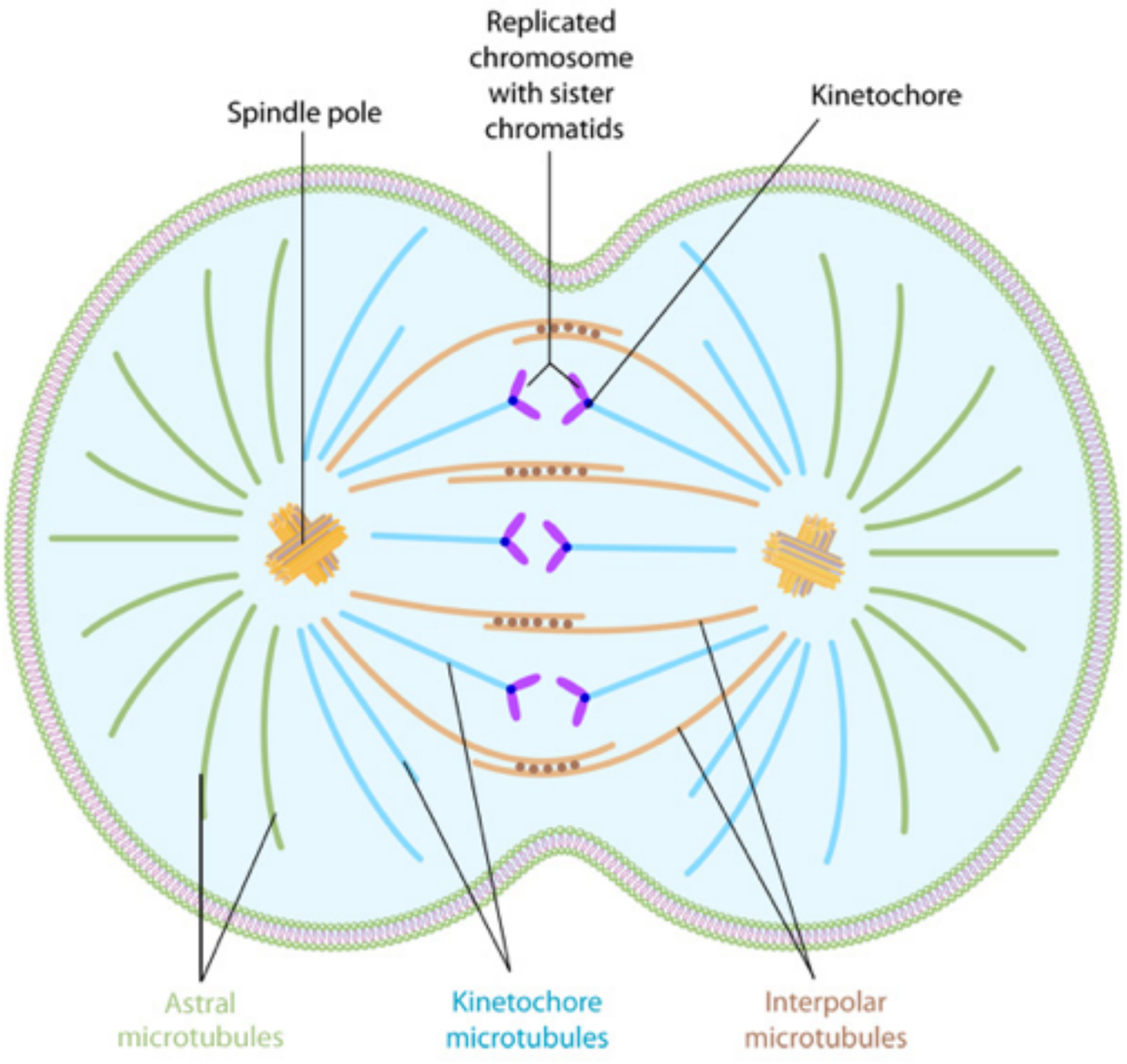
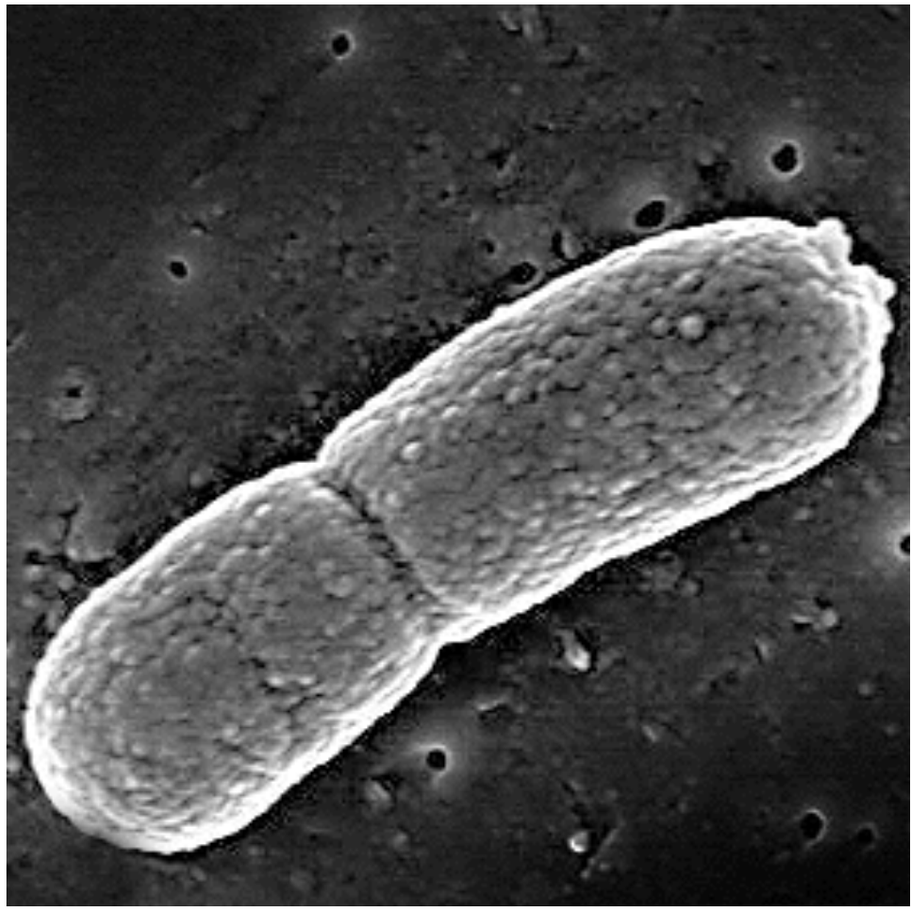
MAE 545: Lecture 9 (10/15)

Cell division in higher organisms

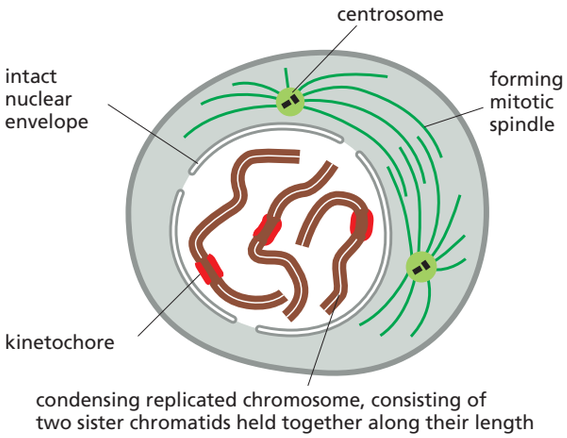


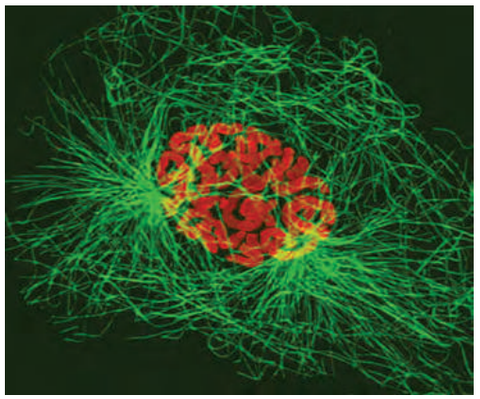
Cell division in bacteria



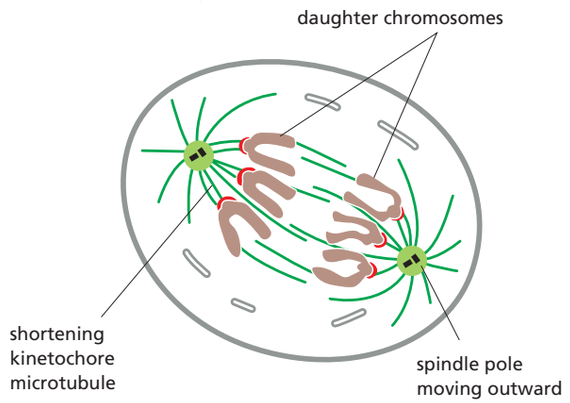
Cell division in higher organisms

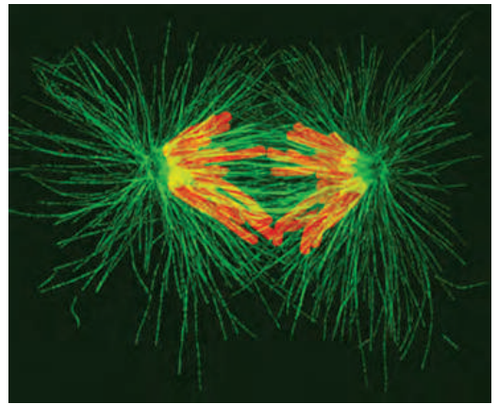
Prophase



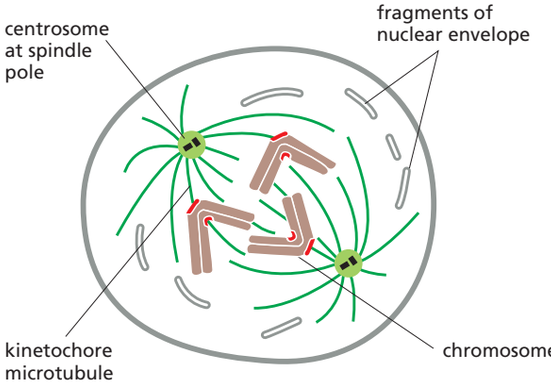


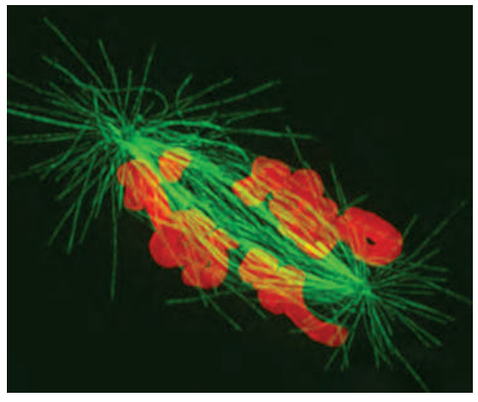
Anaphase



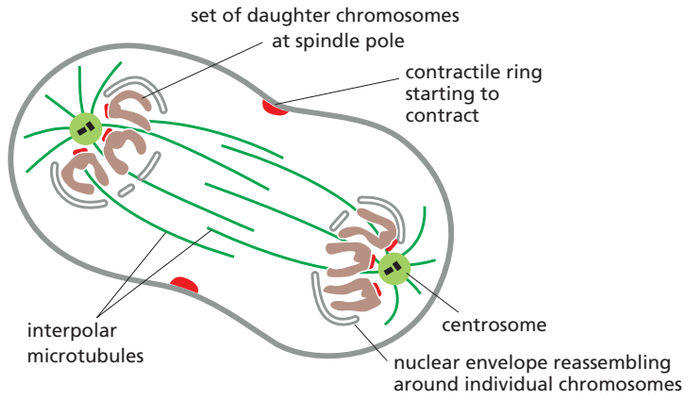


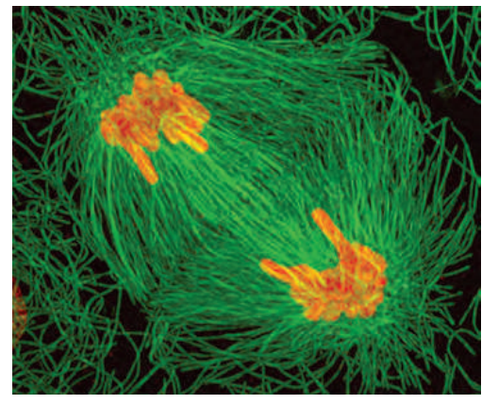
Prometaphase



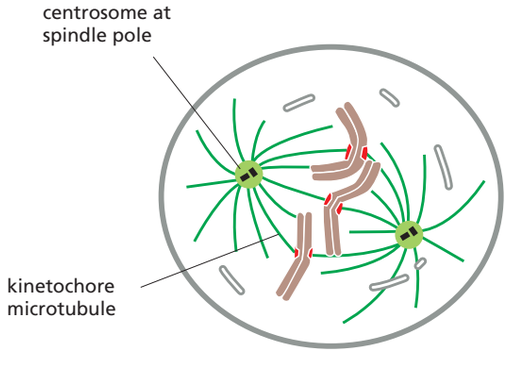


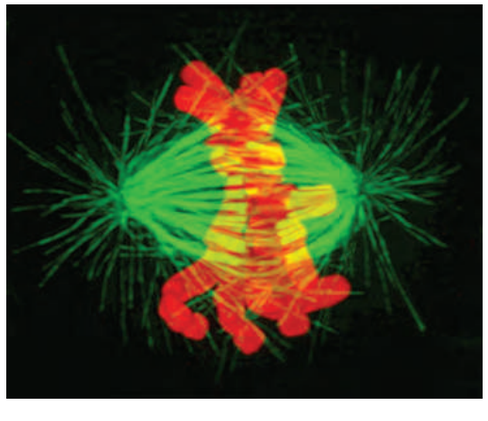
Telophase



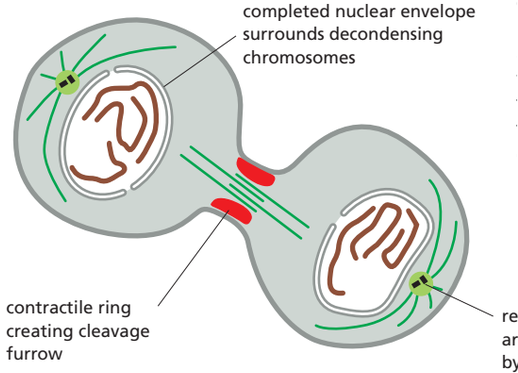


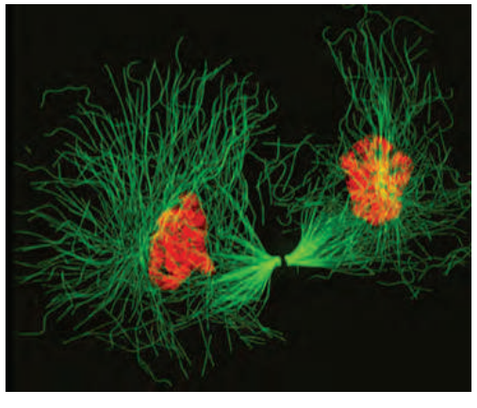
Metaphase





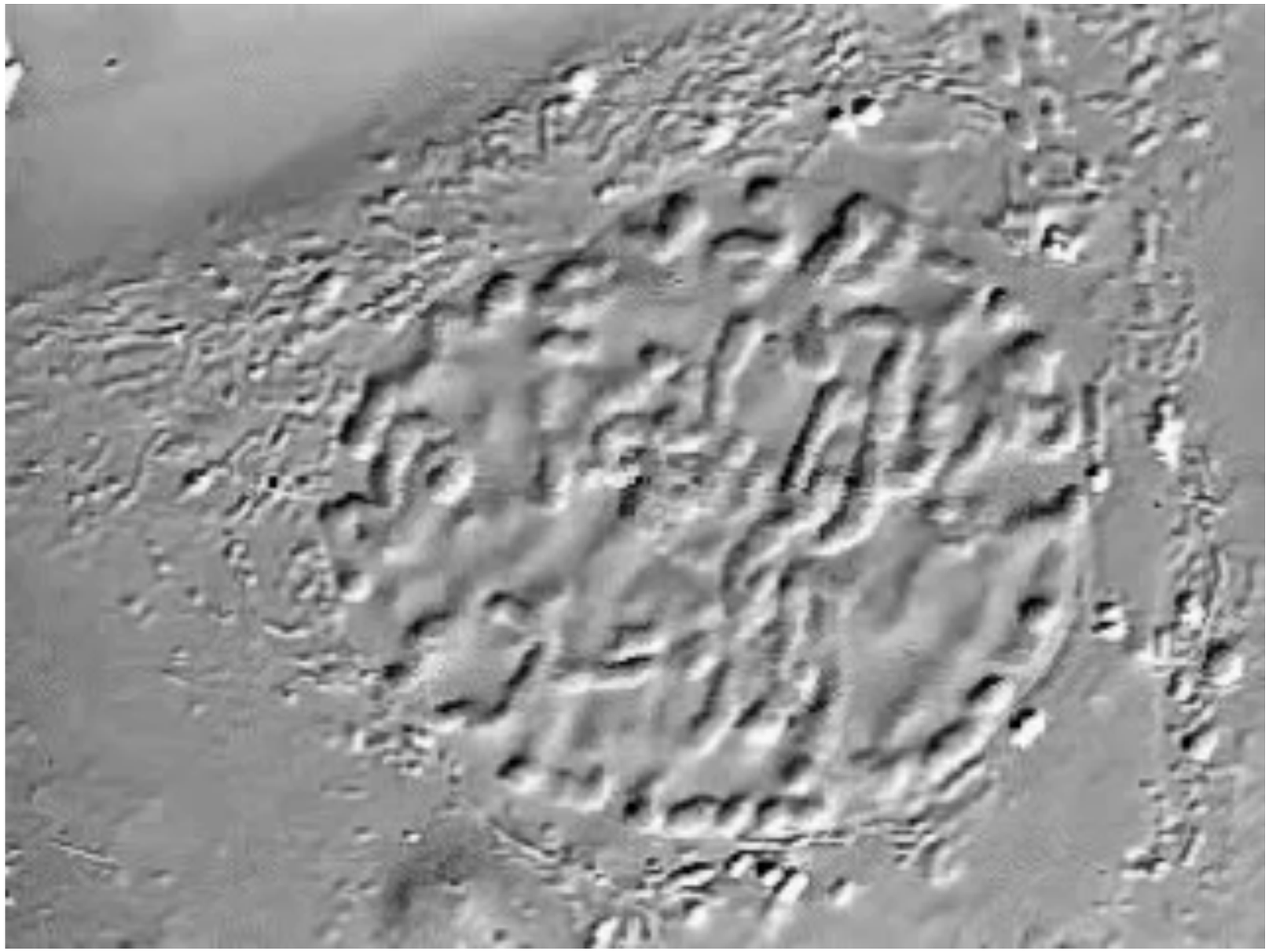
Cytokinesis



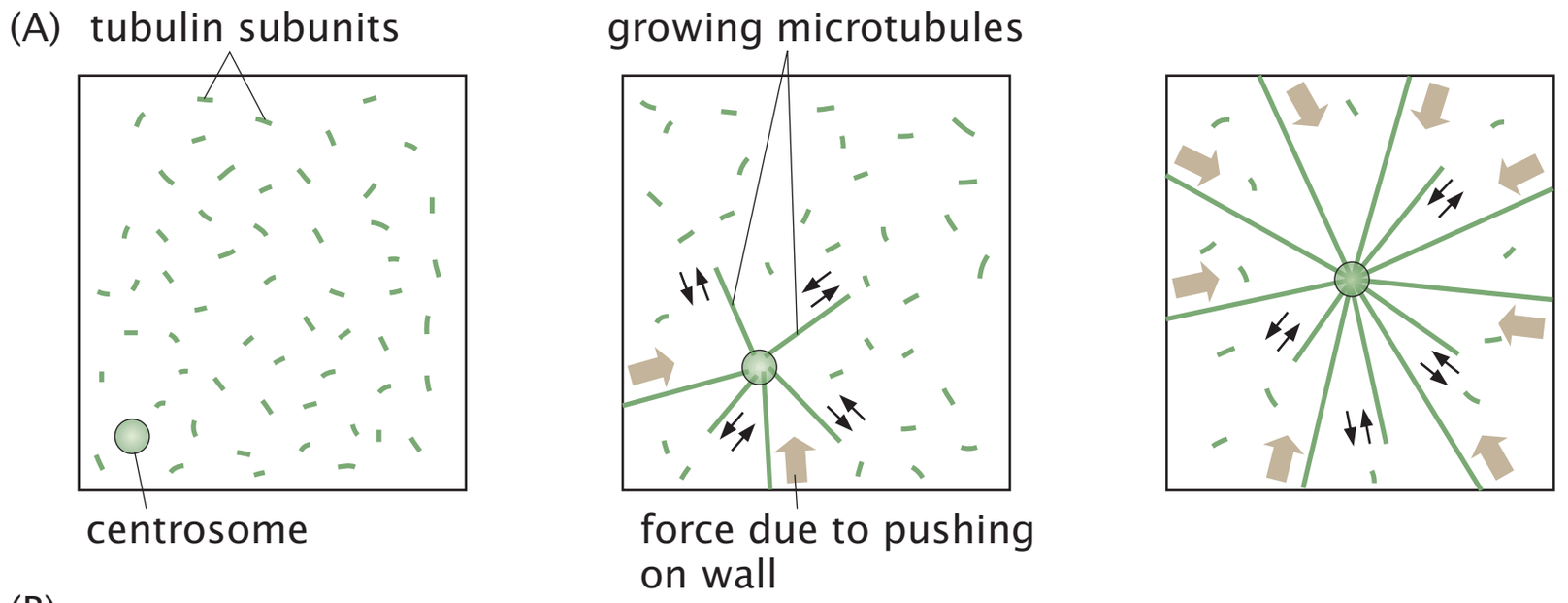


Alberts et al., Molecular Biology of the Cell

Cell division

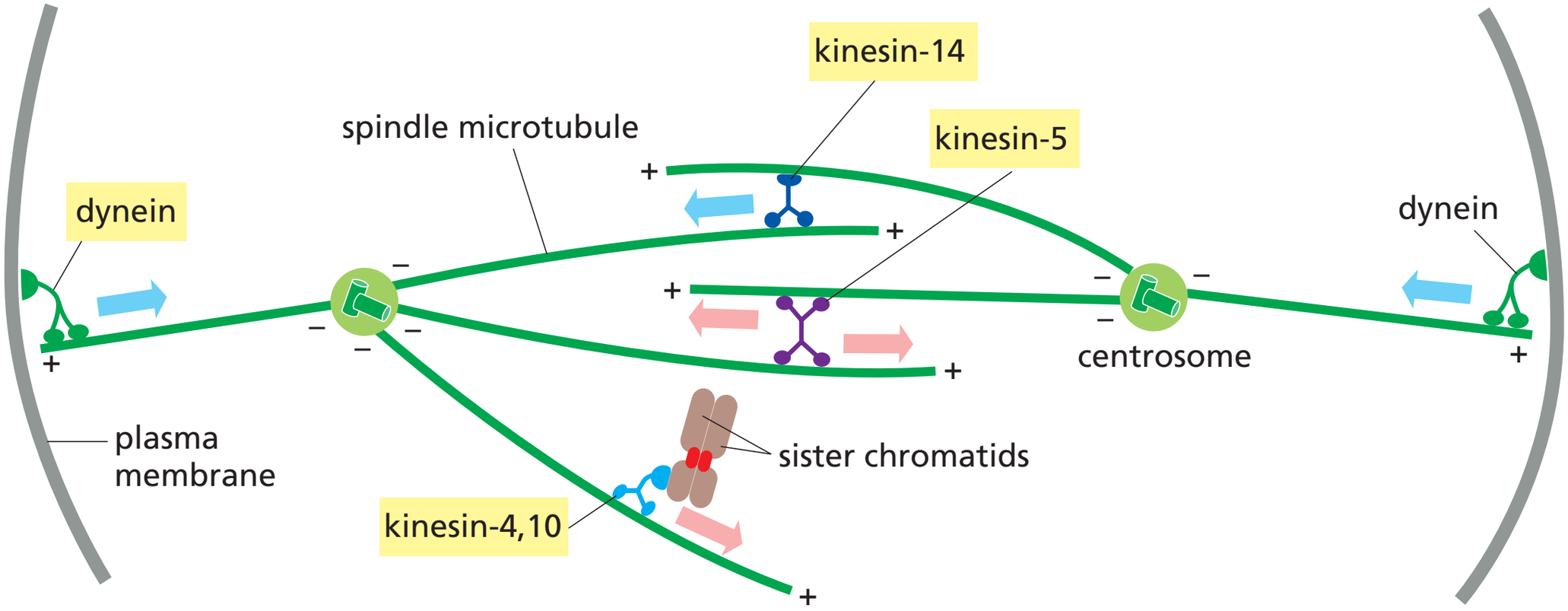


Growing microtubules can push centrosomes to the middle of the cell

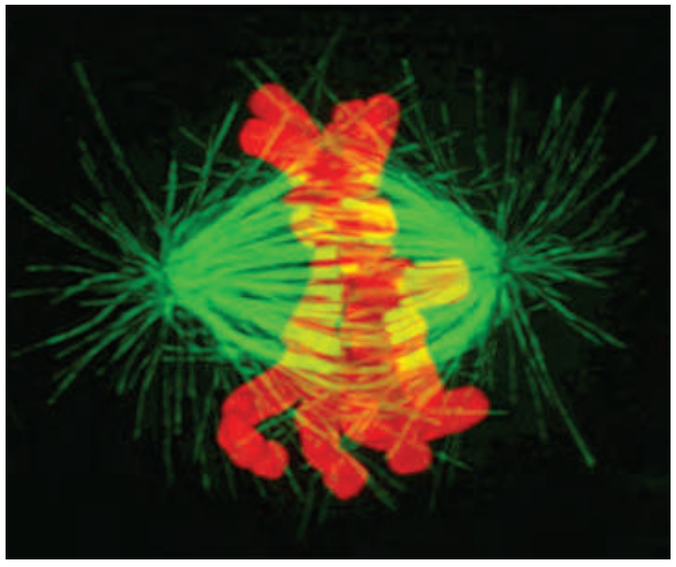


R. Phillips et al., Physical Biology of the Cell

Spindle is organized by molecular motors

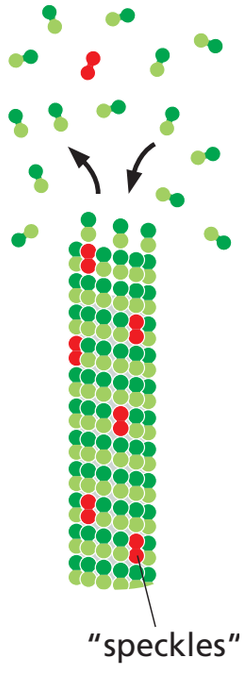


spindle (metaphase)

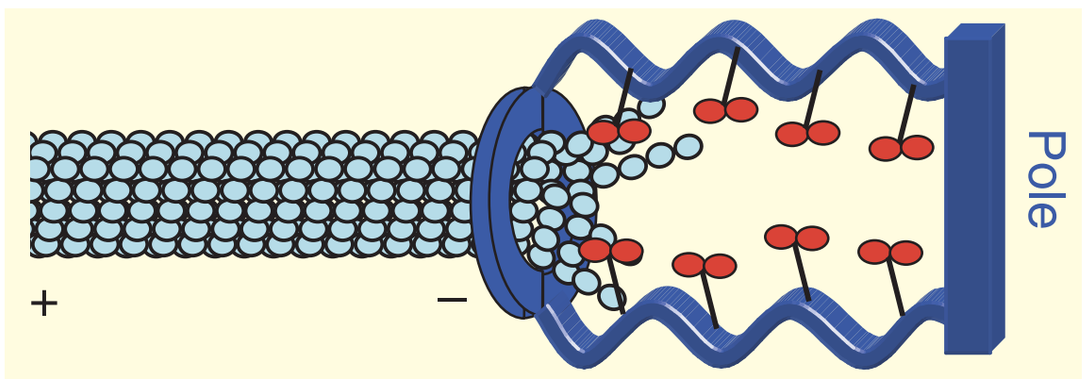


Alberts et al., Molecular Biology of the Cell

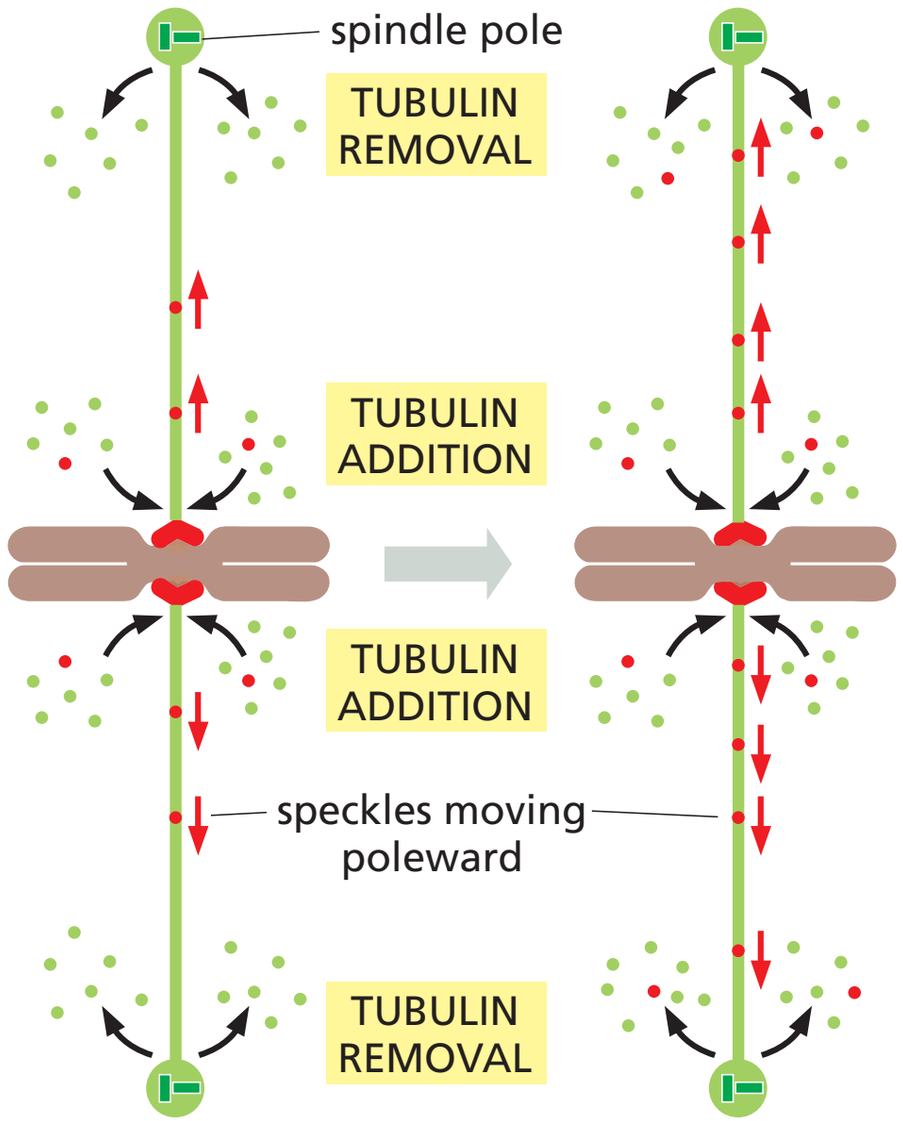
Microtubules are depolymerized at spindle poles



Depolymerization is done by molecular motors

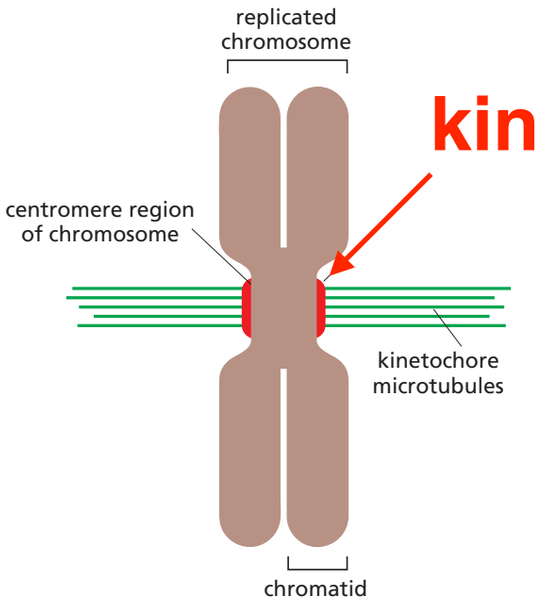


D.J. Odde, Current Biol. 15, R956-R959 (2005)



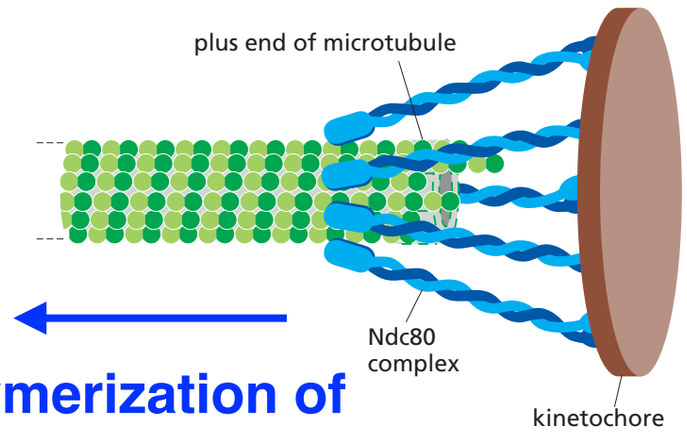
Alberts et al., Molecular Biology of the Cell

Microtubules attach to chromosomes via kinetochore

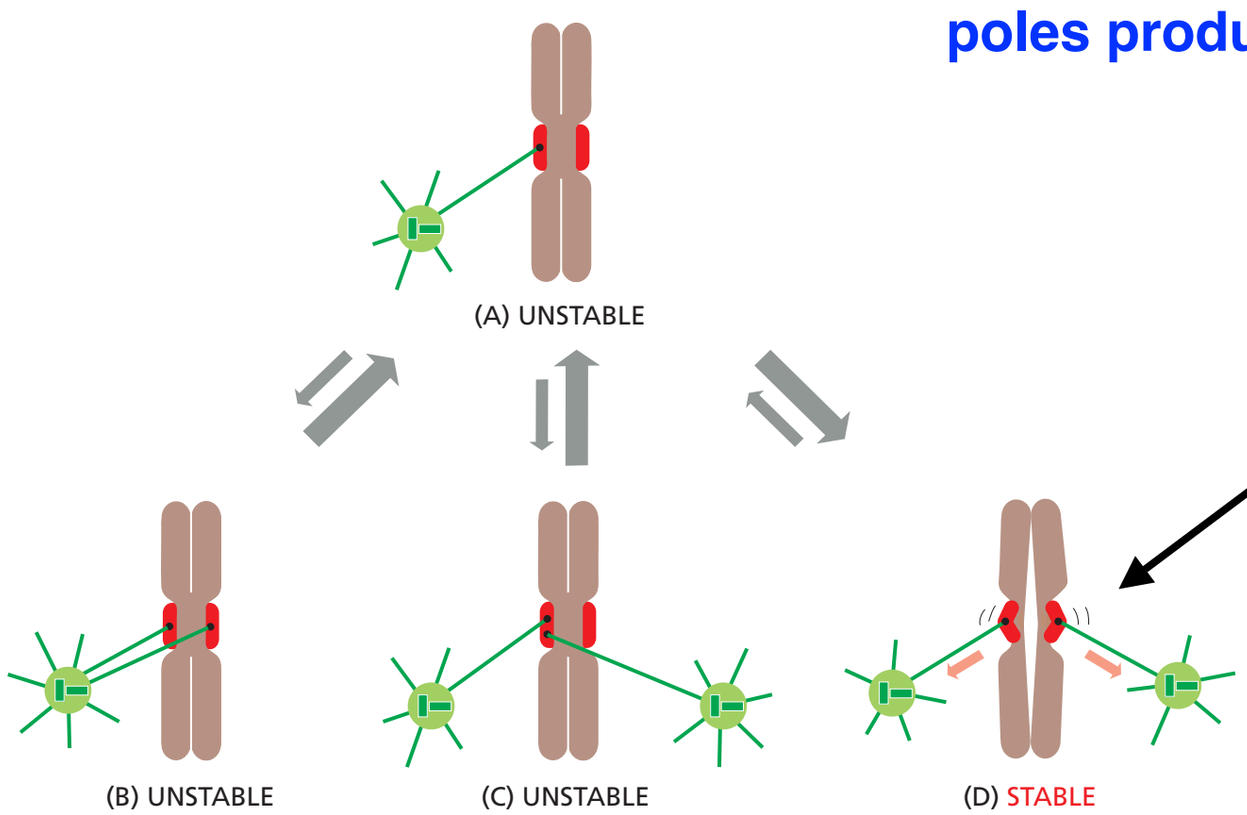


kinetochore

kinetochore



depolymerization of microtubules at spindle poles produces tension

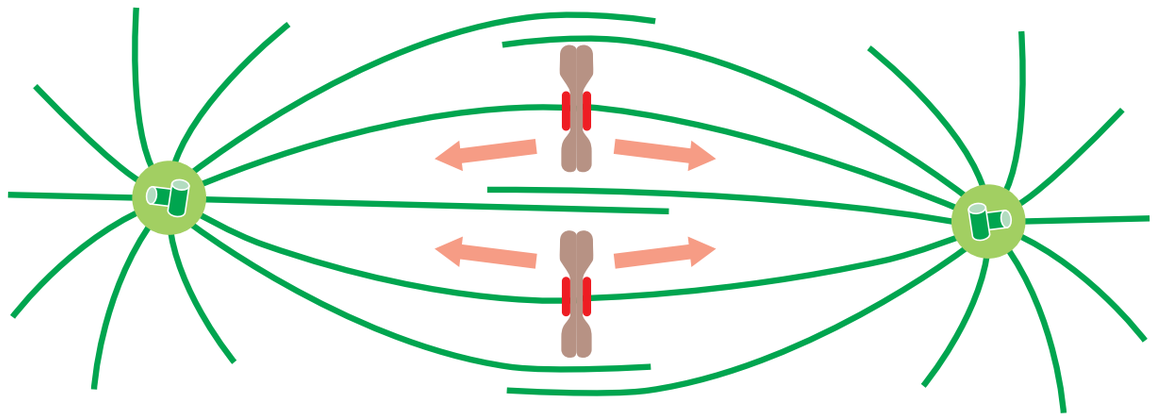


Tension sensed by sister kinetochores increases binding affinity for microtubules and locks them in the correct attachment

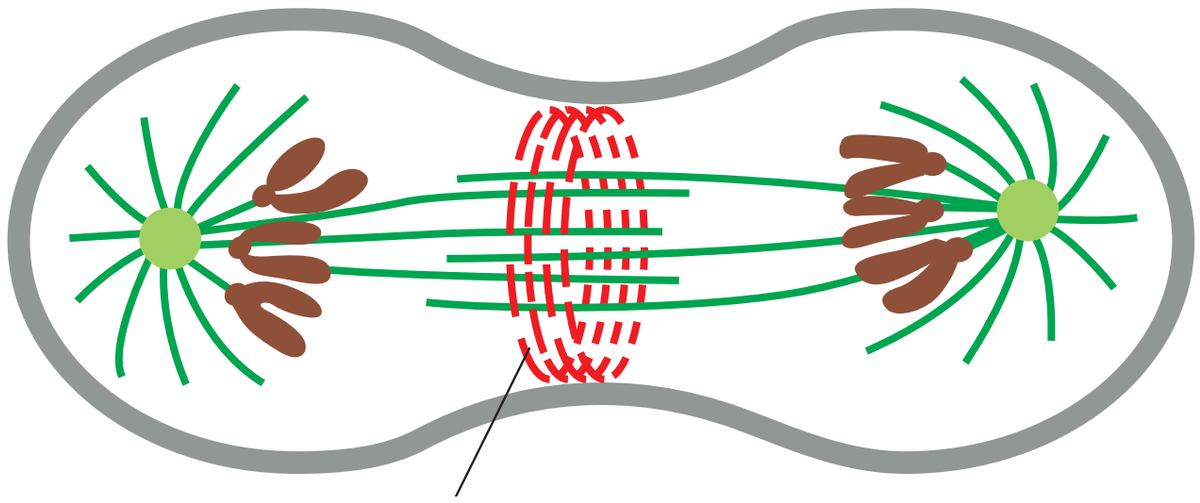
Alberts et al., Molecular Biology of the Cell

Cell division

Once all chromosomes are correctly attached to microtubules, they break into pair of chromatids, which are then pulled towards centrosomes



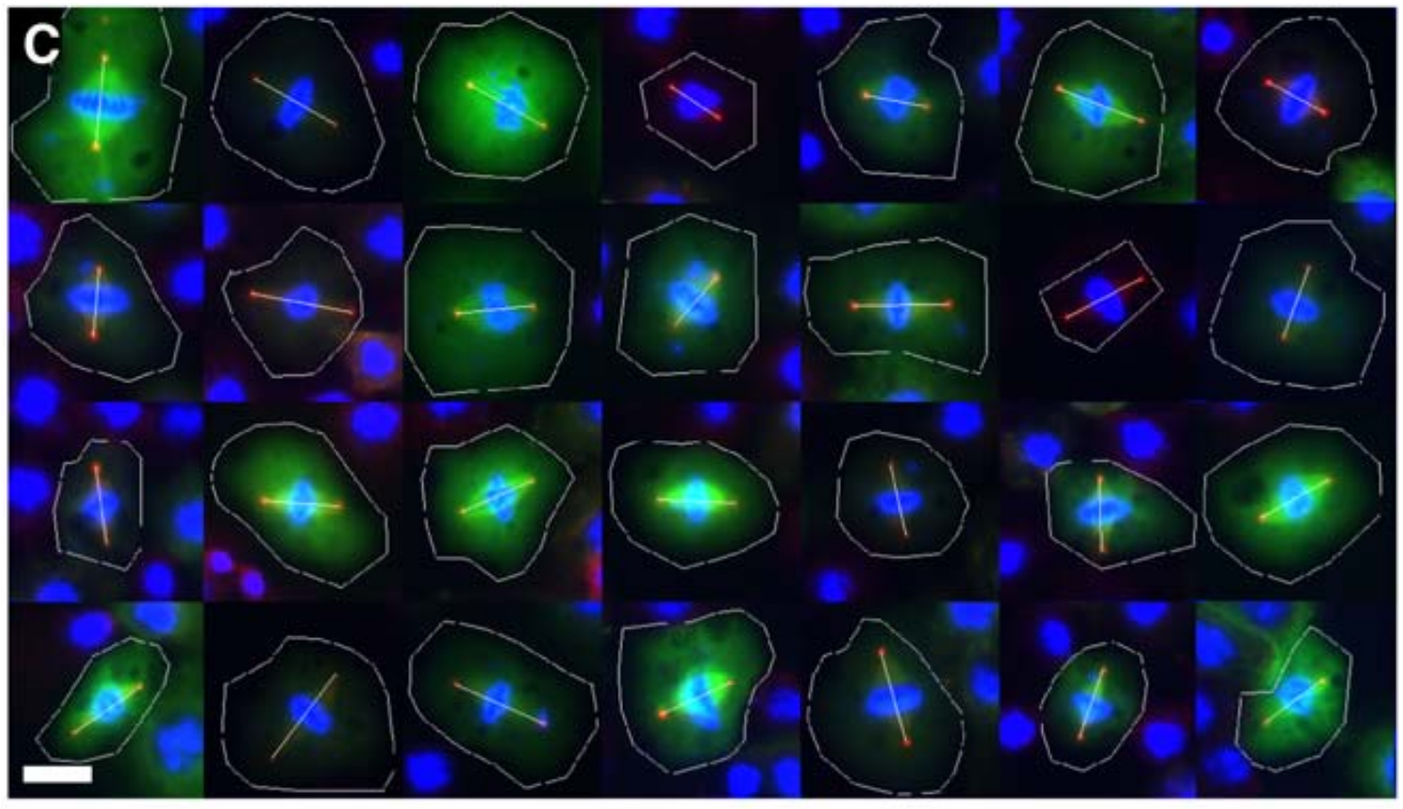
Contractile ring involving actin and myosin motors divides the cell in two



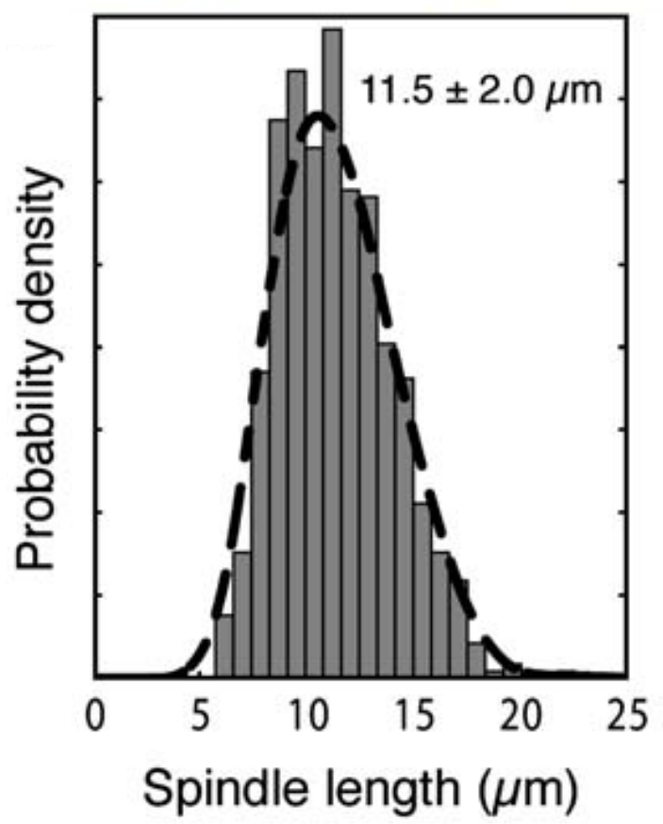
Alberts et al., Molecular Biology of the Cell

Spindle length is similar across the cells

Spindles in Drosophila cells



$10\mu\mathrm{m}$



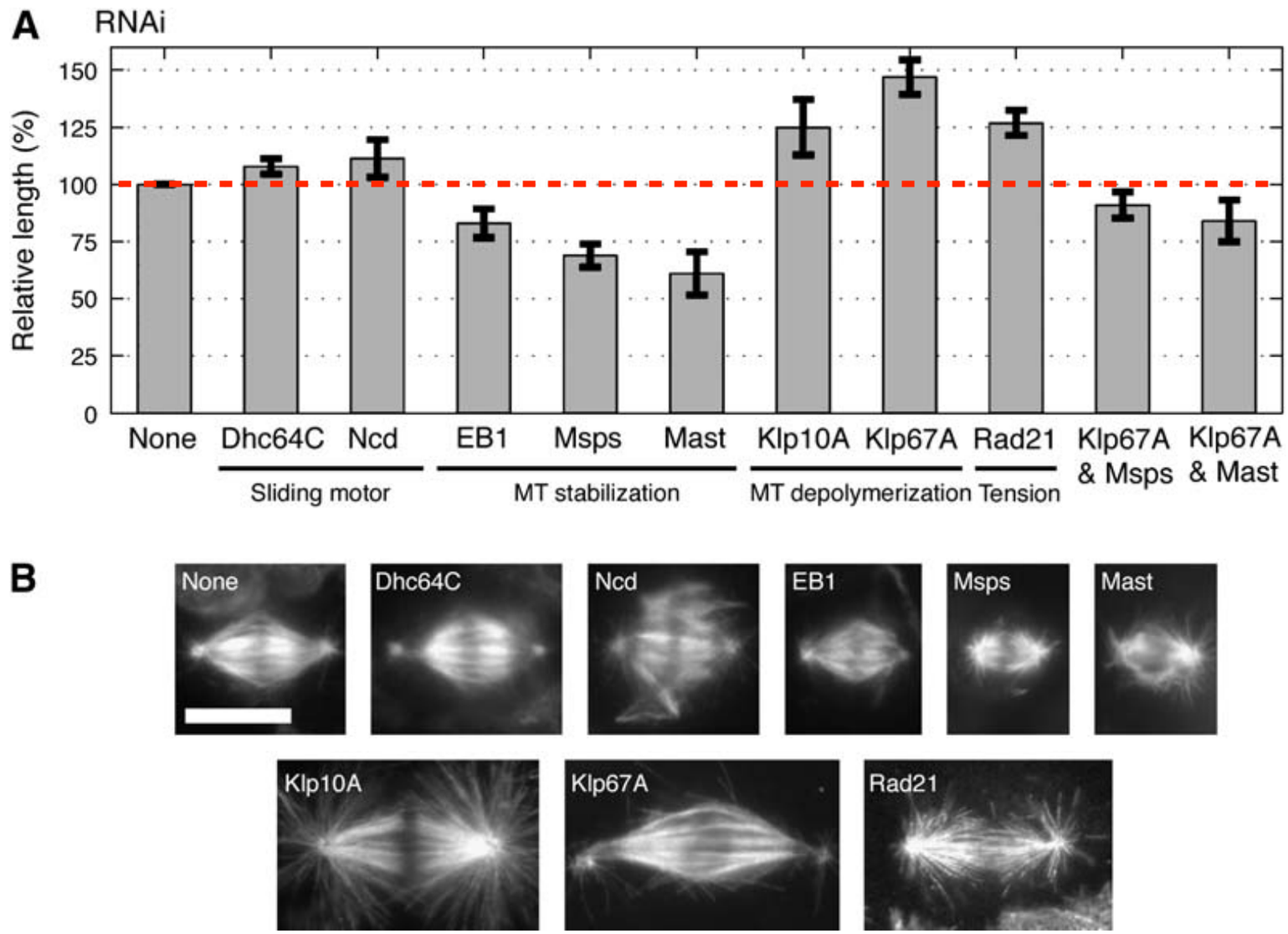
cell nuclei **microtubules**

spindle poles

G. Goshima *et al.*, Current Biol. 15, 1979-1988 (2005)

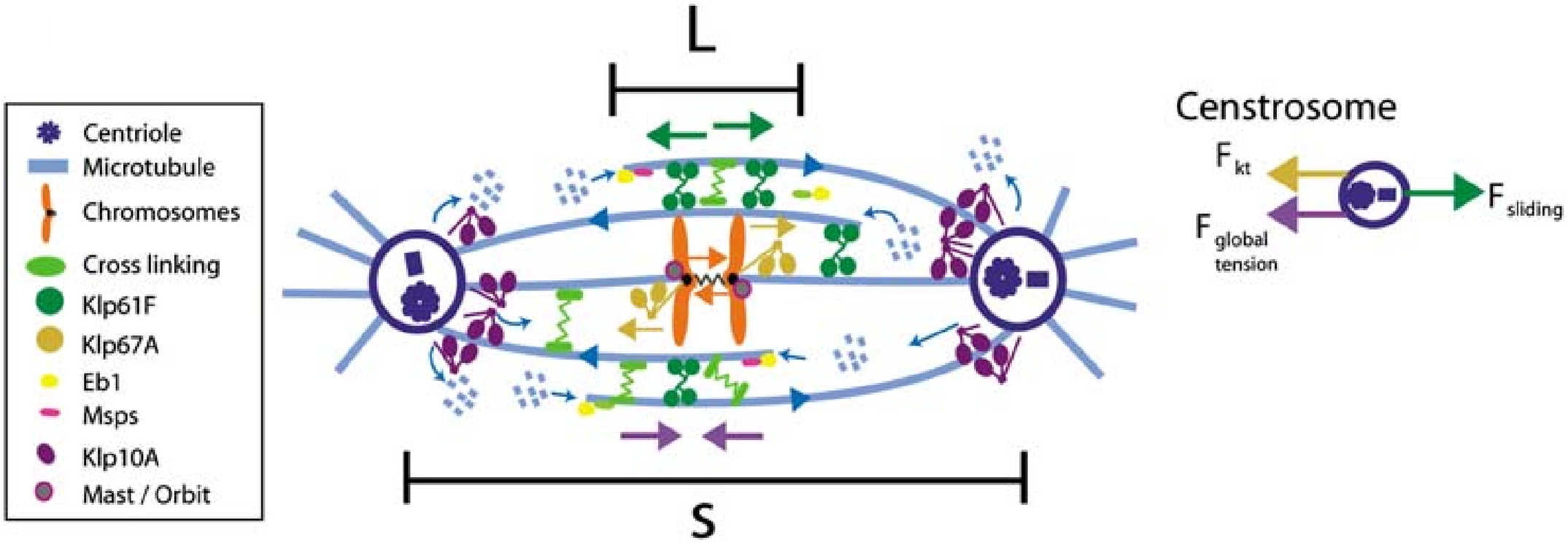
How various factors affect the spindle length?

Certain factors are removed with RNA interference



G. Goshima *et al.*, Current Biol. 15, 1979-1988 (2005)

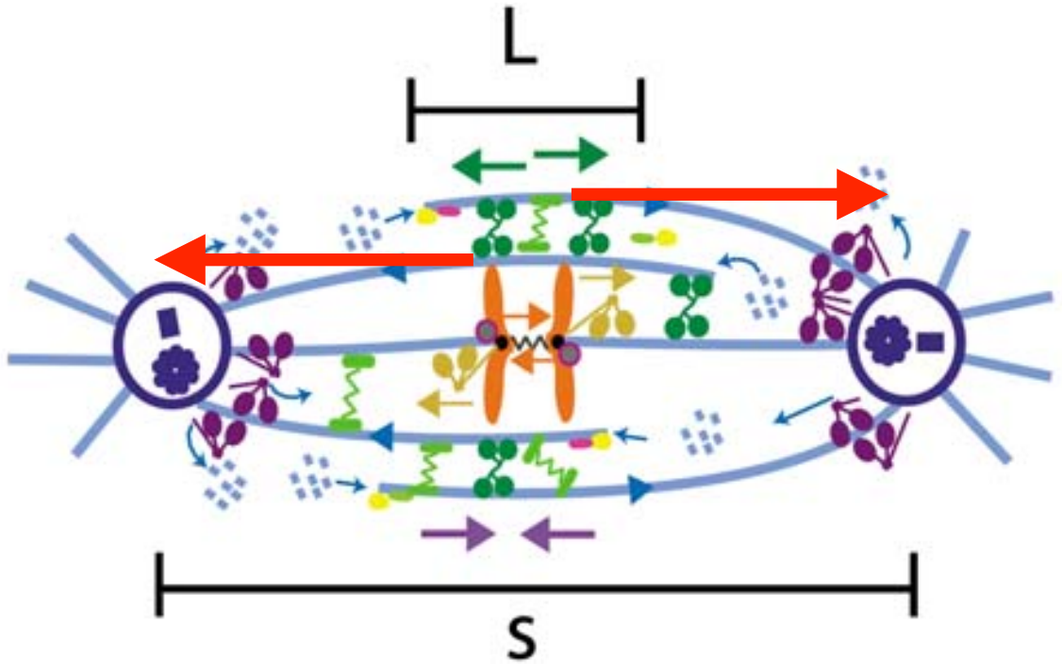
Model for spindle length control



G. Goshima *et al.*, Current Biol. 15, 1979-1988 (2005)

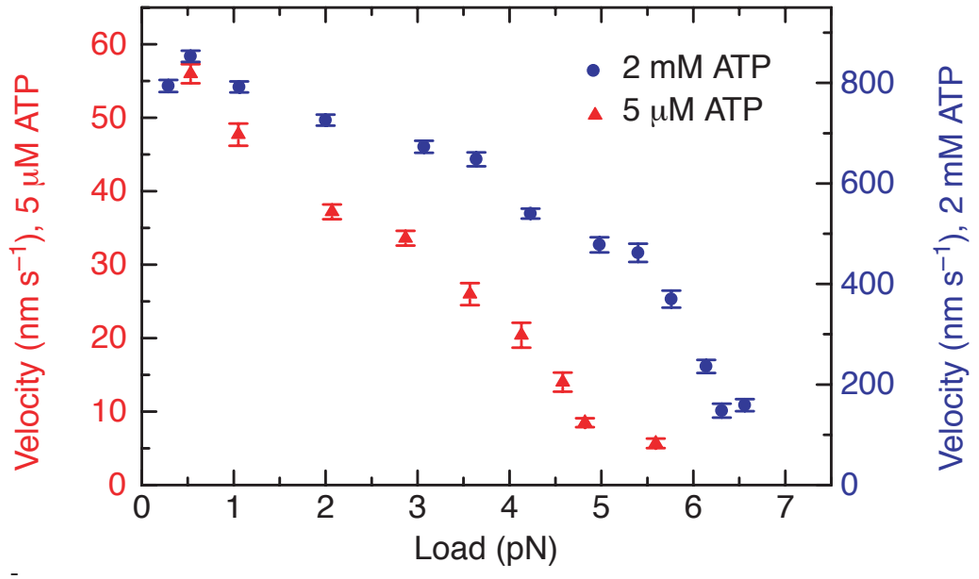
Sliding force pushes centrosomes apart

G. Goshima *et al.*, Current Biol. 15, 1979-1988 (2005)



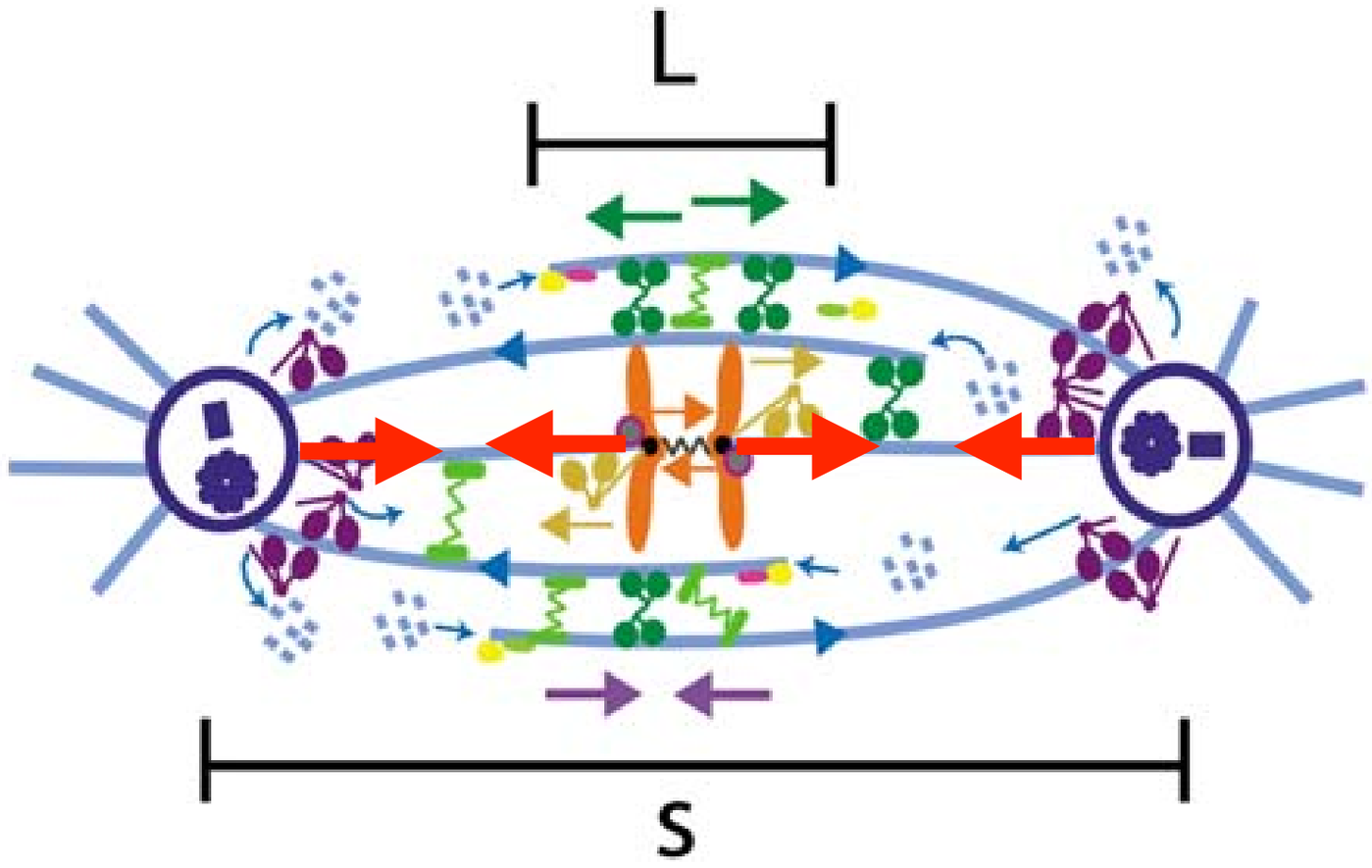
$$F_{\text{sliding}} = \alpha L \left(1 - \frac{v_{\text{sliding}}}{v_{\text{sliding}}^{(\max)}} \right)$$

α **proportional to density of sliding motors**



K. Visscher et al., Nature 400, 184-189 (1999)

Kinetochore pulls centrosome inwards

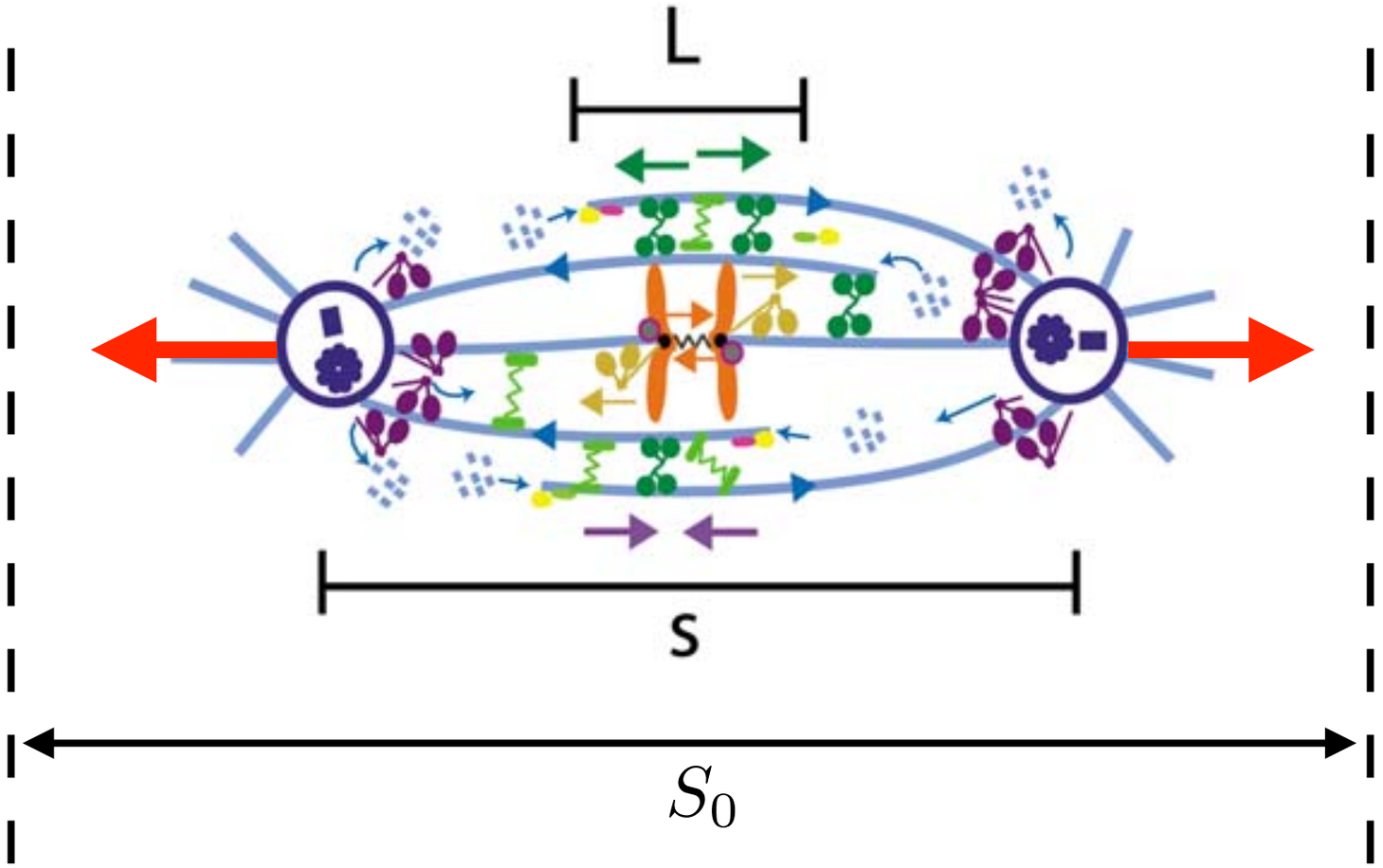


$$F_{\mathrm{kt}} = F_{\mathrm{kt},0}$$

constant tension force between chromosomes and centrosomes

G. Goshima *et al.*, Current Biol. 15, 1979-1988 (2005)

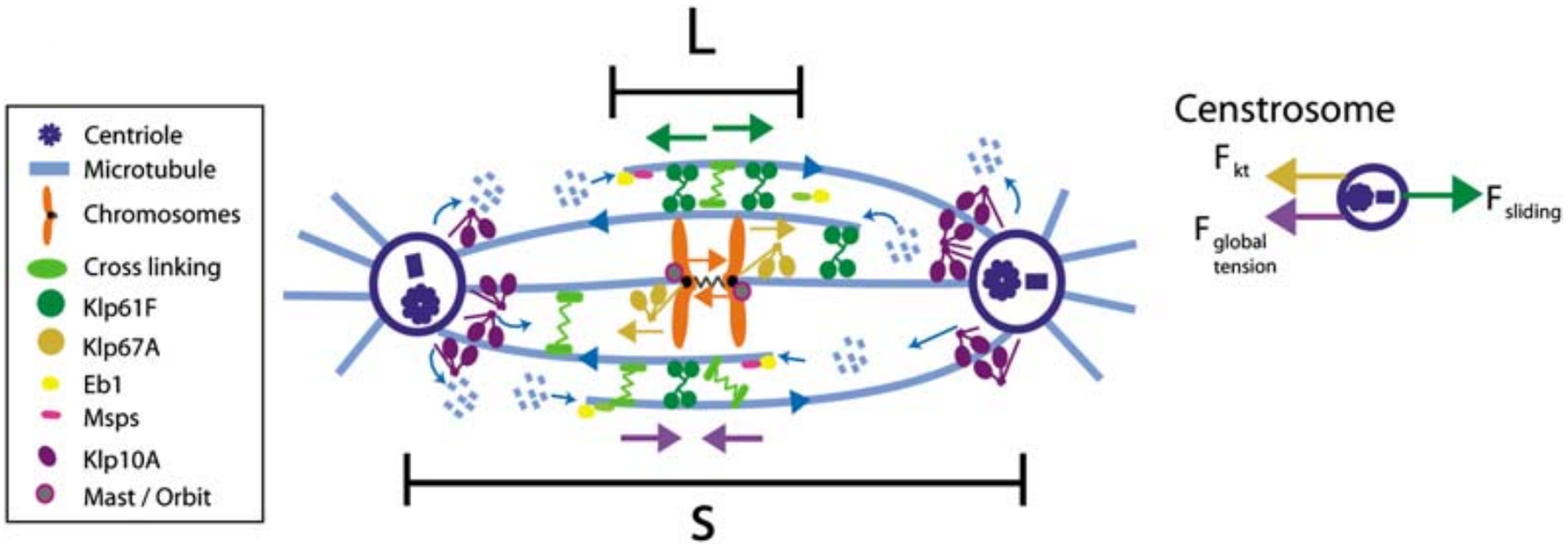
Restoring spring forces try to keep spindle at rest length S_0



$$F_{\text{tension}} = \beta(S - S_0)$$

G. Goshima *et al.*, Current Biol. 15, 1979-1988 (2005)

Model for spindle length control



$$F_{\text{sliding}} = \alpha L \left(1 - \frac{v_{\text{sliding}}}{v_{\text{sliding}}^{(\max)}}\right)$$

$$F_{\text{kt}} = F_{\text{kt},0}$$

$$F_{\text{tension}} = \beta(S - S_0)$$

$$\frac{dS}{dt} = \frac{2\left(F_{\text{sliding}} - F_{\text{kt}} - F_{\text{tension}}\right)}{\mu}$$

assuming viscous drag

G. Goshima *et al.*, Current Biol. 15, 1979-1988 (2005)

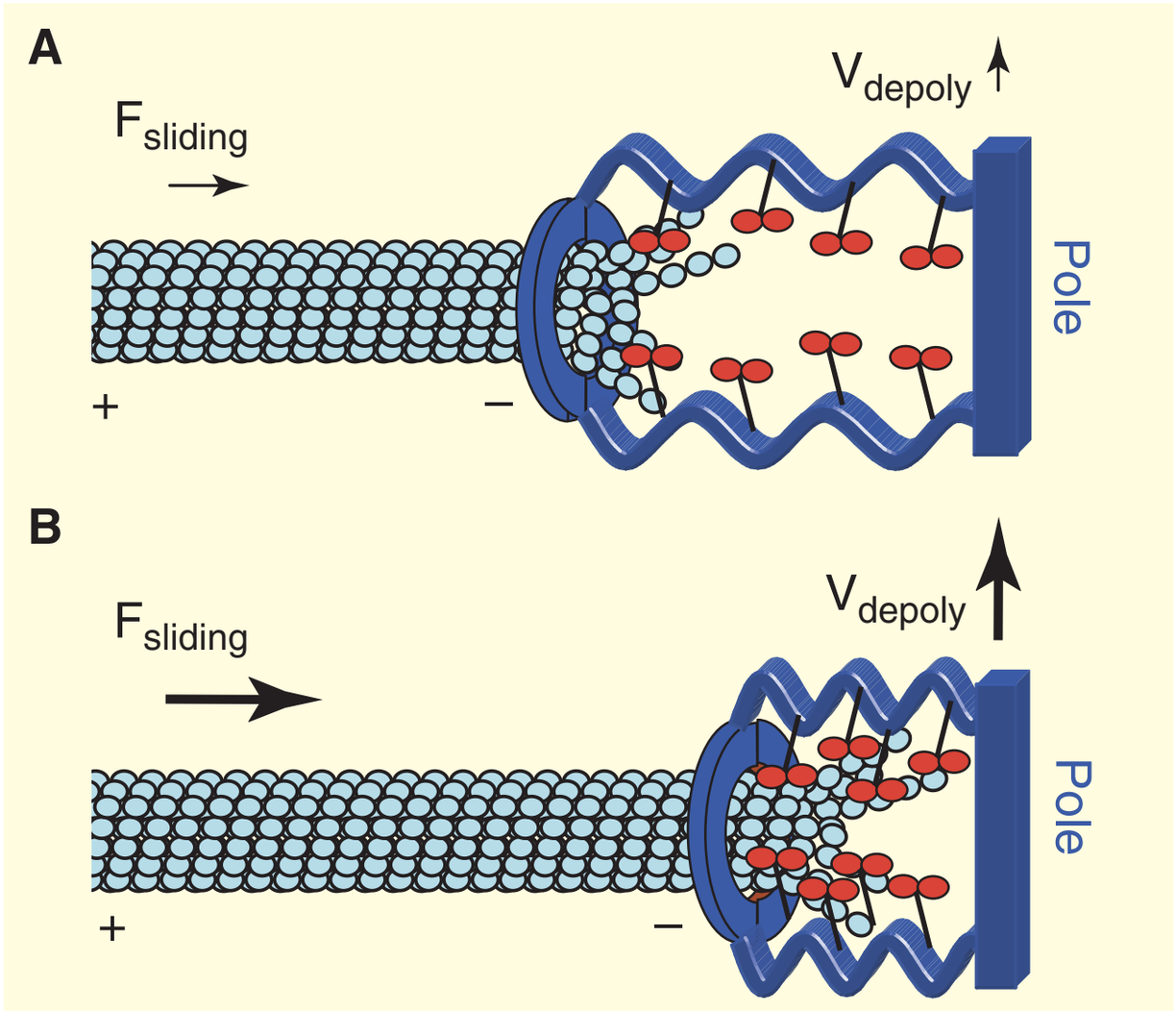
$$\frac{dL}{dt} = 2\left(v_{\text{poly}} - v_{\text{sliding}}\right)$$

$$\frac{dS}{dt} = 2\left(v_{\text{sliding}} - v_{\text{depoly}}\right)$$

$$\frac{dL}{dt} + \frac{dS}{dt} = 2\left(v_{\text{poly}} - v_{\text{depoly}}\right)$$

No steady state if rates of microtubule polymerization and depolymerization are different!

Depolymerization rate depends on the sliding force

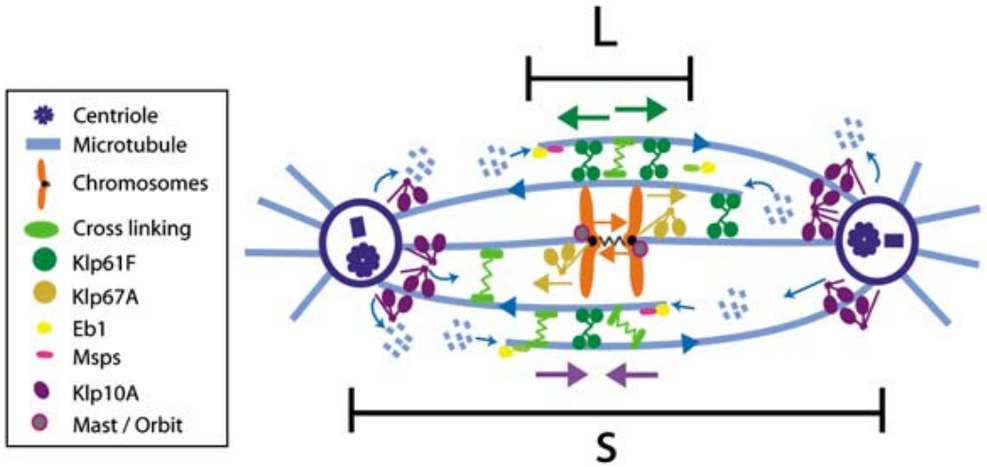


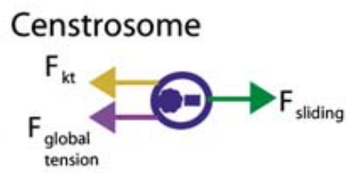
$$v_{\mathrm{depoly}} = v_{\mathrm{dep}}^{0} + v_{\mathrm{dep}}^{(\max)} \left(1 - e^{-F_{\mathrm{sliding}}/\gamma}\right)$$

D.J. Odde, Current Biol. 15, R956-R959 (2005)

G. Goshima *et al.*, Current Biol. 15, 1979-1988 (2005)

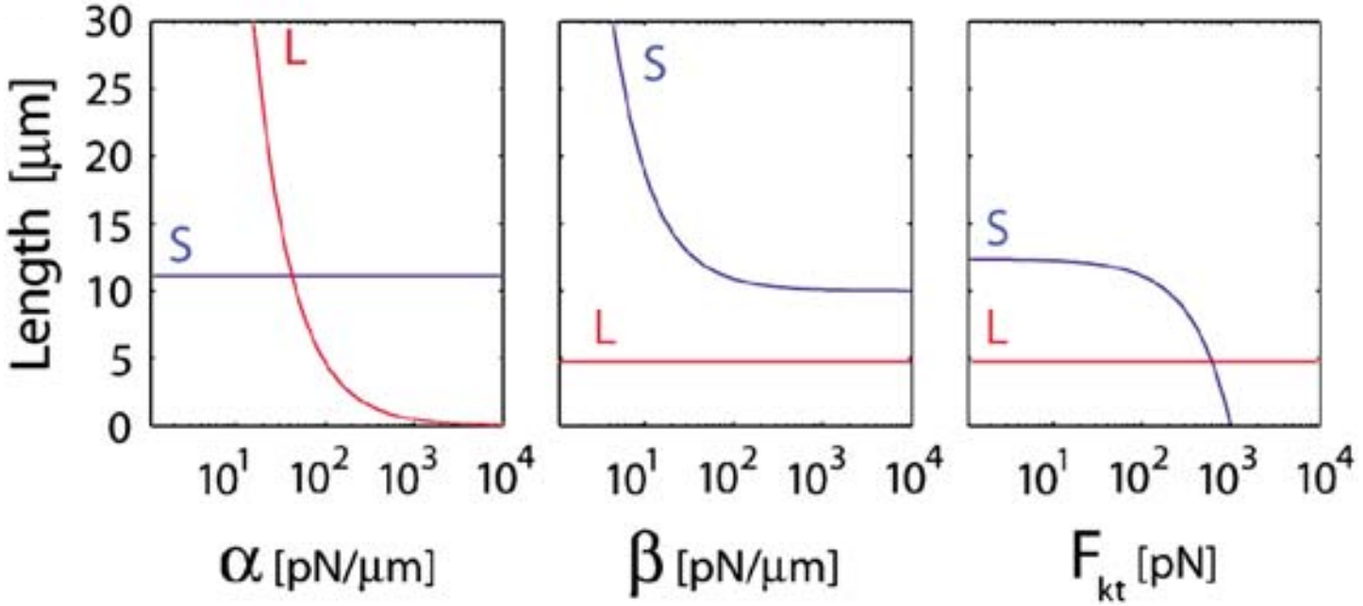
Model for spindle length control





$$L = \frac{\gamma}{\alpha} \frac{\ln\left(\frac{v_{\rm dep}^{(\max)}}{v_{\rm dep}^{(\max)} + v_{\rm dep}^{0} - v_{\rm poly}}\right)}{\left(1 - \frac{v_{\rm poly}}{v_{\rm sliding}^{(\max)}}\right)}$$

$$S = S_0 - \frac{F_{\rm kt}}{\beta} + \frac{\gamma}{\beta} \ln\left(\frac{v_{\rm dep}^{(\max)}}{v_{\rm dep}^{(\max)} + v_{\rm dep}^{0} - v_{\rm poly}}\right)$$



proportional to density of sliding motors

global spindle spring constant

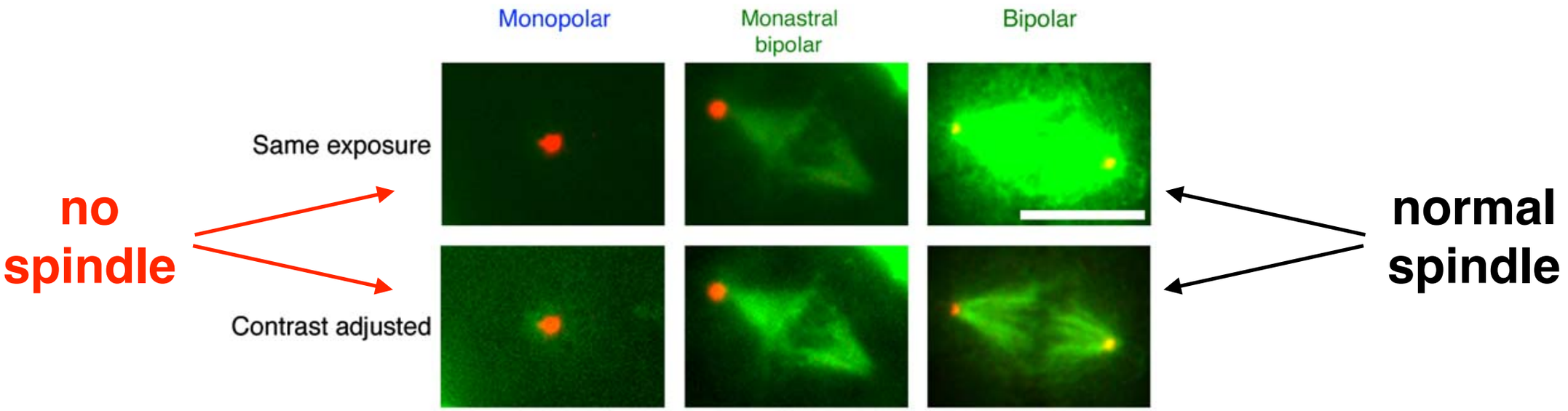
tension between centrosomes and kinetochores

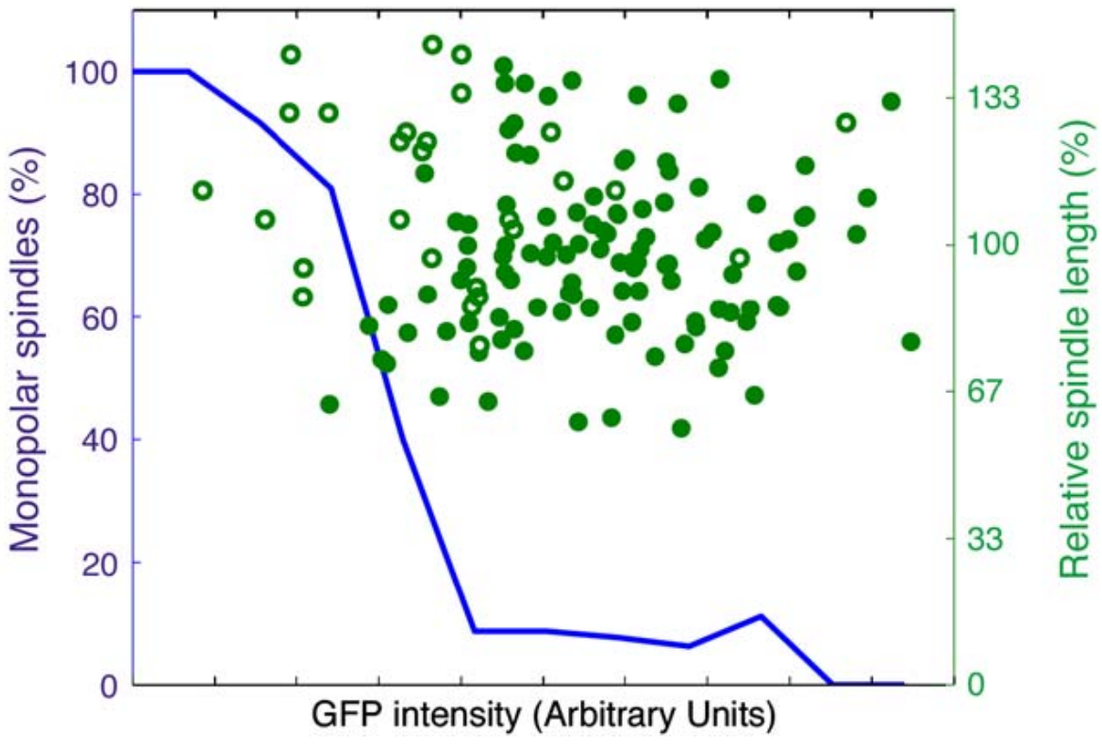
L<S under normal conditions in experiments.

Is there a new spindle phase when L>S?

G. Goshima *et al.*, Current Biol. 15, 1979-1988 (2005)

Spindle bistability

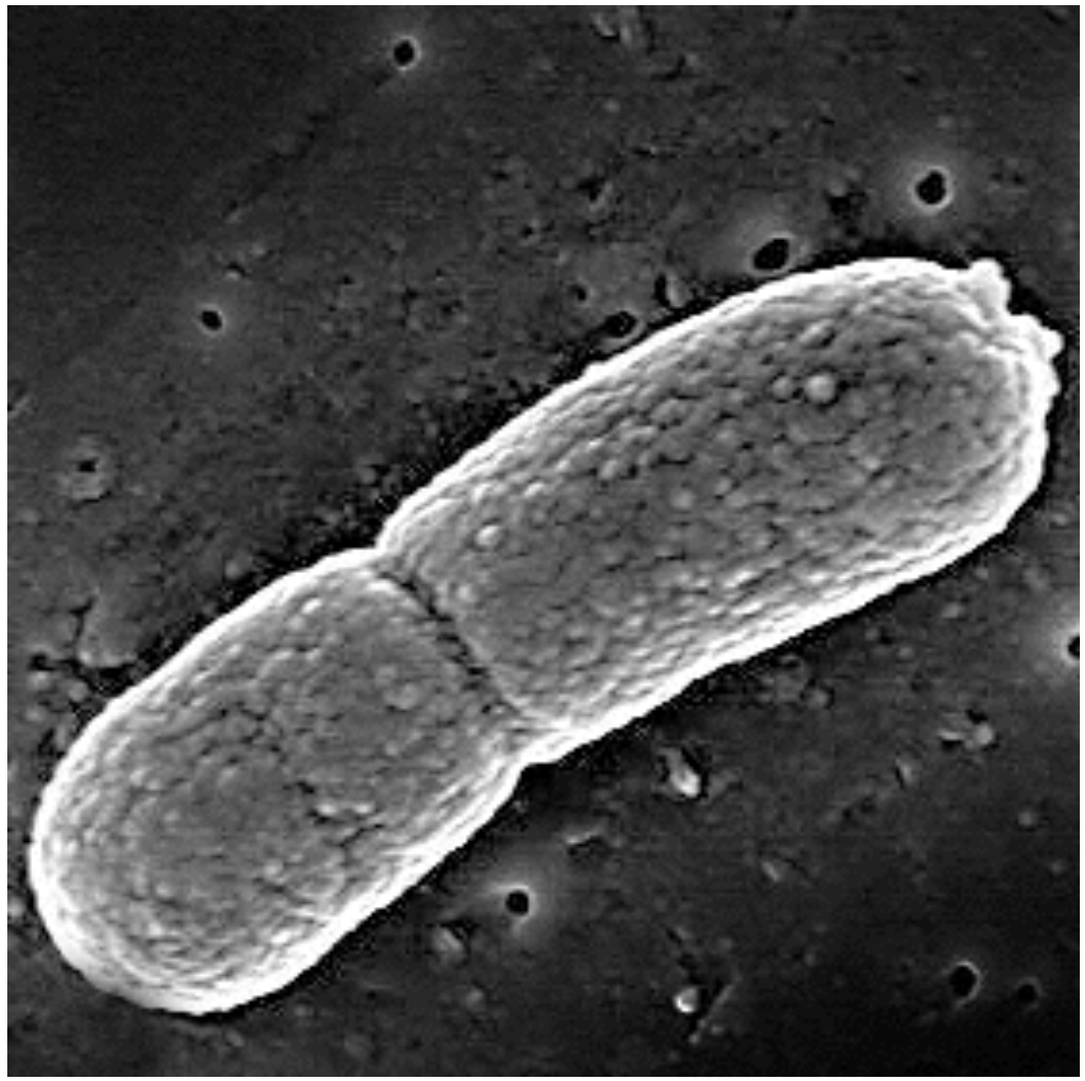




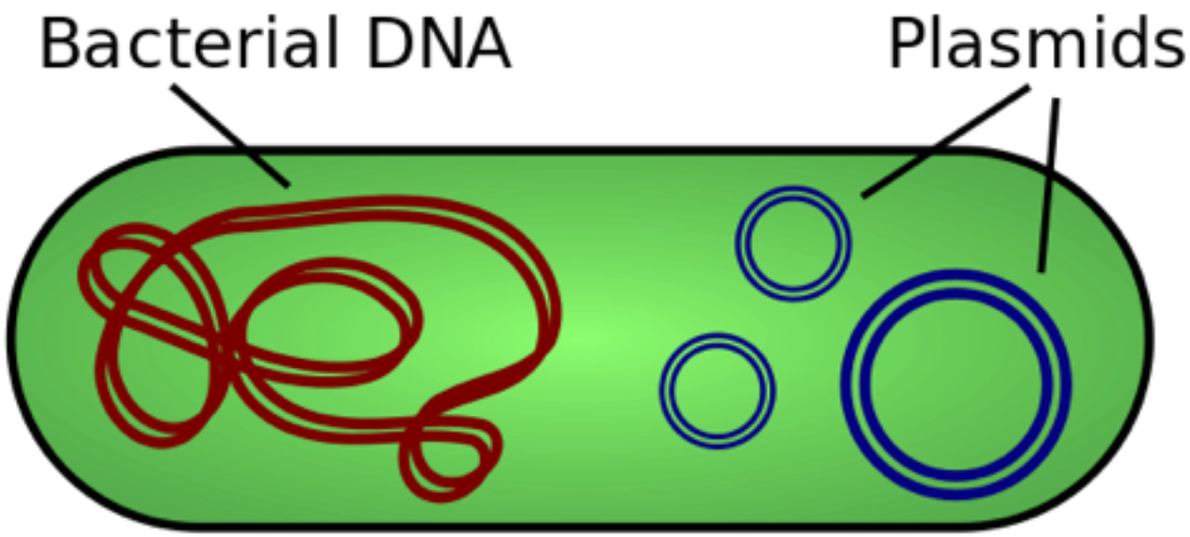
concentration of sliding motors

G. Goshima *et al.*, Current Biol. 15, 1979-1988 (2005)

Cell division in bacteria



Genetic information in bacteria

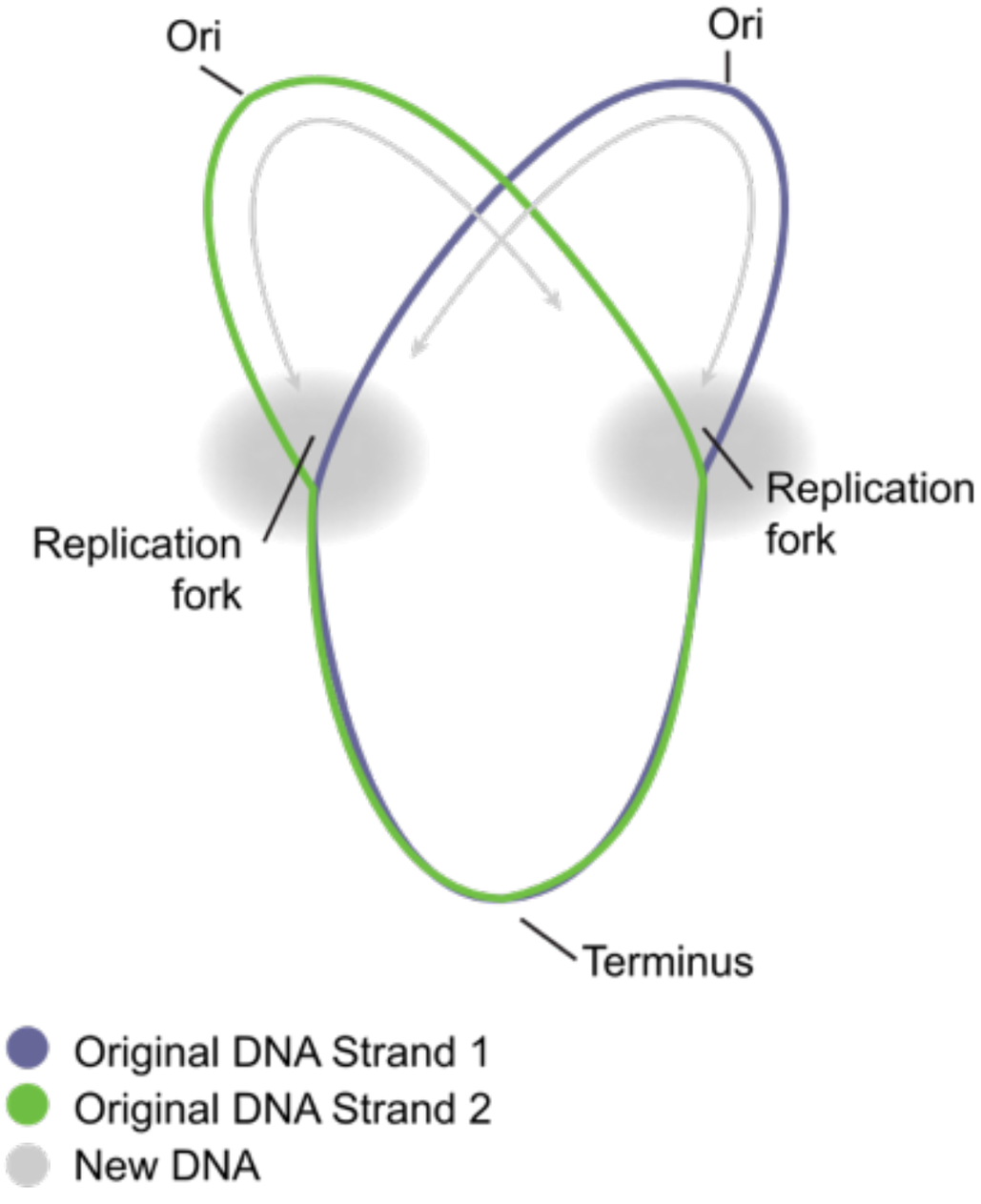


One large circular DNA

A few small circular plasmids

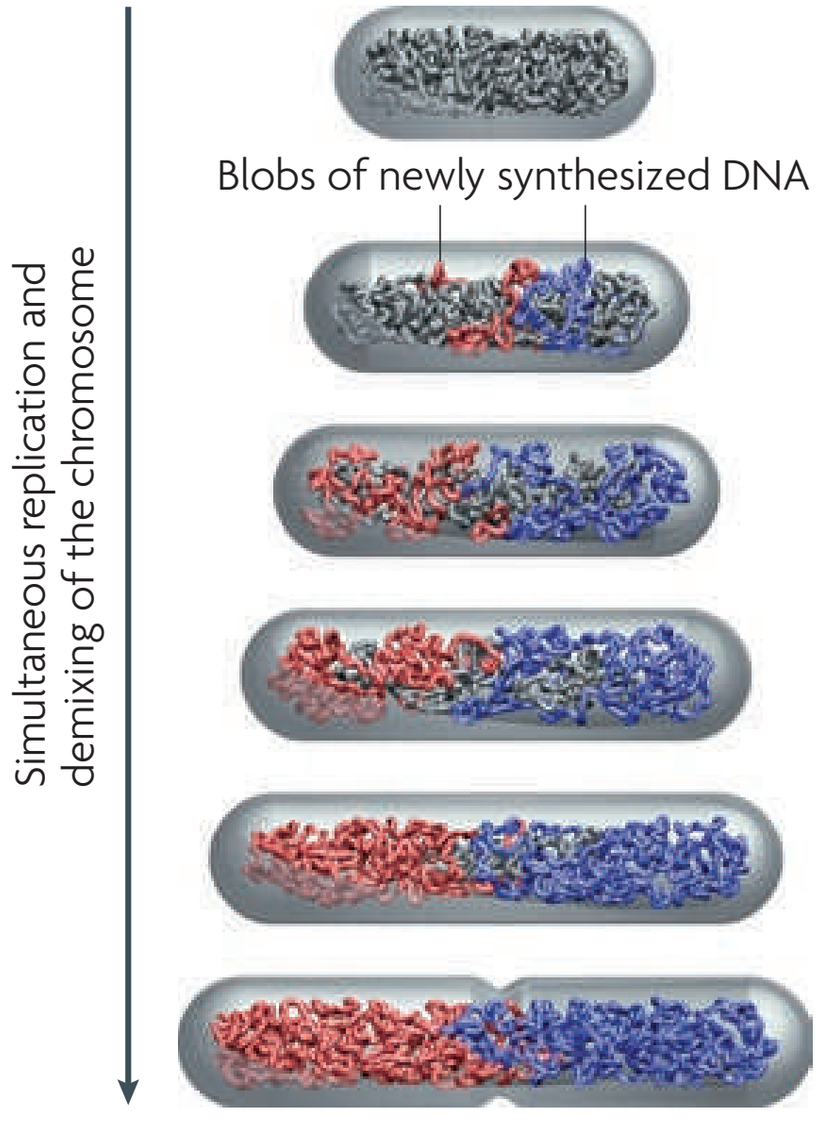
Plasmids carry additional genes that have recently evolved and may benefit survival (e.g. antibiotic resistance)

DNA replication and segregation



Wikipedia

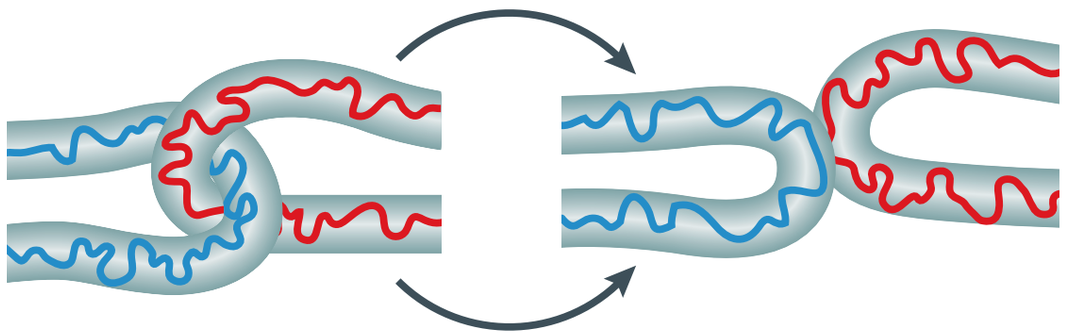
Spontaneous demixing due to steric excluded volume interactions



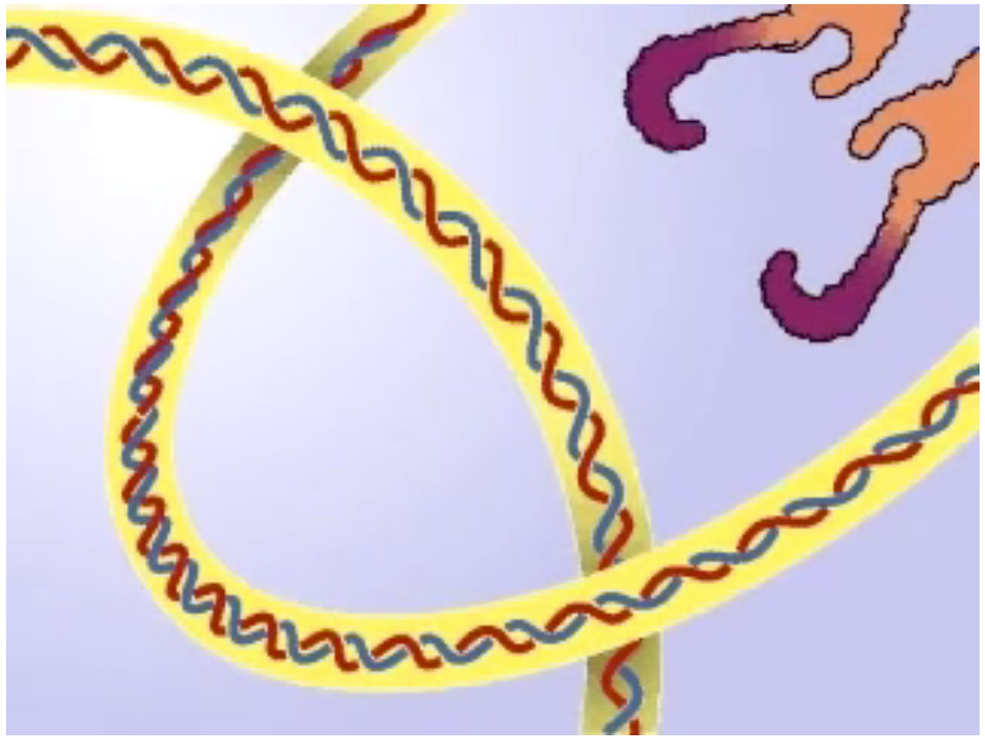
S. Jun and A. Wright, Nat. Rev. Microbiology 8, 600-607 (2010)

Topoisomerase 1 and 2 release tension along the DNA and speed up the separation process

Separation by reptation is slow



Separation by type II topoisomerase can be fast despite occasional reverse strand-passing



S. Jun and A. Wright, Nat. Rev. Microbiology 8, 600-607 (2010)

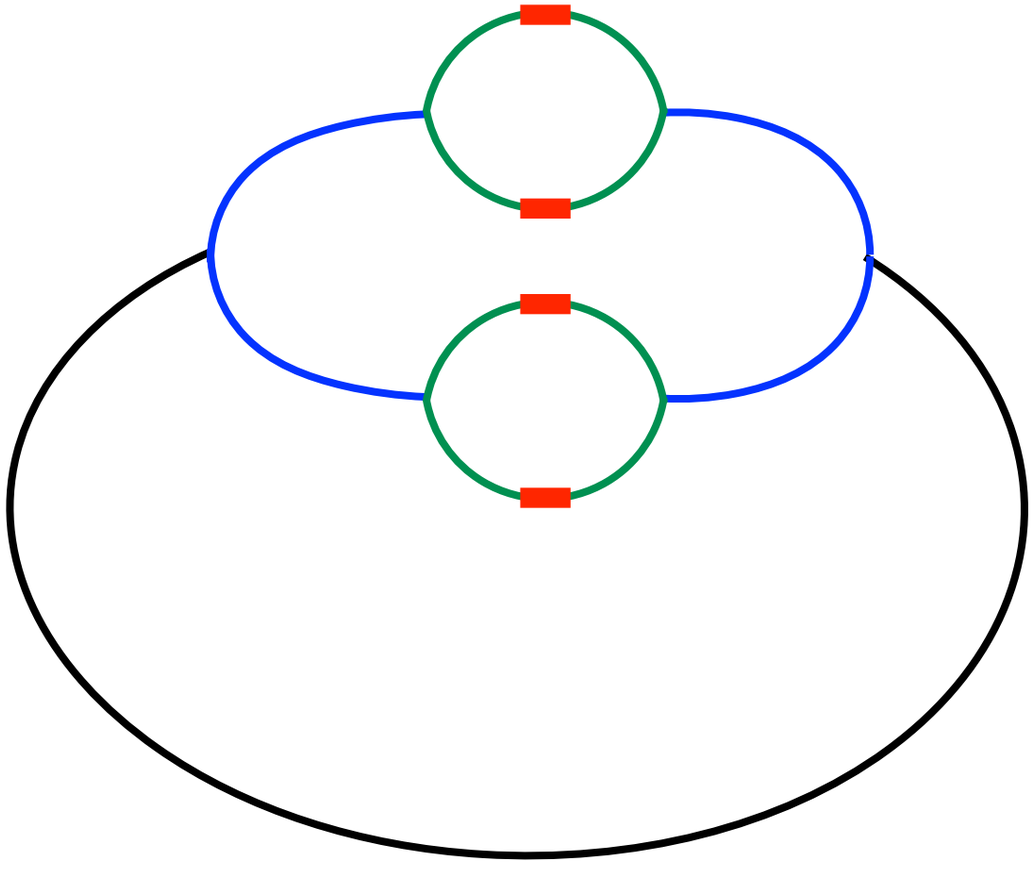
Bacteria divide faster than DNA replicates

Under normal conditions E. coli divides every 15-20 min

In E. coli it takes ~40 min to replicate DNA

How can bacteria divide faster than DNA replicates?

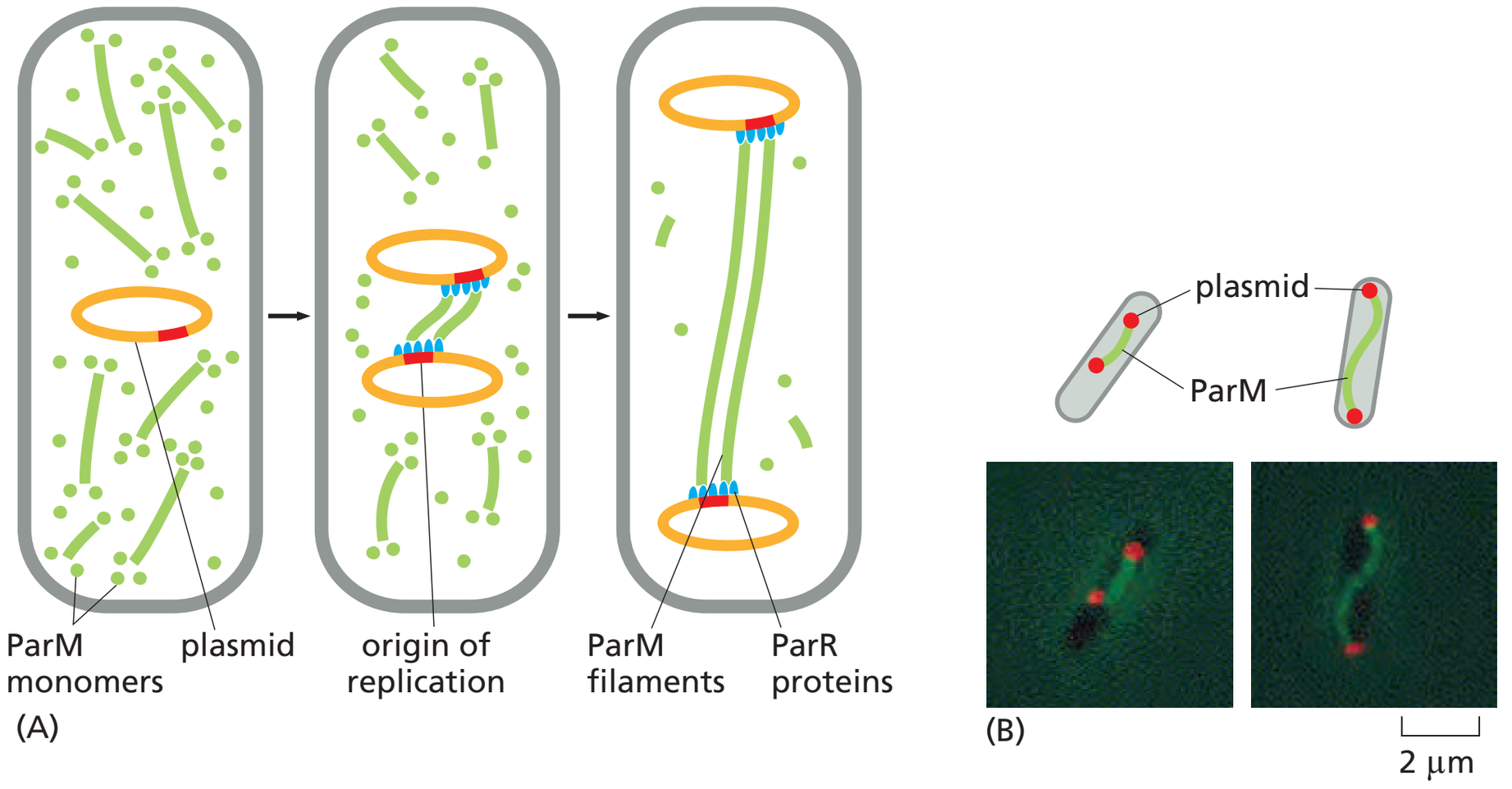
Multiple replication forks!



Bacteria starts replicating DNA for their daughters, grand daughters, etc.

Plasmid segregation

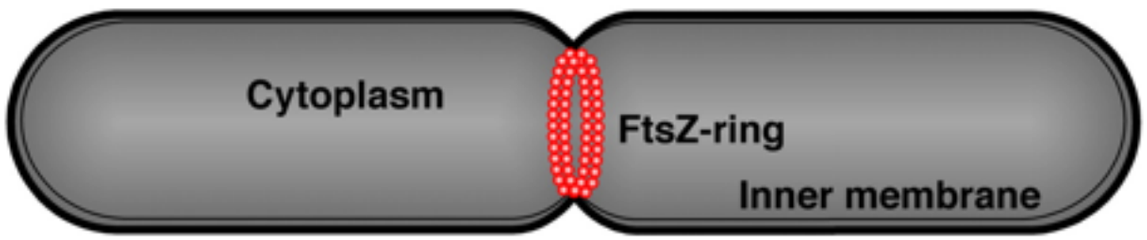
Plasmids are too small to spontaneously segregate on different sides of bacteria



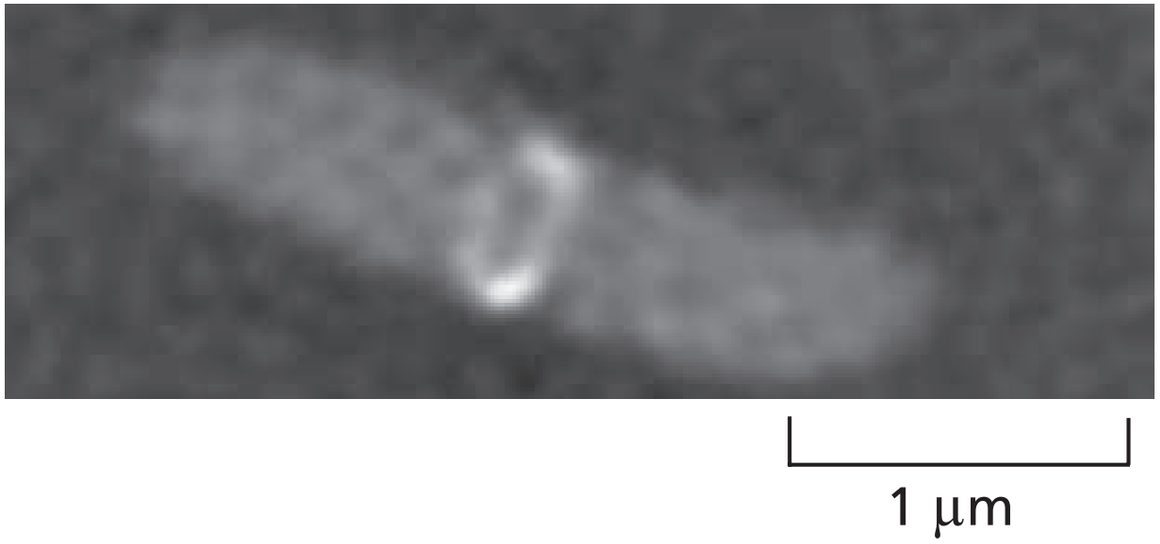
ParM is analogous to actin (assembly by ATP hydrolysis)

Alberts et al., Molecular Biology of the Cell

Contraction of FtsZ-ring divides bacterial cell in two



FtsZ is analogous to tubulin (assembly by GTP hydrolysis)



Bacterial division is extremely precise. FtsZ forms at

$$(0.50 \pm 0.01)\, L$$

How does bacteria know where to place the contractile ring?

Min system oscillations provide cues for the formation of FtsZ ring

FtsZ

⊤

MinC

↑

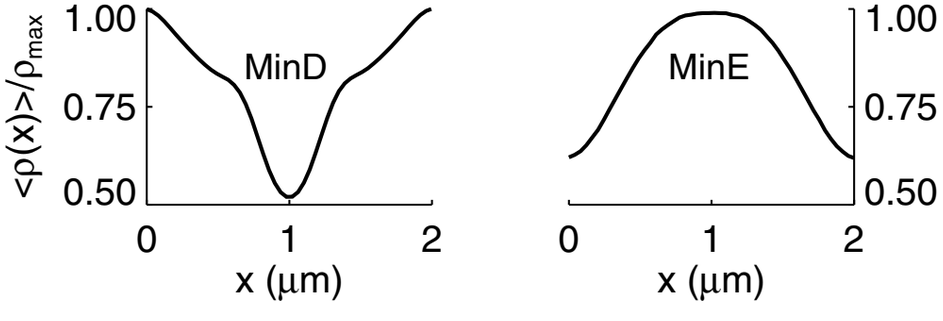
MinD

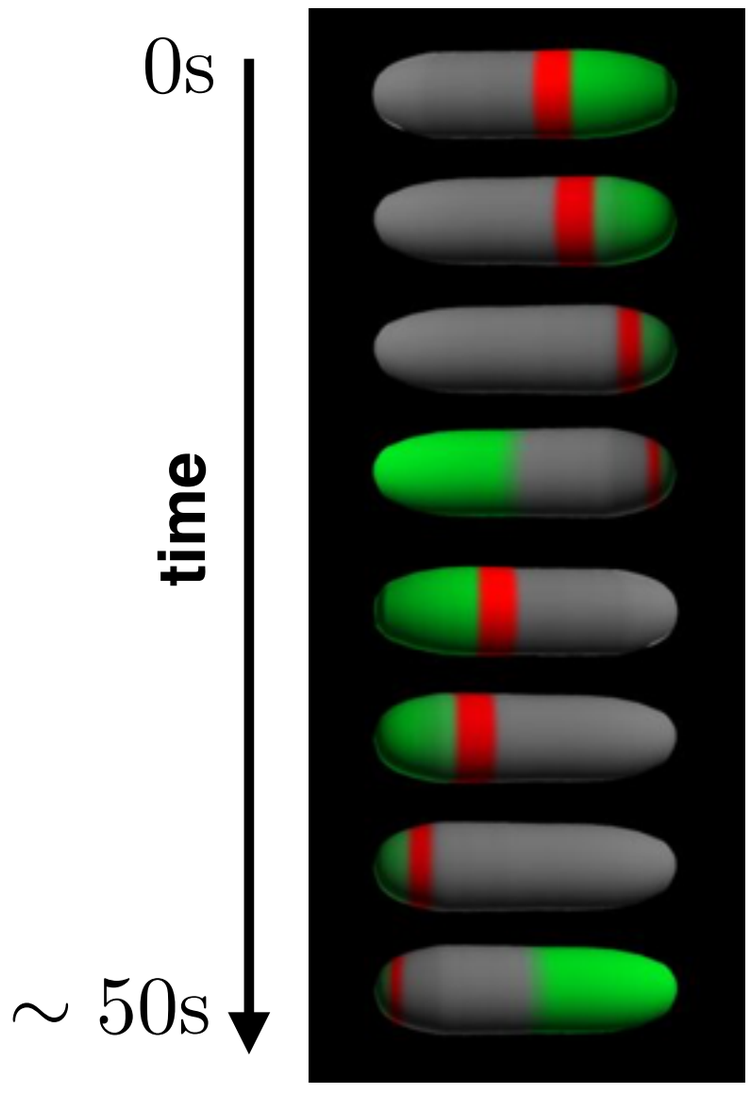
⊤

MinE

Predator-prey like dynamics between MinD and MinE proteins produce oscillations on a minute time scale, which is much shorter than typical division time (~20 min).

On average MinC/MinD proteins are depleted near the cell center, where FtsZ ring forms!

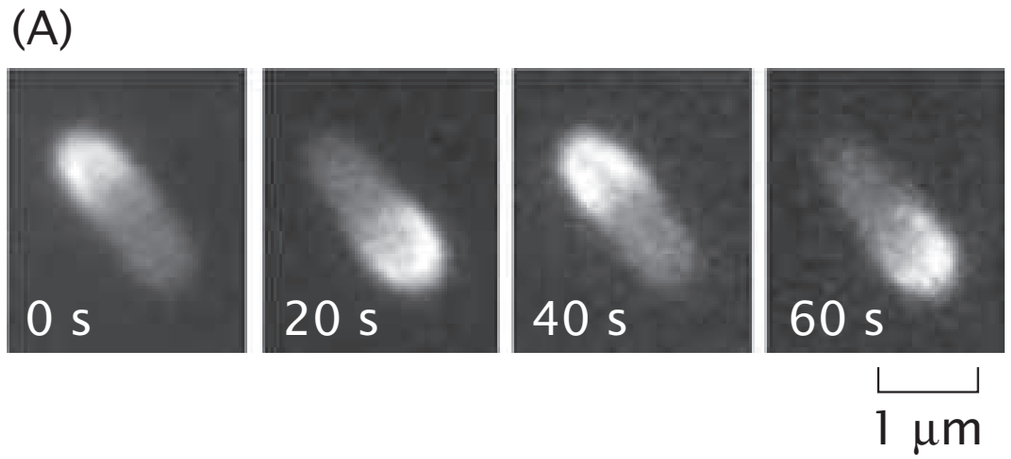




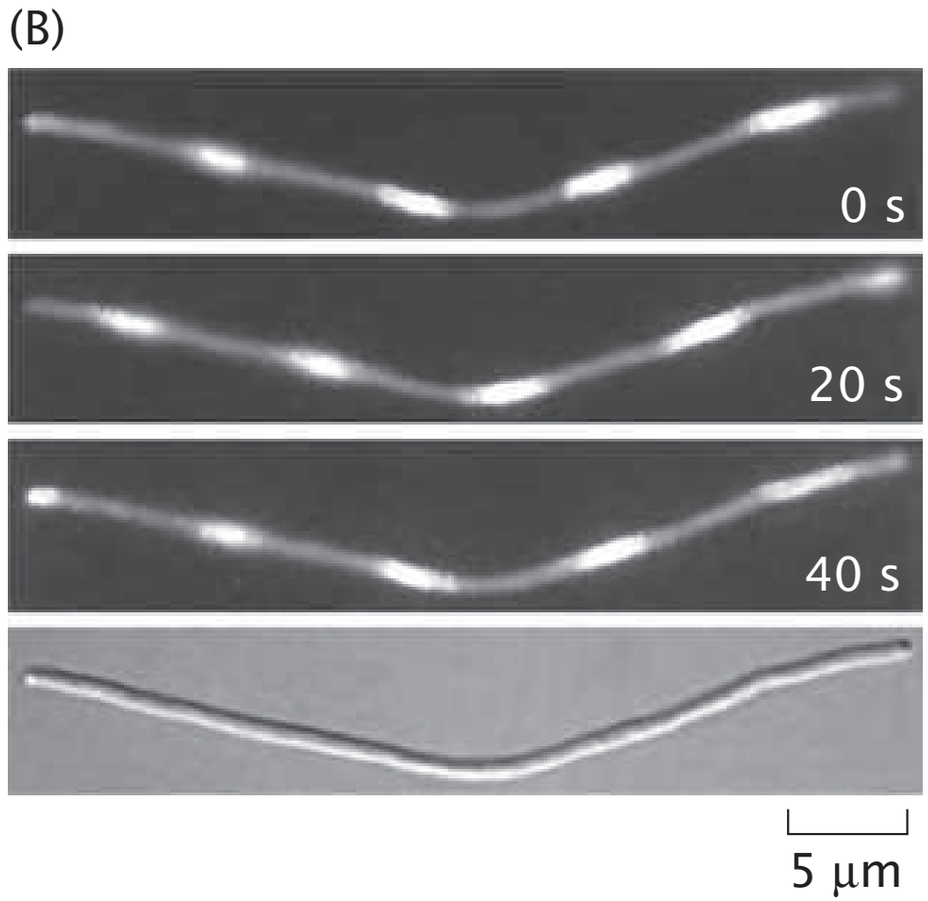
H. Meinhardt and P.A.J. de Boer, PNAS 98, 14202 (2001)

Min system oscillations in large cells

MinD oscillations in normal E. Coli



MinD oscillations in E. Coli, where division is prevented



R. Phillips et al., Physical Biology of the Cell