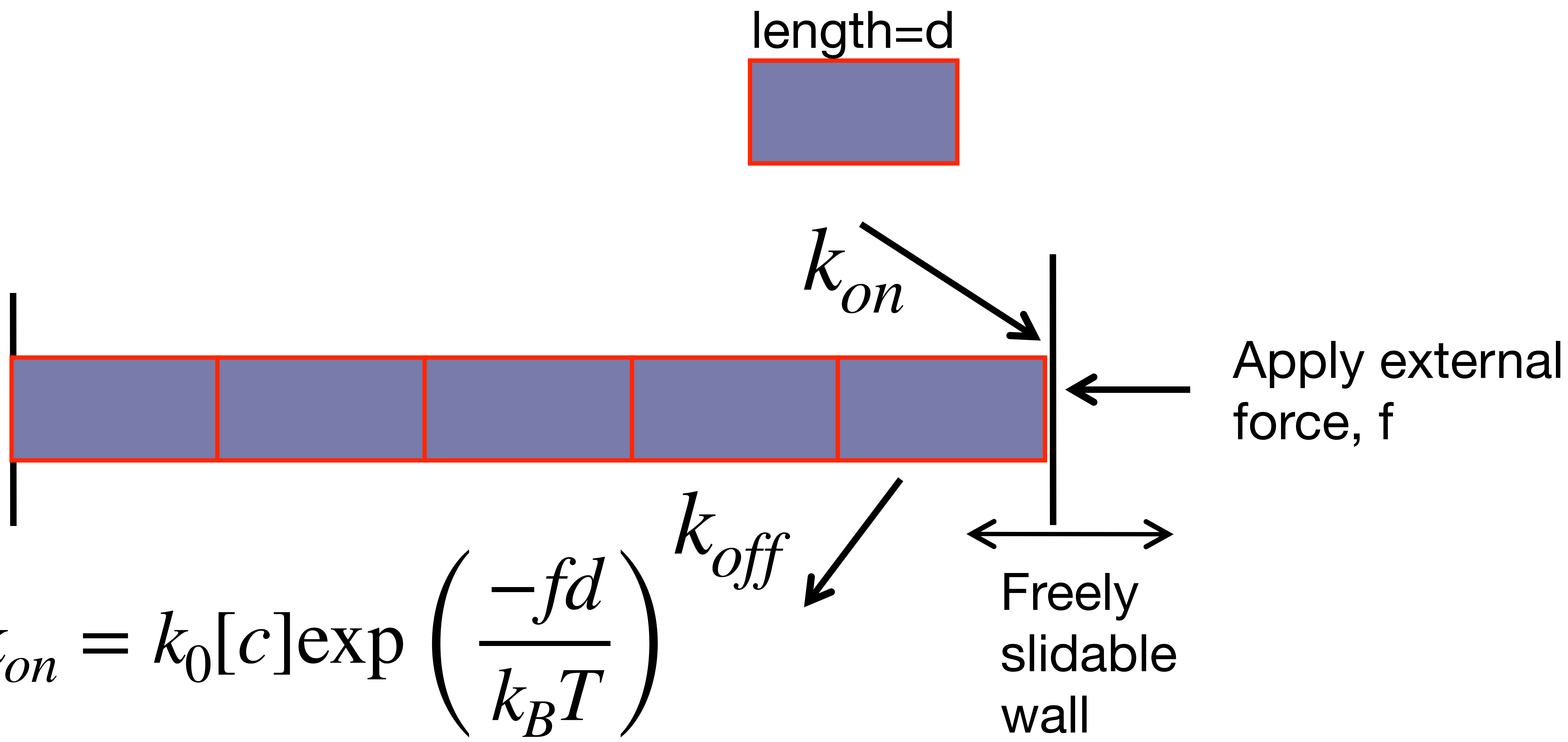
What is the maximum force it can generate?



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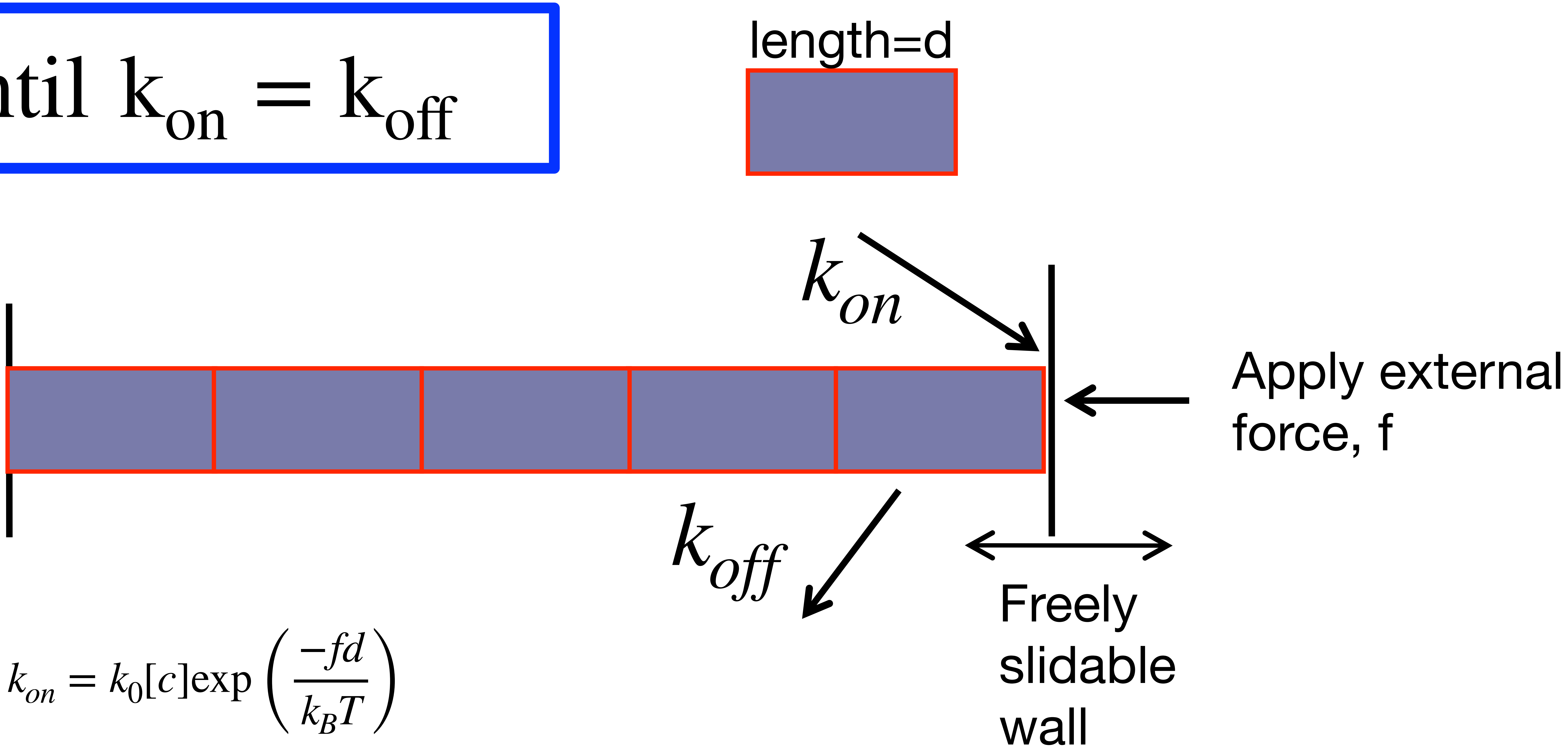
$\boxed{\text{Until } k_{on} = k_{off}}$



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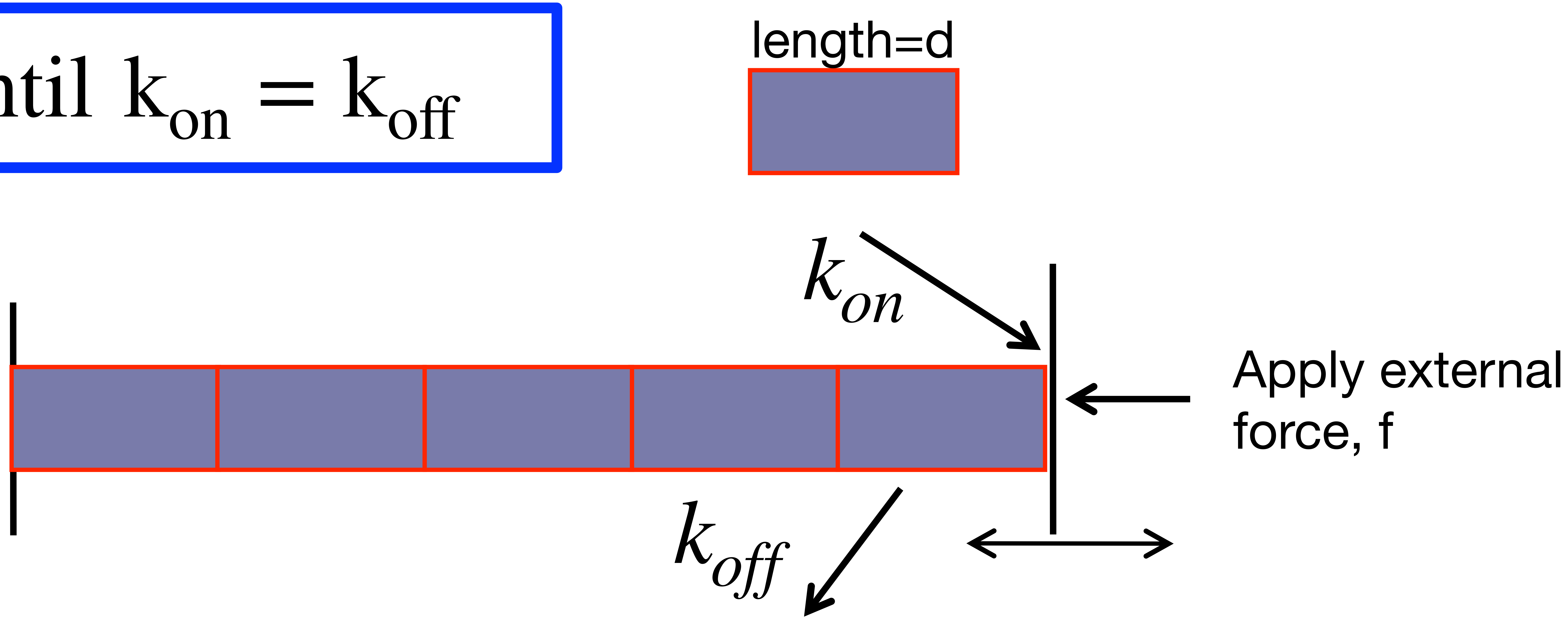


$$k_{on} = k_0[c]\exp\left(\frac{-fd}{k_BT}\right)$$

$$k_{off} = k_{off}^0$$

$$\boxed{f_{max} = -\frac{k_BT}{d}\ln\left(\frac{k_{off}^0}{k_0[c]}\right)}$$

How much force will it generate, if [c]= 10 micro molar?

$$f_{max} = -\frac{k_B T}{d} \ln\left(\frac{k^0_{off}}{k_0[c]}\right)$$

Actin, $k_0 \approx 12\ \mu M^{-1} s^{-1}$

Actin, $k^0_{off} \approx 2\ s^{-1}$

d~3nm

$$f_{max} = -\frac{4\ \mathrm{pN\ nm}}{3\mathrm{nm}} \ln\left(\frac{2\mathrm{s}^{-1}}{12\mu\mathrm{M}^{-1}\mathrm{s}^{-1} \times 10\mu\mathrm{M}}\right) \approx 5\mathrm{pN}$$

This actin transducer converts free energy to mechanical force

$$f_{max} = -\frac{k_B T}{d} \ln\left(\frac{k_{off}^0}{k_0[c]}\right)$$

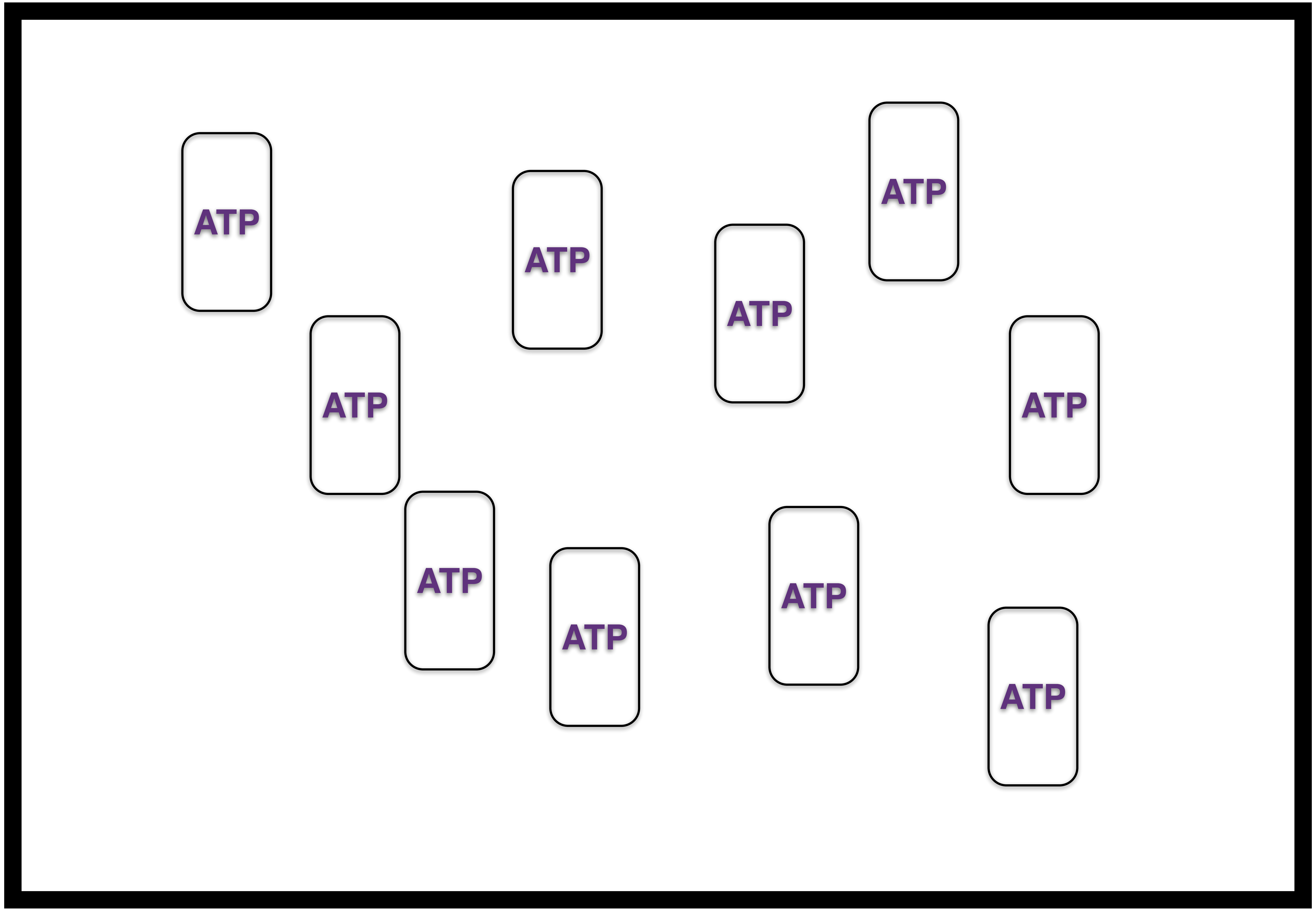
$$f_{max} = -\frac{\Delta G}{d}$$

This is theoretical maximum!

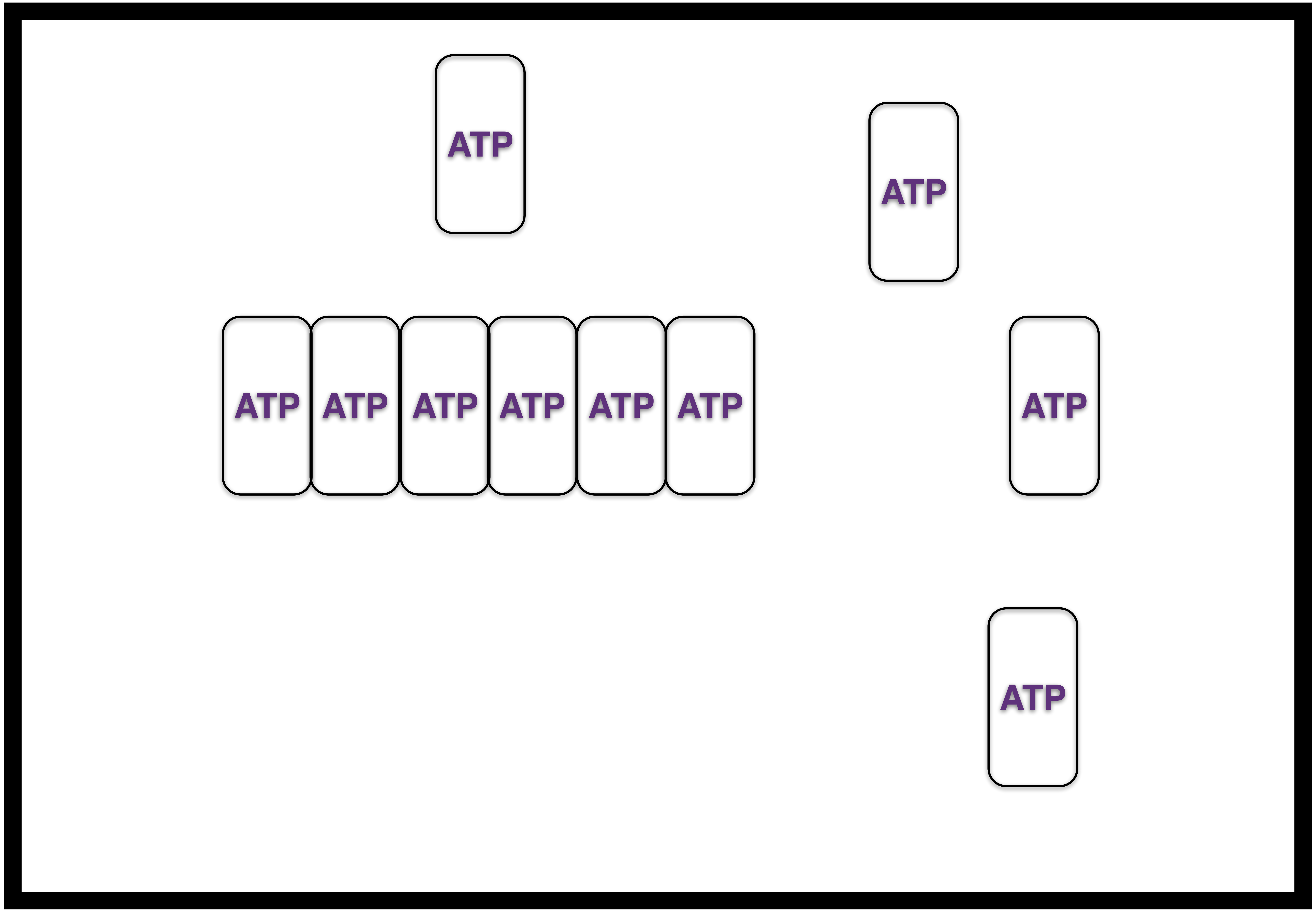
Practically, it will generate a bit less than this

Wait! What I showed was a simplified version of how it works! Reality is more complex (and interesting!)

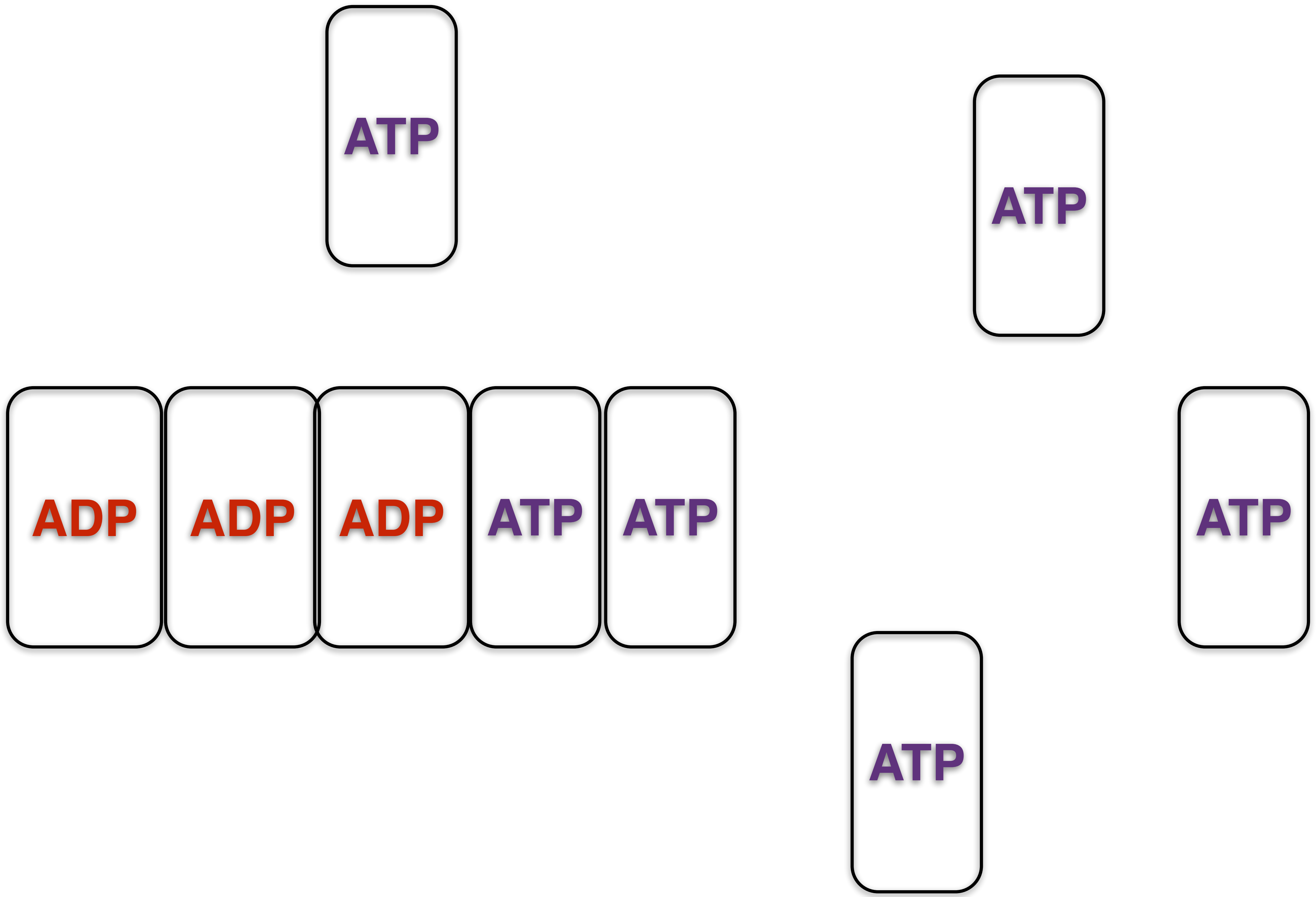
Actin monomers in solution is bound to ATP



ATP-bound actin polymerise

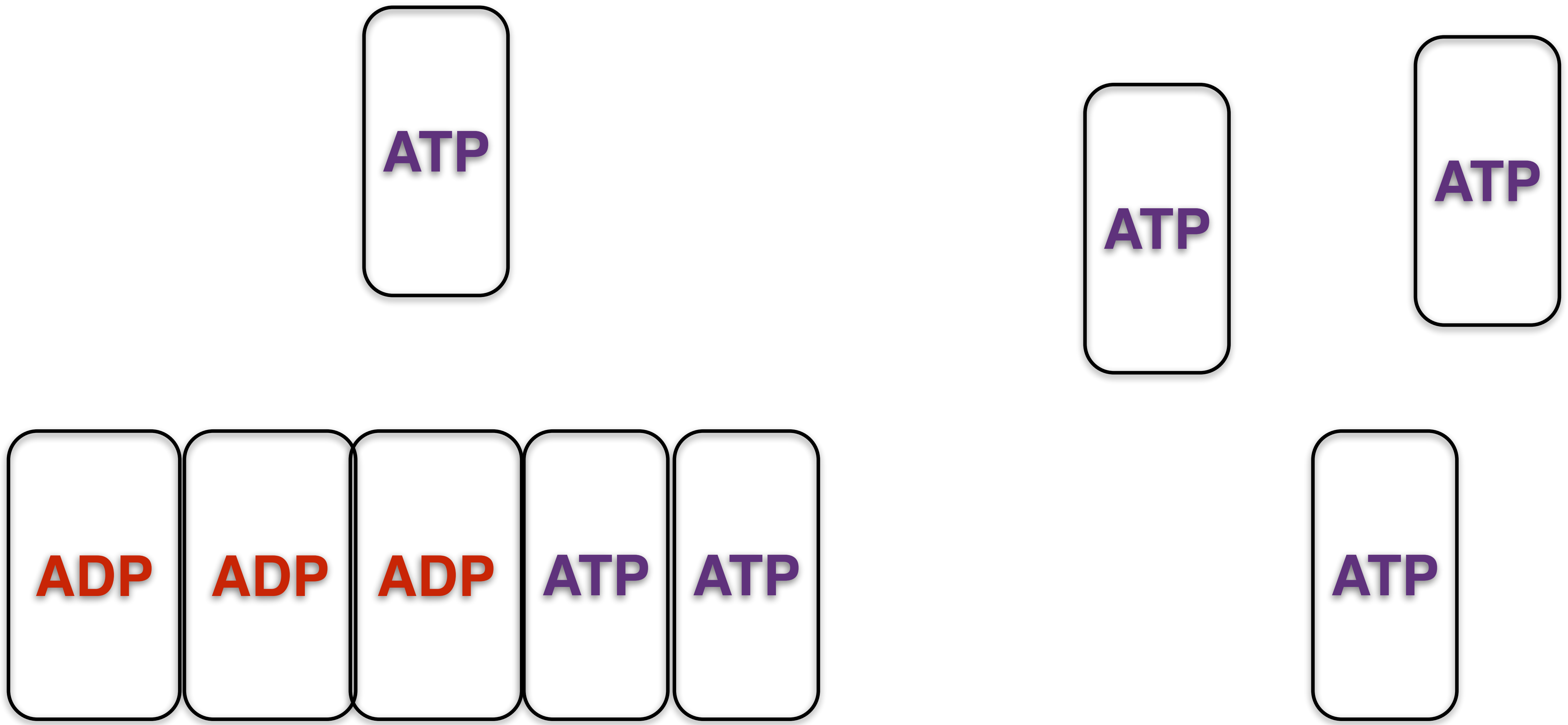


On the polymer, ATP become ADP



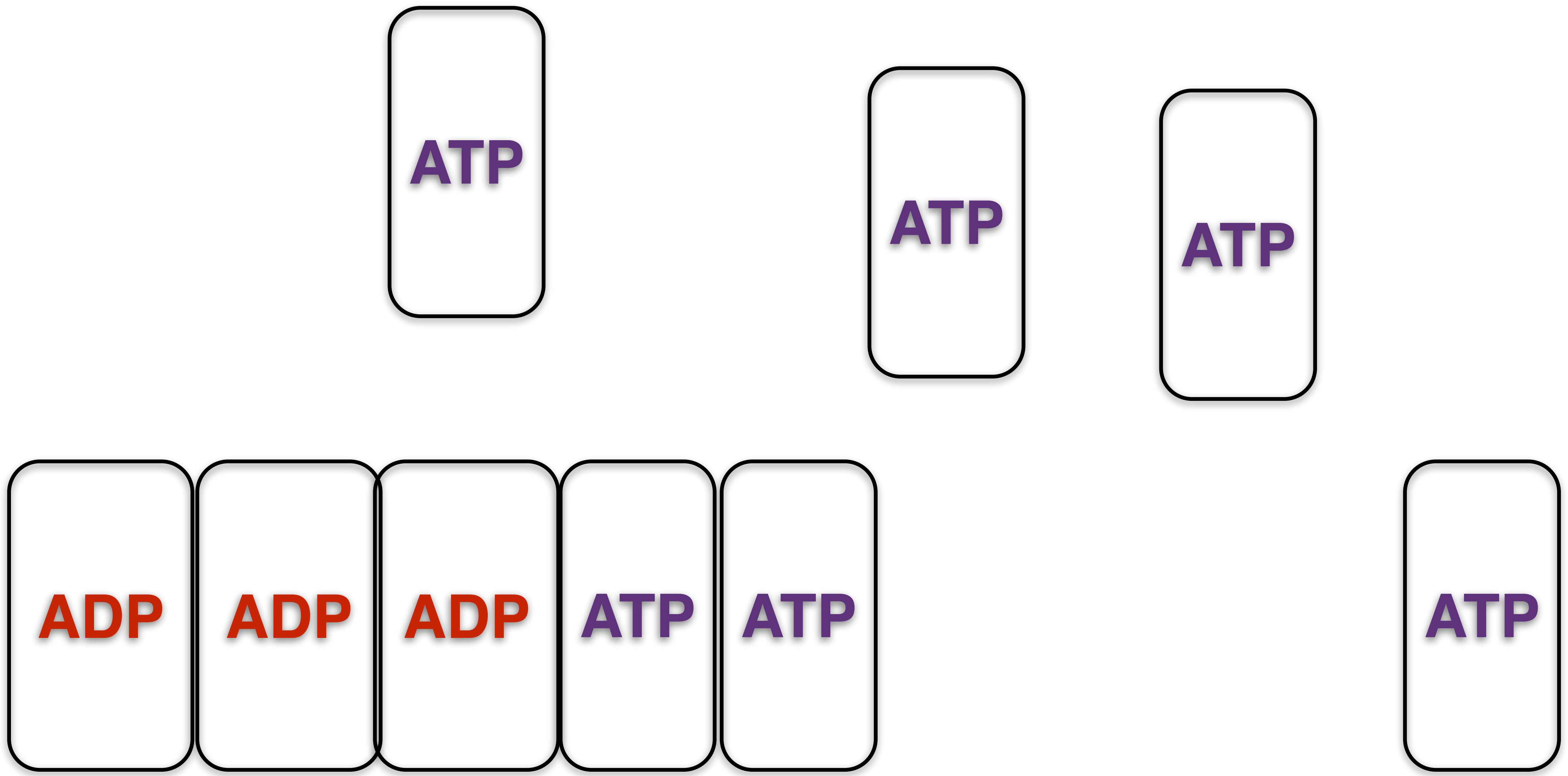
ATP to ADP conversion is known as “hydrolysis”
This happens only when actin is a
part of filament

On the polymer, ATP become ADP



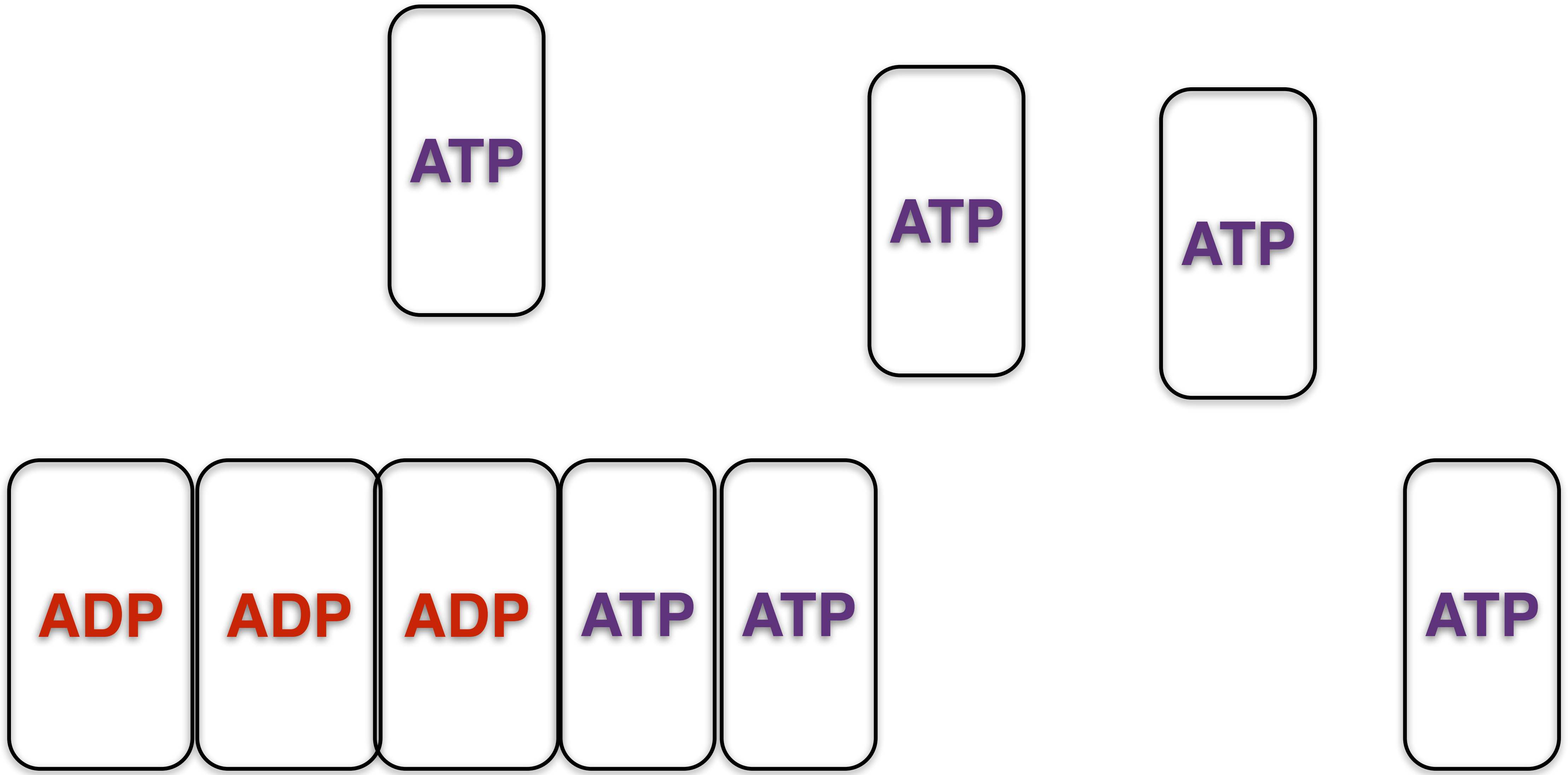
“Hydrolysis” leads to a small structural change in the actin protein. ADP-Actin is now in a different “state”, compared to ATP-actin

This has broken the symmetry — front and back!



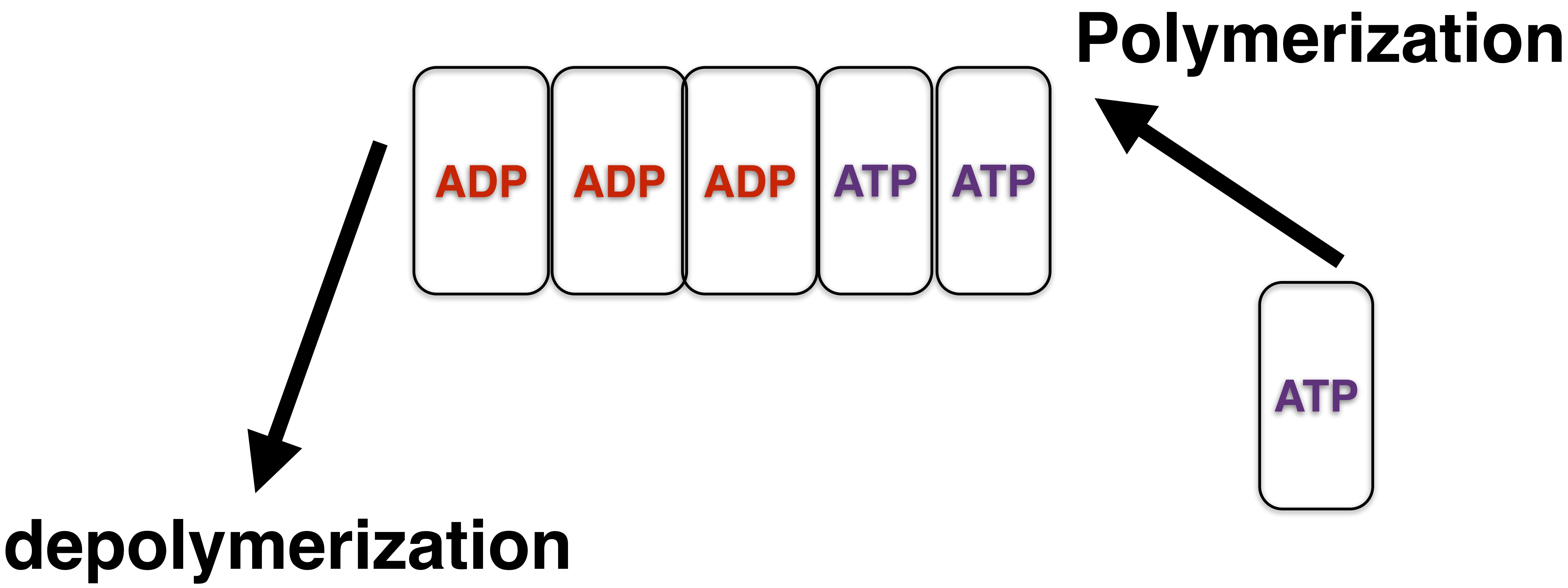
First requirement for any directed motion is “breaking symmetry” and choosing a direction

Asymmetric rates



No monomer can bind on the ADP side!
ADP-monomer can only depolymerise

Centre of mass motion!



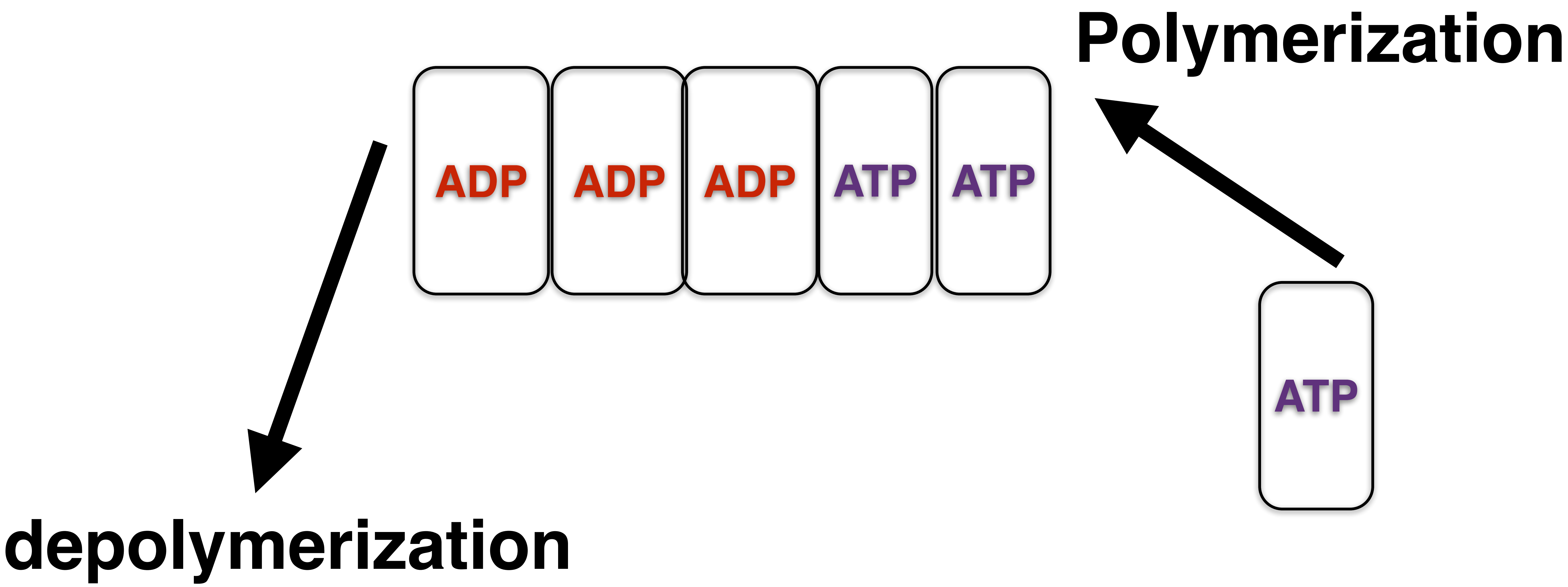
What is the velocity at “ATP” end (+ end)?

What is the velocity at the “ADP” end (minus end)?

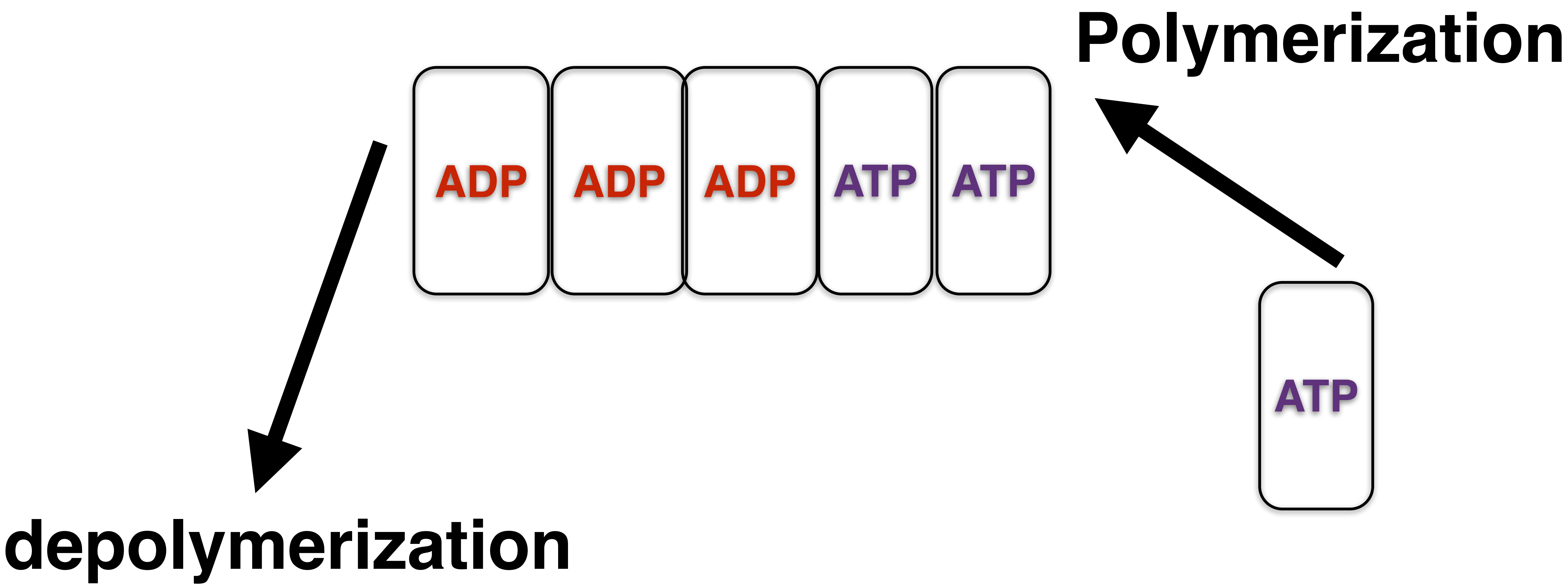
What is the concentration at which the whole filament velocity is zero?

Compare the critical concentration of the whole filament with that of the plus end

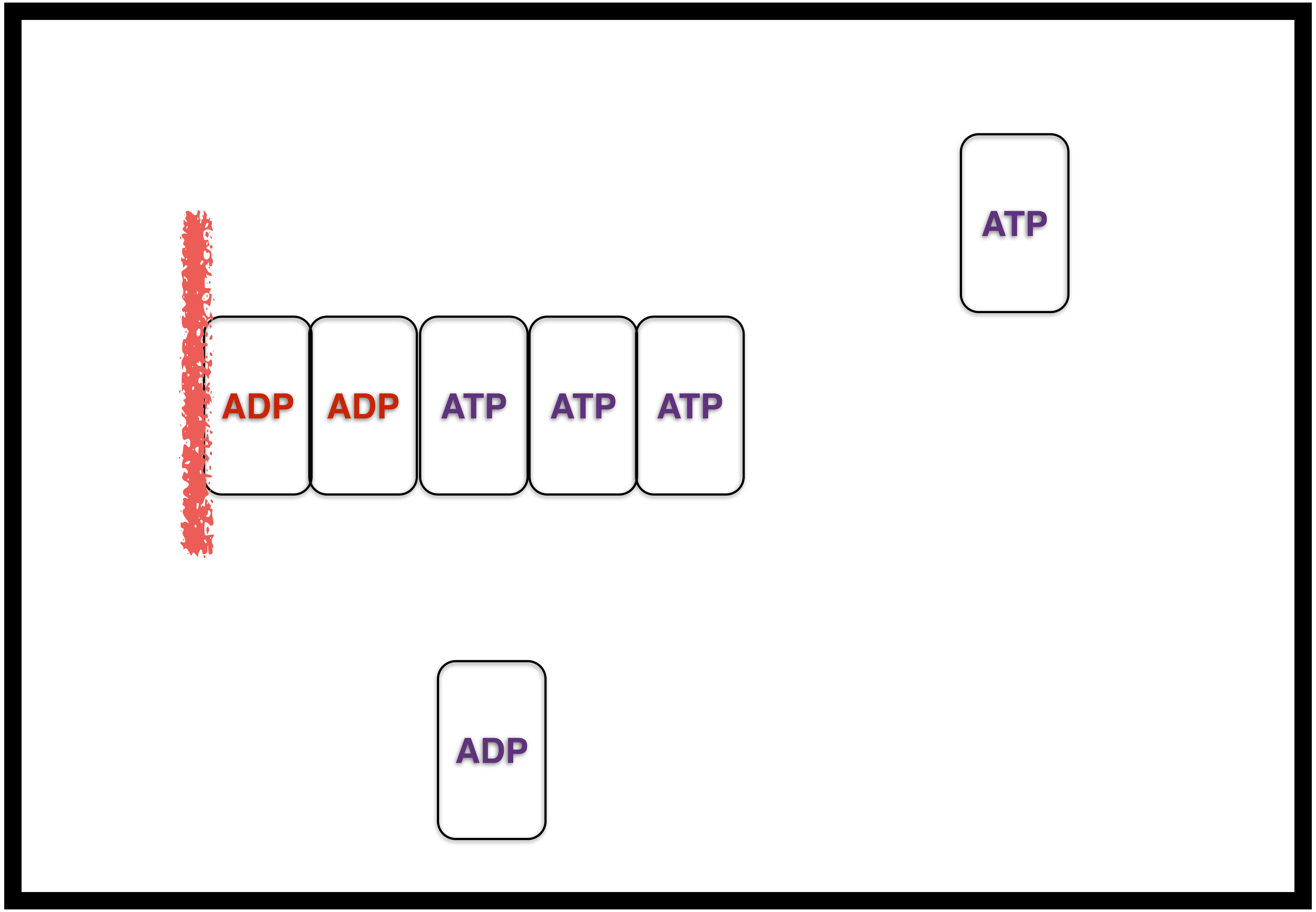
Centre of mass motion!



Treadmilling of actin

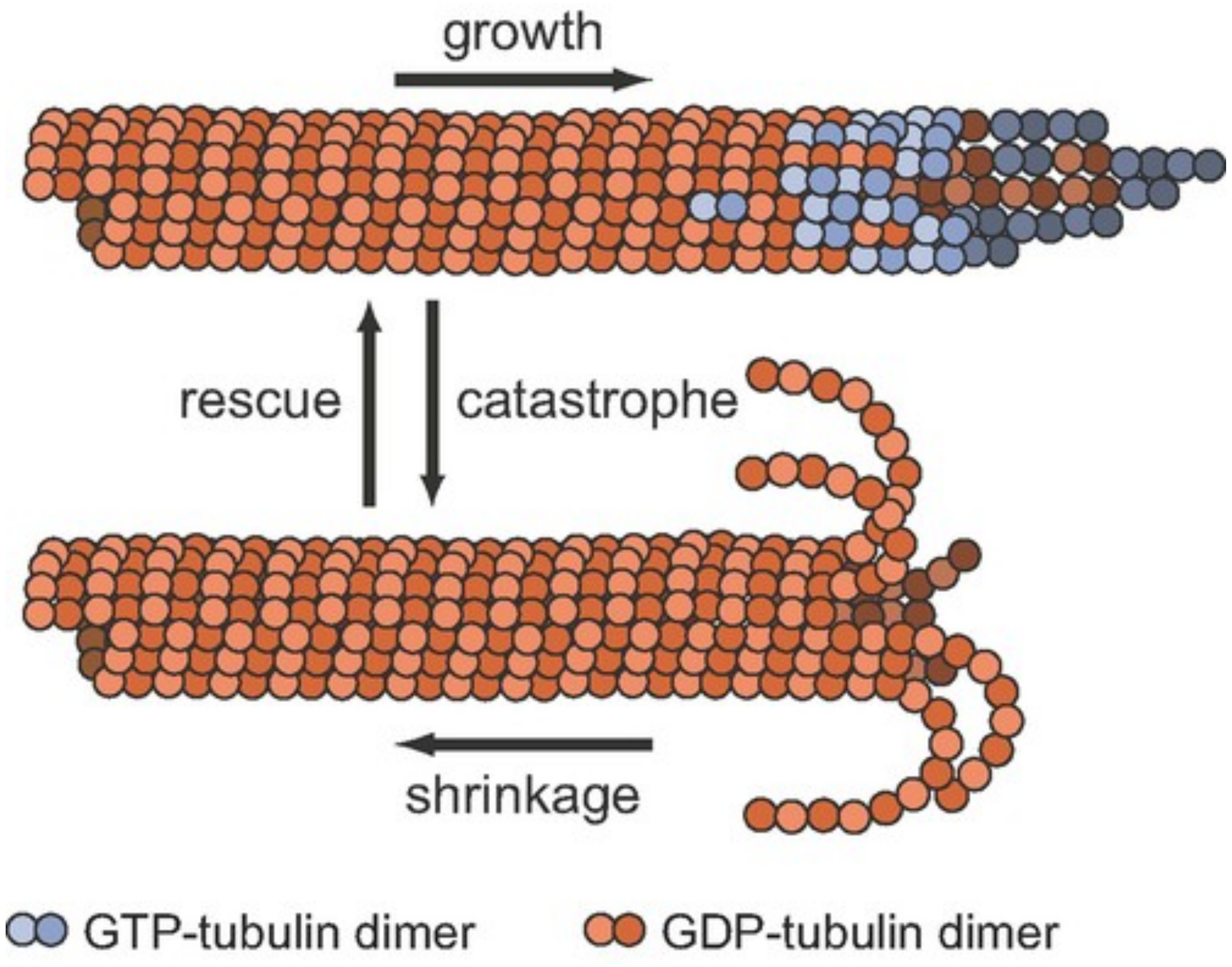


If you block one end, force generation here too

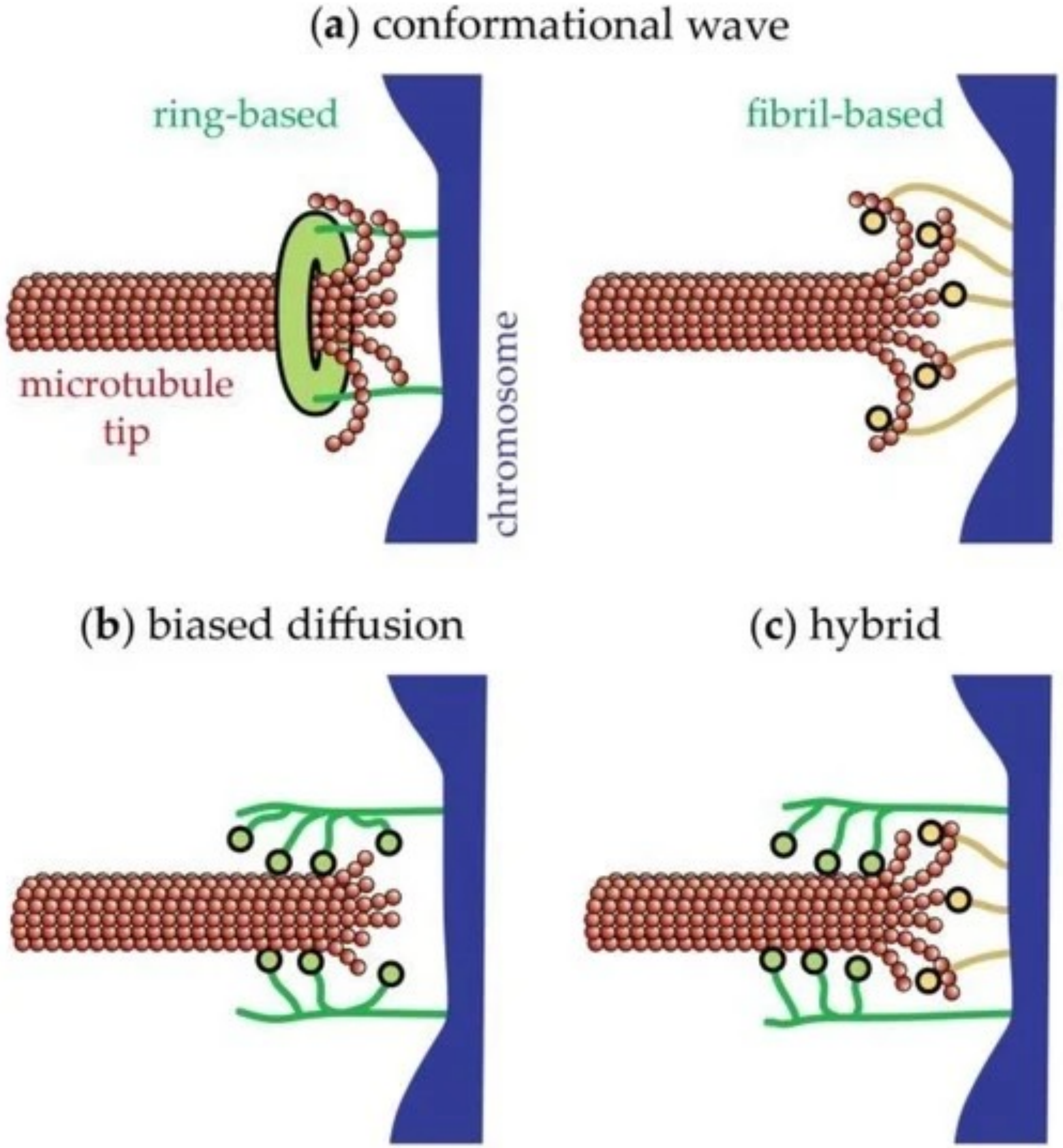


Microtubules are another set of filaments; they have some similarity with actin the way they convert chemical energy to mechanical energy

It uses energy (hydrolysis) to bend



Bending and dynamics together can pull a ring



Summary

- Chemical energy to mechanical energy
- Transducer
- Actin
- Polymerisation/depolymerisation
- Maximum force generated