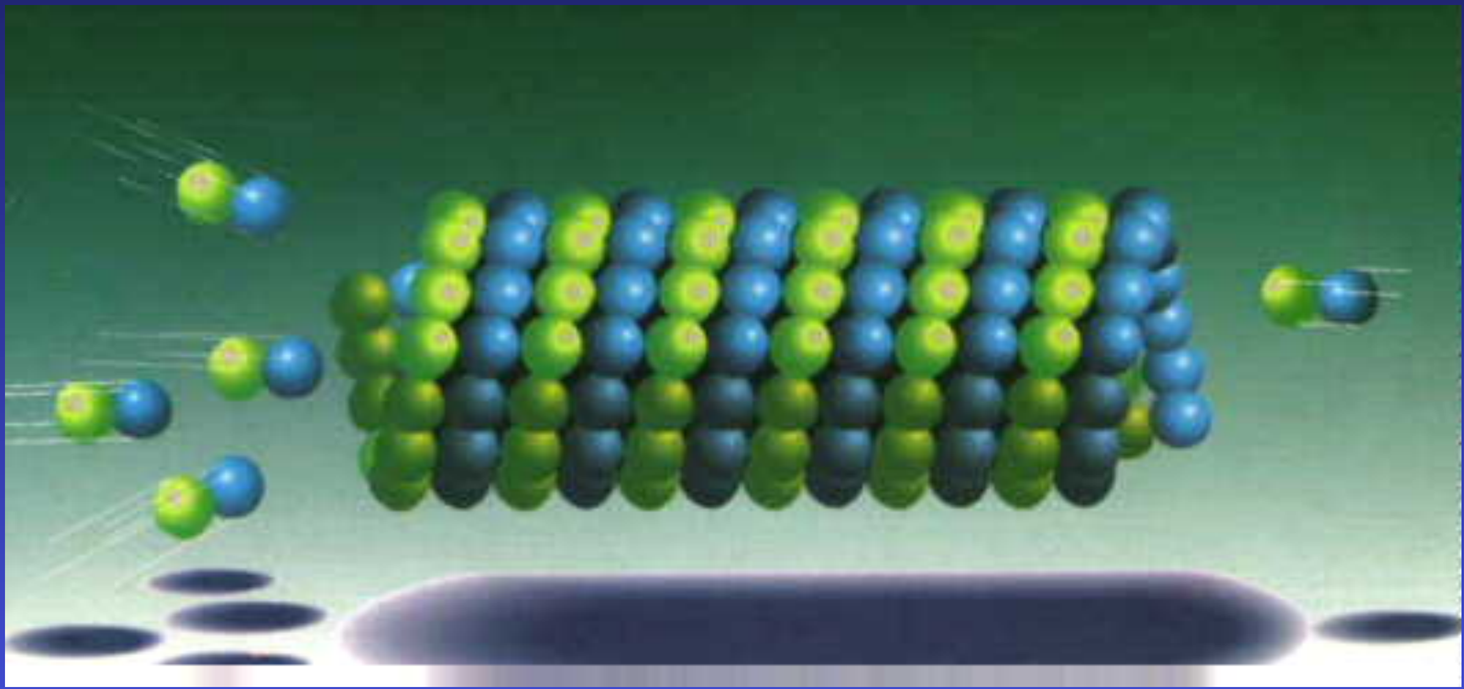
Basics of actin polymerization

Actin filament:

Microtubule:



Actin growth is concentrated close to the leading edge of the cell

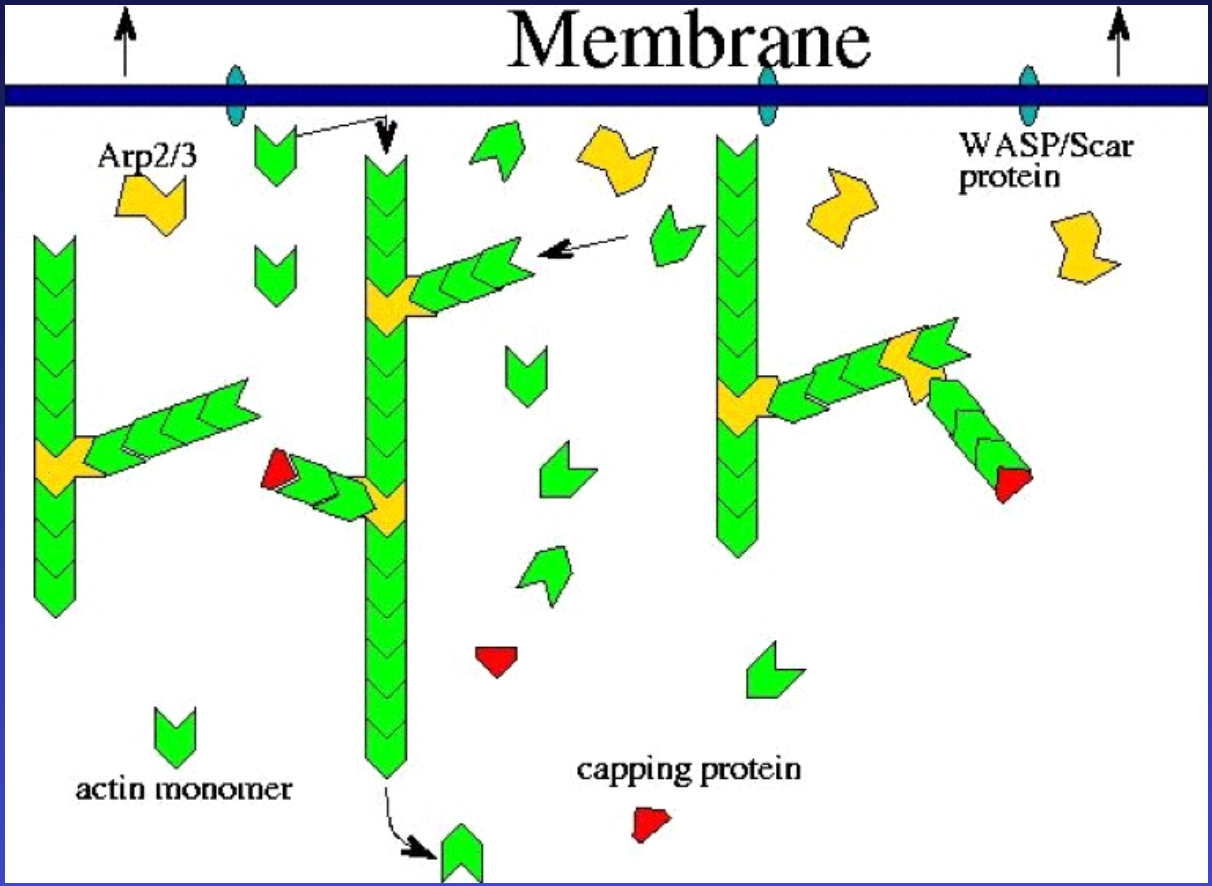


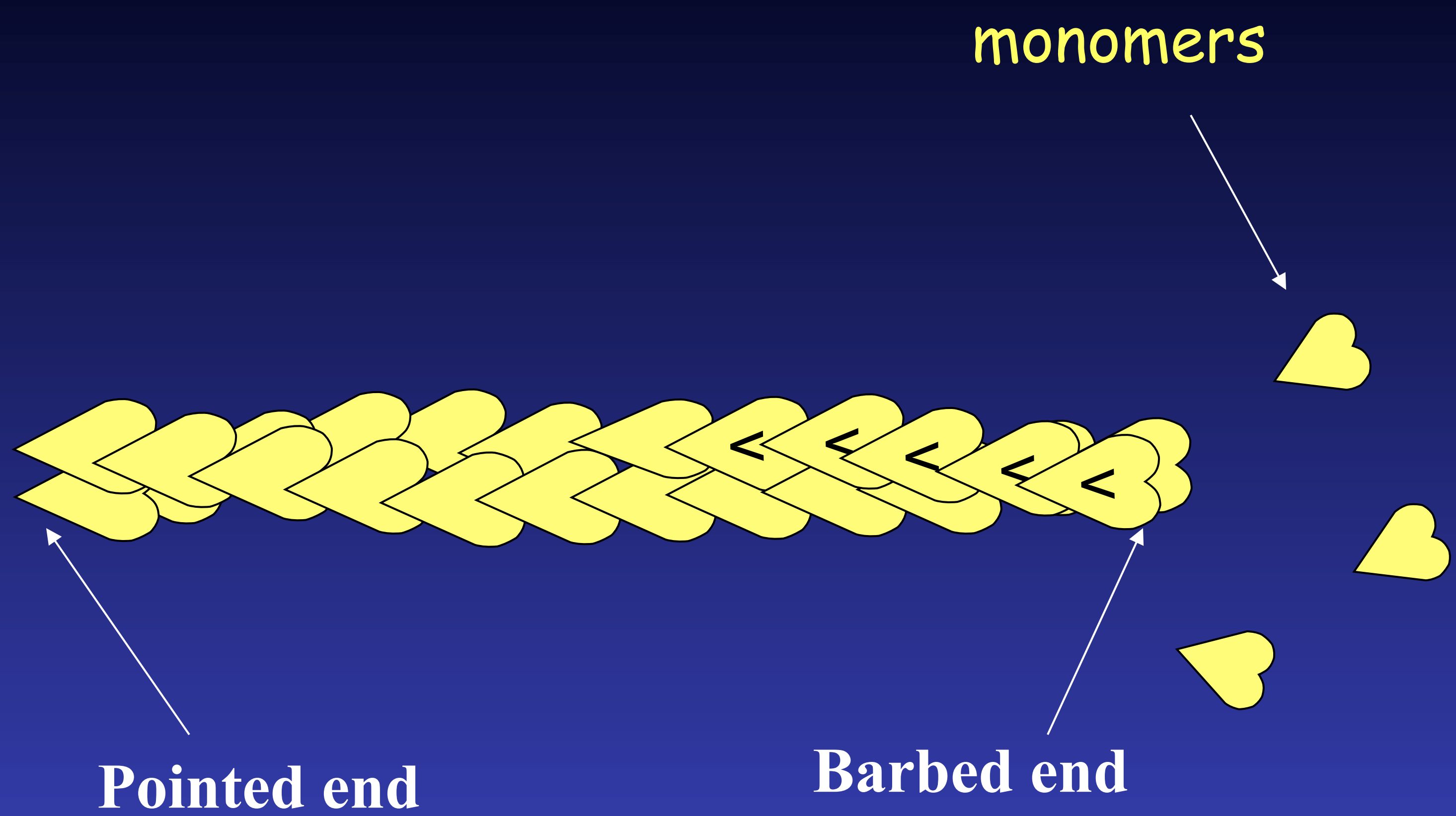
Fig courtesy: A.T. Dawes

Models of the single actin filament

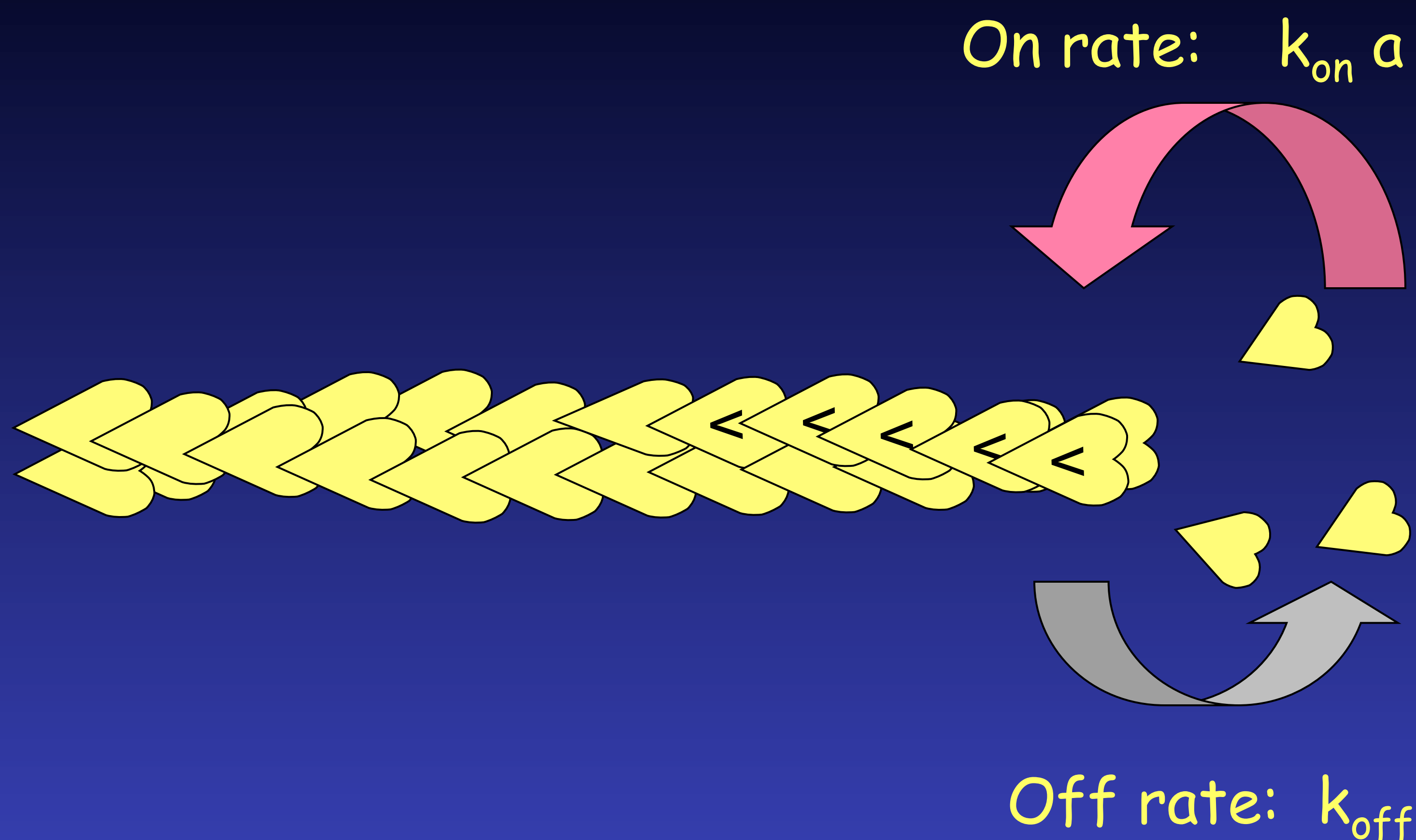
Simple actin polymerization

What do properties of actin monomers and their filaments imply ?

- about rates that filaments grow/shrink
- about level of monomer needed for growth?

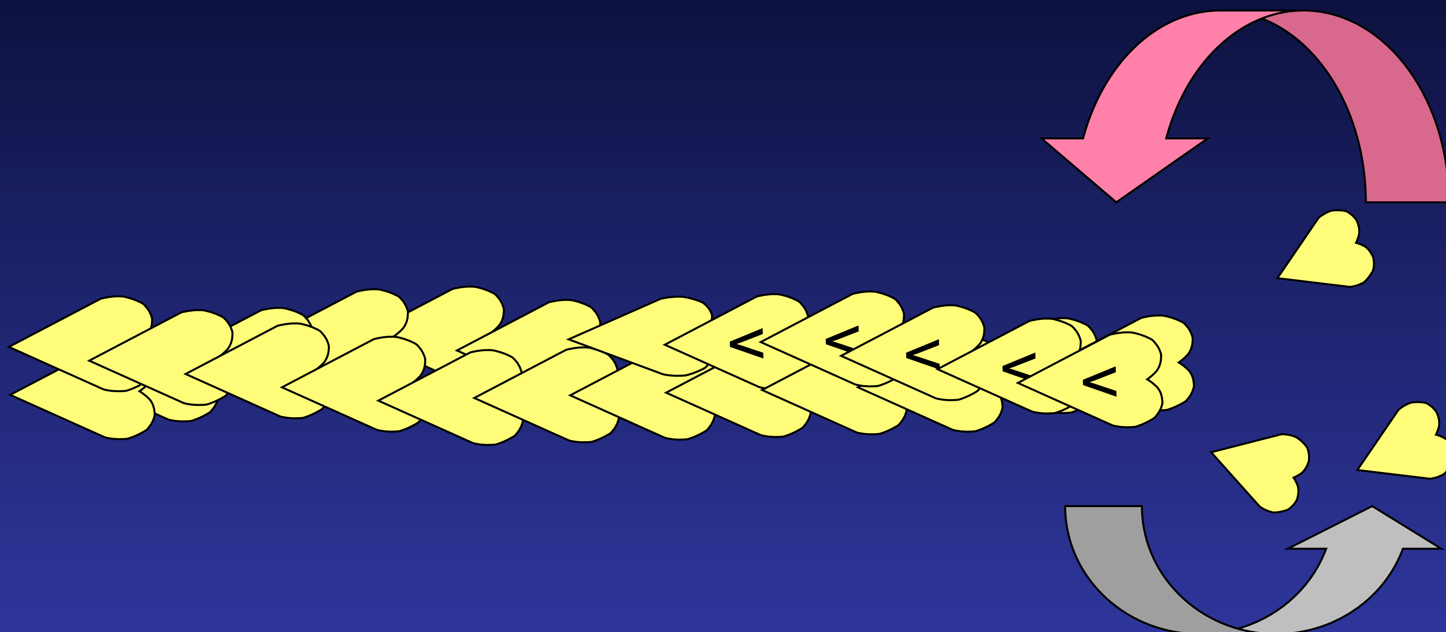


Actin filament



Polymerization kinetics

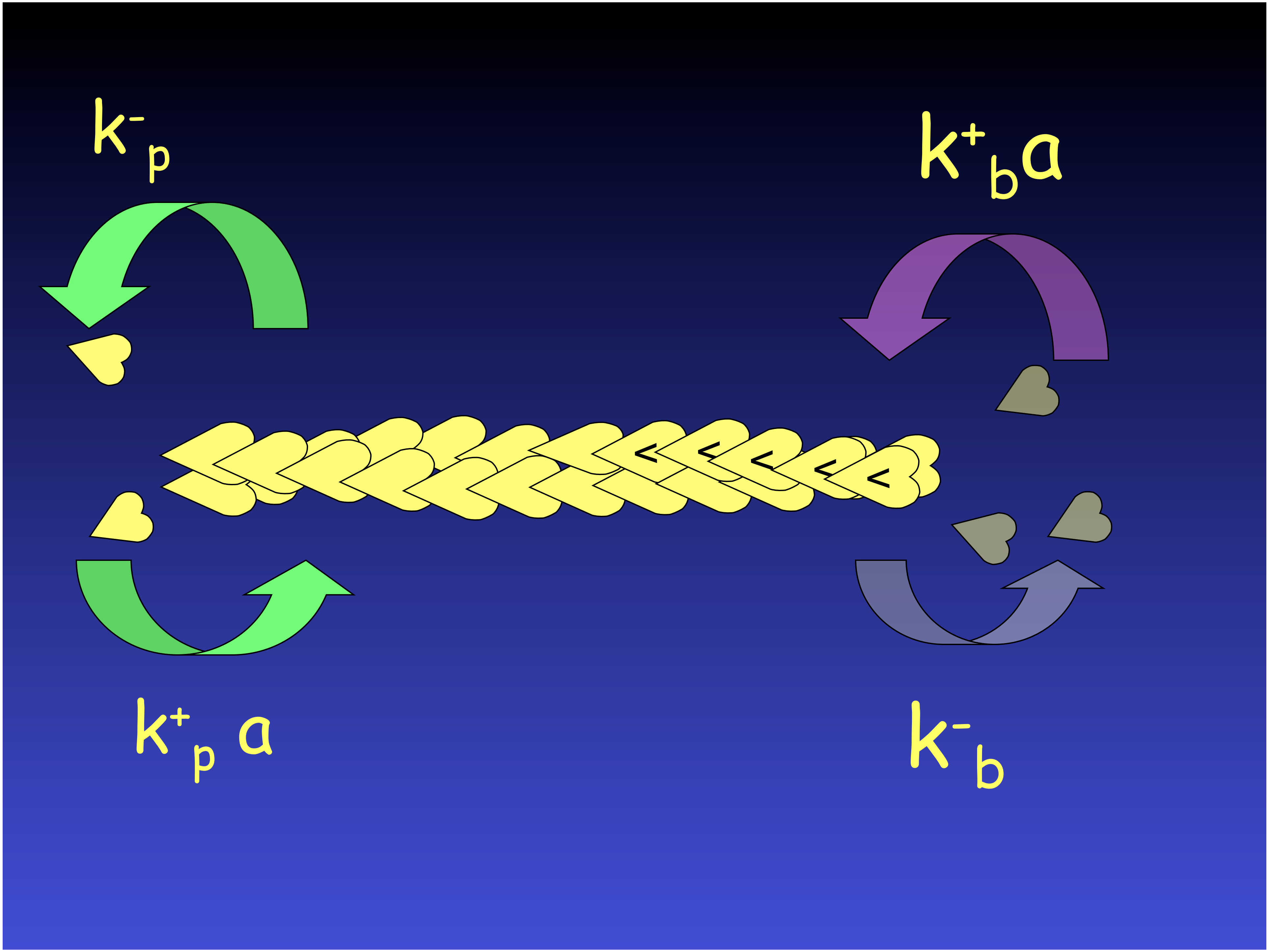
On rate: $k^{+}_{b}a$

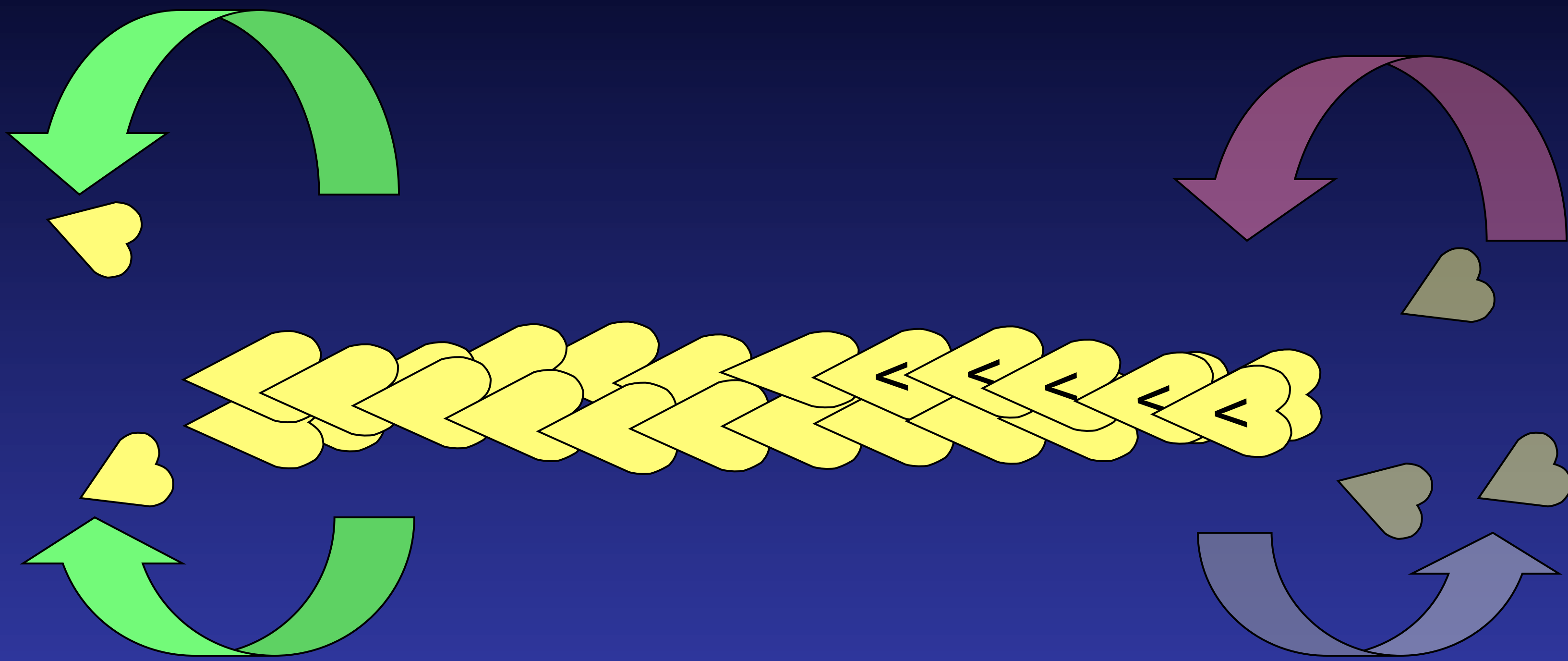


Off rate: k^{-}_{b}

Barbed end grows rapidly

$$k^{+}_{b}a \gg k^{-}_{b}$$


k^-_p
$k^+_b a$
$k^+_p\ a$
k^-_b



Depolymerization dominates at pointed end

Length of actin monomer	2.72 nm	Abraham et al 1999
actin monomer on-rate	11.6 /μM /s	Pollard 1986
actin monomer off-rate	1.4/s	Pollard 1986
number b-ends at margin	240/μ	Abraham et al 1999
monomers in 1 μM actin	600/μ^3	conversion factor

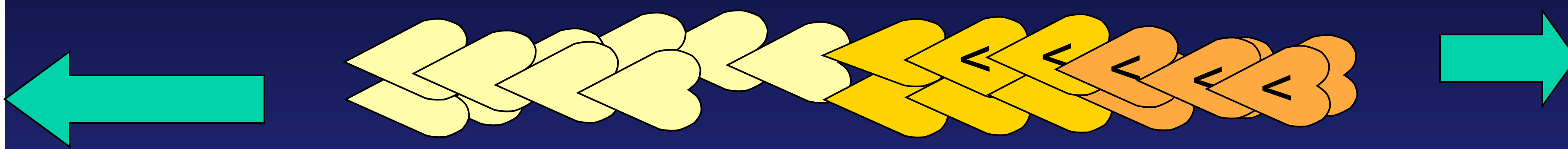
The total length of a filament would change as each end grows or shrinks due to monomer addition or loss

$$\frac{dl}{dt} = (k_b^+ a - k_b^-) + (k_p^+ a - k_p^-)$$

Barbed end

Pointed end

Rate of growth at barbed/pointed ends:



depend on the actin monomer concentration:

$$(k_p^+ a - k_p^-)$$

$$(k_b^+ a - k_b^-)$$

Because monomers can be gained at the barbed end and lost at the pointed end, the filament can appear to move.

This is called treadmilling.

In treadmilling, the length of the filament is constant, so

$$\frac{dl}{dt} = 0$$

Putting these two facts together:

$$\frac{dl}{dt} = (k_b^+ a - k_b^-) + (k_p^+ a - k_p^-)$$

$$\frac{dl}{dt} = 0$$

implies

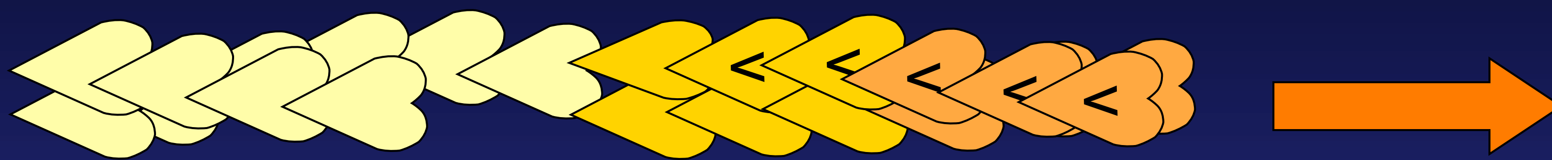
$$(k_b^+ a - k_b^-) + (k_p^+ a - k_p^-) = 0$$

We can find out at what monomer concentration this is possible by solving for a:

$$(k_b^+ a - k_b^-) + (k_p^+ a - k_p^-) = 0$$

$$a = \frac{k_p^- + k_b^-}{k_p^+ + k_b^+}$$

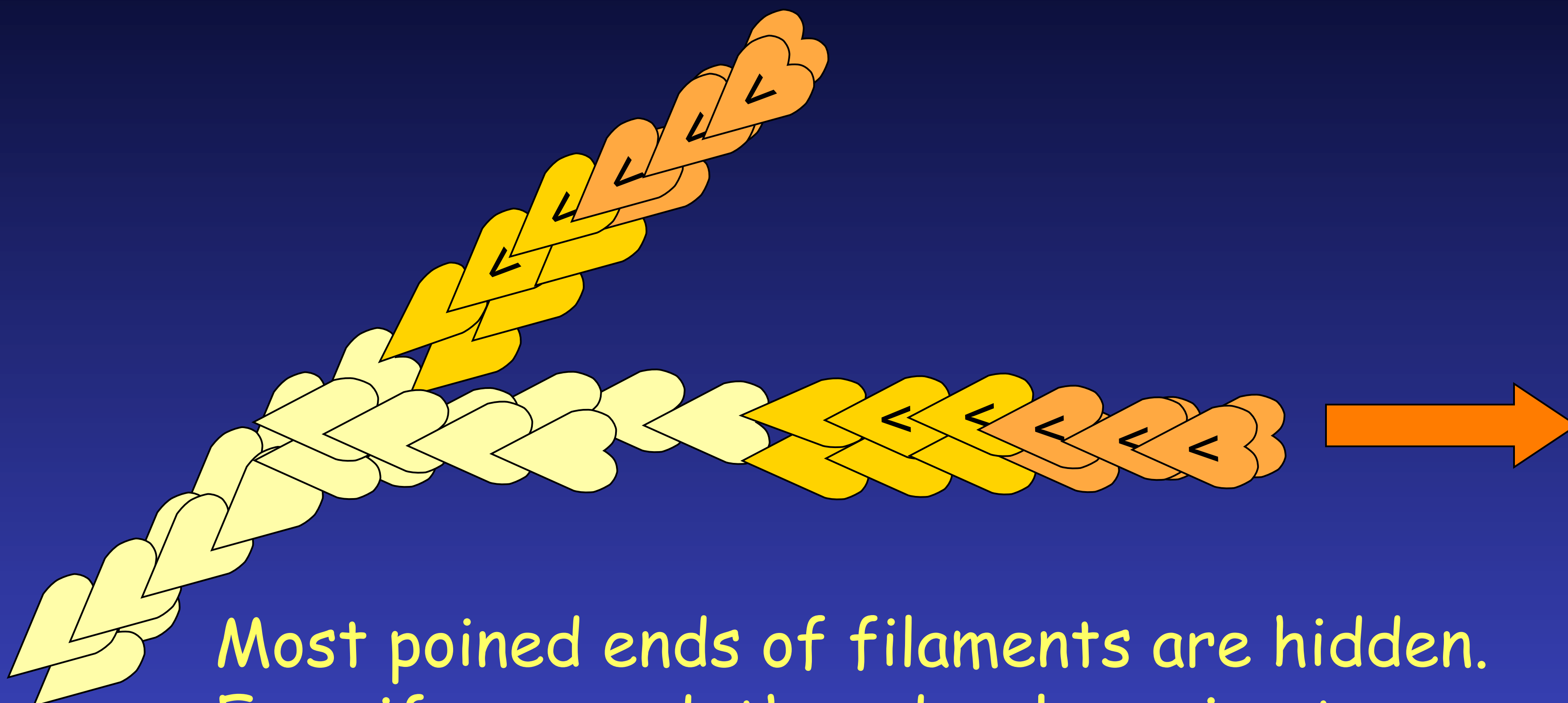
The treadmilling concentration:



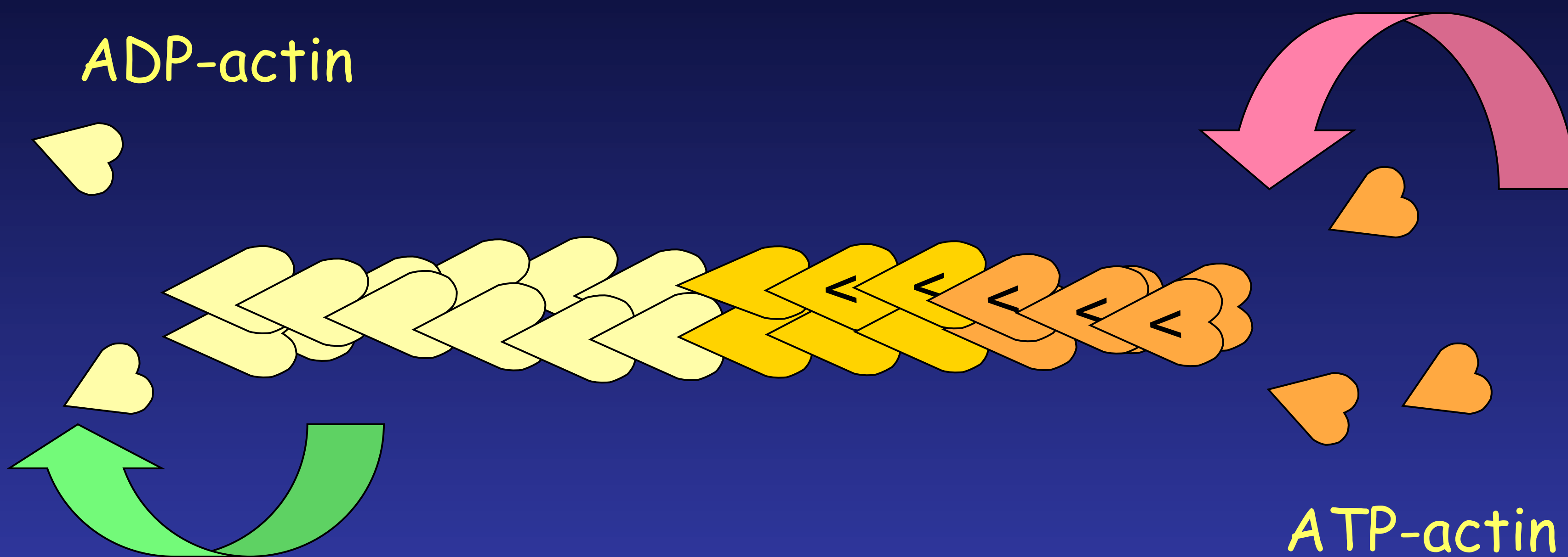
$$a_{tread} = \frac{k_p^- + k_b^-}{k_p^+ + k_b^+}$$

At this concentration, monomers add to the barbed end at the same rate as they are lost at the pointed end.

Treadmilling not so relevant in the cell



Most poined ends of filaments are hidden.
Even if exposed, they depolymerize too
slowly to keep up with growing barbed ends.



The actin monomers are modified by attached nucleotides (ATP, ADP)

ATP-actin polymerizes fastest at barbed end

Actin dynamics and polymerization

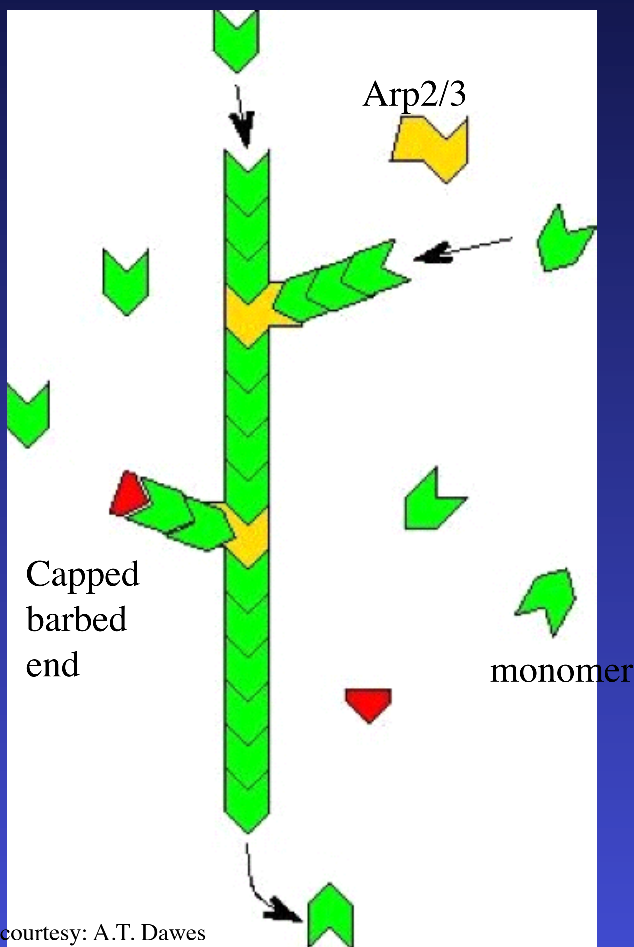


Fig courtesy: A.T. Dawes

- Polar filaments polymerize fastest at their “barbed” ends, slower kinetics at the “pointed ends”
- Barbed ends regulated by capping, branching
- Filaments depolymerize further back