# How to convert the chemical free energy to mechanical work?

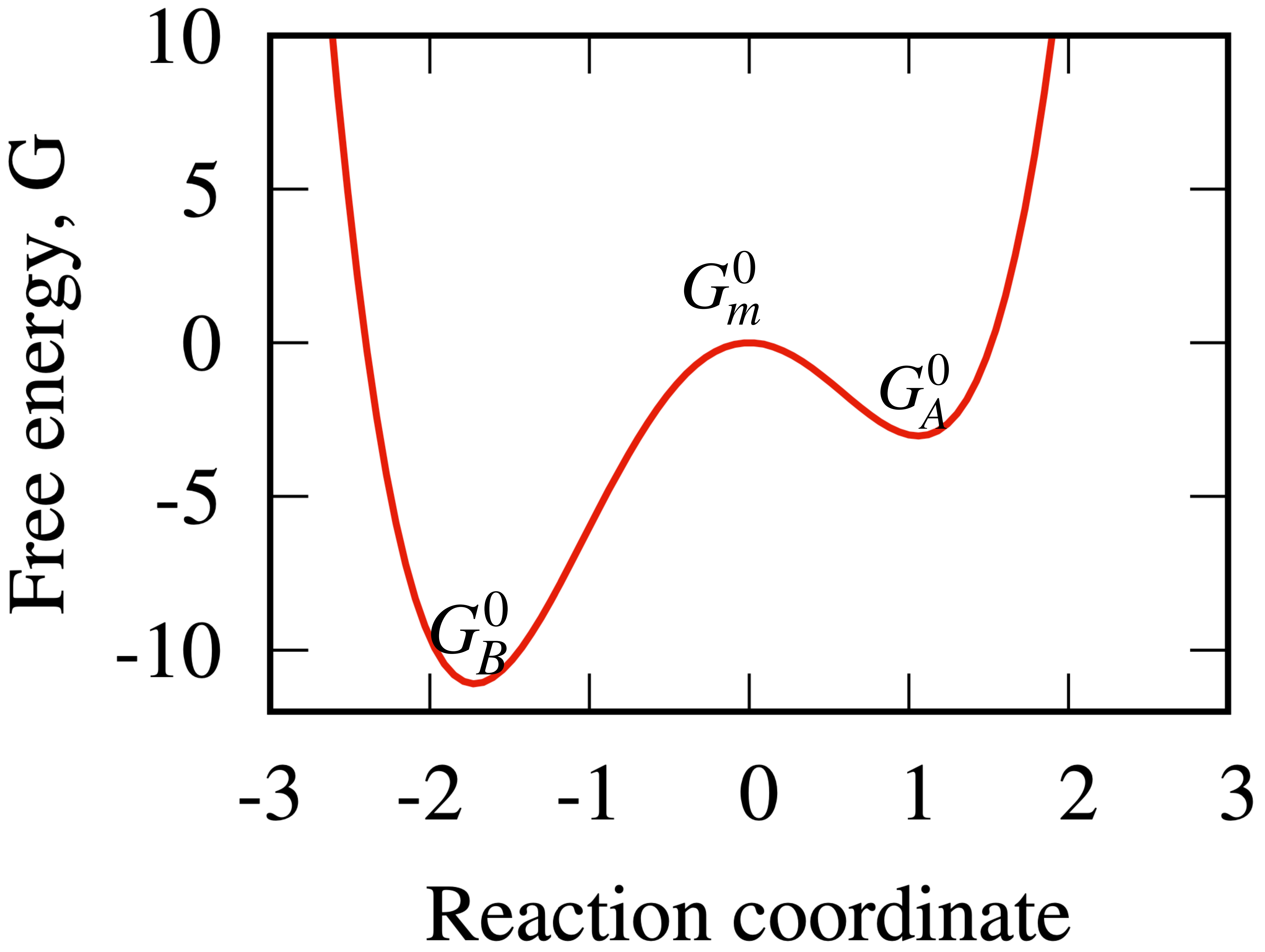
**What is the simplest molecular robot that can move?**

**Energy transducer**

# What is chemical work

# Chemical reactions and movements in a landscape

# Rate of reactions (at standard conditions)



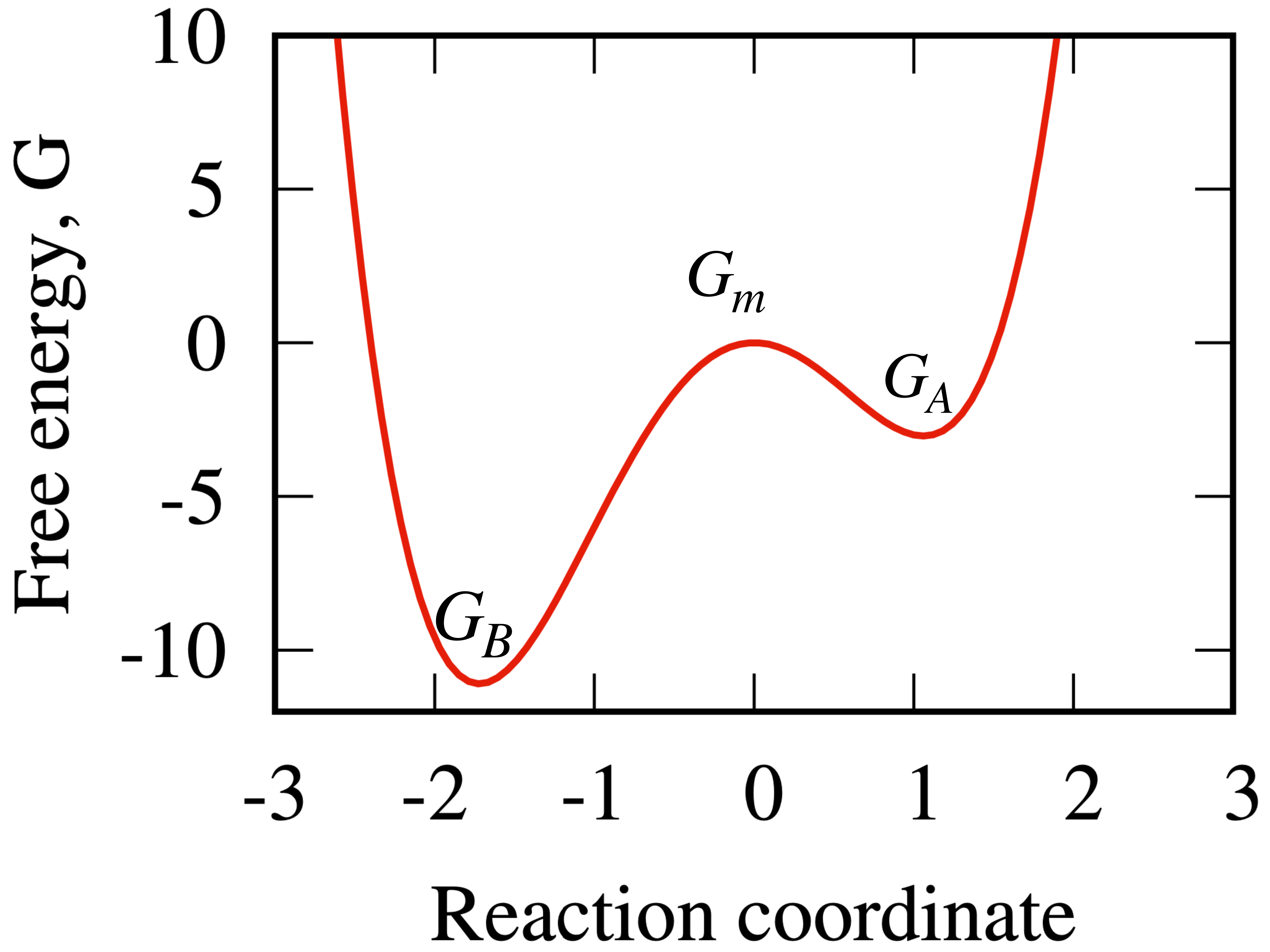

$$r_{AB}^0 = r_0 \exp\left(-\frac{G_m^0 - G_A^0}{k_B T}\right)$$

$$r_{BA}^0 = r_0 \exp\left(-\frac{G_m^0 - G_B^0}{k_B T}\right)$$

**Height of the hill decides the rate of reactions**

$$G_m^0 - G_B^0 = \text{activiation energy}$$

## Ratio of rates determine equilibrium




$$r_{AB}^0 = r_0 \exp\left(-\frac{G_m^0 - G_A^0}{k_B T}\right)$$

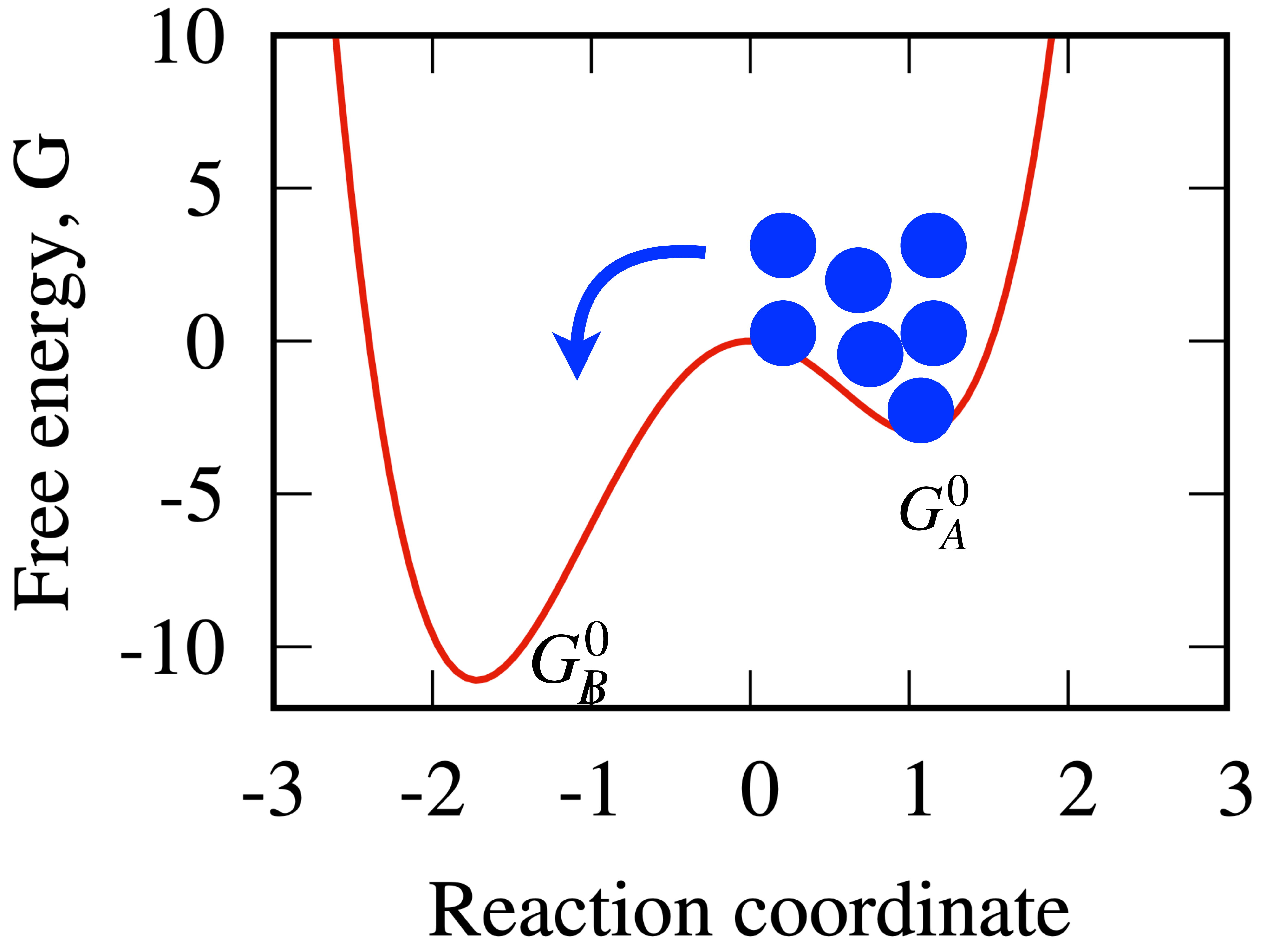
$$r_{BA}^0 = r_0 \exp\left(-\frac{G_m^0 - G_B^0}{k_B T}\right)$$

$$\frac{r_{AB}^0}{r_{BA}^0} = \exp\left(-\frac{G_A^0 - G_B^0}{k_B T}\right)$$

$$\frac{r_{AB}^0}{r_{BA}^0} = \exp\left(-\frac{\Delta G^0}{k_B T}\right)$$

**Only difference in Free energy matters**

# Concentration can change rate

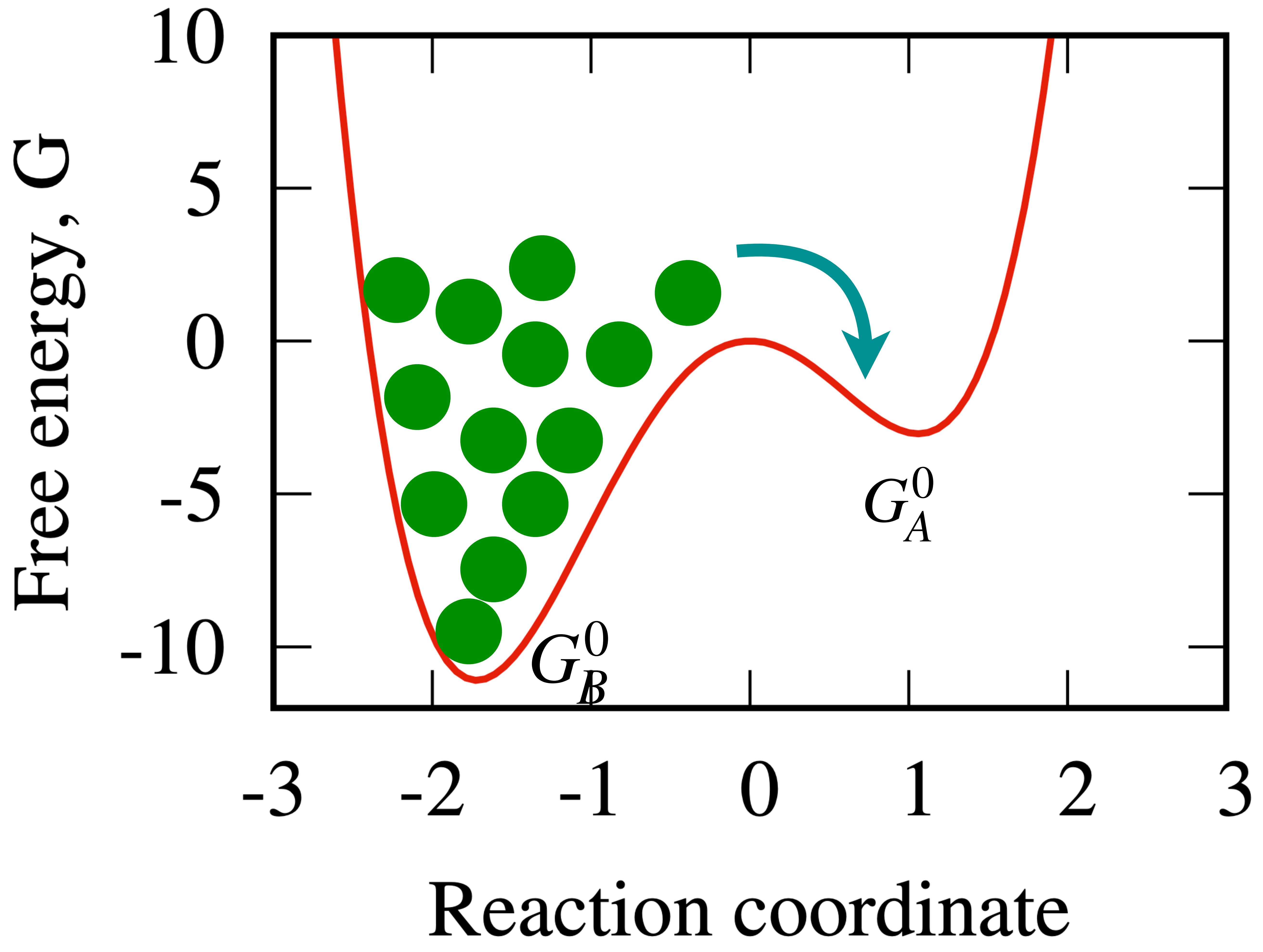



**A lot of [A] can make A to B reaction easy**

$$r_{AB} = r_0[A]\exp\left(-\frac{G_m^0 - G_A^0}{k_B T}\right)$$

$$r_{AB} = r_{AB}^0[A]$$

# Concentration can change rate

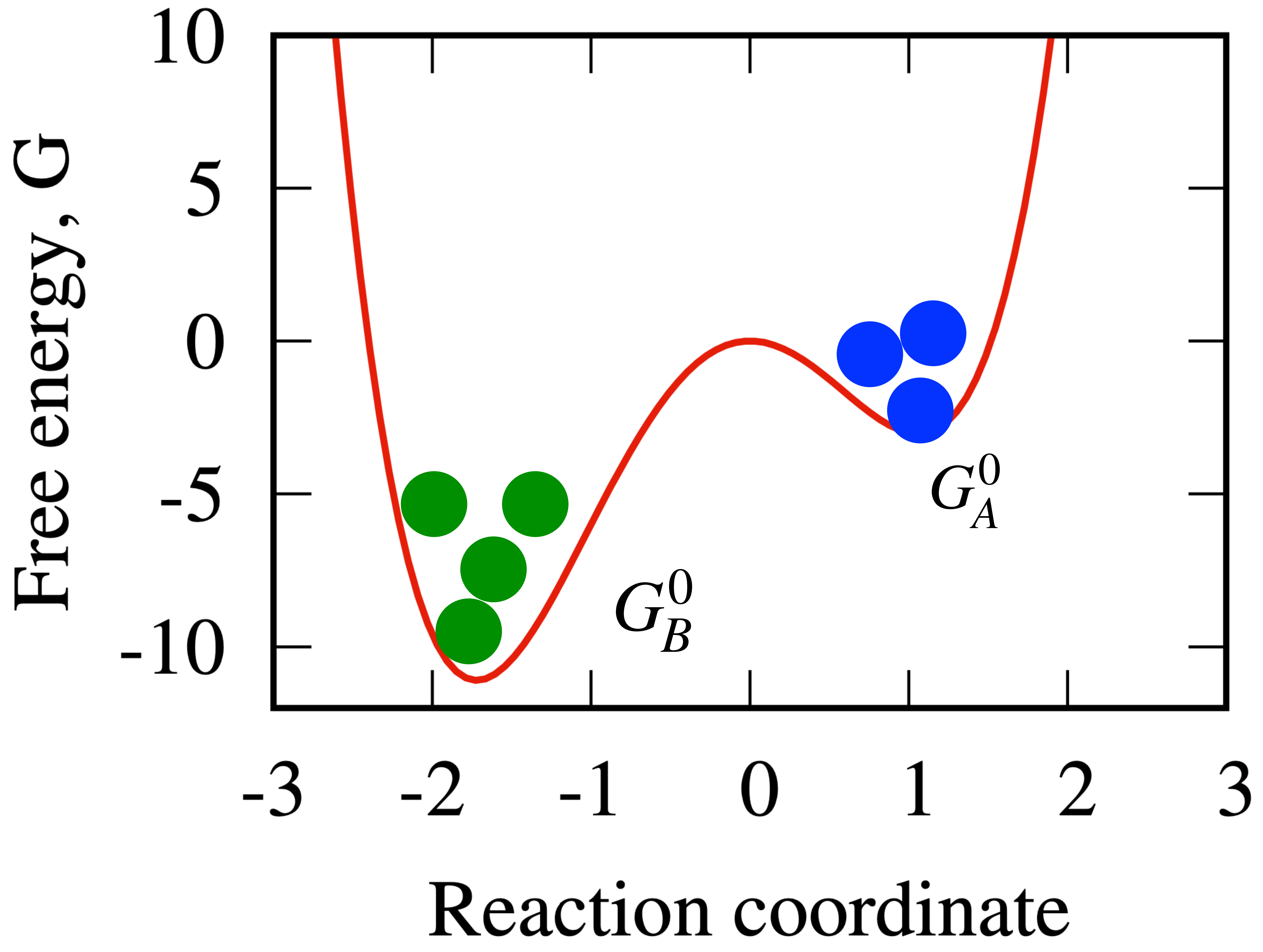



**A lot of [B] can make B to A reaction quicker**

$$r_{BA} = r_0[B]\exp\left(-\frac{G_m^0 - G_B^0}{k_B T}\right)$$

$$r_{BA} = r_{BA}^0[B]$$

## At equilibrium: Ratio of rates



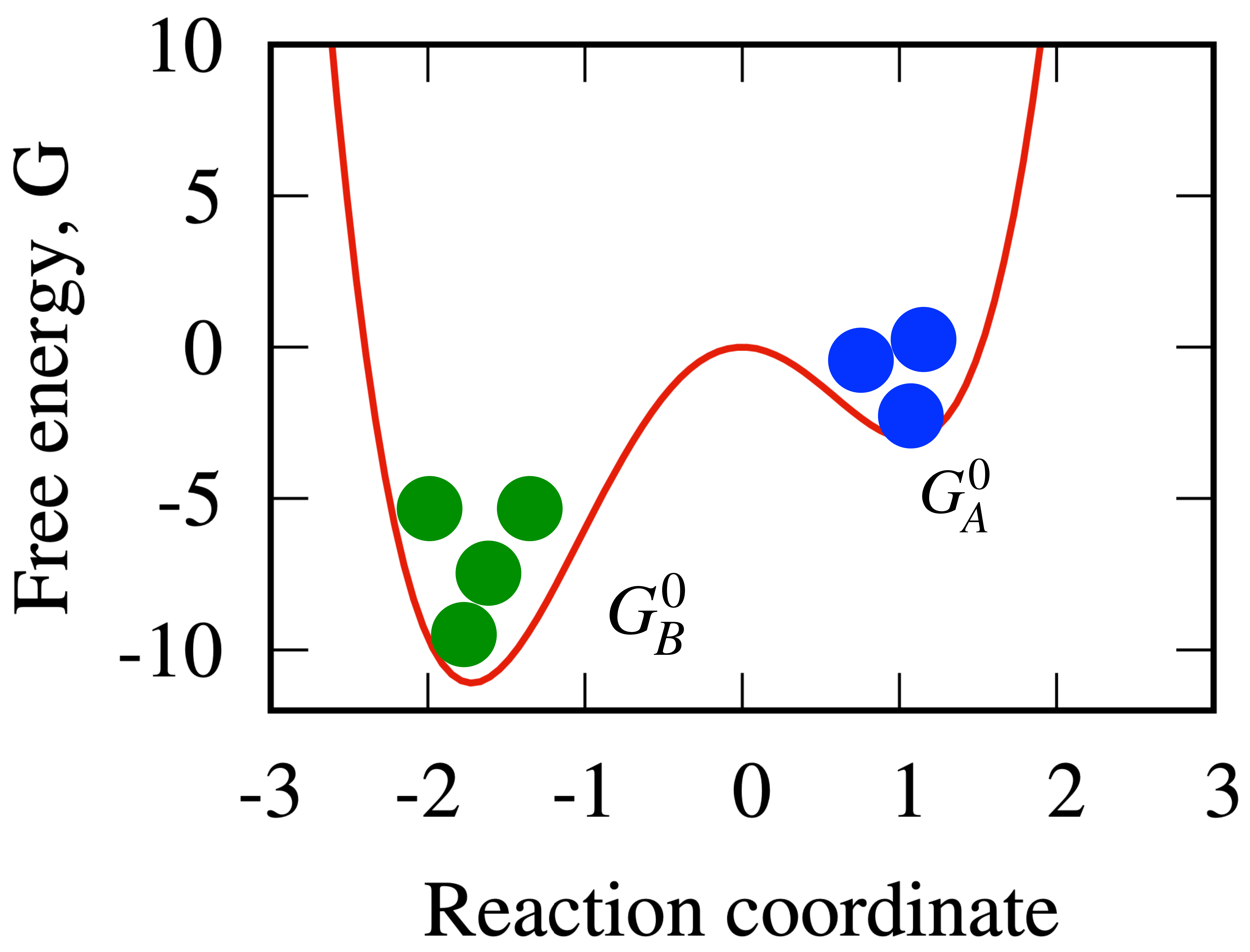

$$\frac{r_{AB}}{r_{BA}} = \frac{[A]}{[B]} \exp\left(-\frac{G_A^0 - G_B^0}{k_B T}\right)$$

$$\frac{r_{AB}}{r_{BA}} = \frac{[A]}{[B]} \exp\left(-\frac{\Delta G^0}{k_B T}\right)$$

At equilibrium, if $r_{AB} = r_{BA}$,

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

## At equilibrium: Ratio of rates




$$\frac{r_{AB}}{r_{BA}} = \frac{[A]}{[B]} \exp\left(-\frac{G_A^0 - G_B^0}{k_B T}\right)$$

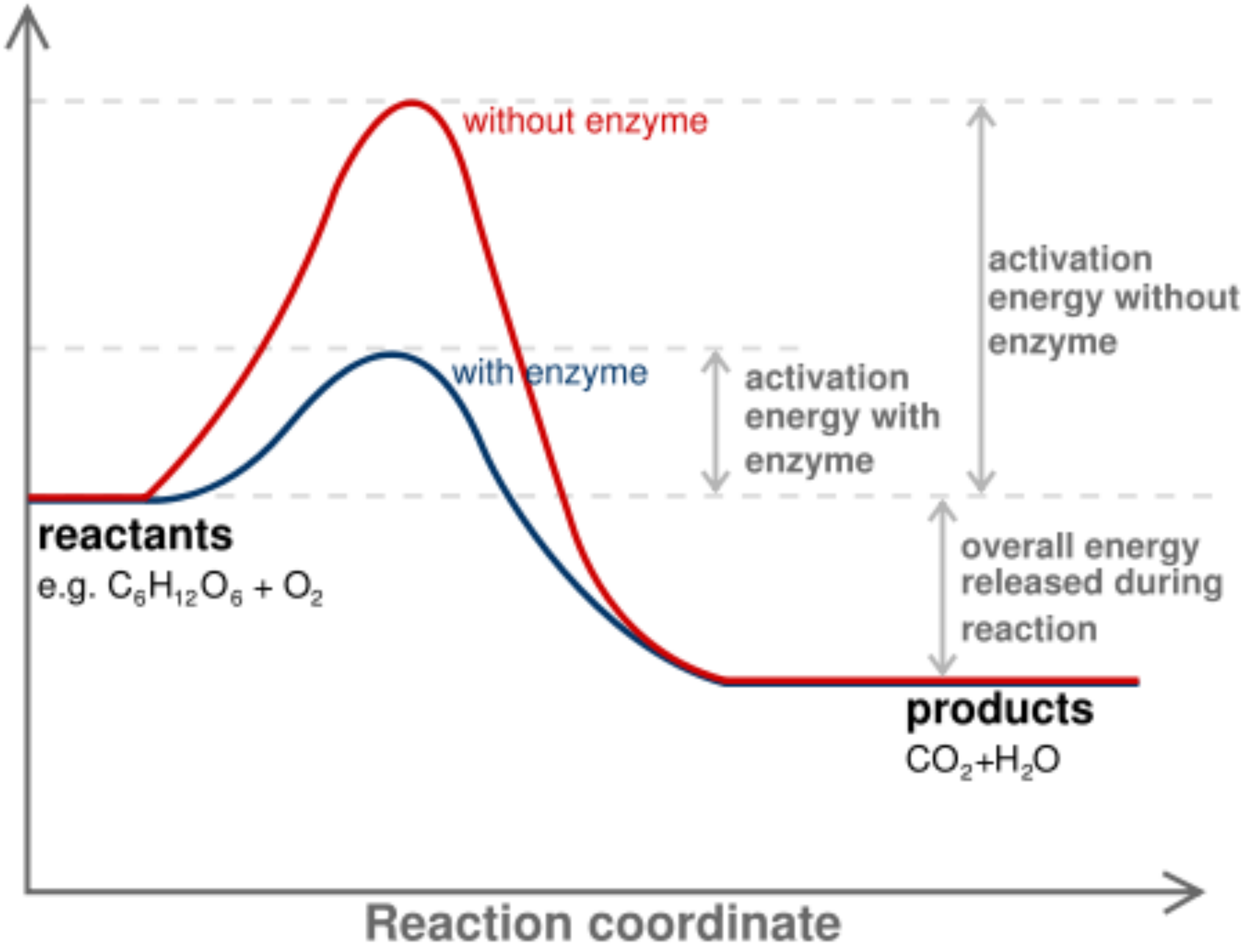
$$\frac{r_{AB}}{r_{BA}} = \frac{[A]}{[B]} \exp\left(-\frac{\Delta G^0}{k_B T}\right)$$

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

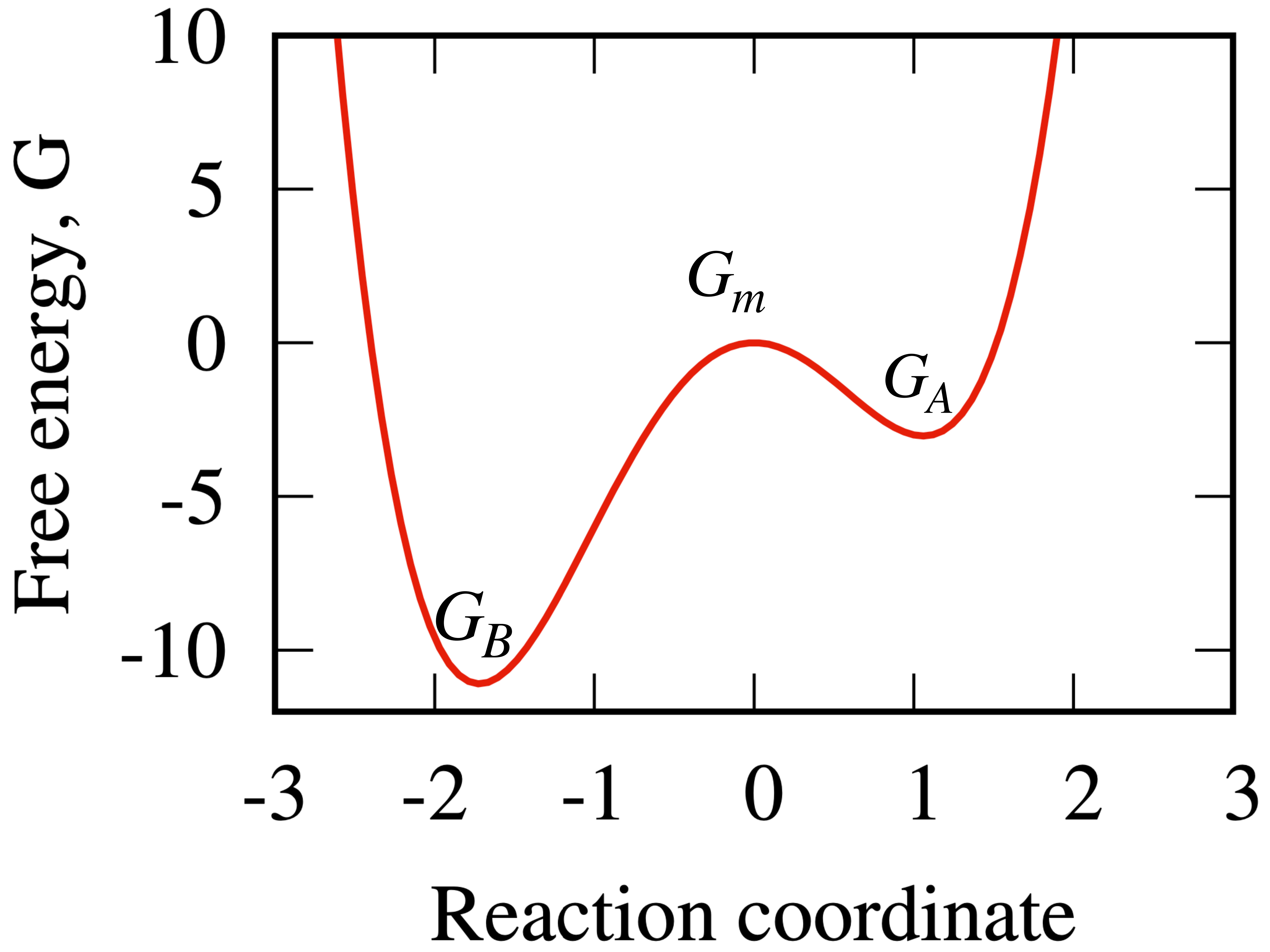
Enzymes influence the landscape by changing the height of the barrier

Enzyme reduces barrier height (activation energy)

Free energy



**Enzyme changing barrier height does not change equilibrium (ratio)**




$$r_{AB}^0 = r_0 \exp\left(-\frac{G_m^0 - G_A^0 - G_e}{k_B T}\right)$$

$$r_{BA}^0 = r_0 \exp\left(-\frac{G_m^0 - G_B^0 - G_e}{k_B T}\right)$$

$$\frac{r_{AB}^0}{r_{BA}^0} = \exp\left(-\frac{G_A^0 - G_B^0}{k_B T}\right)$$

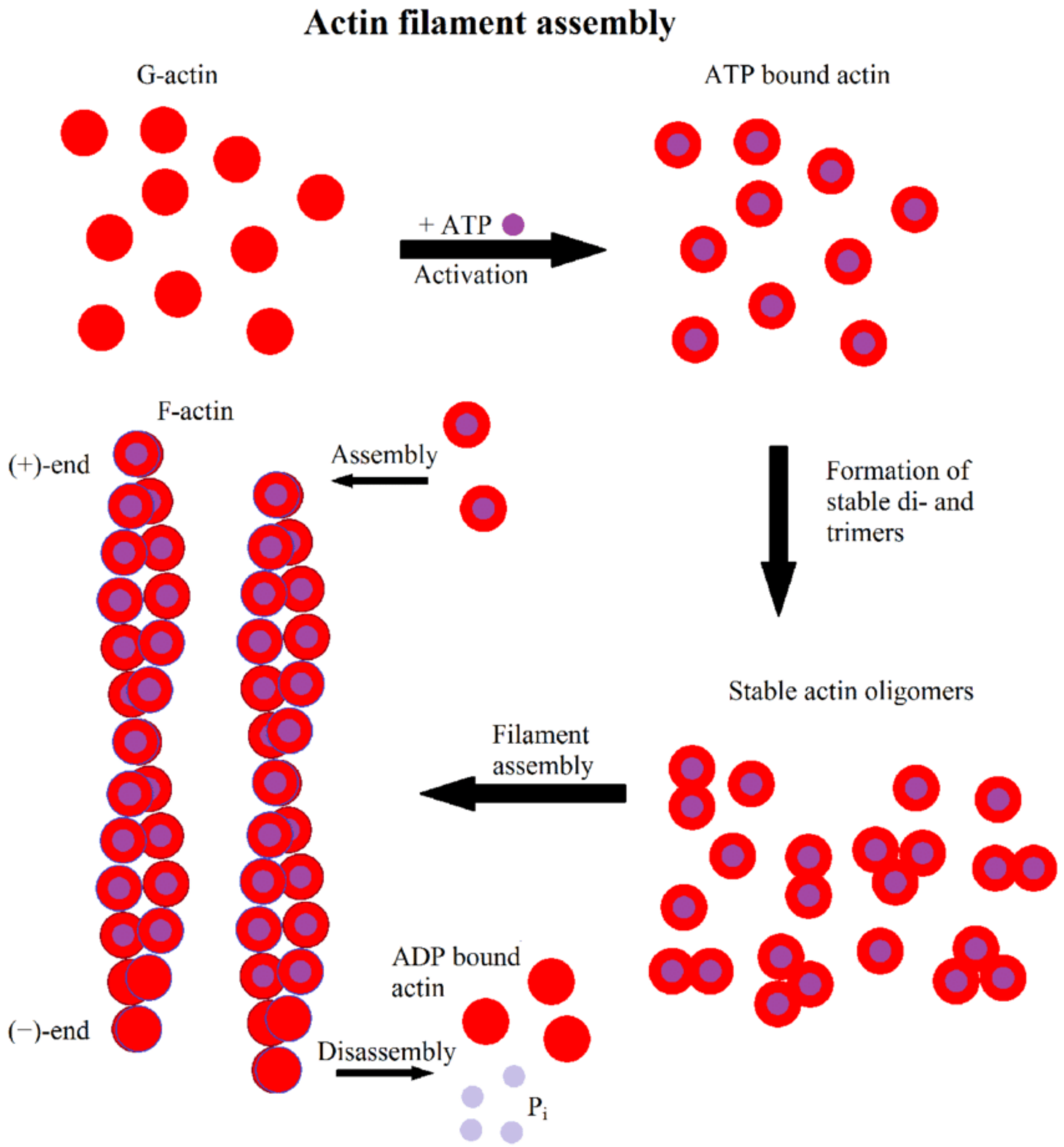
$$\frac{r_{AB}^0}{r_{BA}^0} = \exp\left(-\frac{\Delta G^0}{k_B T}\right)$$

**Only difference in Free energy matters**

# ATP Hydrolysis

$$ATP \rightleftharpoons ADP + P_i$$

# Actin is probably the simplest machine

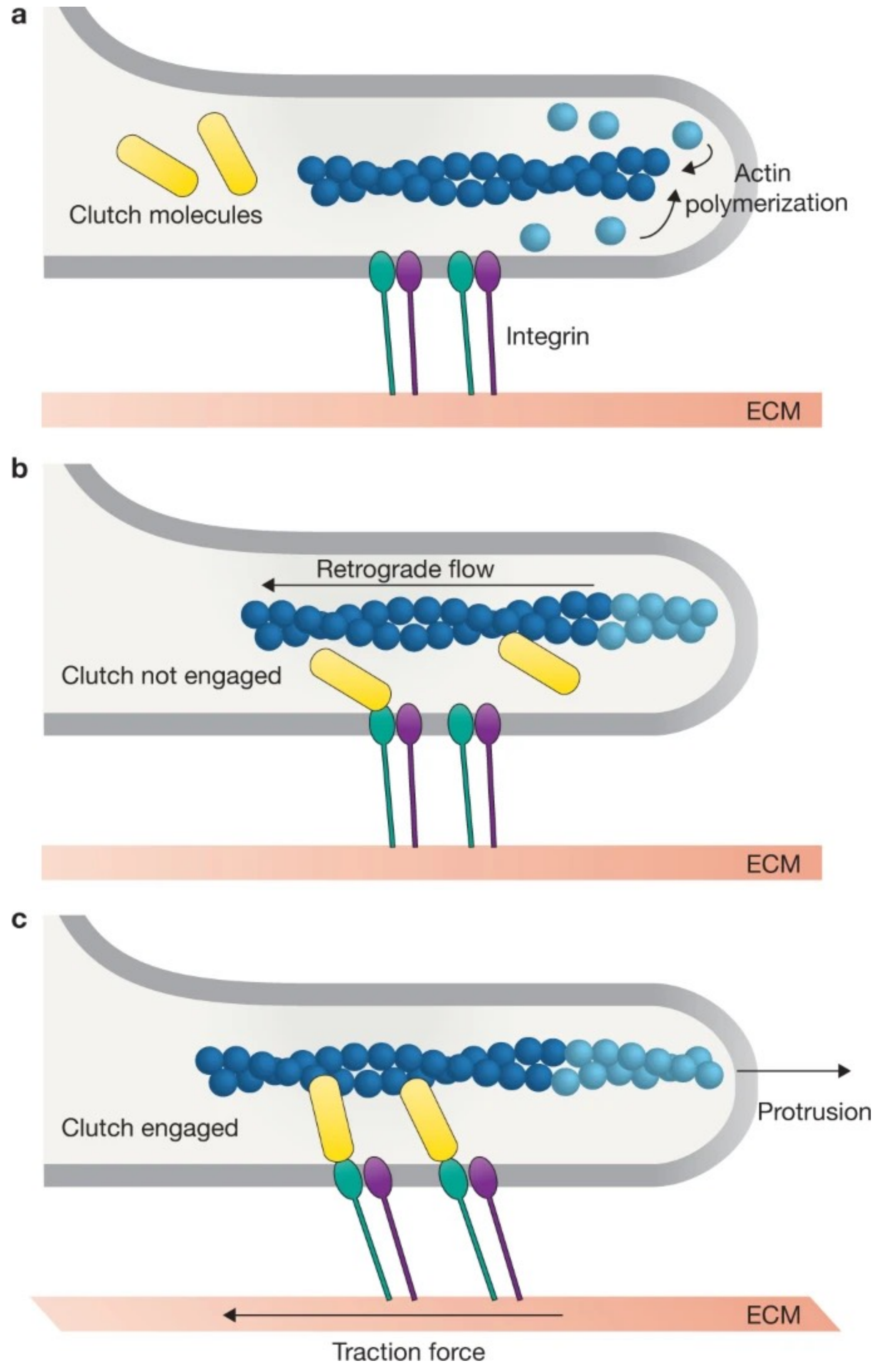


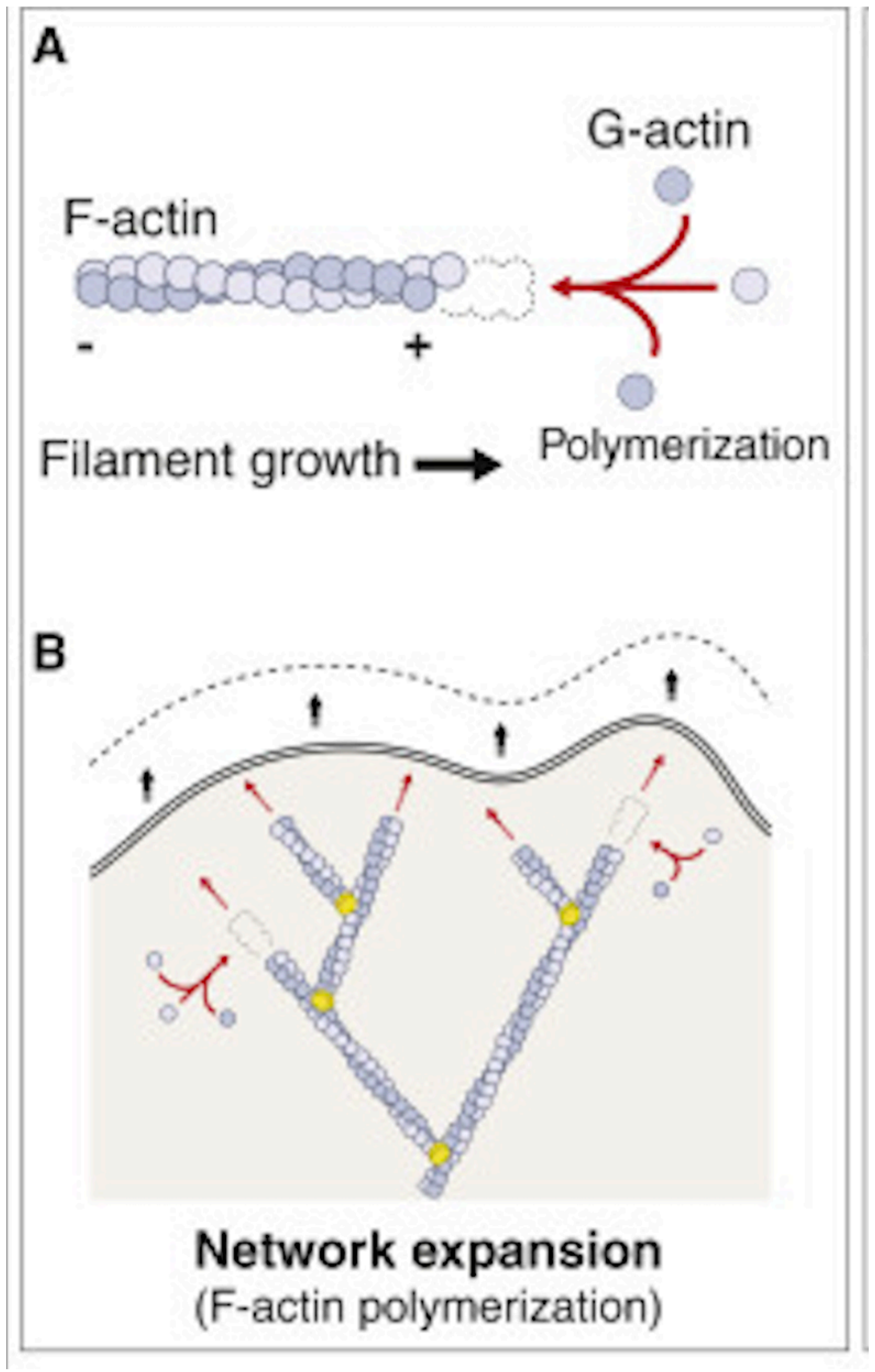

Actin is a protein

Many actin monomers self-assemble and form long filaments

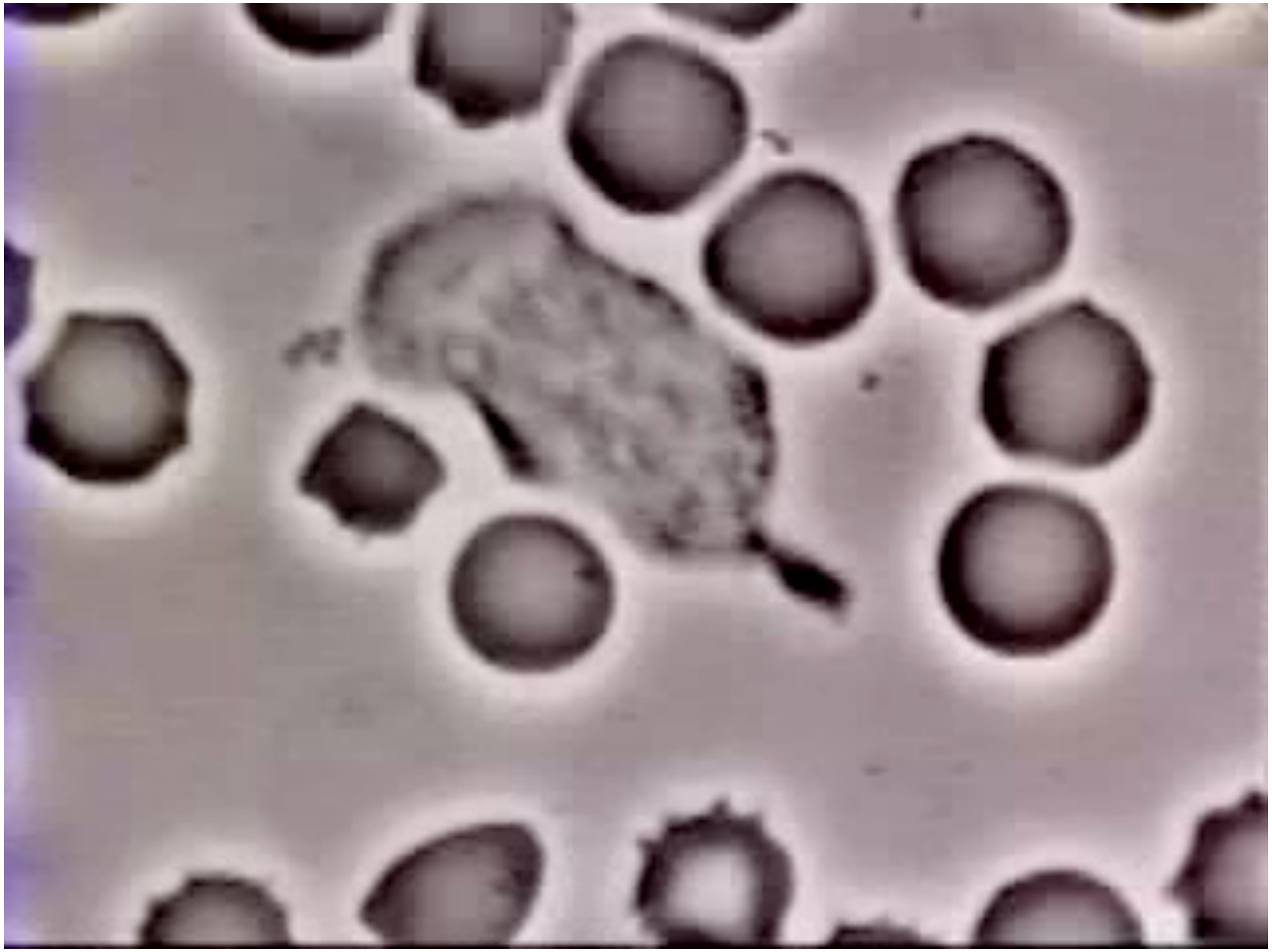
These filaments generate force

# Actin polymerisation can push cell membrane



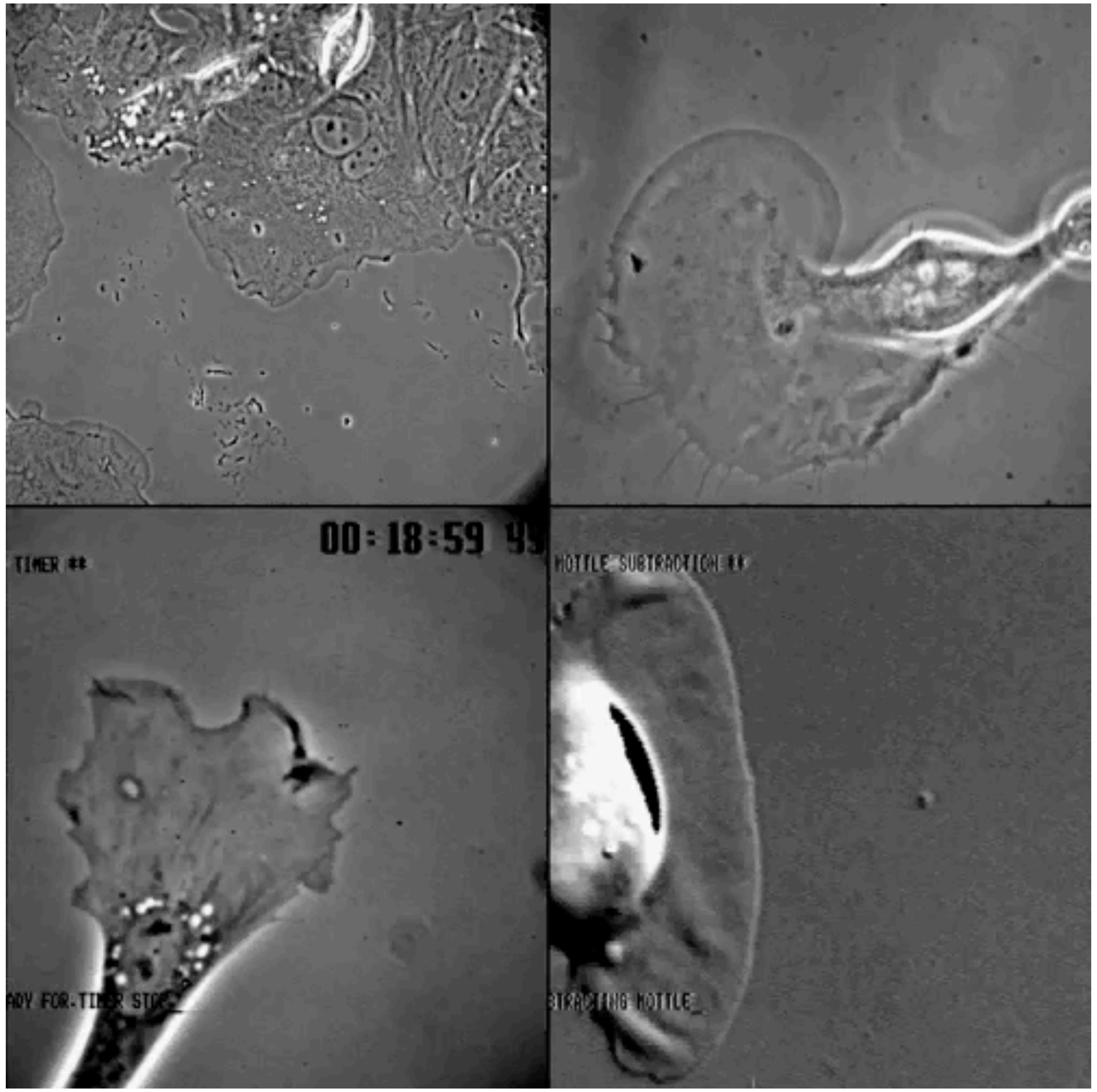
# White blood cell chasing bacteria



# Cells can generate force and move

Mouse fibroblasts: Wound healing

Mouse melanoma cell




Chick fibroblast

Trout epidermal keratocyte

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

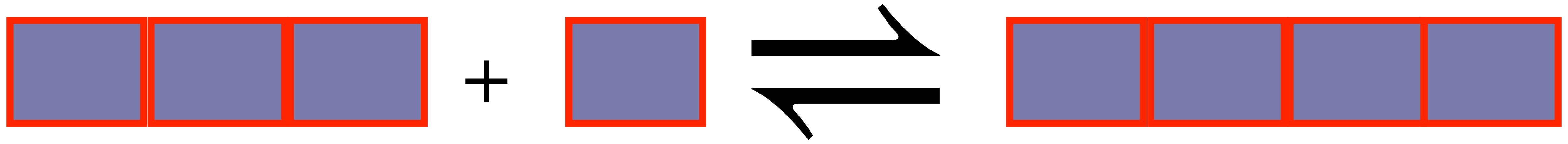
When actin polymerises how is chemical energy getting converted to mechanical energy?

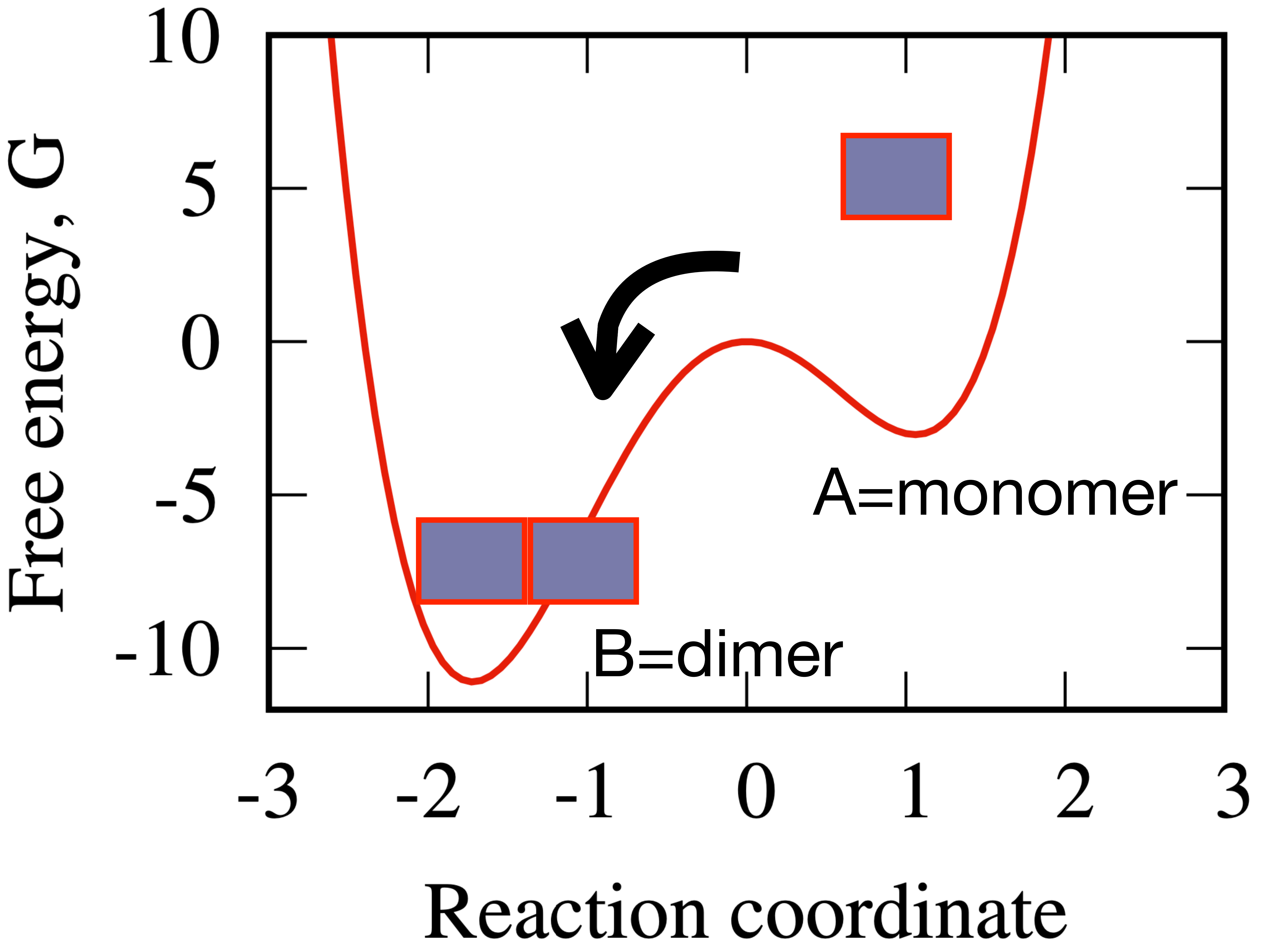
# Polymerisation

$$\text{Monomer} \rightleftharpoons \text{Dimer}$$

$$\text{kmer} \rightleftharpoons (k+1)\text{mer}$$

Consider the following reaction



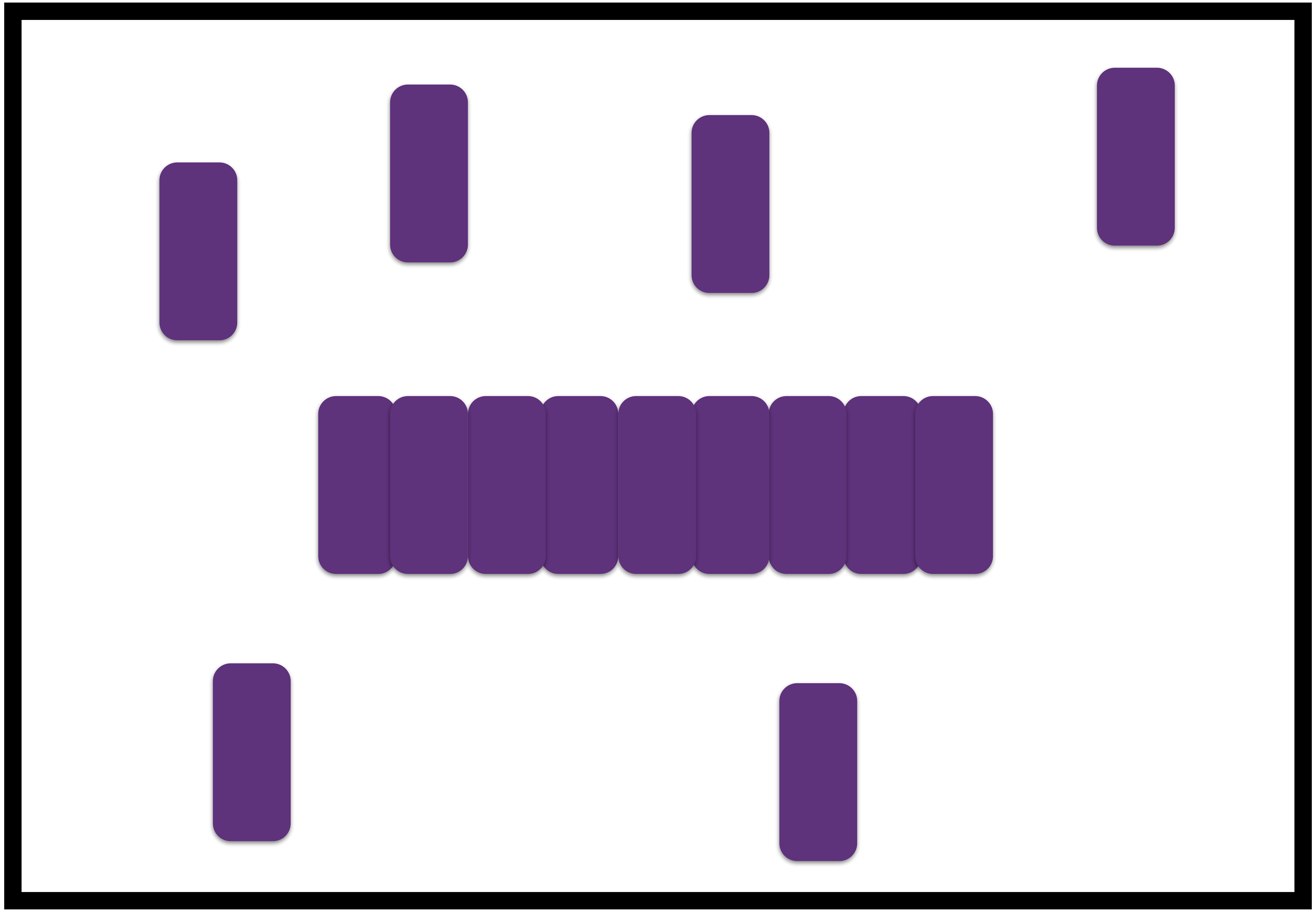
Imagine you put a bunch of monomers into a beaker

What will happen?

# Imagine you put a bunch of monomers into a beaker

What will happen?

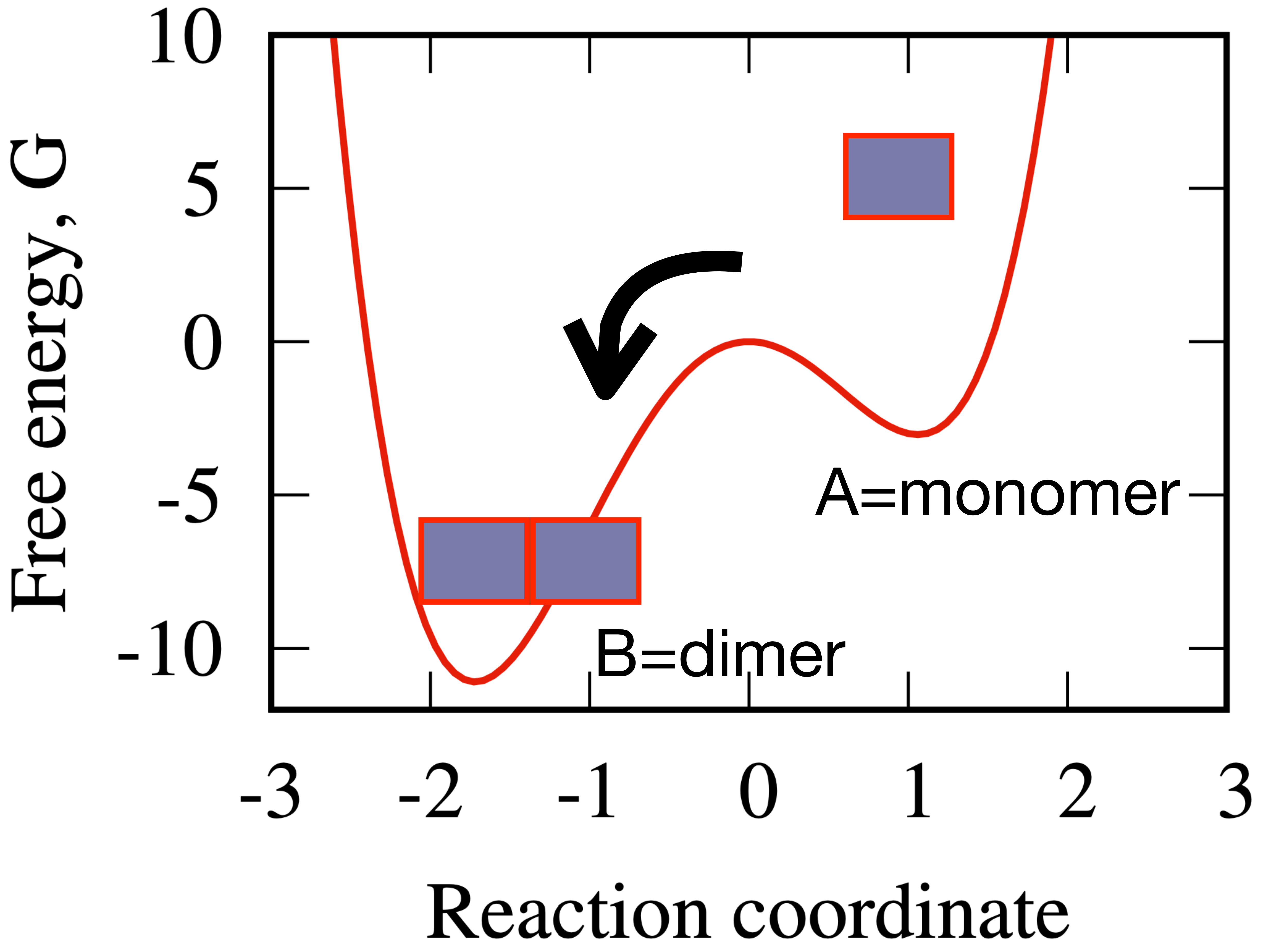
# They will polymerise



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

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

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

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

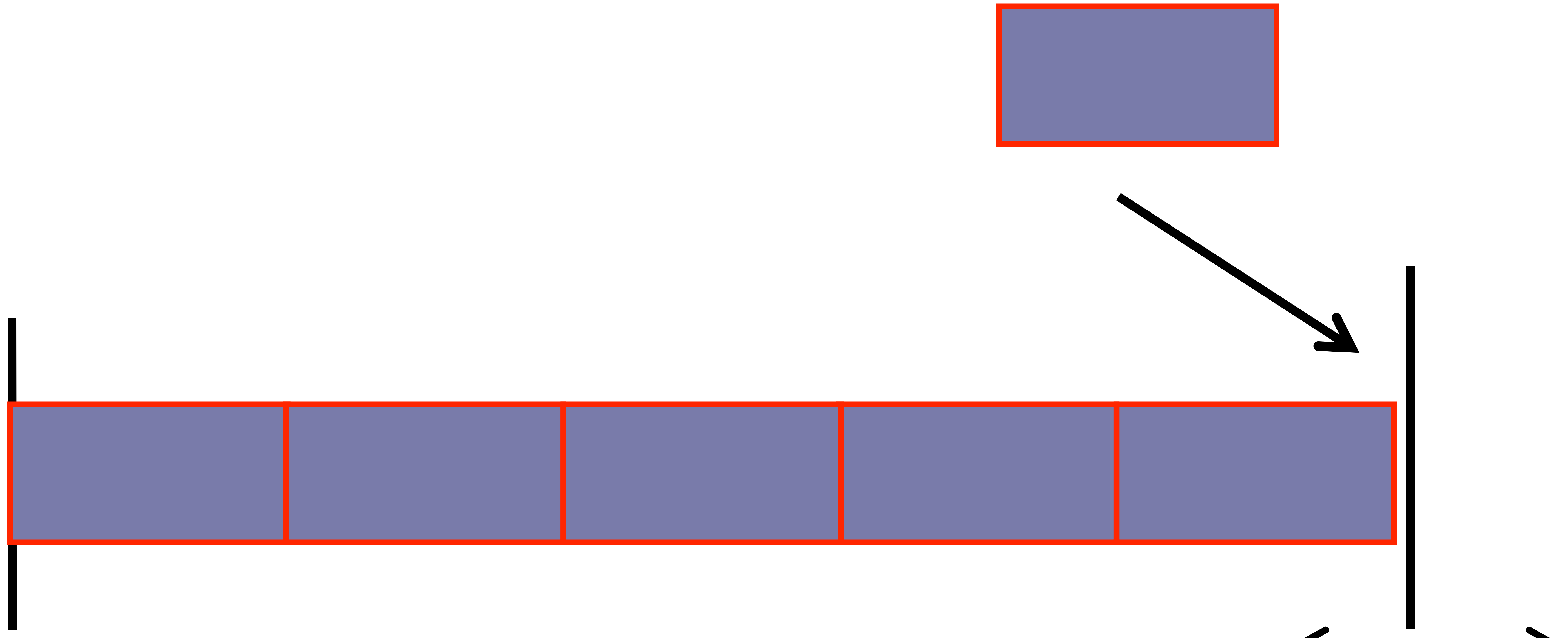
$$\text{When,}\ \ [c] = \frac{k_{\text{off}}}{k_0}$$

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

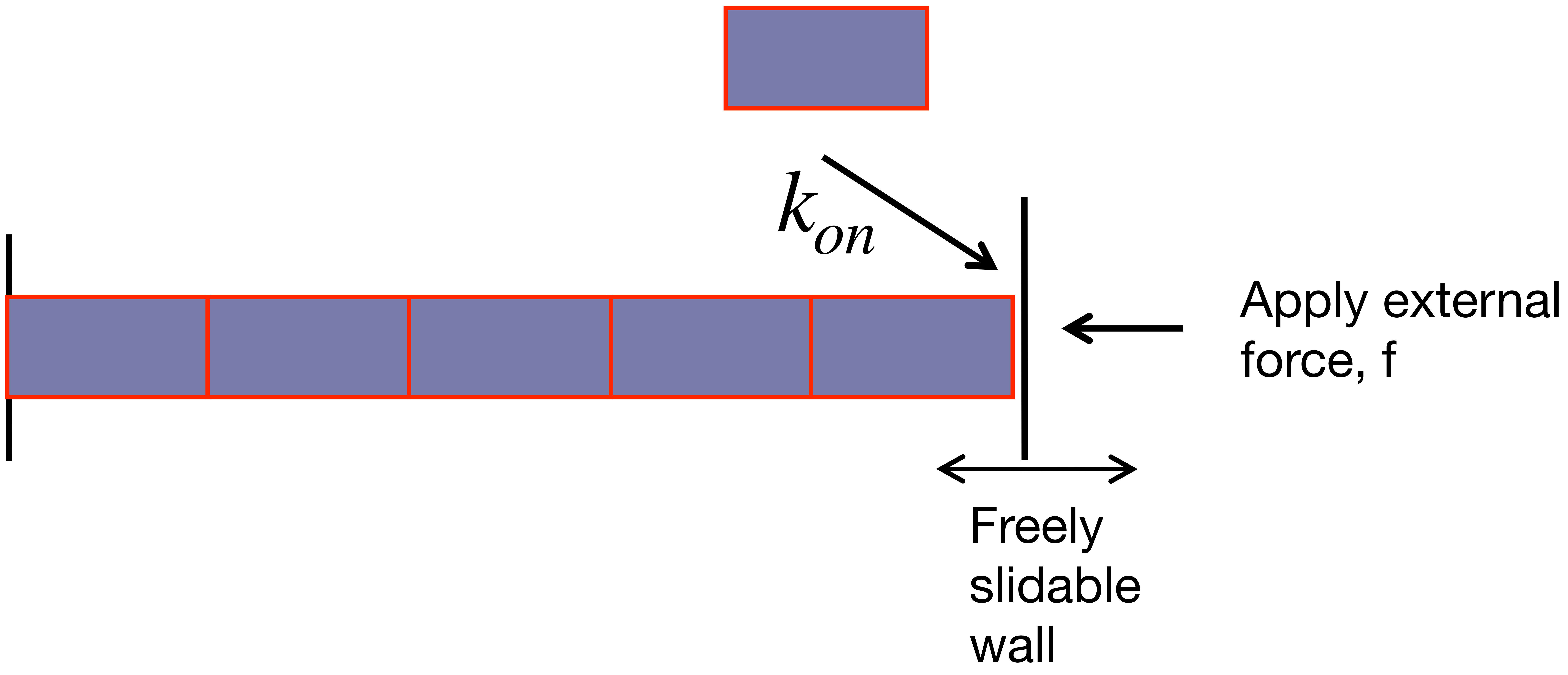
$$\text{Actin, } k_0 \approx 12\ \mu M^{-1} s^{-1}$$

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

# Polymerization can push against a wall = generate force

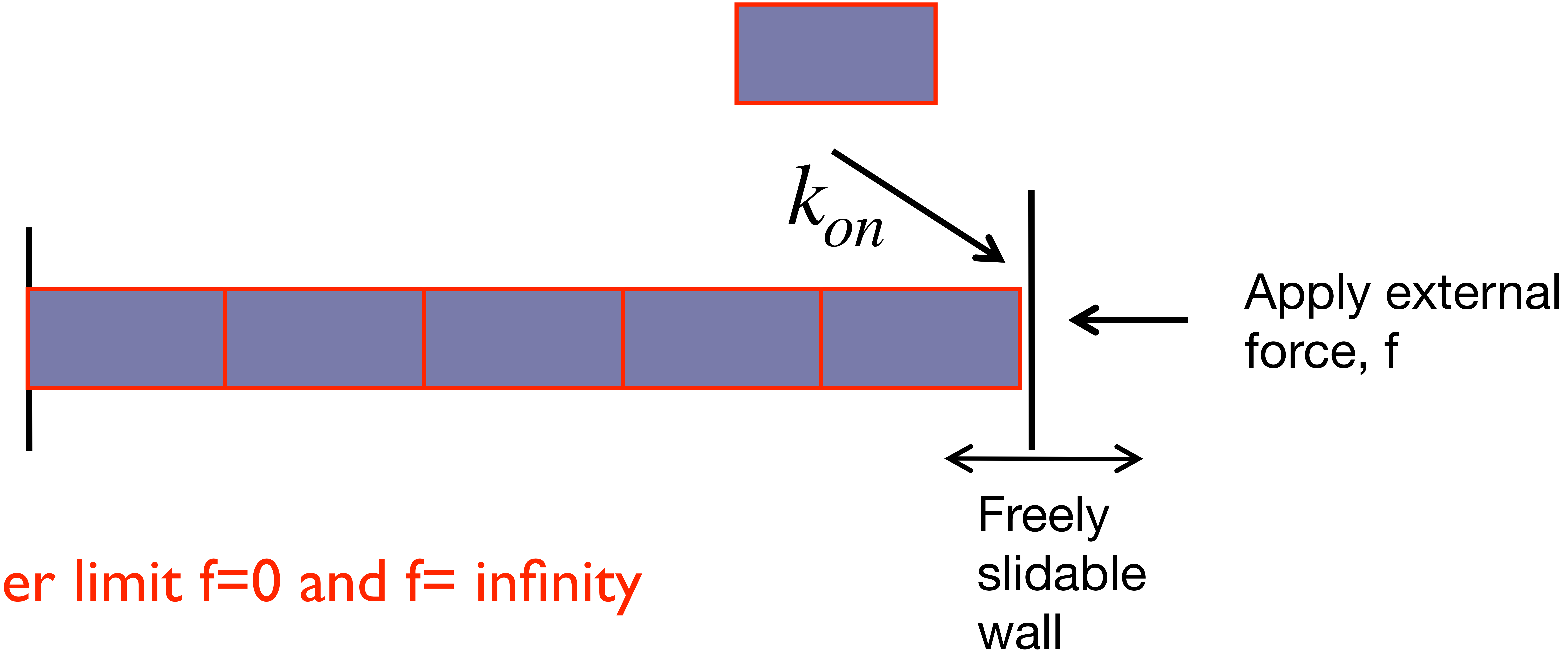


# Imagine an experimental setup where you apply an external force, f, against a polymerising actin



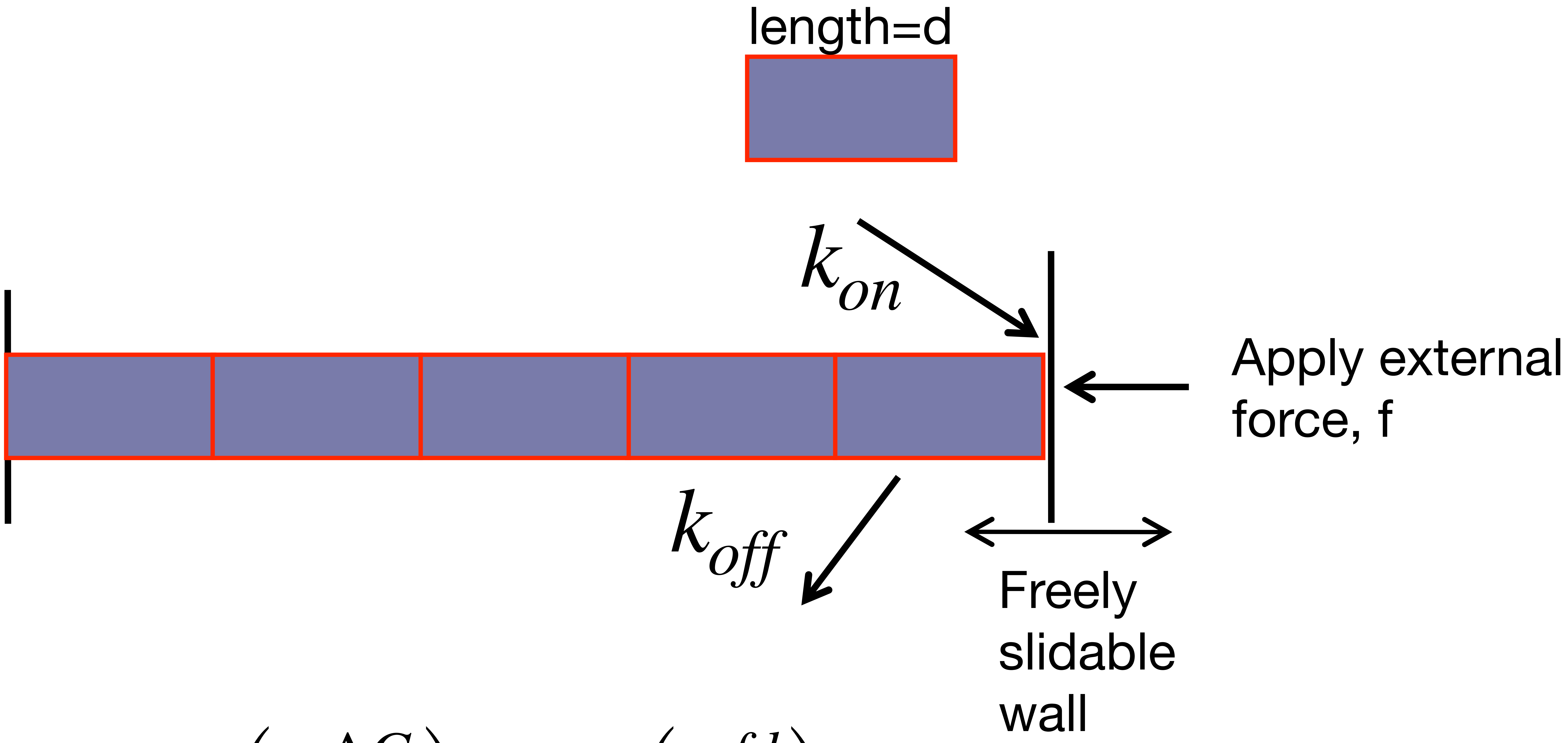

If the external force is high, what happens to the polymerisation rate?

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




Consider limit f=0 and f= infinity

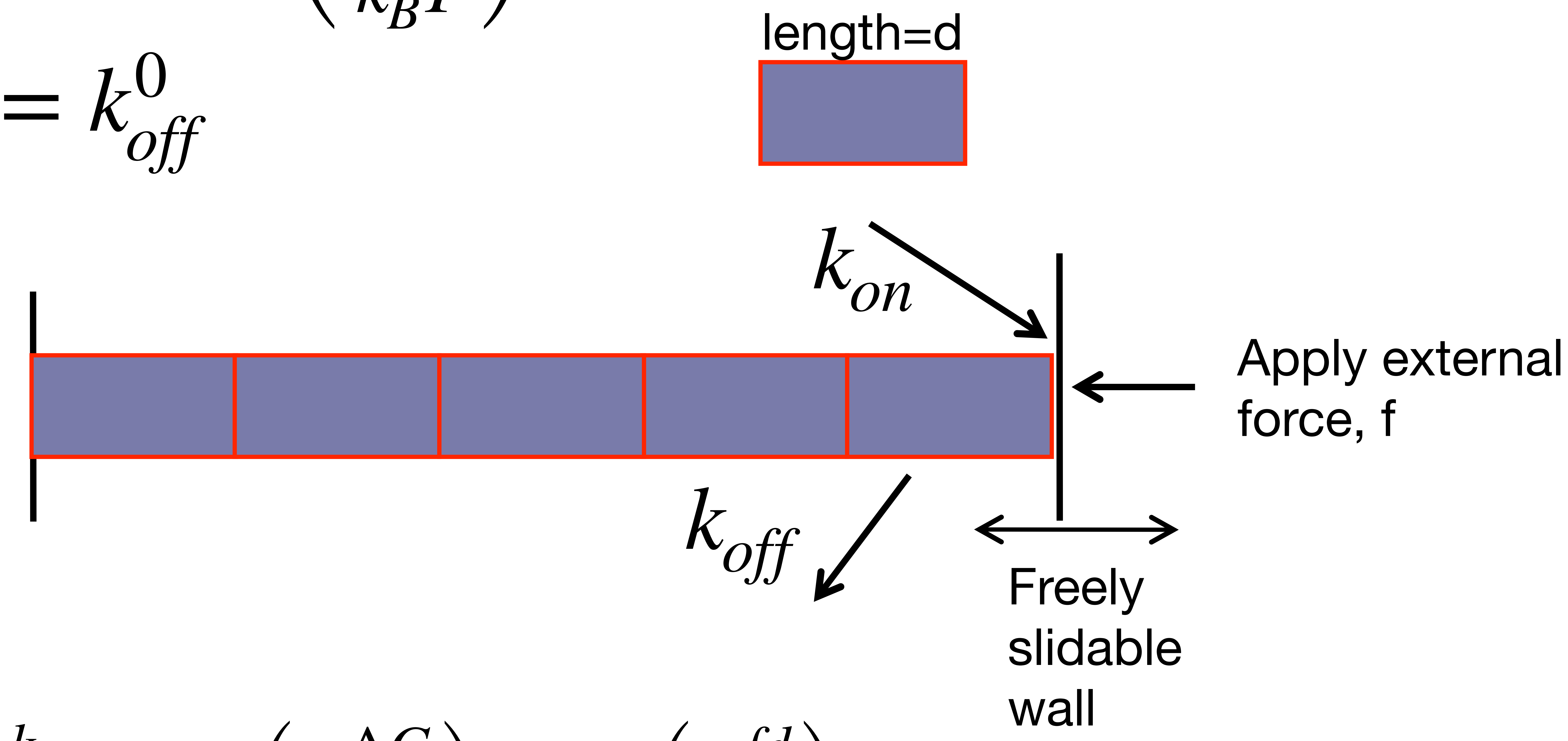
# Can you think of a functional form using which polymerisation force will decrease.




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

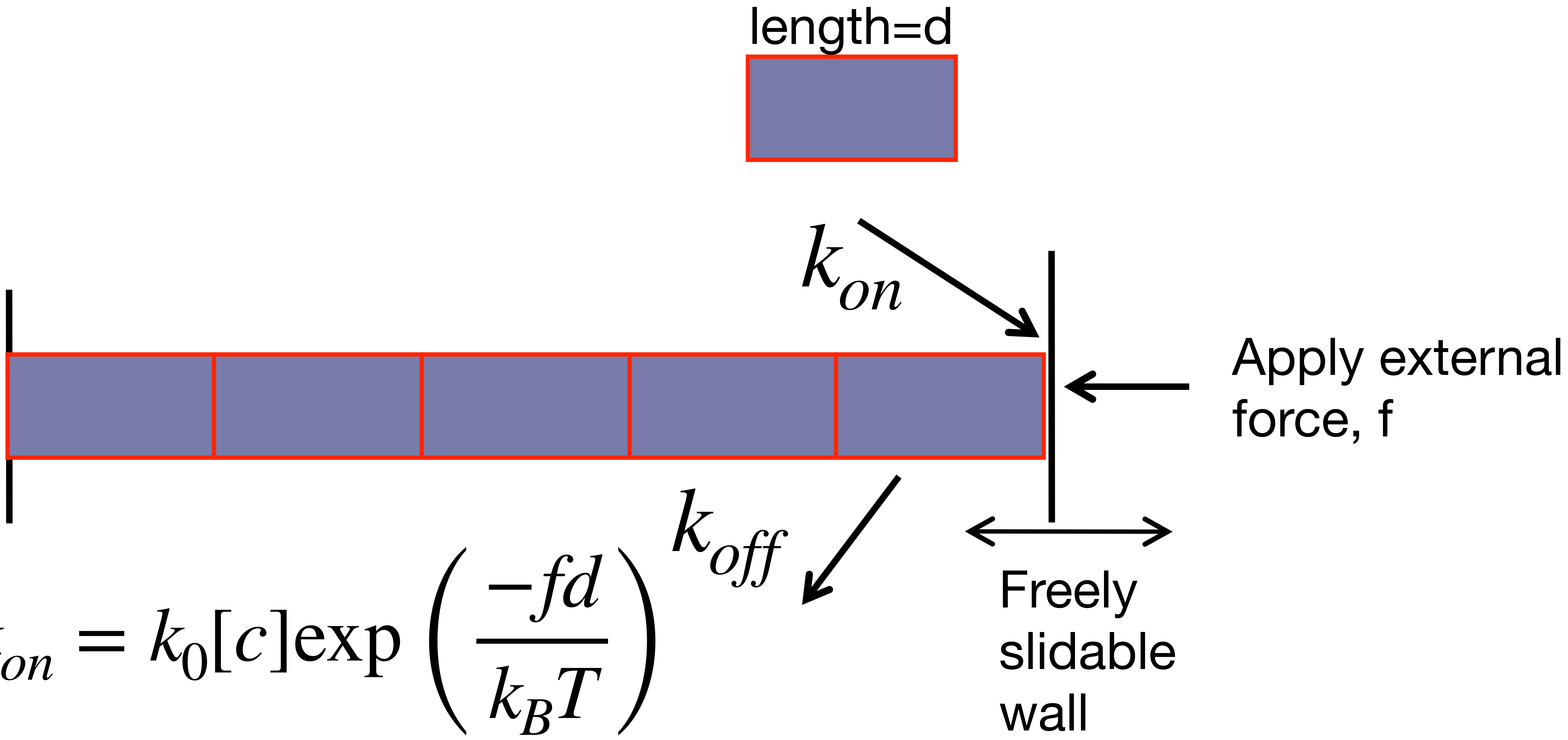
$$k_{on} = k_0[c]\exp\left(\frac{-fd}{k_BT}\right)$$

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




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

# What is the maximum force it can generate?

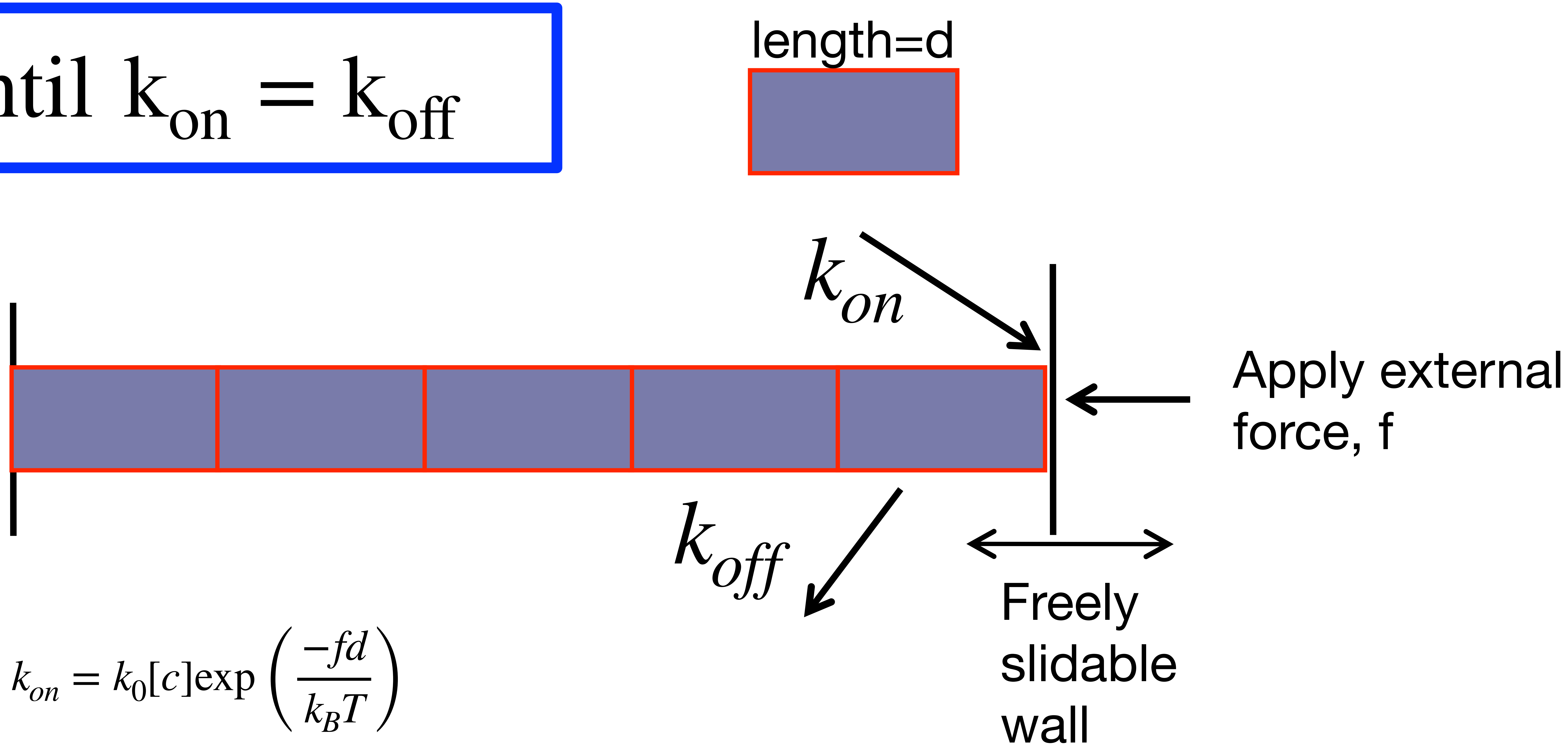



$$k_{on} = k_0[c]\exp\left(\frac{-fd}{k_BT}\right)$$

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

# What is the maximum force it can generate?

Until $k_{on} = k_{off}$

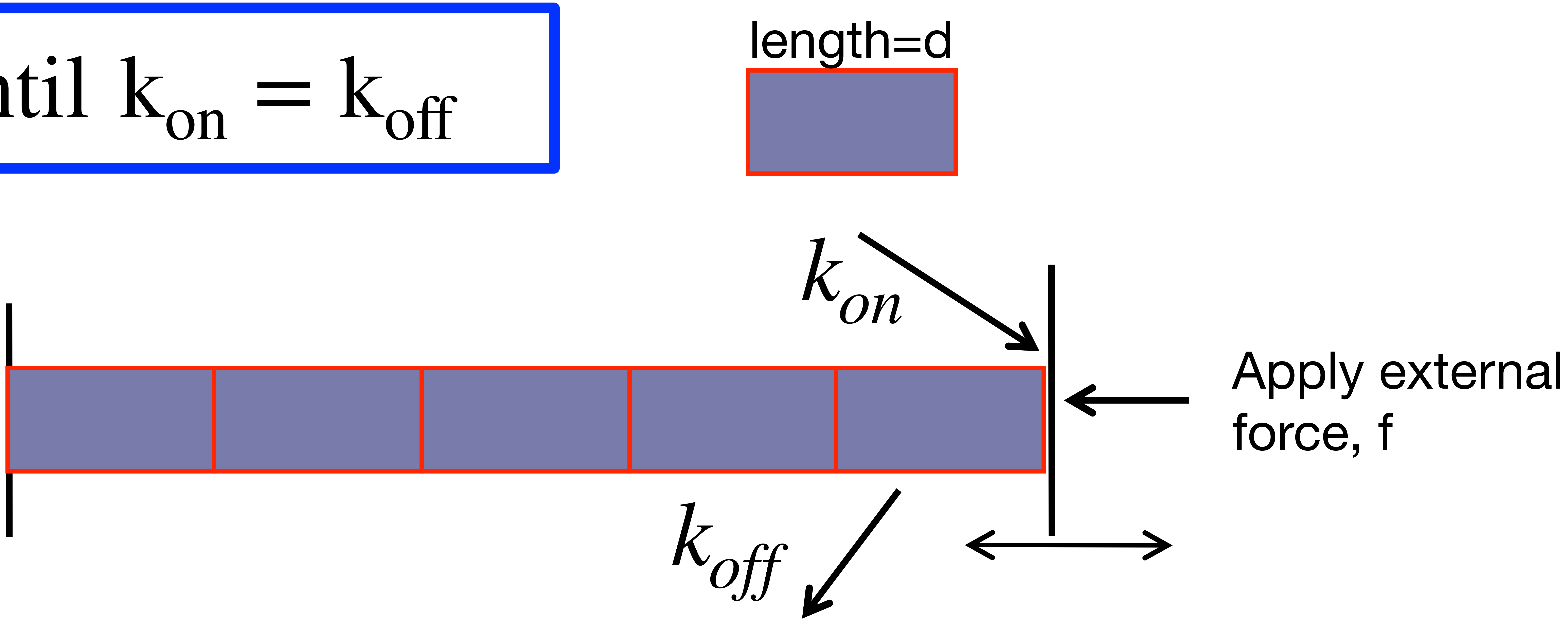



$$k_{on} = k_0[c]\exp\left(\frac{-fd}{k_B T}\right)$$

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

# What is the maximum force it can generate?

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




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

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

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

# 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

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

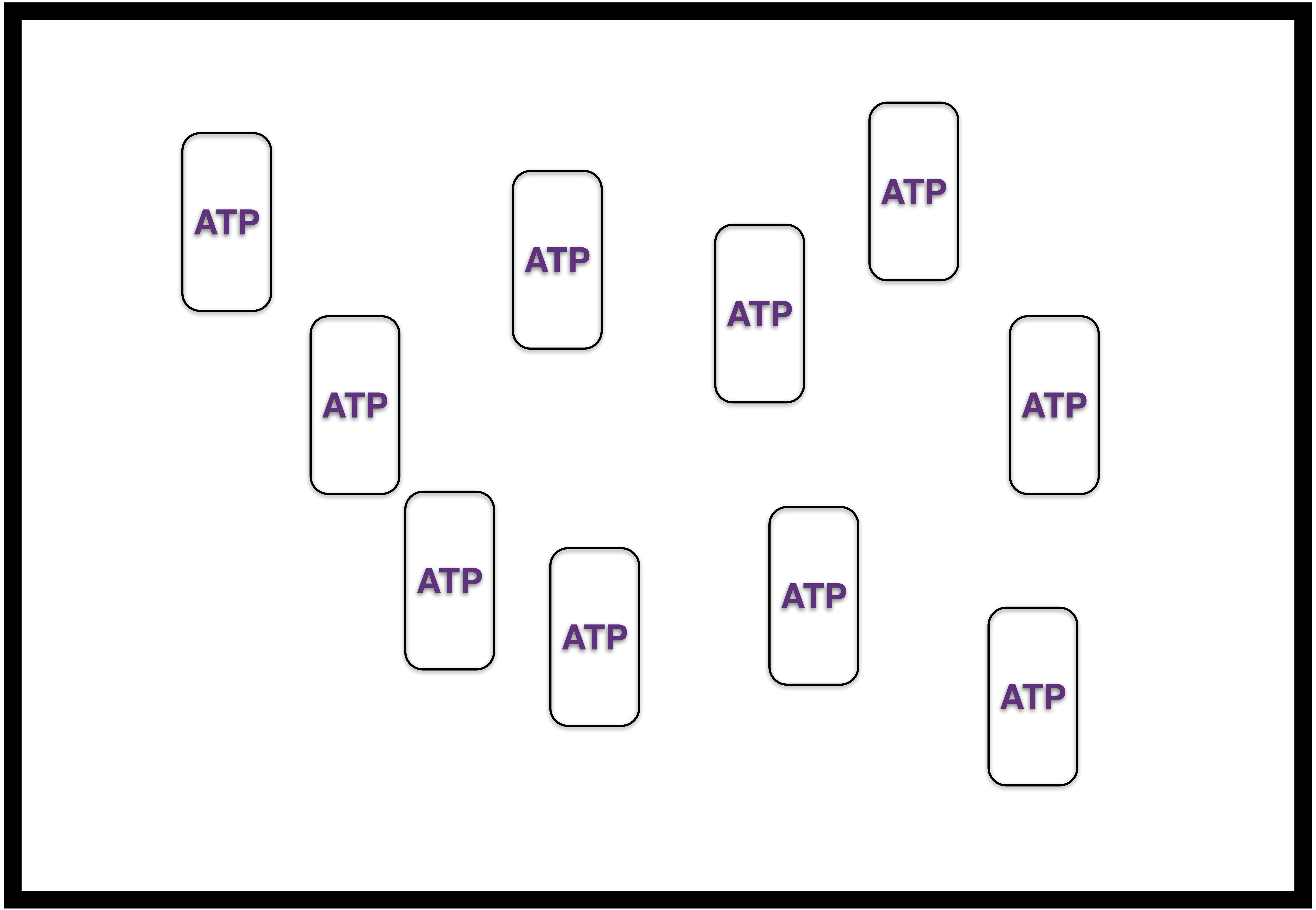
$$f_{max} = -\frac{\Delta G}{d}$$

This is theoretical maximum!

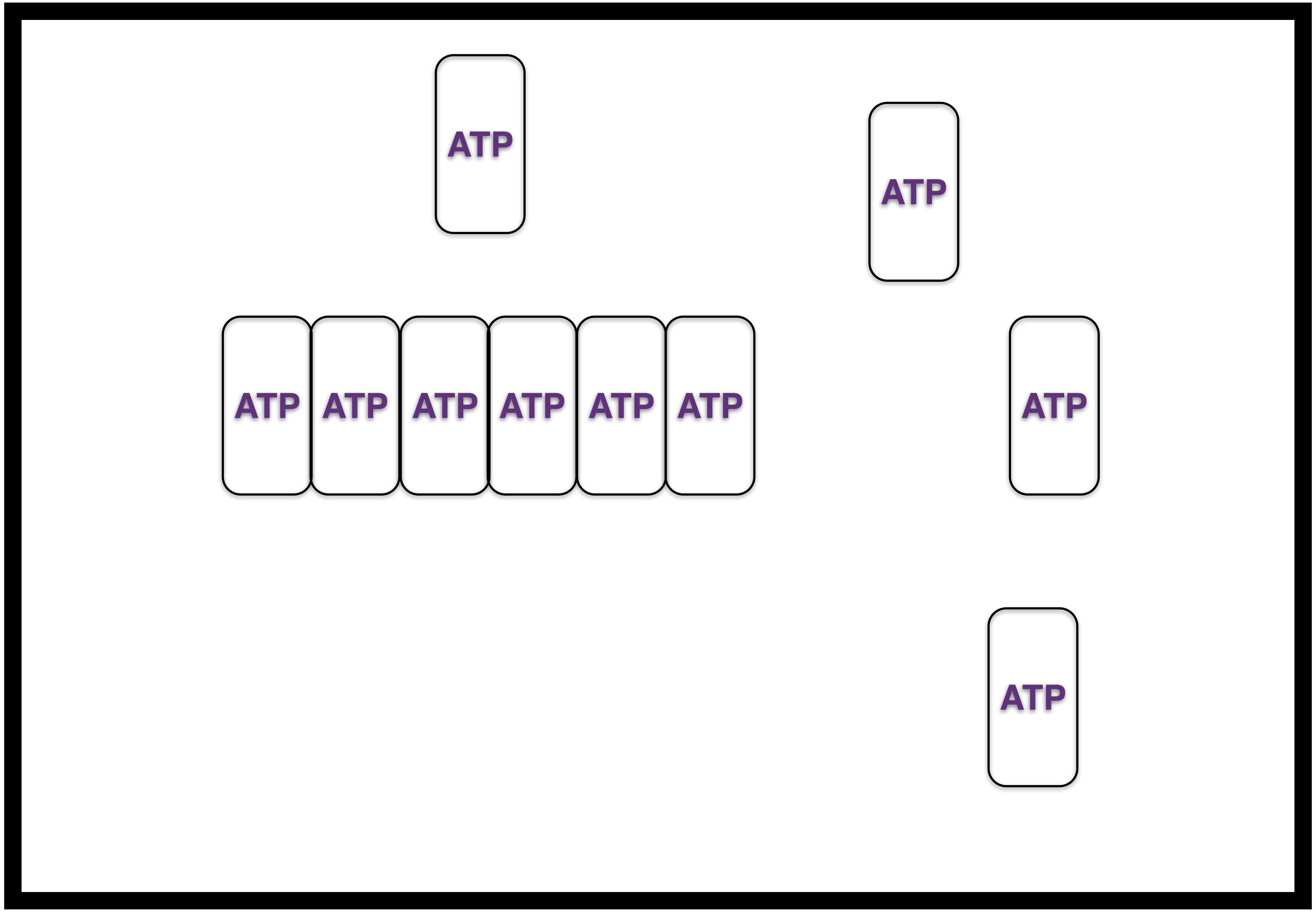
Practically, it will generate a bit less than this

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

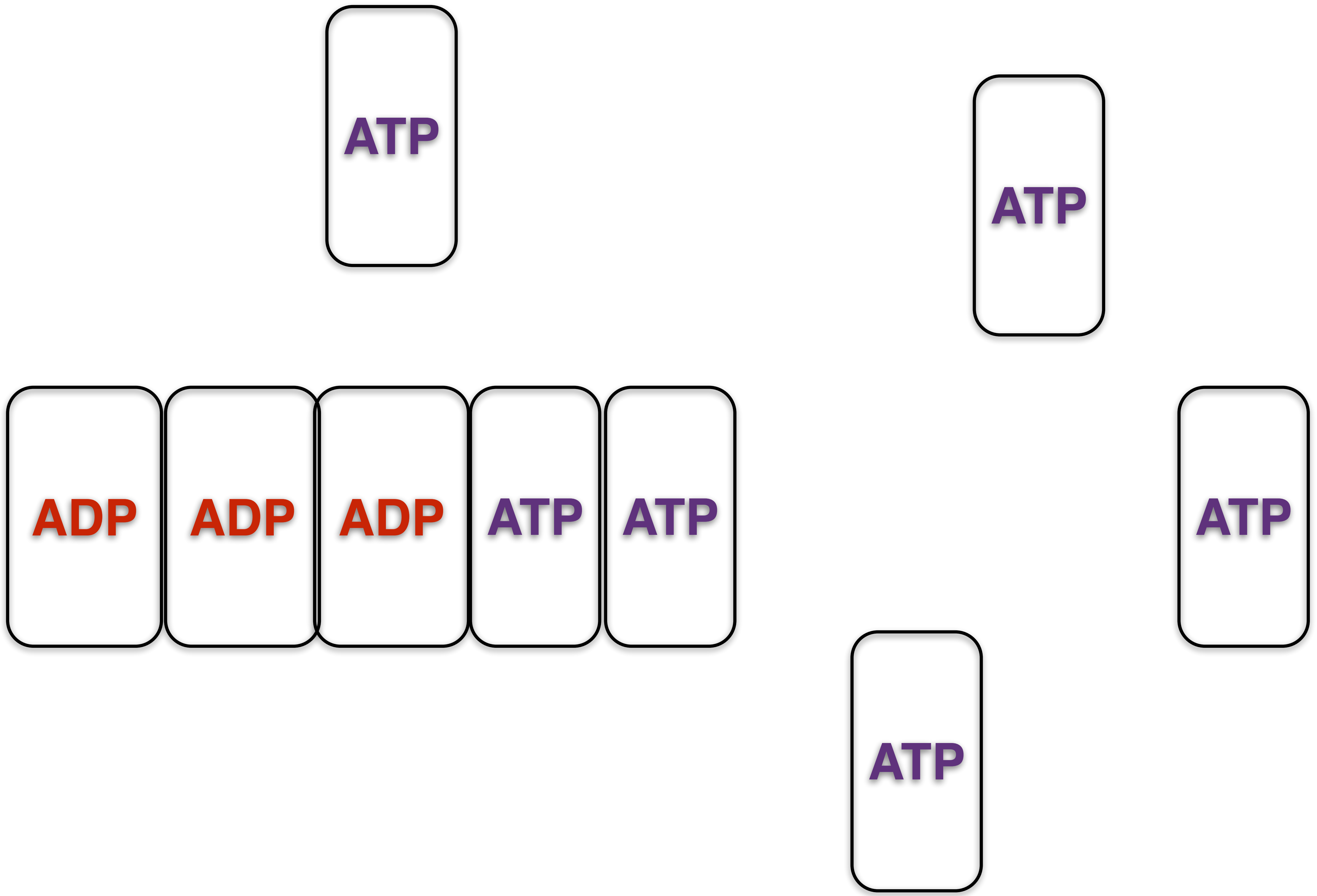
# Actin monomers in solution is bound to ATP



# ATP-bound actin polymerise

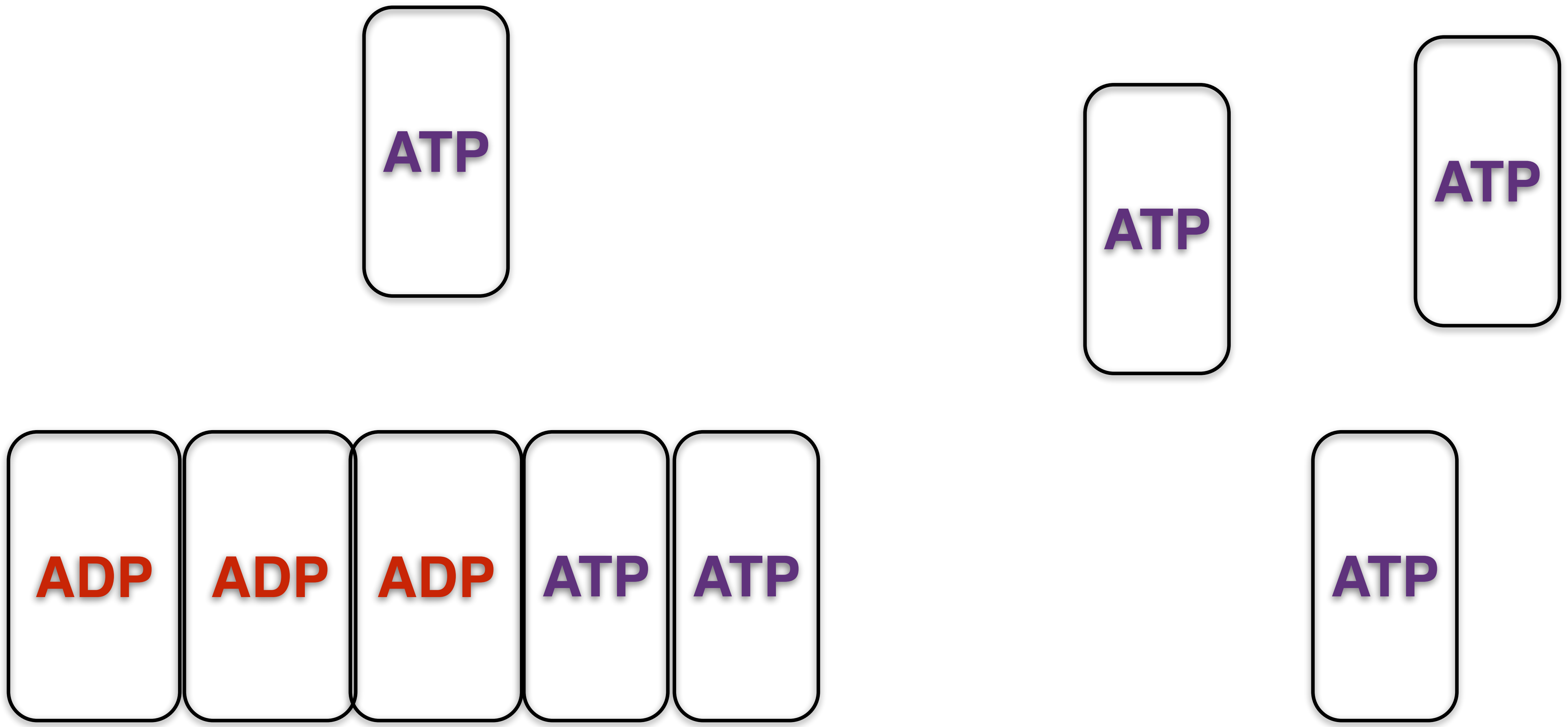


# On the polymer, ATP become ADP



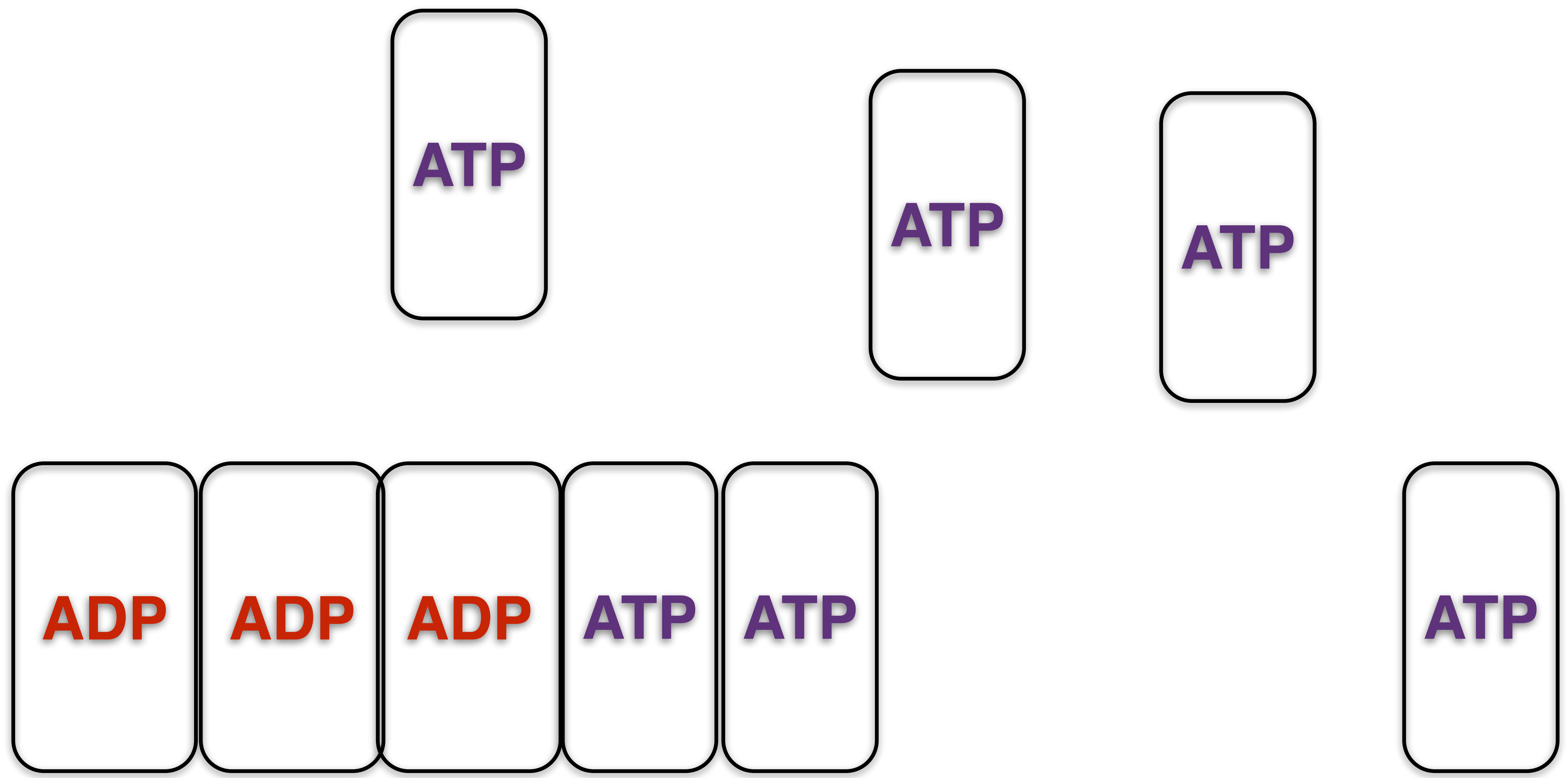

ATP to ADP conversion is known as "hydrolysis"
This happens only when actin is a
part of filament

# On the polymer, ATP become ADP



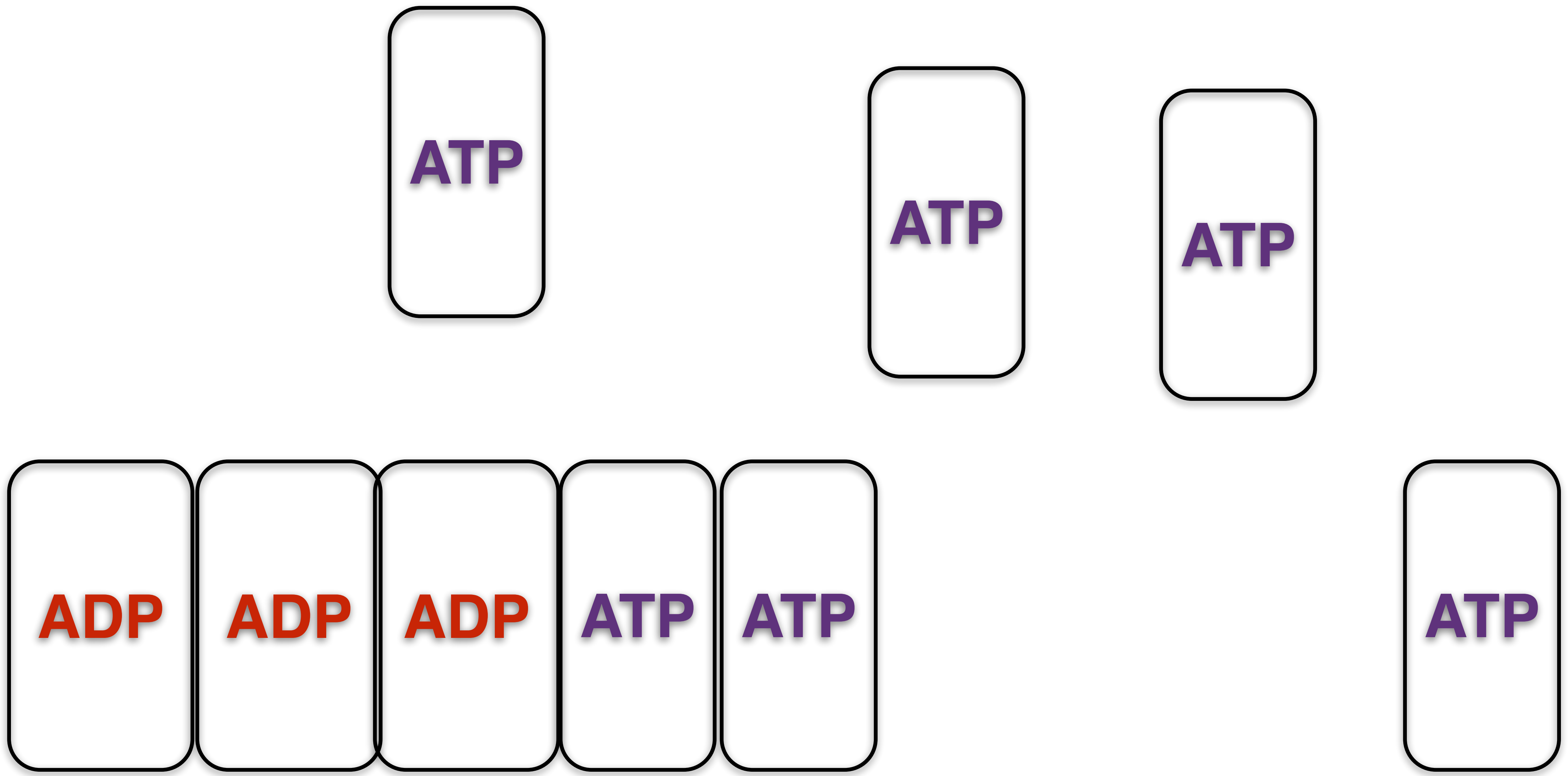

“Hydrolysis” leads to a small structural change in the actin protein. ADP-Actin is now in a different “state”, compared to ATP-actin

# This has broken the symmetry — front and back!



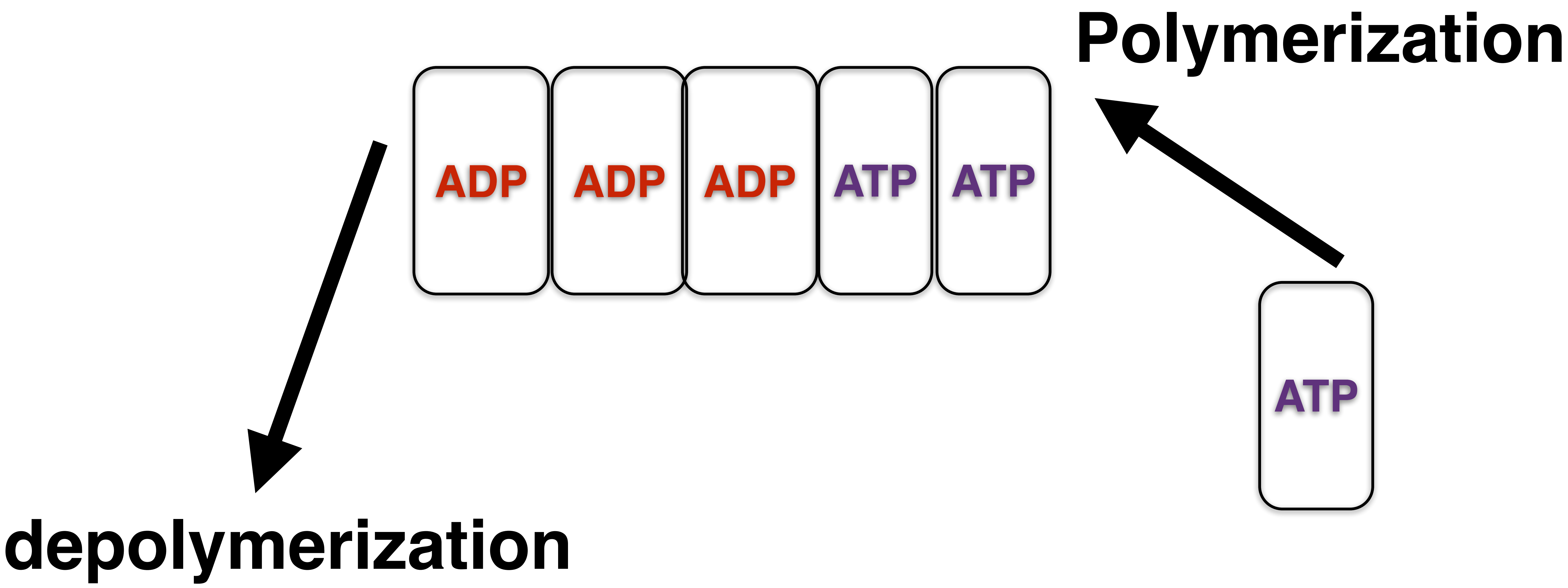

First requirement for any directed motion is "breaking symmetry" and choosing a direction

# Asymmetric rates




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

# Centre of mass motion!



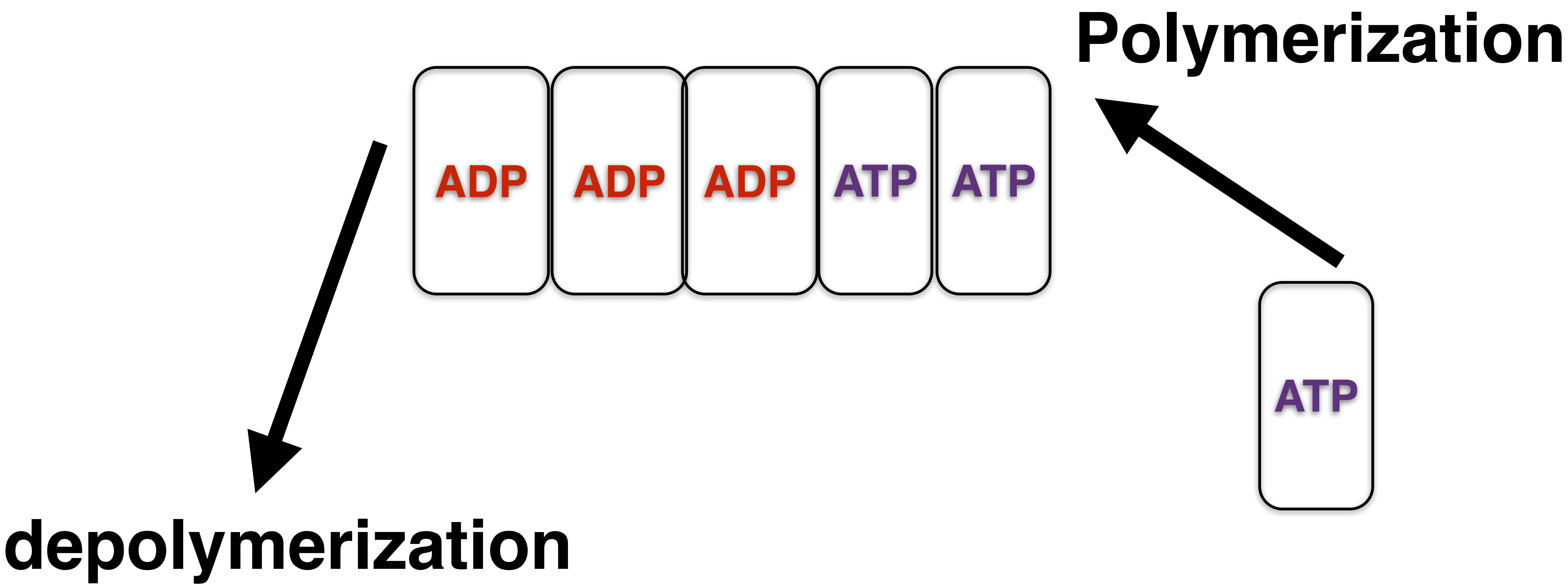
What is the velocity at “ATP” end (+ end)?

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

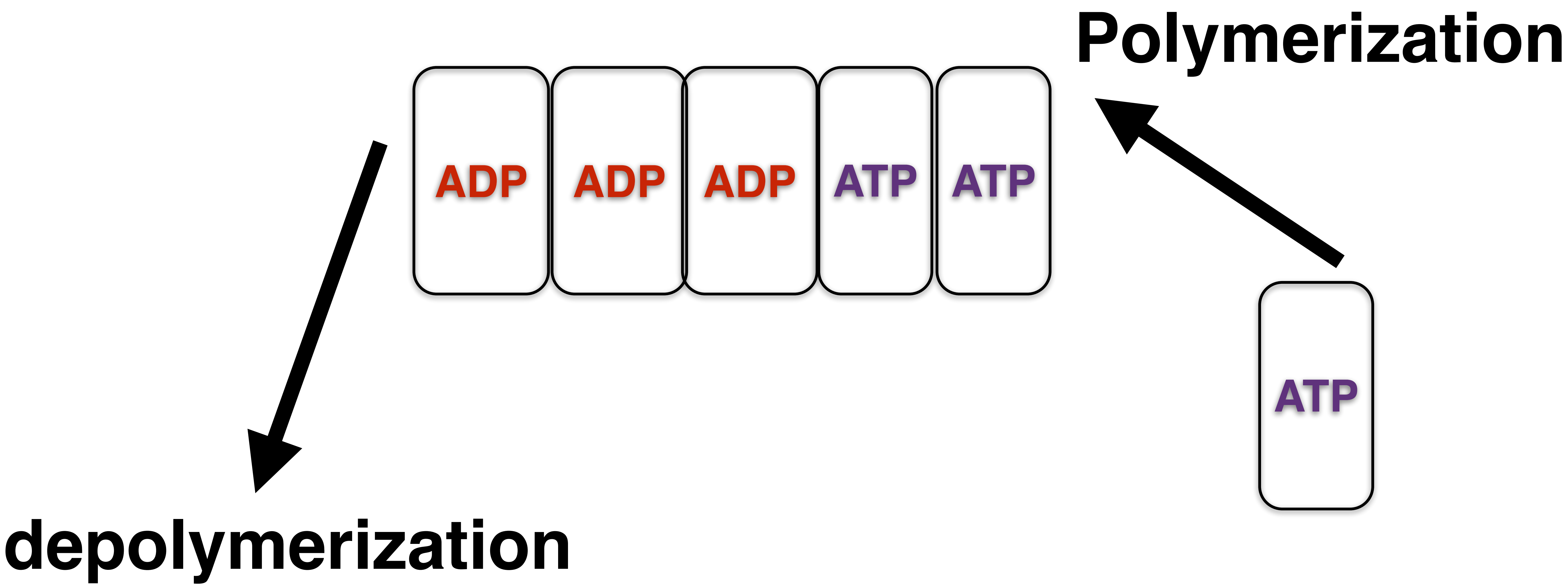
What is the concentration at which the whole filament velocity is zero?

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

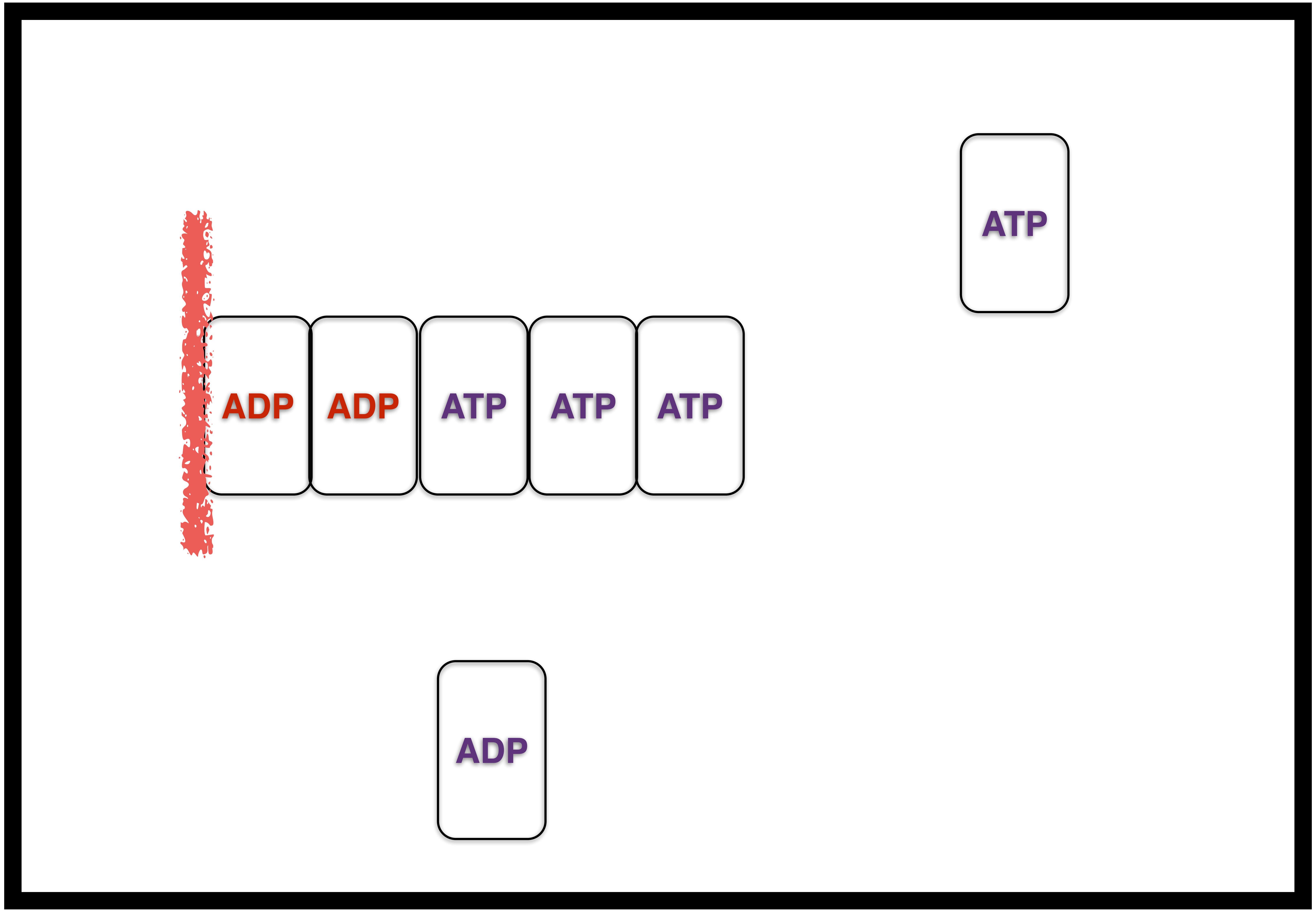
# Centre of mass motion!



# Treadmilling of actin

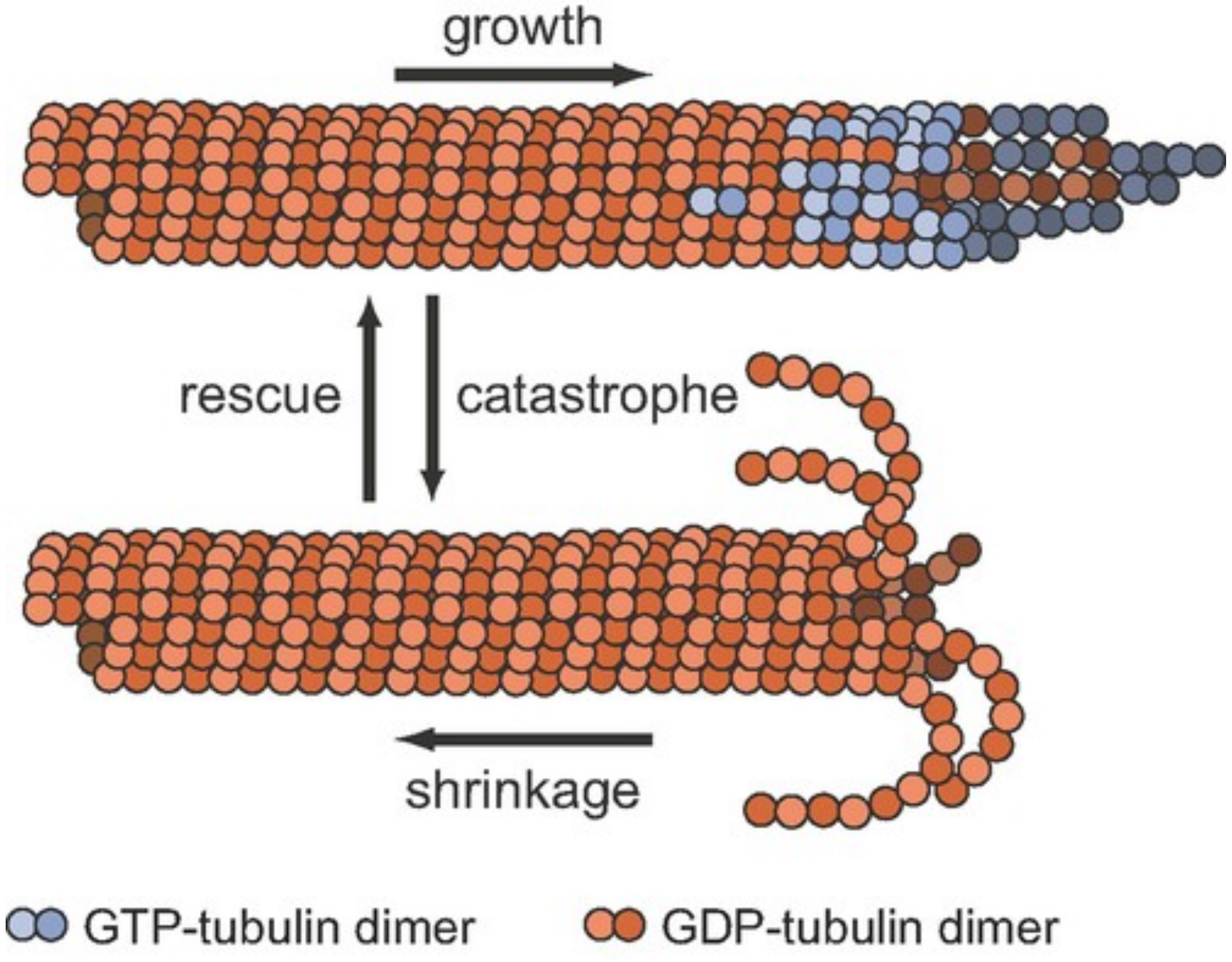


# If you block one end, force generation here too

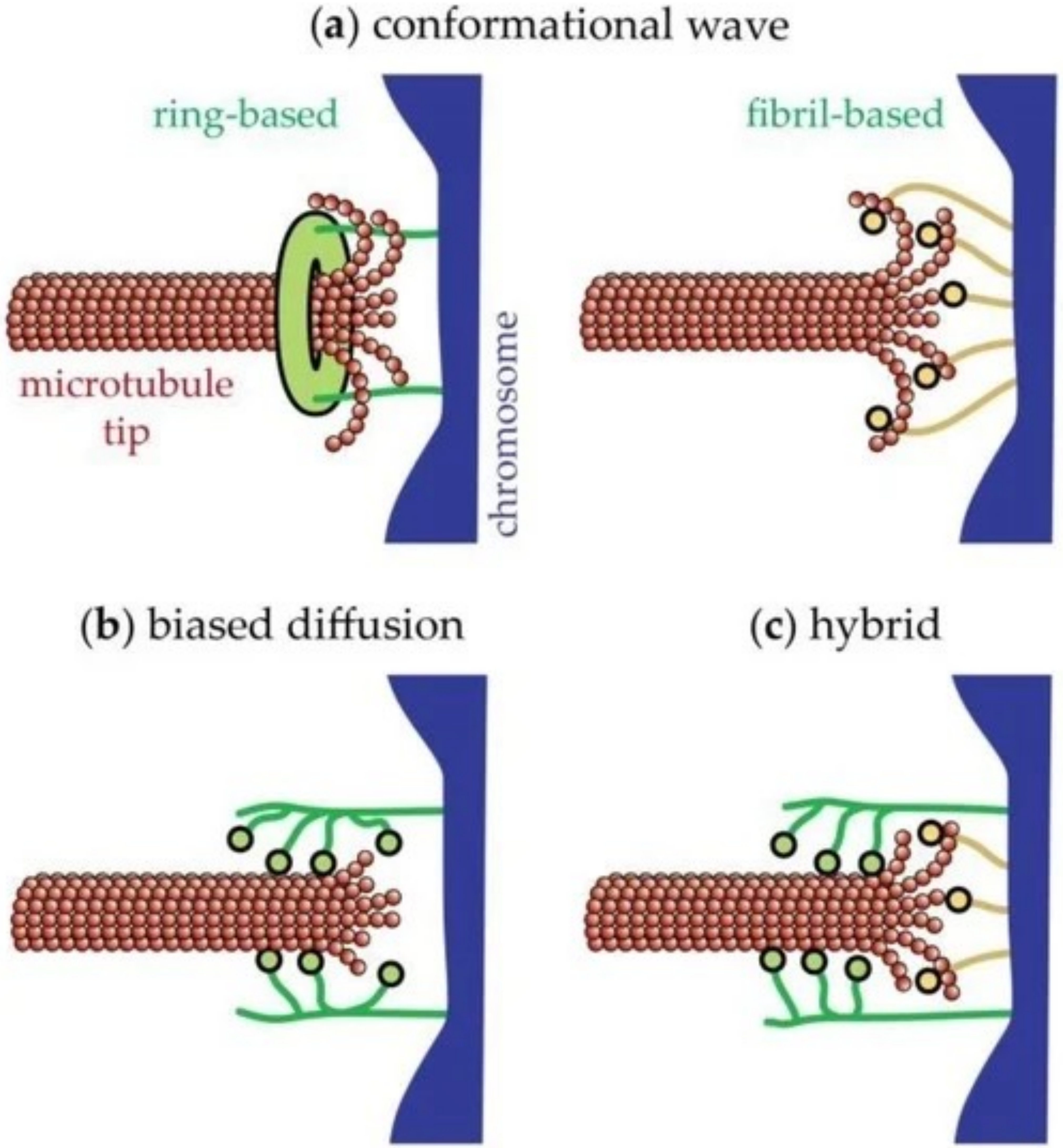


Microtubules are another set of filaments; they have some similarity with actin the way they convert chemical energy to mechanical energy

# 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