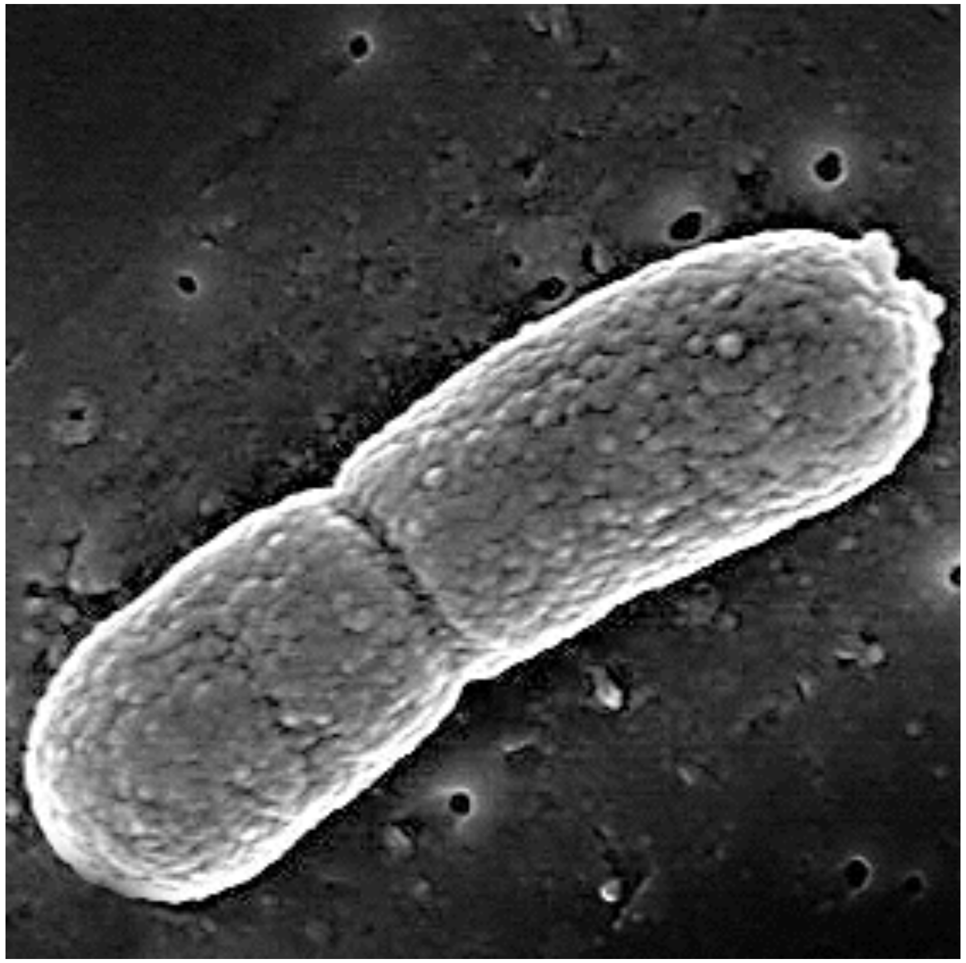
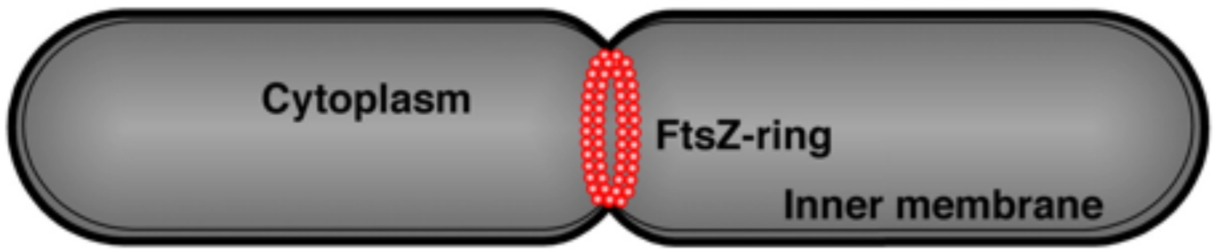
MAE 545: Lecture 10 (10/20)

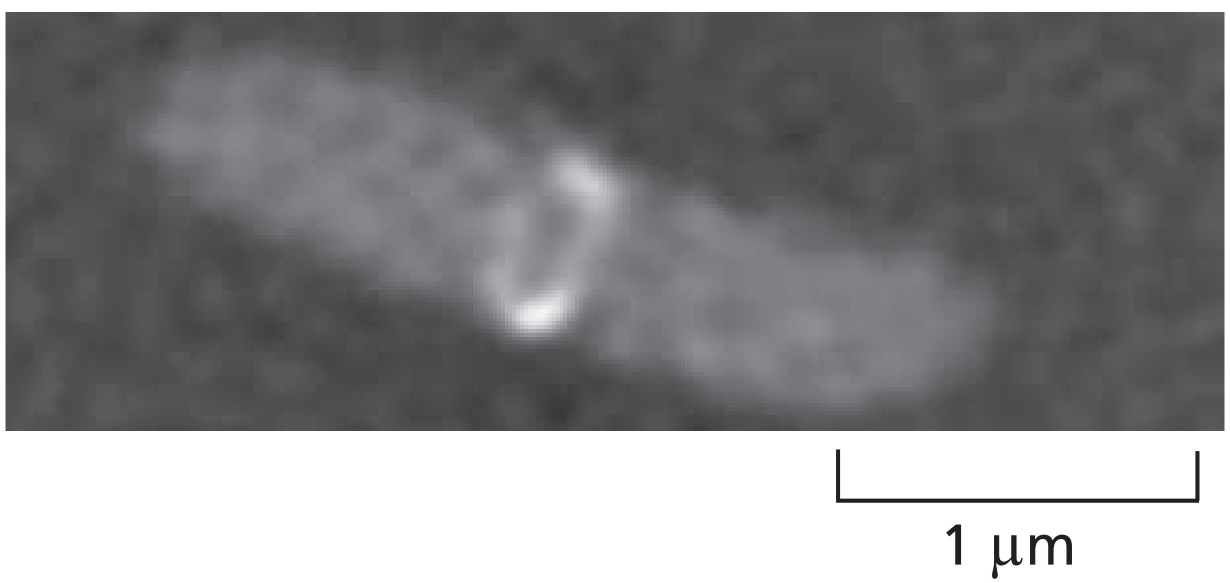
How bacteria find midline for cell division?



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

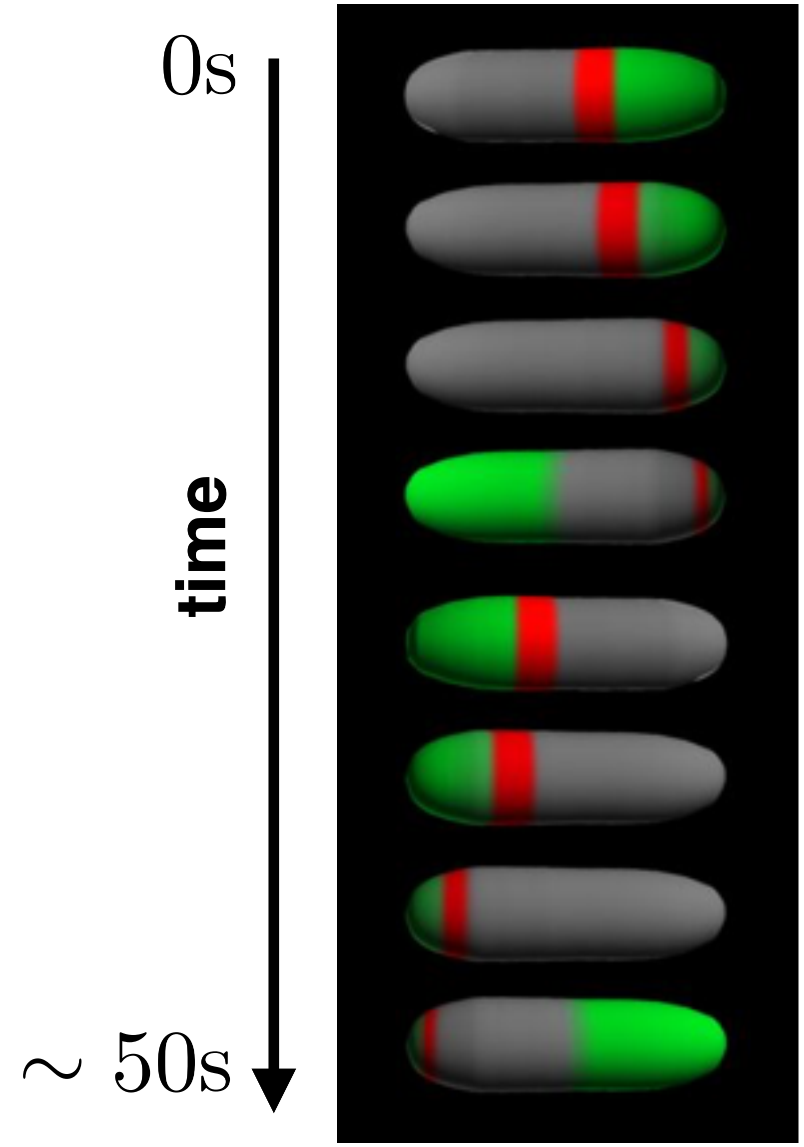
MinC

MinD

MinE

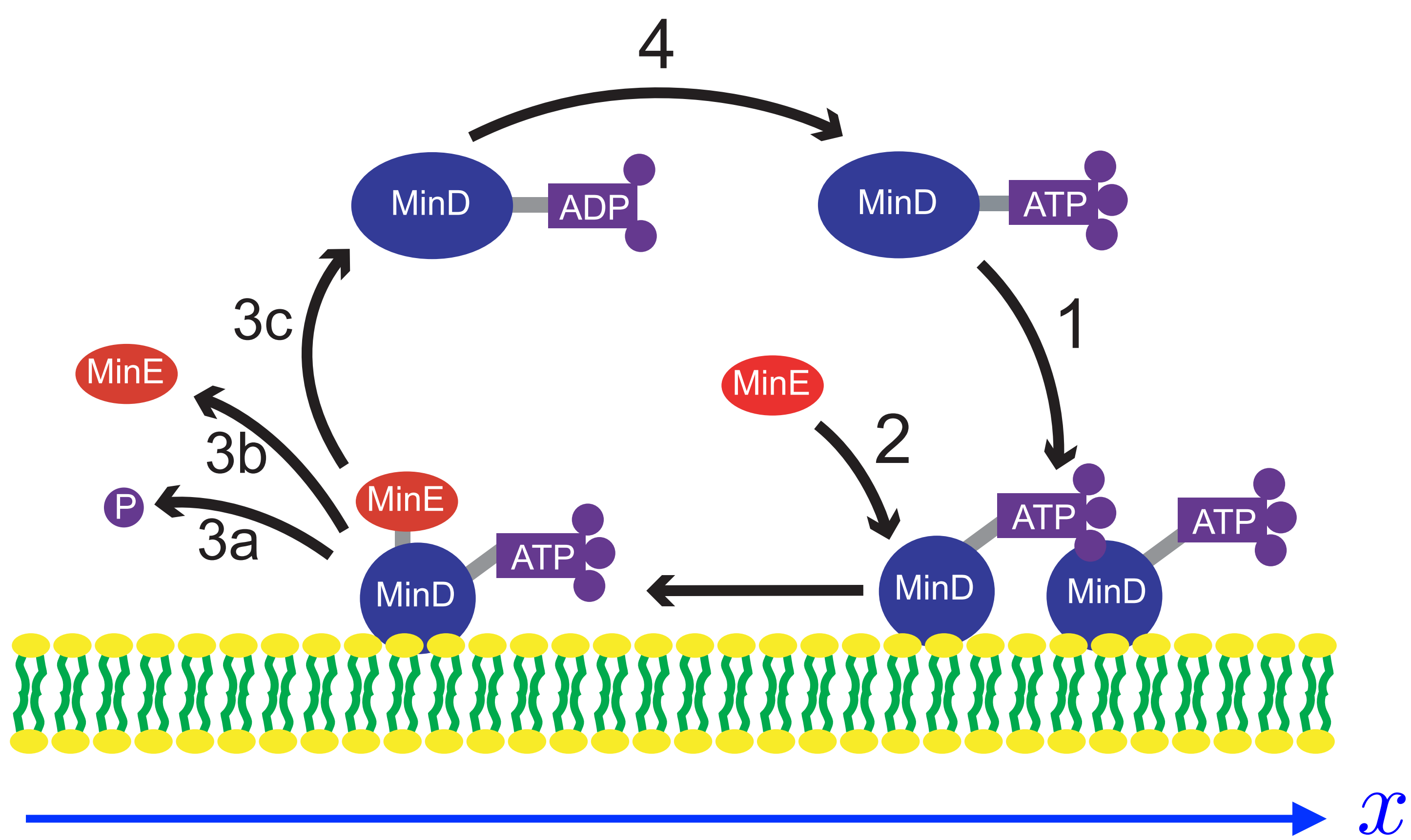
Predator-prey like dynamics between MinD and MinE proteins produce oscillations on a minute time scale, which is much shorter than typical division time (~20 min).

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)

1D model of Min system



Concentrations of proteins in the cytoplasm

$$C_{\mathrm{D:ADP}}(x,t) \qquad C_{\mathrm{D:ATP}}(x,t) \qquad C_{\mathrm{E}}(x,t)$$

Concentrations of membrane bound proteins

$$C_{\mathrm{d}}(x,t) \qquad C_{\mathrm{de}}(x,t)$$

Note: in paper they treat the full 3D model

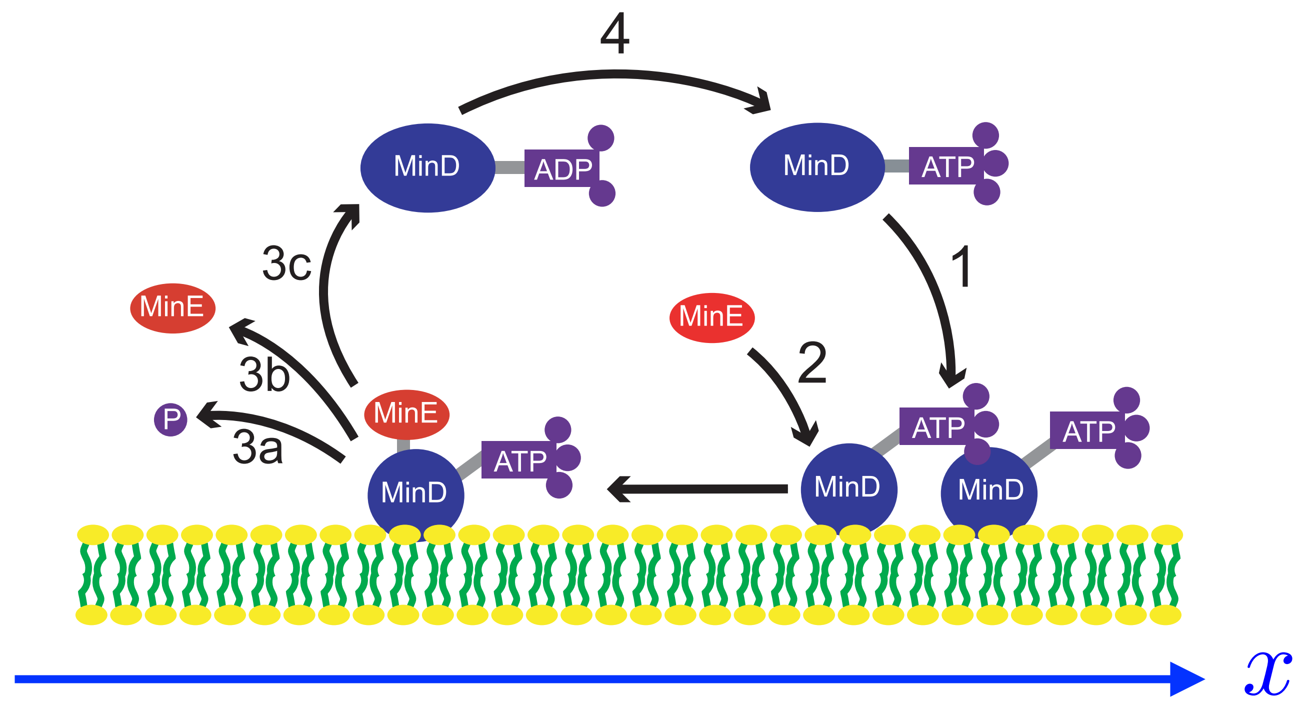
K.C. Huang *et al.*, PNAS 100, 12724 (2003)

Diffusion of Min proteins

Diffusion of Min proteins in cytoplasm

$$D_D \approx D_E \approx 2.5\mu\mathrm{m}^2/\mathrm{s}$$

Diffusion of membrane bound Min proteins is negligible!



$$\frac{\partial C_{\mathrm{D:ADP}}}{\partial t} = \boxed{D_D \frac{\partial^2 C_{\mathrm{D:ADP}}}{\partial x^2}}$$

$$\frac{\partial C_{\mathrm{D:ATP}}}{\partial t} = \boxed{D_D \frac{\partial^2 C_{\mathrm{D:ATP}}}{\partial x^2}}$$

$$\frac{\partial C_{\mathrm{E}}}{\partial t} = \boxed{D_E \frac{\partial^2 C_{\mathrm{E}}}{\partial x^2}}$$

$$\frac{\partial C_{\mathrm{d}}}{\partial t} =$$

$$\frac{\partial C_{\mathrm{de}}}{\partial t} =$$

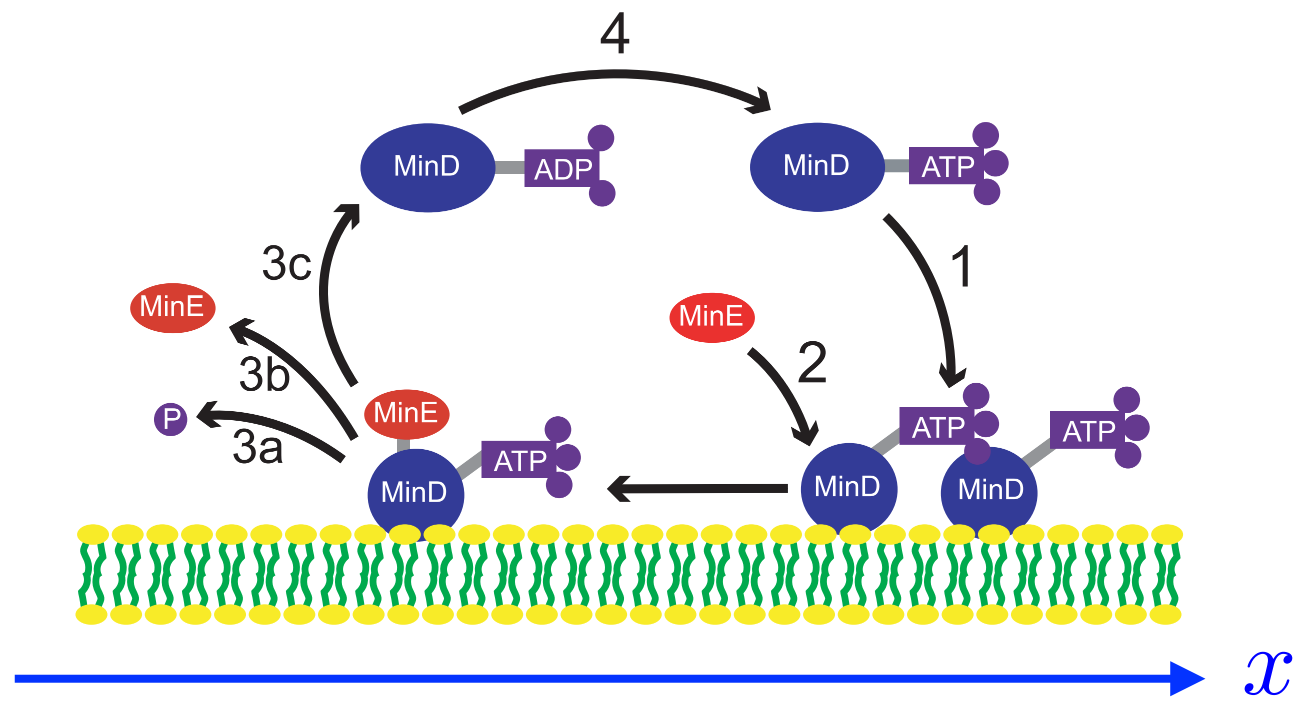
Reaction 1

MinD-ATP binds to the membrane

$$\sigma_D \approx 0.1\mathrm{s}^{-1}$$

MinD-ATP in the membrane recruits more MinD-ATP proteins

$$\sigma_{dD} \approx 0.002\mu\mathrm{m\,s}^{-1}$$



$$\frac{\partial C_{\mathrm{D:ADP}}}{\partial t} = D_D \frac{\partial^2 C_{\mathrm{D:ADP}}}{\partial x^2}$$

$$\frac{\partial C_{\mathrm{D:ATP}}}{\partial t} = D_D \frac{\partial^2 C_{\mathrm{D:ATP}}}{\partial x^2} \boxed{- \sigma_D C_{\mathrm{D:ATP}} - \sigma_{dD} C_{\mathrm{D:ATP}} \left[C_{\mathrm{d}} + C_{\mathrm{de}}\right]}$$

$$\frac{\partial C_{\mathrm{E}}}{\partial t} = D_E \frac{\partial^2 C_{\mathrm{E}}}{\partial x^2}$$

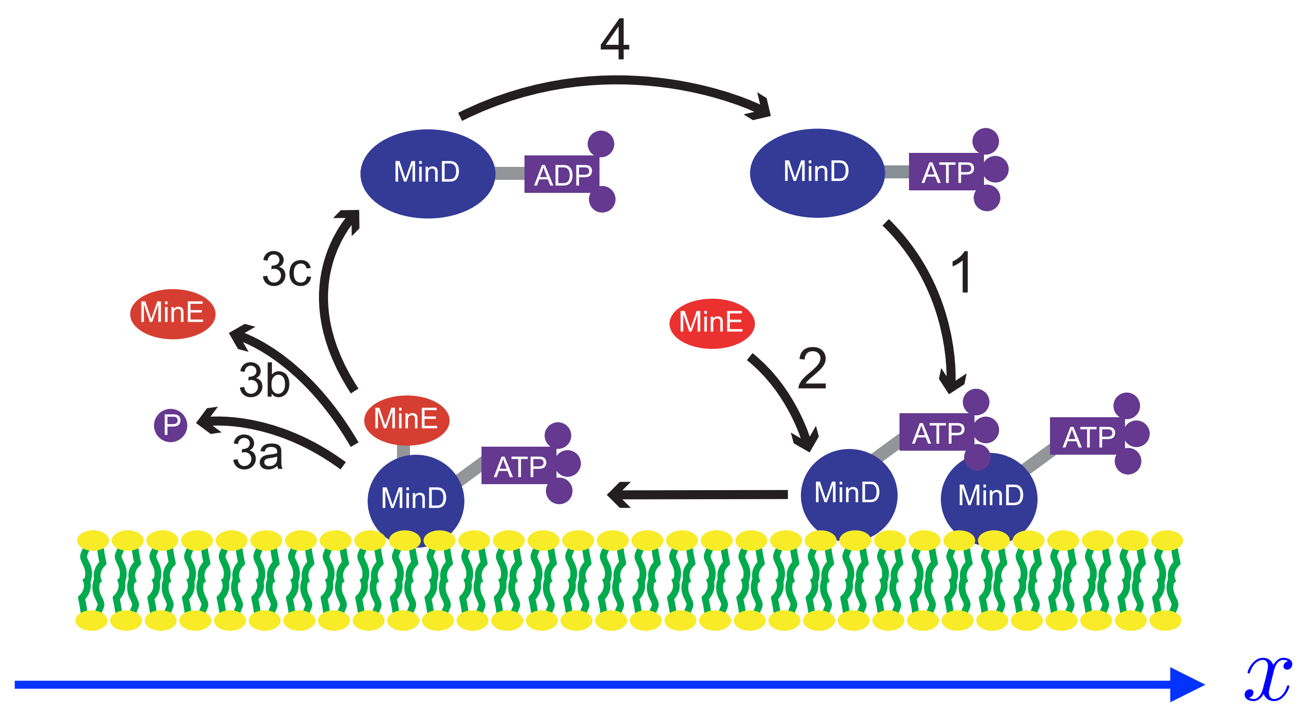
$$\frac{\partial C_{\mathrm{d}}}{\partial t} = \boxed{\sigma_D C_{\mathrm{D:ATP}} + \sigma_{dD} C_{\mathrm{D:ATP}} \left[C_{\mathrm{d}} + C_{\mathrm{de}}\right]}$$

$$\frac{\partial C_{\mathrm{de}}}{\partial t} =$$

Reaction 2

MinE binds to MinD-ATP in the membrane

$$\sigma_E \approx 0.12 \mu\mathrm{m\,s}^{-1}$$



$$\frac{\partial C_{\mathrm{D:ADP}}}{\partial t} = D_D \frac{\partial^2 C_{\mathrm{D:ADP}}}{\partial x^2}$$

$$\frac{\partial C_{\mathrm{D:ATP}}}{\partial t} = D_D \frac{\partial^2 C_{\mathrm{D:ATP}}}{\partial x^2} - \sigma_D C_{\mathrm{D:ATP}} - \sigma_{dD} C_{\mathrm{D:ATP}} \left[C_{\mathrm{d}} + C_{\mathrm{de}}\right]$$

$$\frac{\partial C_{\mathrm{E}}}{\partial t} = D_E \frac{\partial^2 C_{\mathrm{E}}}{\partial x^2} \boxed{- \sigma_E C_{\mathrm{d}} C_{\mathrm{E}}}$$

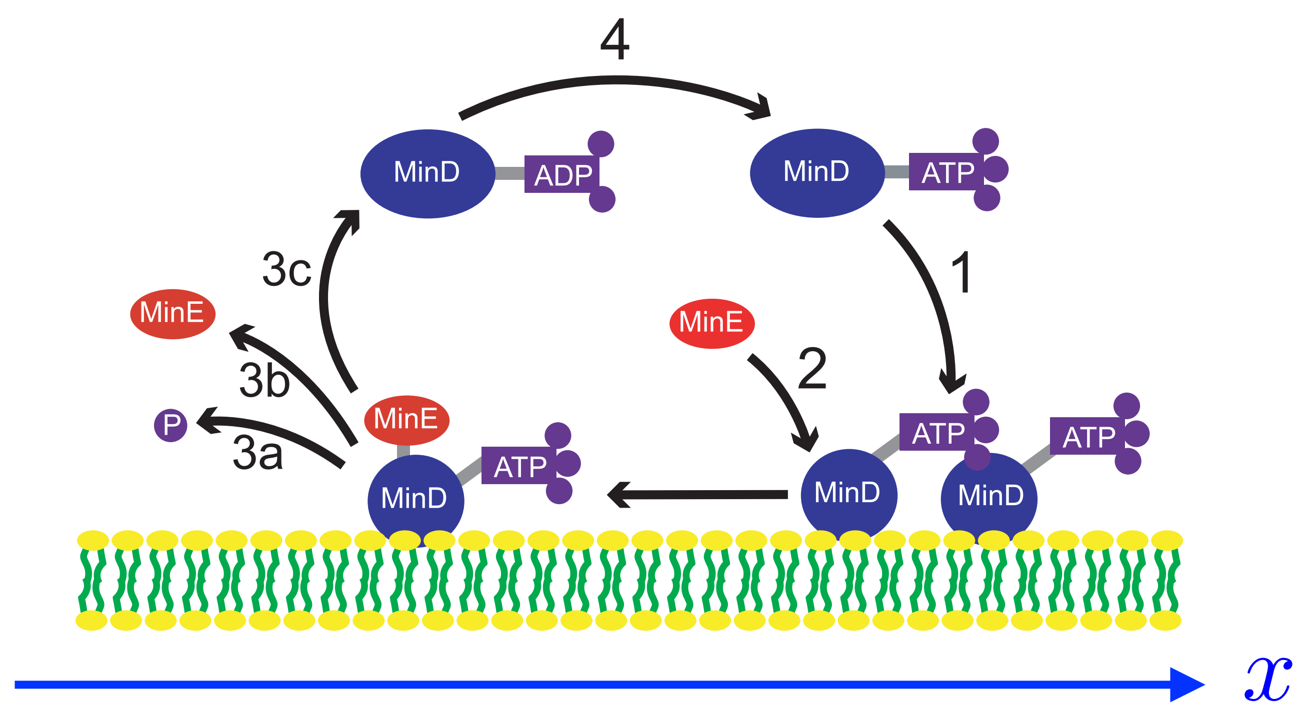
$$\frac{\partial C_{\mathrm{d}}}{\partial t} = \sigma_D C_{\mathrm{D:ATP}} + \sigma_{dD} C_{\mathrm{D:ATP}} \left[C_{\mathrm{d}} + C_{\mathrm{de}}\right] \boxed{- \sigma_E C_{\mathrm{d}} C_{\mathrm{E}}}$$

$$\frac{\partial C_{\mathrm{de}}}{\partial t} = \boxed{\sigma_E C_{\mathrm{d}} C_{\mathrm{E}}}$$

Reaction 3

MinE increases the rate of ATP hydrolysis and afterwards both MinE and MinD fall off the membrane

$\sigma_{de} \approx 0.7\text{s}^{-1}$



$$\frac{\partial C_{\text{D:ADP}}}{\partial t} = D_D \frac{\partial^2 C_{\text{D:ADP}}}{\partial x^2} \boxed{+ \sigma_{de} C_{\text{de}}}$$

$$\frac{\partial C_{\text{D:ATP}}}{\partial t} = D_D \frac{\partial^2 C_{\text{D:ATP}}}{\partial x^2} - \sigma_D C_{\text{D:ATP}} - \sigma_{dD} C_{\text{D:ATP}} \left[C_{\text{d}} + C_{\text{de}} \right]$$

$$\frac{\partial C_{\text{E}}}{\partial t} = D_E \frac{\partial^2 C_{\text{E}}}{\partial x^2} - \sigma_E C_{\text{d}} C_{\text{E}} \boxed{+ \sigma_{de} C_{\text{de}}}$$

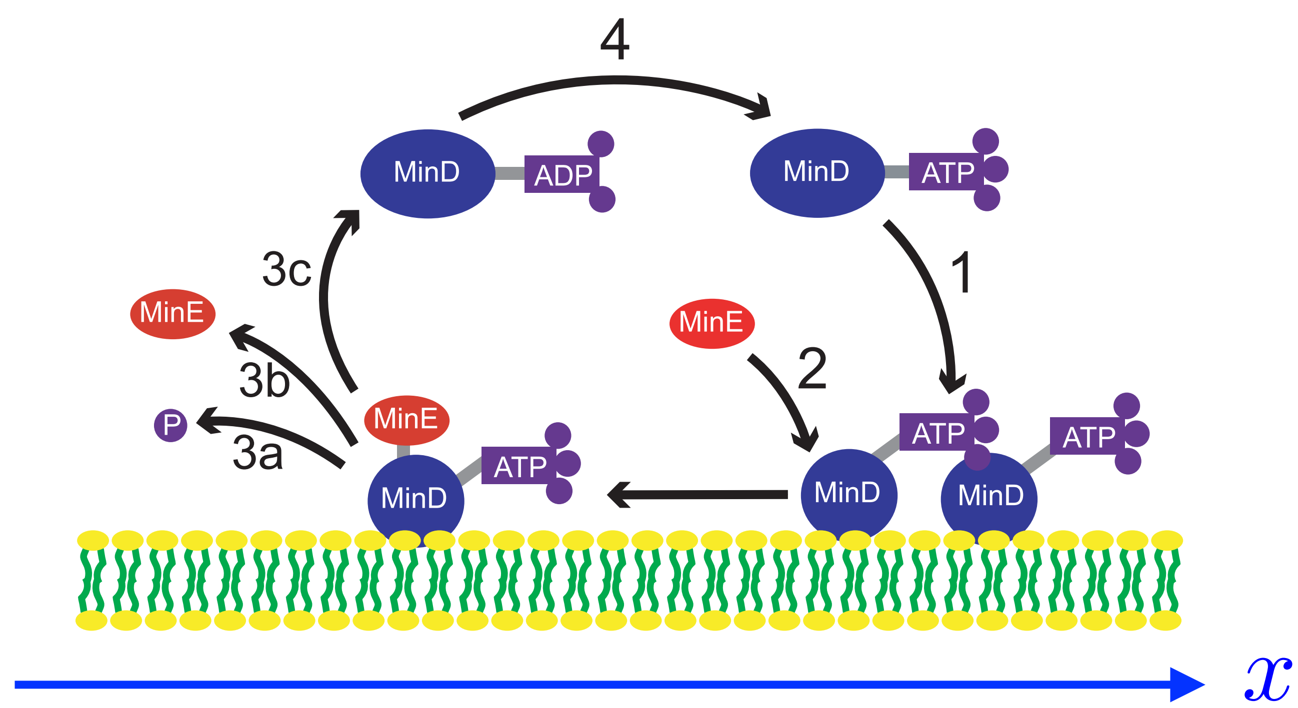
$$\frac{\partial C_{\text{d}}}{\partial t} = \sigma_D C_{\text{D:ATP}} + \sigma_{dD} C_{\text{D:ATP}} \left[C_{\text{d}} + C_{\text{de}} \right] - \sigma_E C_{\text{d}} C_{\text{E}}$$

$$\frac{\partial C_{\text{de}}}{\partial t} = \sigma_E C_{\text{d}} C_{\text{E}} \boxed{- \sigma_{de} C_{\text{de}}}$$

Reaction 4

Replacement of ADP with ATP for MinD proteins in the cytoplasm

$$\sigma_D^{\mathrm{ADP}\to\mathrm{ATP}} \sim 1\mathrm{s}^{-1}$$



$$\frac{\partial C_{\mathrm{D:ADP}}}{\partial t} = D_D \frac{\partial^2 C_{\mathrm{D:ADP}}}{\partial x^2} + \sigma_{de} C_{\mathrm{de}} \boxed{- \sigma_D^{\mathrm{ADP}\to\mathrm{ATP}} C_{\mathrm{D:ADP}}}$$

$$\frac{\partial C_{\mathrm{D:ATP}}}{\partial t} = D_D \frac{\partial^2 C_{\mathrm{D:ATP}}}{\partial x^2} - \sigma_D C_{\mathrm{D:ATP}} - \sigma_{dD} C_{\mathrm{D:ATP}} \left[C_{\mathrm{d}} + C_{\mathrm{de}}\right] \boxed{+ \sigma_D^{\mathrm{ADP}\to\mathrm{ATP}} C_{\mathrm{D:ADP}}}$$

$$\frac{\partial C_{\mathrm{E}}}{\partial t} = D_E \frac{\partial^2 C_{\mathrm{E}}}{\partial x^2} - \sigma_E C_{\mathrm{d}} C_{\mathrm{E}} + \sigma_{de} C_{\mathrm{de}}$$

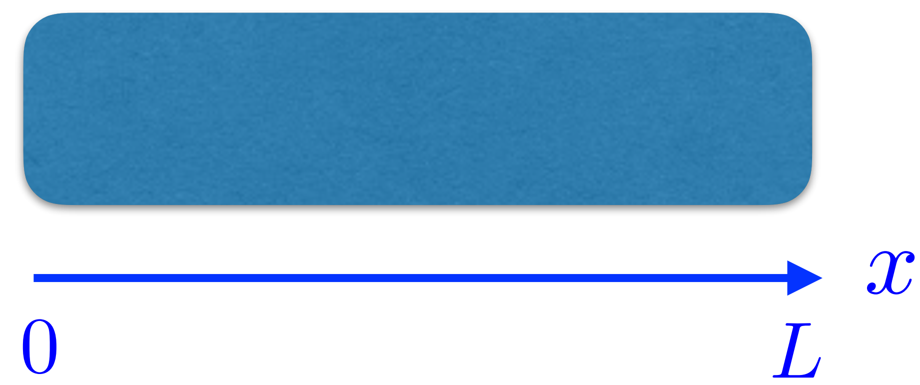
$$\frac{\partial C_{\mathrm{d}}}{\partial t} = \sigma_D C_{\mathrm{D:ATP}} + \sigma_{dD} C_{\mathrm{D:ATP}} \left[C_{\mathrm{d}} + C_{\mathrm{de}}\right] - \sigma_E C_{\mathrm{d}} C_{\mathrm{E}}$$

$$\frac{\partial C_{\mathrm{de}}}{\partial t} = \sigma_E C_{\mathrm{d}} C_{\mathrm{E}} - \sigma_{de} C_{\mathrm{de}}$$

Boundary conditions

No flux of proteins through the edge

$$\frac{\partial C_{\mathrm{D:ADP}}}{\partial x}(x=0,t) = \frac{\partial C_{\mathrm{D:ADP}}}{\partial x}(x=L,t) = 0$$
$$\frac{\partial C_{\mathrm{D:ATP}}}{\partial x}(x=0,t) = \frac{\partial C_{\mathrm{D:ATP}}}{\partial x}(x=L,t) = 0$$
$$\frac{\partial C_{\mathrm{E}}}{\partial x}(x=0,t) = \frac{\partial C_{\mathrm{E}}}{\partial x}(x=L,t) = 0$$



$$\frac{\partial C_{\mathrm{D:ADP}}}{\partial t} = D_D \frac{\partial^2 C_{\mathrm{D:ADP}}}{\partial x^2} + \sigma_{de} C_{\mathrm{de}} - \sigma_D^{\mathrm{ADP}\to\mathrm{ATP}} C_{\mathrm{D:ADP}}$$

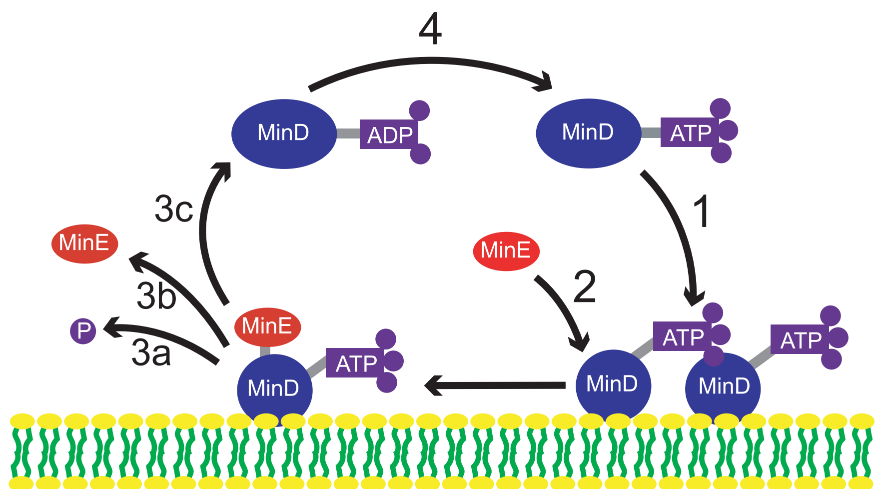
$$\frac{\partial C_{\mathrm{D:ATP}}}{\partial t} = D_D \frac{\partial^2 C_{\mathrm{D:ATP}}}{\partial x^2} - \sigma_D C_{\mathrm{D:ATP}} - \sigma_{dD} C_{\mathrm{D:ATP}} \left[C_{\mathrm{d}} + C_{\mathrm{de}}\right] + \sigma_D^{\mathrm{ADP}\to\mathrm{ATP}} C_{\mathrm{D:ADP}}$$

$$\frac{\partial C_{\mathrm{E}}}{\partial t} = D_E \frac{\partial^2 C_{\mathrm{E}}}{\partial x^2} - \sigma_E C_{\mathrm{d}} C_{\mathrm{E}} + \sigma_{de} C_{\mathrm{de}}$$

$$\frac{\partial C_{\mathrm{d}}}{\partial t} = \sigma_D C_{\mathrm{D:ATP}} + \sigma_{dD} C_{\mathrm{D:ATP}} \left[C_{\mathrm{d}} + C_{\mathrm{de}}\right] - \sigma_E C_{\mathrm{d}} C_{\mathrm{E}}$$

$$\frac{\partial C_{\mathrm{de}}}{\partial t} = \sigma_E C_{\mathrm{d}} C_{\mathrm{E}} - \sigma_{de} C_{\mathrm{de}}$$

How do we analyze such system of PDEs?



$$\frac{\partial C_{\mathrm{D:ADP}}}{\partial t} = D_D \frac{\partial^2 C_{\mathrm{D:ADP}}}{\partial x^2} + \sigma_{de} C_{\mathrm{de}} - \sigma_D^{\mathrm{ADP} \to \mathrm{ATP}} C_{\mathrm{D:ADP}}$$

$$\frac{\partial C_{\mathrm{D:ATP}}}{\partial t} = D_D \frac{\partial^2 C_{\mathrm{D:ATP}}}{\partial x^2} - \sigma_D C_{\mathrm{D:ATP}} - \sigma_{dD} C_{\mathrm{D:ATP}} \left[C_{\mathrm{d}} + C_{\mathrm{de}}\right] + \sigma_D^{\mathrm{ADP} \to \mathrm{ATP}} C_{\mathrm{D:ADP}}$$

$$\frac{\partial C_{\mathrm{E}}}{\partial t} = D_E \frac{\partial^2 C_{\mathrm{E}}}{\partial x^2} - \sigma_E C_{\mathrm{d}} C_{\mathrm{E}} + \sigma_{de} C_{\mathrm{de}}$$

$$\frac{\partial C_{\mathrm{d}}}{\partial t} = \sigma_D C_{\mathrm{D:ATP}} + \sigma_{dD} C_{\mathrm{D:ATP}} \left[C_{\mathrm{d}} + C_{\mathrm{de}}\right] - \sigma_E C_{\mathrm{d}} C_{\mathrm{E}}$$

$$\frac{\partial C_{\mathrm{de}}}{\partial t} = \sigma_E C_{\mathrm{d}} C_{\mathrm{E}} - \sigma_{de} C_{\mathrm{de}}$$

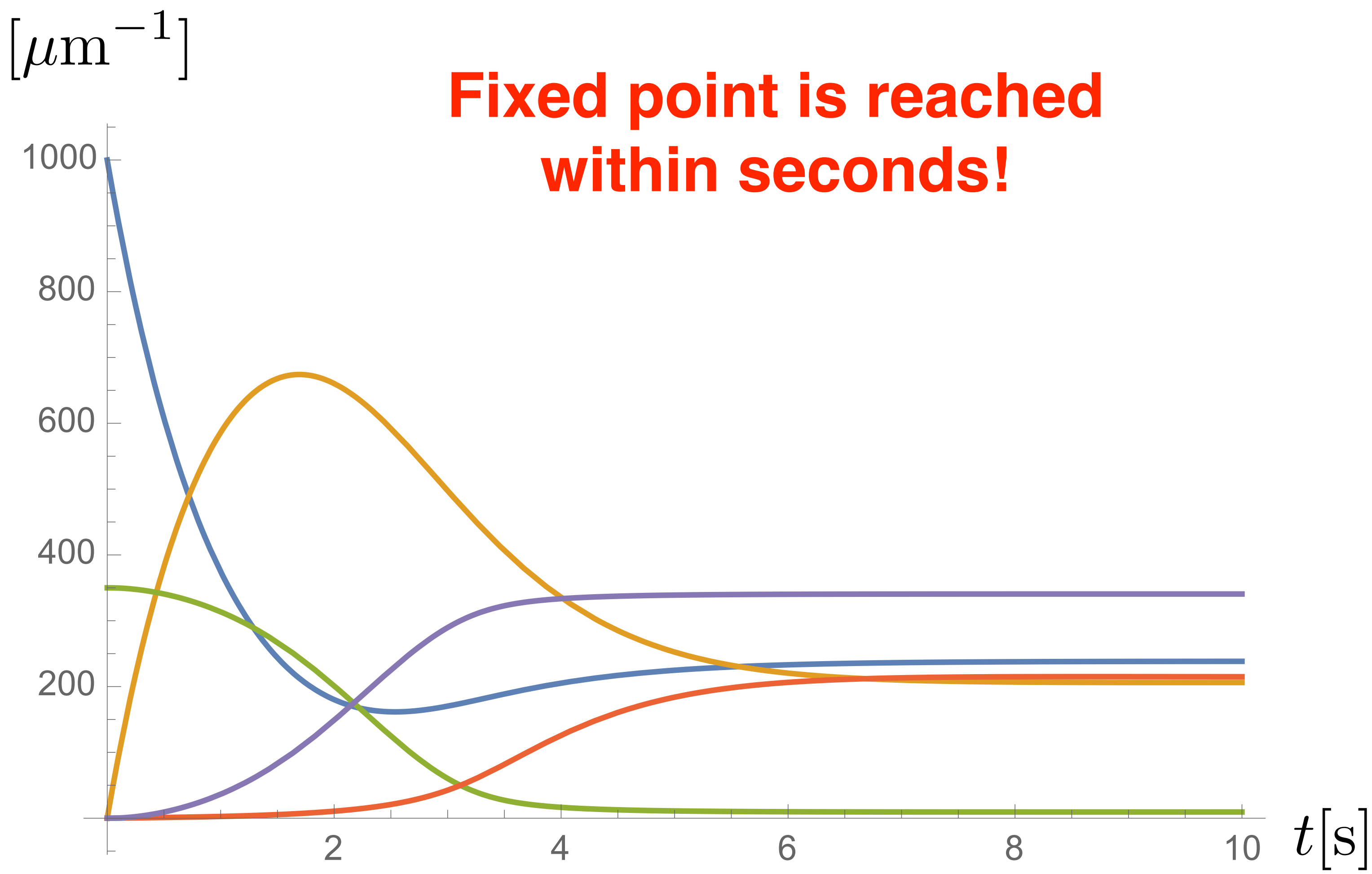
$$\boxed{\frac{\partial C_i(x,t)}{\partial t} = F_i\big(\{C_j(x,t)\}\big) + D_i \frac{\partial^2 C_i(x,t)}{\partial x^2}}$$

Stable fixed point for uniformly distributed concentrations

$$\frac{\partial C_i(x,t)}{\partial t} = F_i\big(\{C_j(x,t)\}\big) + D_i \frac{\partial^2 C_i(x,t)}{\partial x^2}$$

First let us assume that concentration profiles are independent of *x* and find stable fixed point concentrations.

$$\boxed{F_i\big(\{C_j^*\}\big) = 0}$$



Fixed point is reached within seconds!

$C^*_{\mathrm{D:ADP}} \approx 240\mu\mathrm{m}^{-1}$

$C^*_{\mathrm{D:ATP}} \approx 210\mu\mathrm{m}^{-1}$

$C^*_{\mathrm{E}} \approx 10\mu\mathrm{m}^{-1}$

$C^*_{\mathrm{d}} \approx 210\mu\mathrm{m}^{-1}$

$C^*_{\mathrm{de}} \approx 340\mu\mathrm{m}^{-1}$

Linear stability analysis of fixed point

$$\frac{\partial C_i(x,t)}{\partial t} = F_i\big(\,\{C_j(x,t)\}\,\big) + D_i \frac{\partial^2 C_i(x,t)}{\partial x^2}$$

Let's assume small perturbations around the fixed point

$$c_i(x,t) = C_i(x,t) - C_i^*$$

and linearize the PDE

$$\boxed{\frac{\partial c_i(x,t)}{\partial t} = \sum_j M^0_{ij} c_j(x,t) + D_i \frac{\partial^2 c_i(x,t)}{\partial x^2}}$$

$$M^0_{ij} = \frac{\partial F_i}{\partial C_j}\bigg|_{C^*} = \begin{pmatrix} -\sigma_D^{\mathrm{ADP}\to\mathrm{ATP}}, & 0, & 0, & 0, & \sigma_{de} \\ +\sigma_D^{\mathrm{ADP}\to\mathrm{ATP}}, & -\sigma_D - \sigma_{dD}\left(C^*_{\mathrm{d}} + C^*_{\mathrm{de}}\right), & 0, & -\sigma_{dD} C^*_{\mathrm{D:ATP}}, & -\sigma_{dD} C^*_{\mathrm{D:ATP}} \\ 0, & 0, & -\sigma_E C^*_{\mathrm{d}} & -\sigma_E C^*_{\mathrm{E}}, & \sigma_{de} \\ 0, & \sigma_D + \sigma_{dD}\left(C^*_{\mathrm{d}} + C^*_{\mathrm{de}}\right), & -\sigma_E C^*_{\mathrm{d}}, & \sigma_{dD} C^*_{\mathrm{D:ATP}} - \sigma_E C^*_{\mathrm{E}}, & \sigma_{dD} C^*_{\mathrm{D:ATP}} \\ 0, & 0, & \sigma_E C^*_{\mathrm{d}}, & \sigma_E C^*_{\mathrm{E}}, & -\sigma_{de} \end{pmatrix}$$

Linear stability analysis of fixed point

$$\frac{\partial c_i(x,t)}{\partial t} = \sum_j M^0_{ij} c_j(x,t) + D_i \frac{\partial^2 c_i(x,t)}{\partial x^2}$$

It is convenient to analyze this PDE in Fourier space, but note that only $\cos(kx)$ modes are consistent with boundary conditions.

Boundary conditions also restrict the values for wavenumber *k*

$$\frac{\partial c_i}{\partial x}(x=0,t) = \frac{\partial c_i}{\partial x}(x=L,t) = 0 \longrightarrow \boxed{k = \frac{n\pi}{L}, \quad n = 0, 1, 2, \cdots}$$

Let's rewrite the PDE in Fourier space

$$c_i(x,t) = \sum_k \tilde{c}_i(k,t)\cos(kx)$$

$$\boxed{\frac{\partial \tilde{c}_i(k,t)}{\partial t} = \sum_j M^0_{ij}\tilde{c}_j(k,t) - D_i k^2 \tilde{c}_i(k,t) = \sum_j M_{ij}(k)\tilde{c}_j(k,t)}$$

Note: in higher dimensions use solutions of Helmholtz equation with appropriate boundary conditions $u(\vec{r}) = -k^2\nabla^2 u(\vec{r})$

Linear stability analysis of fixed point

$$\frac{\partial \tilde{c}_i(k,t)}{\partial t} = \sum_j M^0_{ij}\tilde{c}_j(k,t) - D_i k^2 \tilde{c}_i(k,t) = \sum_j M_{ij}(k)\tilde{c}_j(k,t)$$

From linear algebra we know that the solution of this equation can be expressed in terms of eigenvalues and eigenvectors of matrix *$M_{ij}(k)$*:

$$\boxed{\tilde{c}_i(k,t) = \sum_\alpha A_\alpha(k) v_i^\alpha(k) e^{\lambda_\alpha(k)t}}$$

$$\lambda_\alpha v_i^\alpha = \sum_j M_{ij}(k) v_j^\alpha$$

Thus small perturbations from fixed point evolve as

$$\boxed{c_i(x,t) = \sum_{\alpha,k} A_\alpha(k) v_i^\alpha(k) e^{\lambda_\alpha(k)t}\cos(kx)}$$

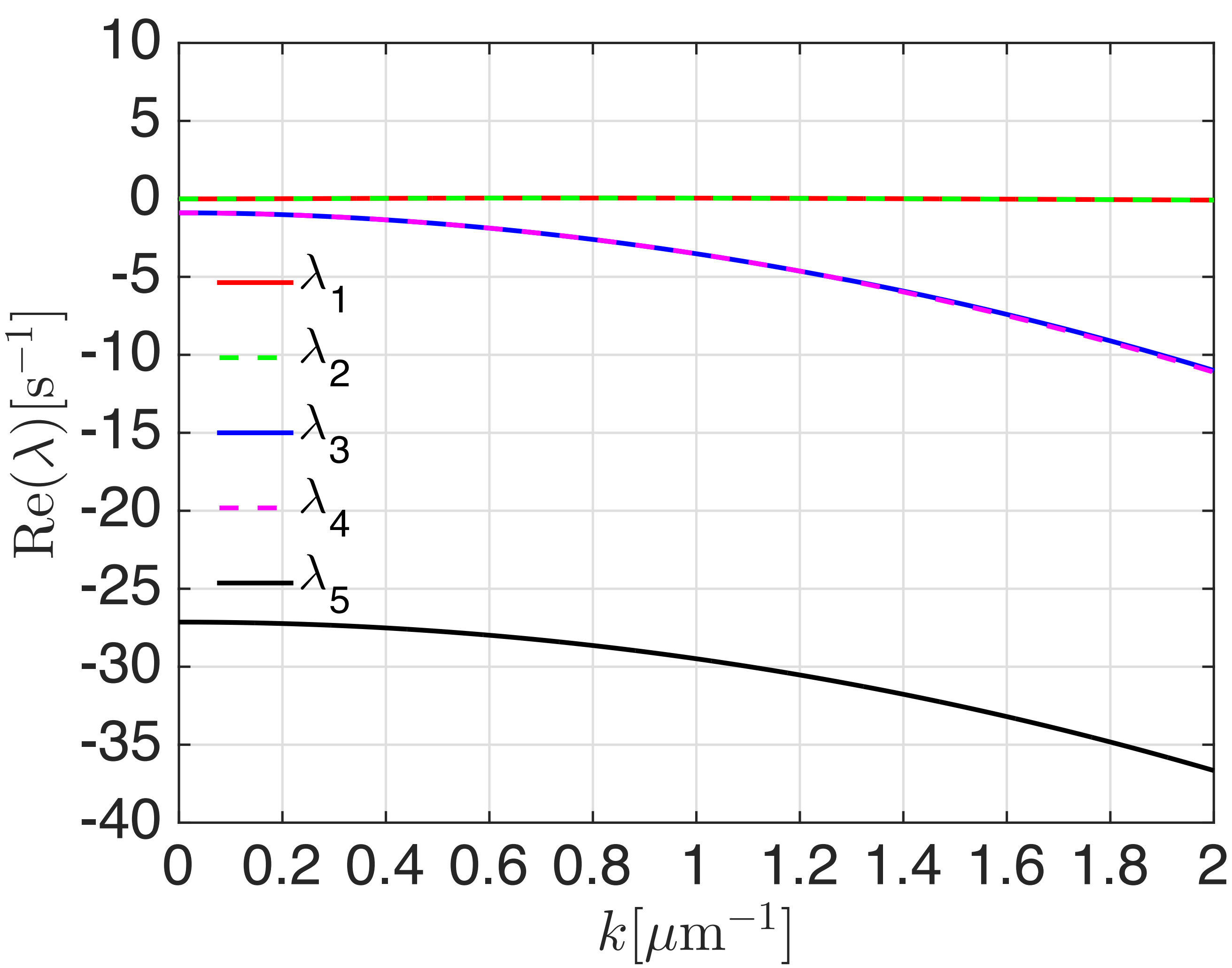
Fixed point is stable if and only if all eigenvalues have negative real parts for all allowed wavenumbers *k*!

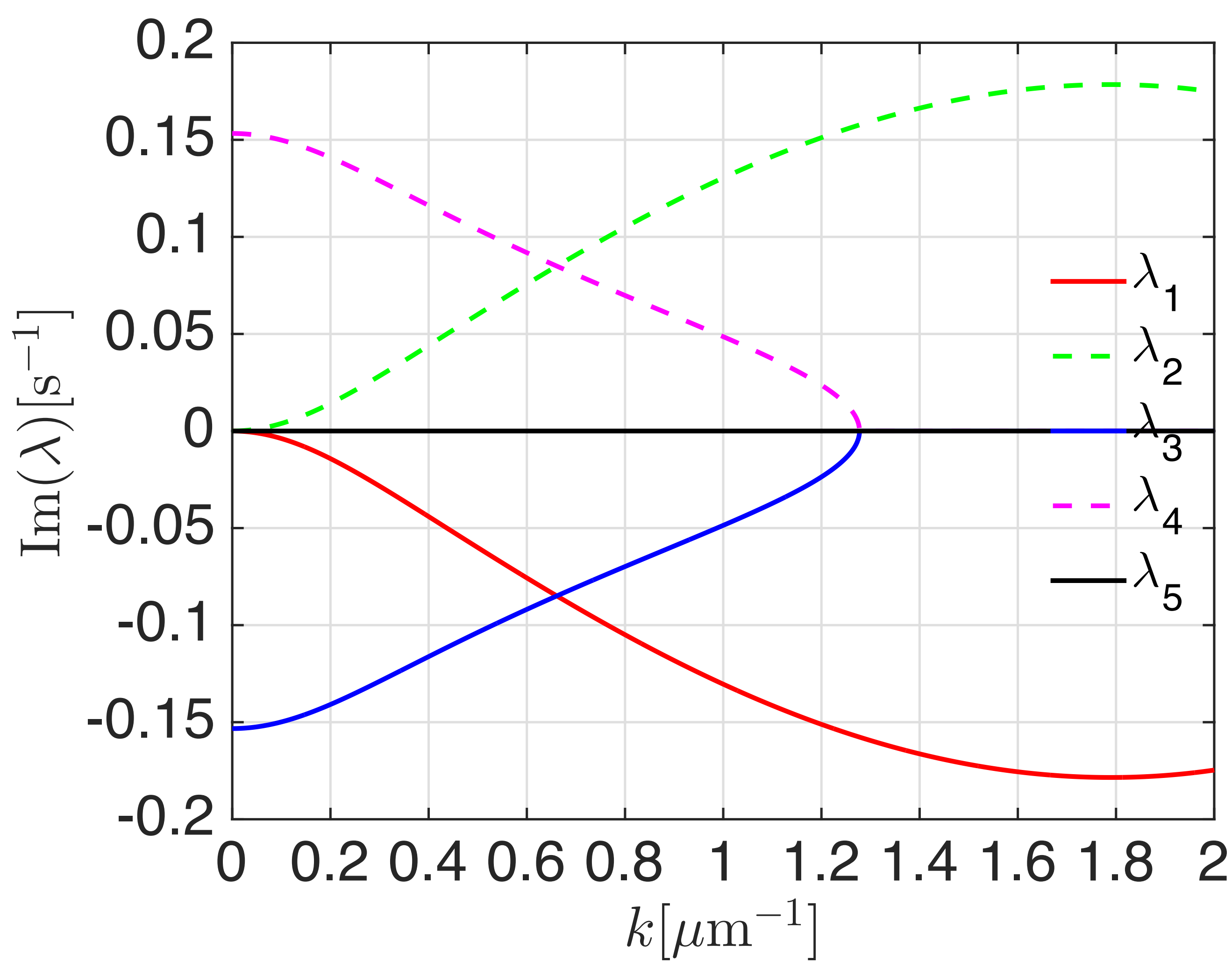
$$\mathrm{Re}\left[\lambda_\alpha(k)\right] < 0$$

For unstable fixed points the mode that corresponds to the eigenvalue with the largest real part dominates!

Eigenvalues in the model Min system

$$M_{ij}(k) = \begin{pmatrix} -\sigma_D^{\mathrm{ADP}\to\mathrm{ATP}} - D_D k^2, & 0, & 0, & 0, & \sigma_{de} \\ +\sigma_D^{\mathrm{ADP}\to\mathrm{ATP}}, & -\sigma_D - \sigma_{dD}\left(C^*_{\mathrm{d}} + C^*_{\mathrm{de}}\right) - D_D k^2, & 0, & -\sigma_{dD} C^*_{\mathrm{D:ATP}}, & -\sigma_{dD} C^*_{\mathrm{D:ATP}} \\ 0, & 0, & -\sigma_E C^*_{\mathrm{d}} - D_E k^2, & -\sigma_E C^*_{\mathrm{E}}, & \sigma_{de} \\ 0, & \sigma_D + \sigma_{dD}\left(C^*_{\mathrm{d}} + C^*_{\mathrm{de}}\right), & -\sigma_E C^*_{\mathrm{d}}, & \sigma_{dD} C^*_{\mathrm{D:ATP}} - \sigma_E C^*_{\mathrm{E}}, & \sigma_{dD} C^*_{\mathrm{D:ATP}} \\ 0, & 0, & \sigma_E C^*_{\mathrm{d}}, & \sigma_E C^*_{\mathrm{E}}, & -\sigma_{de} \end{pmatrix}$$



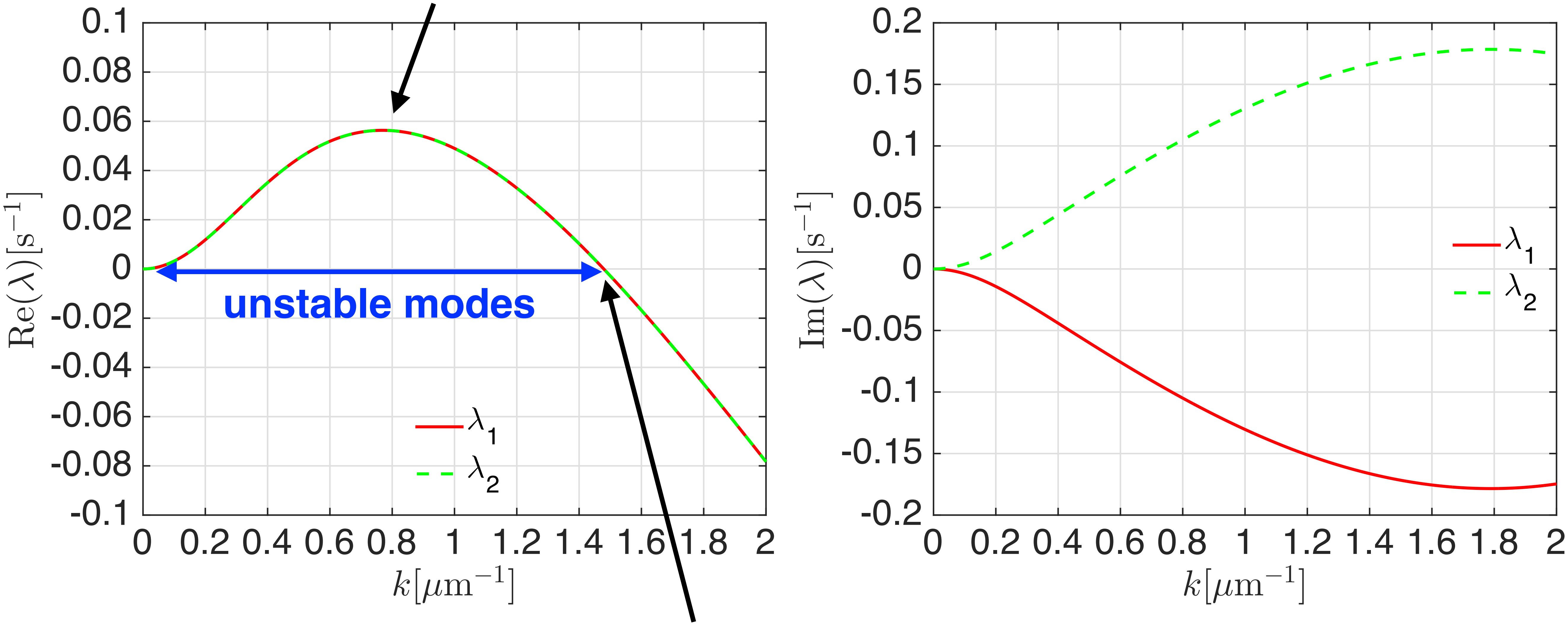


Eigenvalues in the model Min system

wavelength of the most unstable mode

$k_{\rm max} \approx 0.8\mu{\rm m}^{-1}$

$2\pi/k_{\rm max} \approx 8.2\mu{\rm m}^{-1}$



Note that only discrete set of wavenumber is allowed!

$$k = \frac{n\pi}{L}, \quad n = 0, 1, 2, \cdots$$

For bacteria that is shorter than

$$L < (\pi/1.5)\mu{\rm m} \approx 2.1\mu{\rm m}$$

fixed point is stable and there are no oscillations!

For E.coli with $L \approx 4\mu{\rm m}$

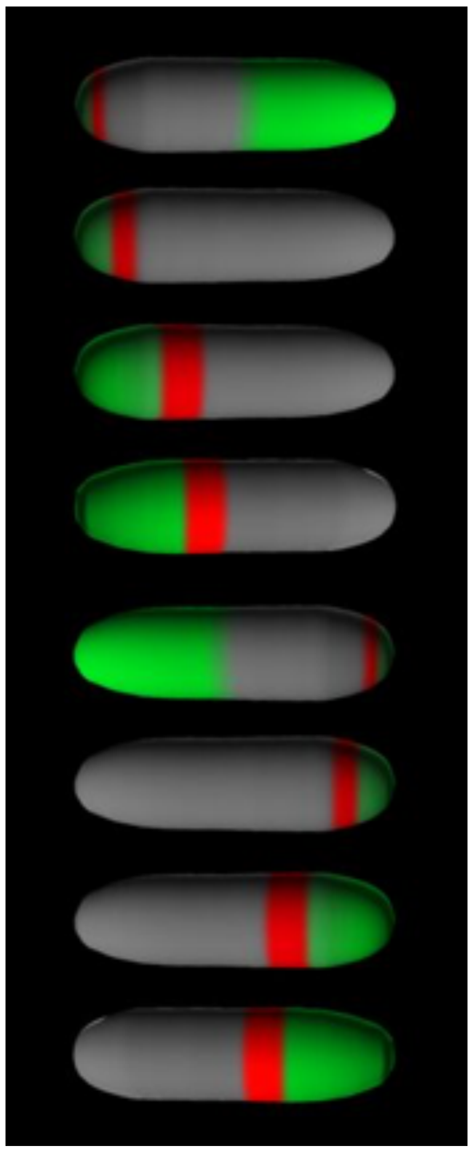
$$k = \pi/L \approx 0.8\mu{\rm m}$$

$$\lambda_{1,2} \approx (0.06 \pm i0.10){\rm s}^{-1}$$

Period of oscillations

$$(2\pi/0.010){\rm s} \approx 60{\rm s}$$

Oscillations in the model Min system

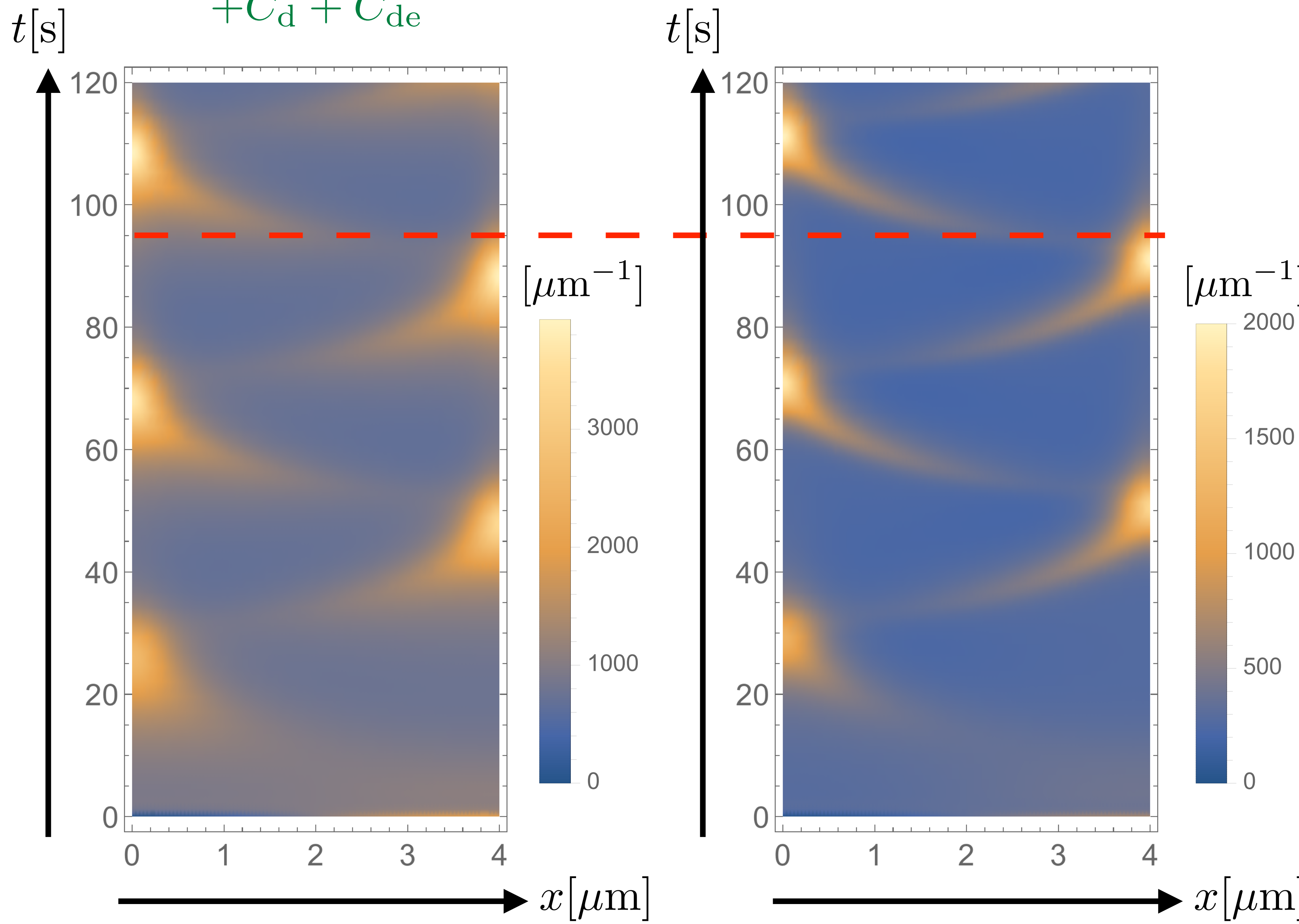


Tot MinD

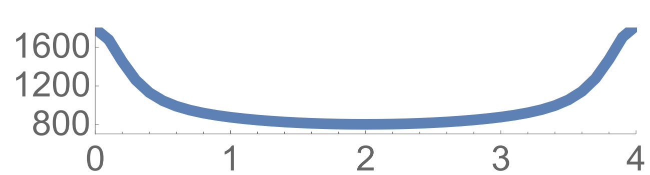
$C_{\mathrm{D:ADP}} + C_{\mathrm{D:ATP}}$
$+ C_{\mathrm{d}} + C_{\mathrm{de}}$

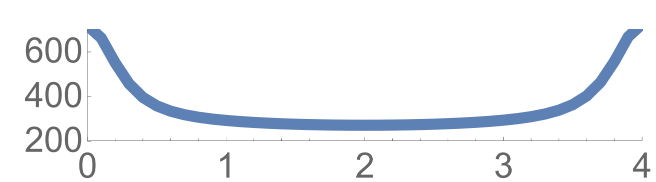
Tot MinE

$C_{\mathrm{E}} + C_{\mathrm{de}}$



time averaged concentrations

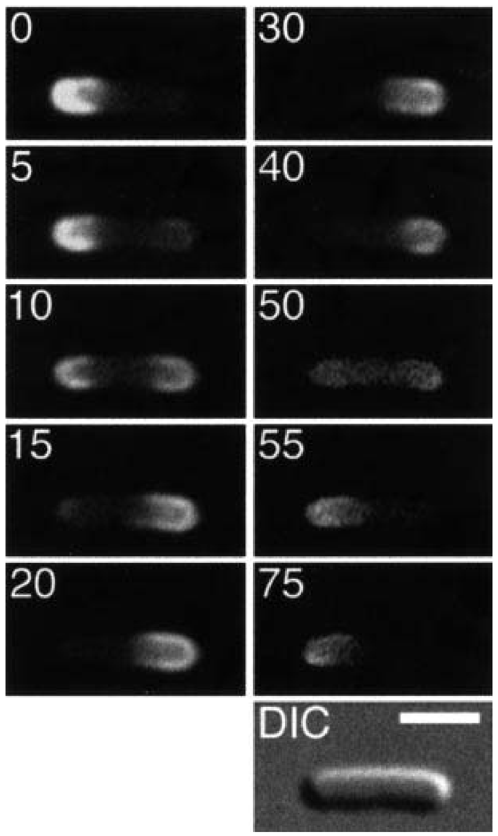




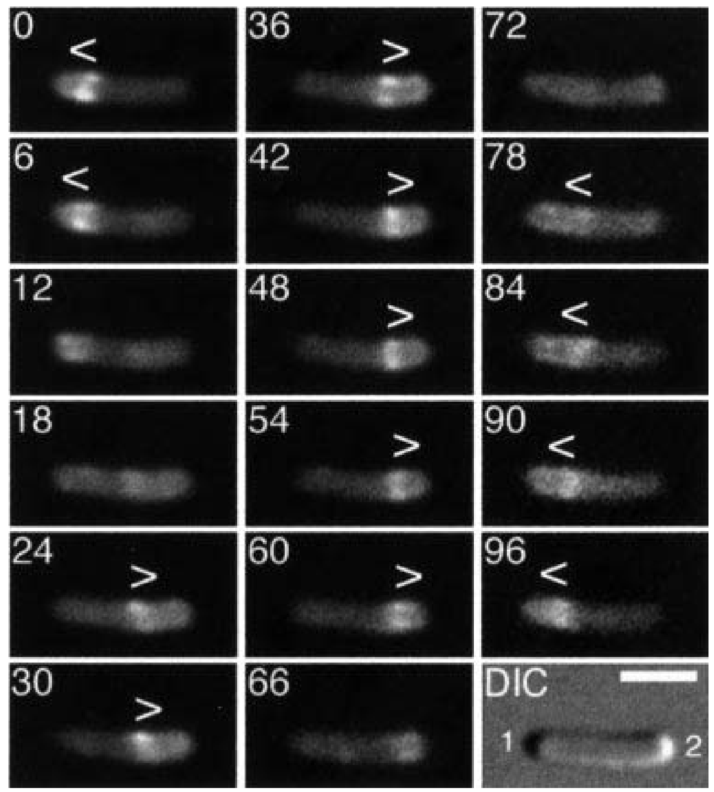
Min system oscillations in larger cells

C.A. Hale *et al.*, EMBO 20, 1563 (2001)

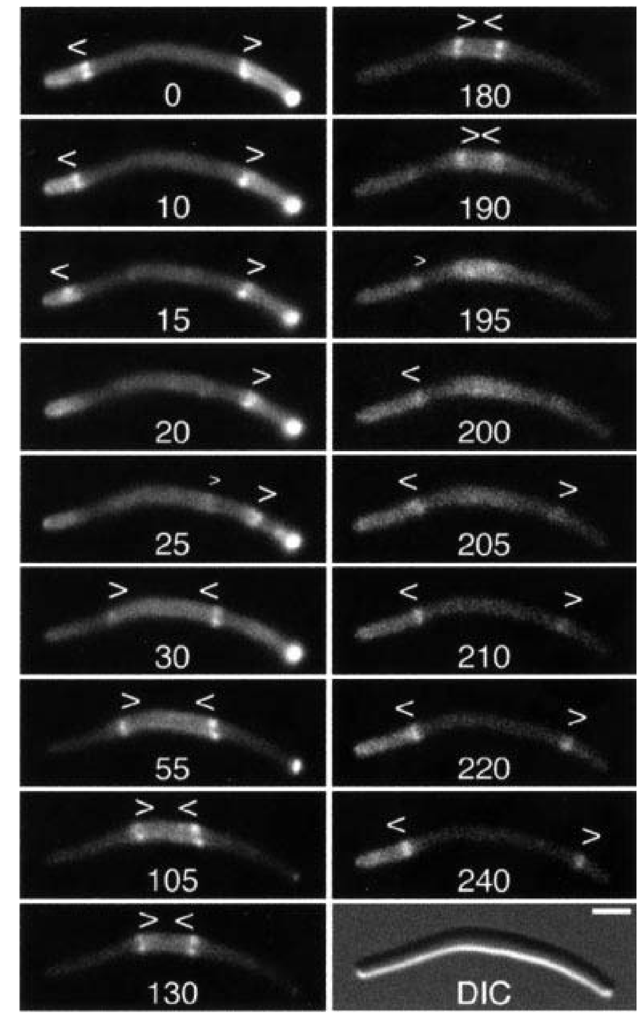
MinD



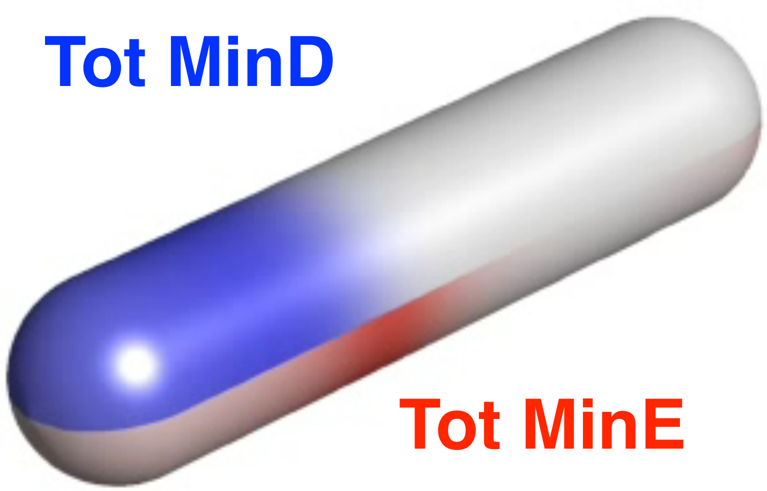
MinE



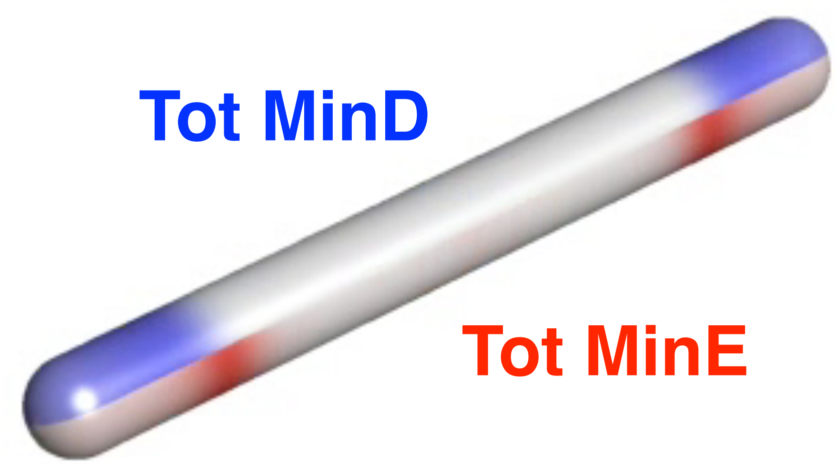
MinE



http://mesord.sourceforge.net



$L = 4\mu\text{m}$

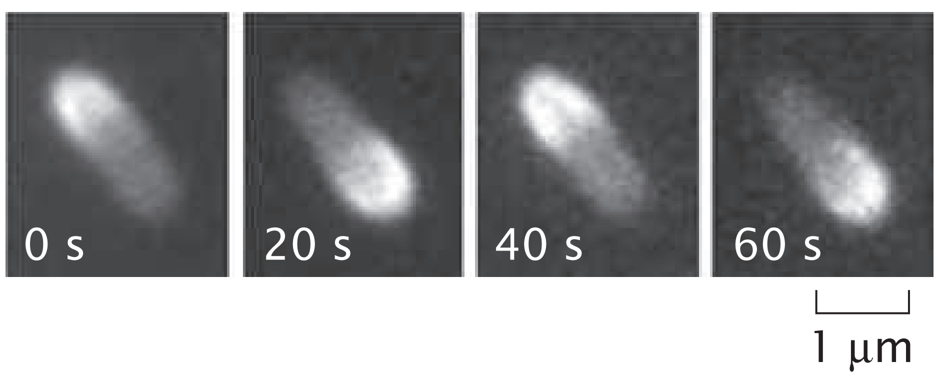


$L = 10\mu\text{m}$

Min system oscillations in large cells

MinD oscillations in normal E. Coli

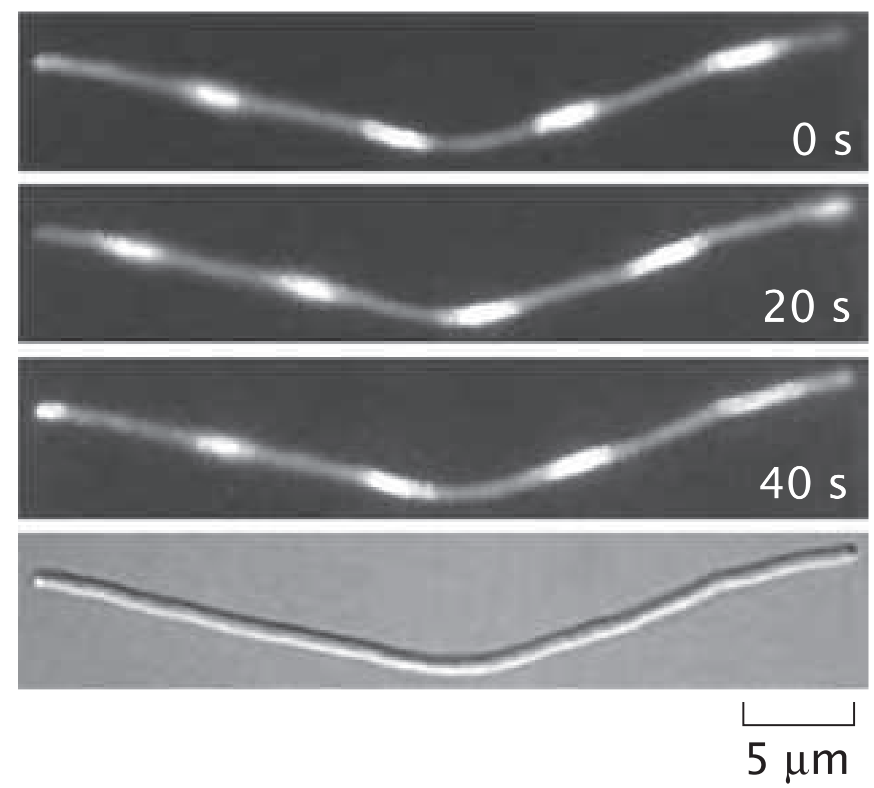
(A)



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

MinD oscillations in E. Coli, where division is prevented by removing FtsZ

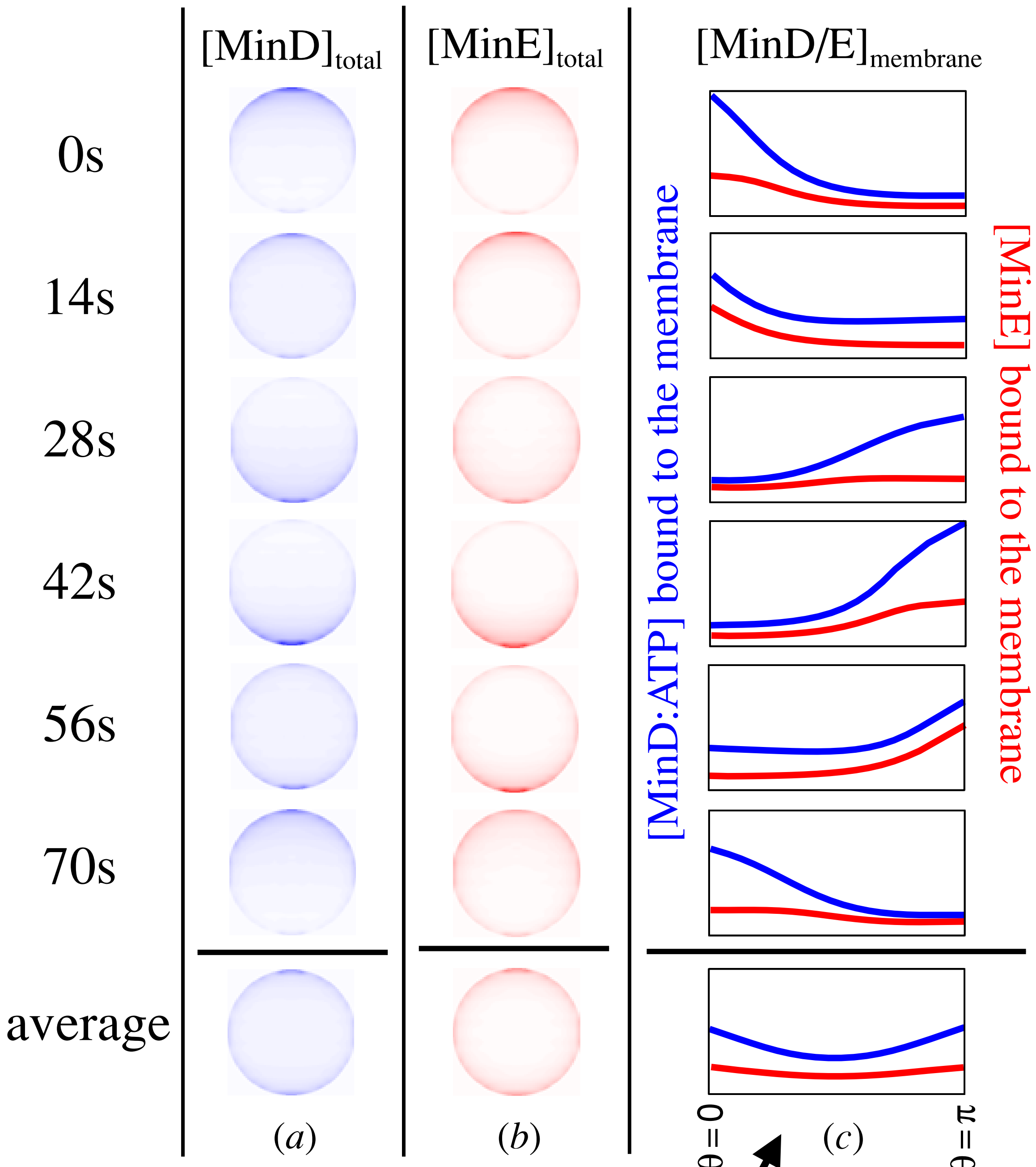
(B)



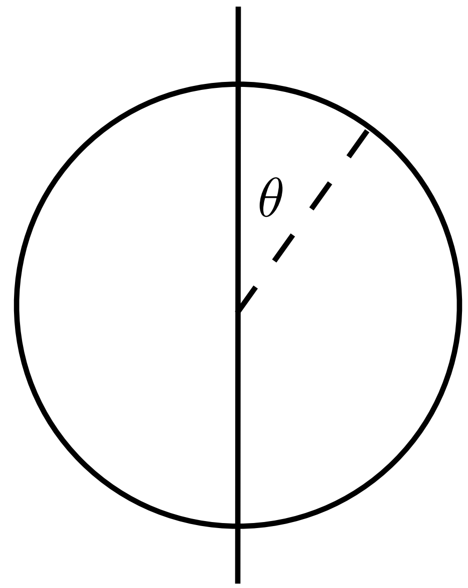
Can the same mechanism work for spherical bacteria?

Min system oscillations in spherical bacteria

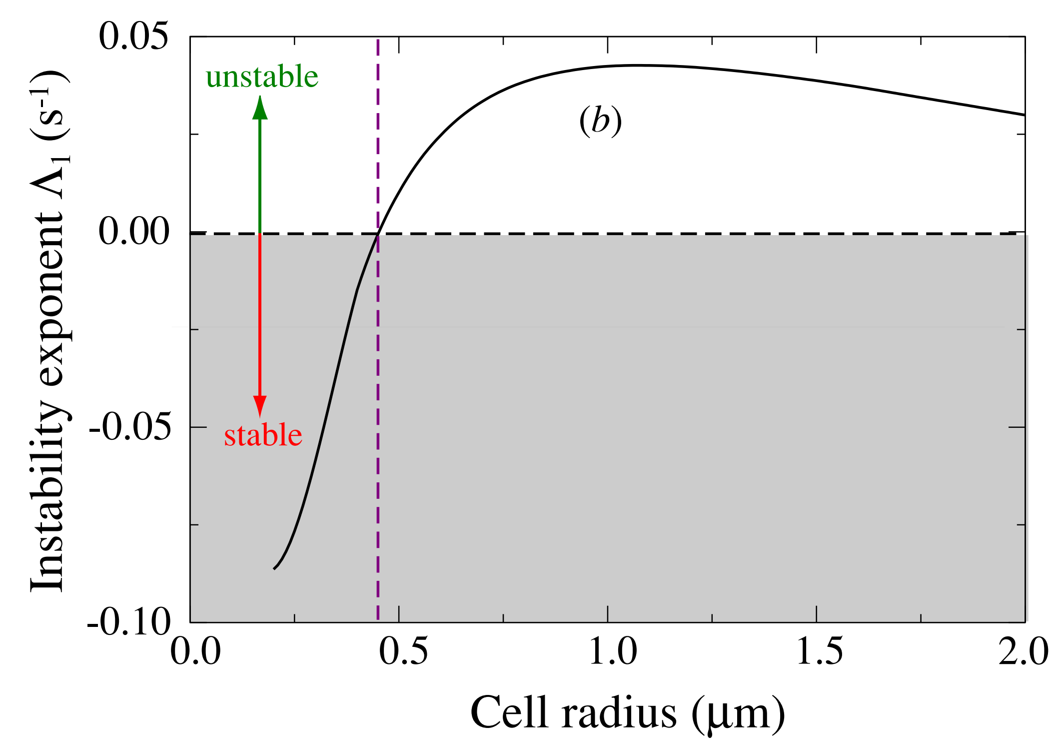
no MinE ring



Min oscillations can identify midline

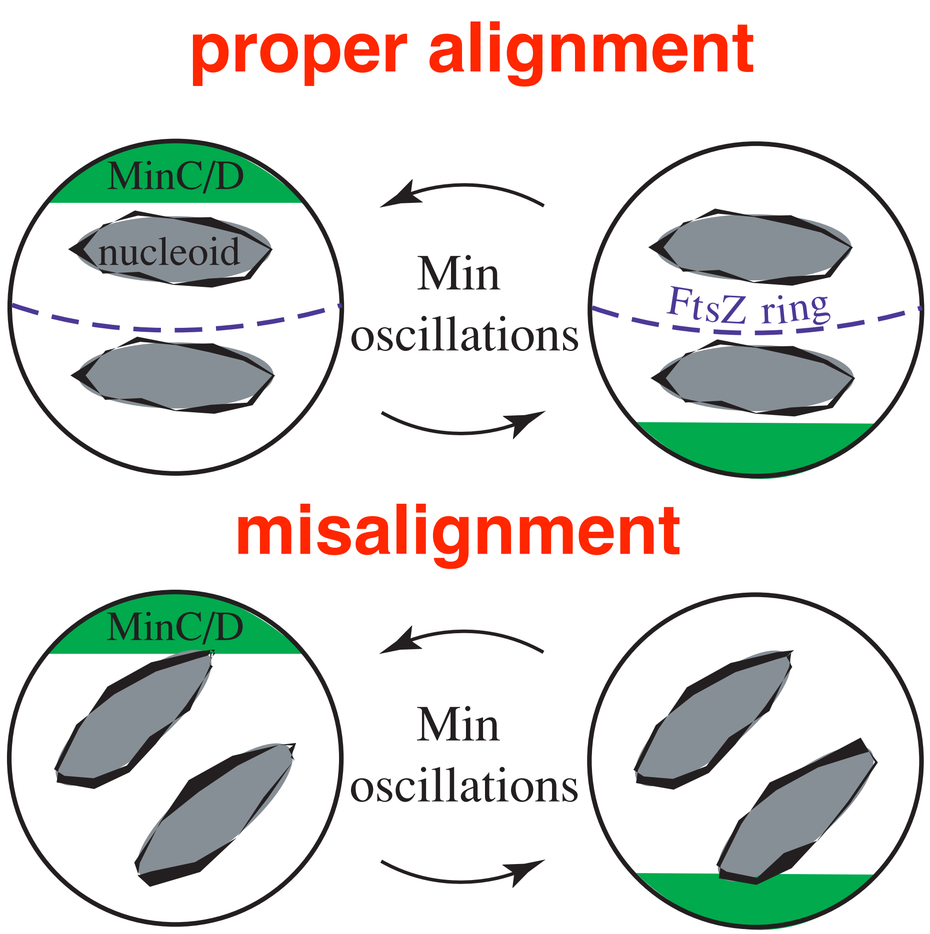


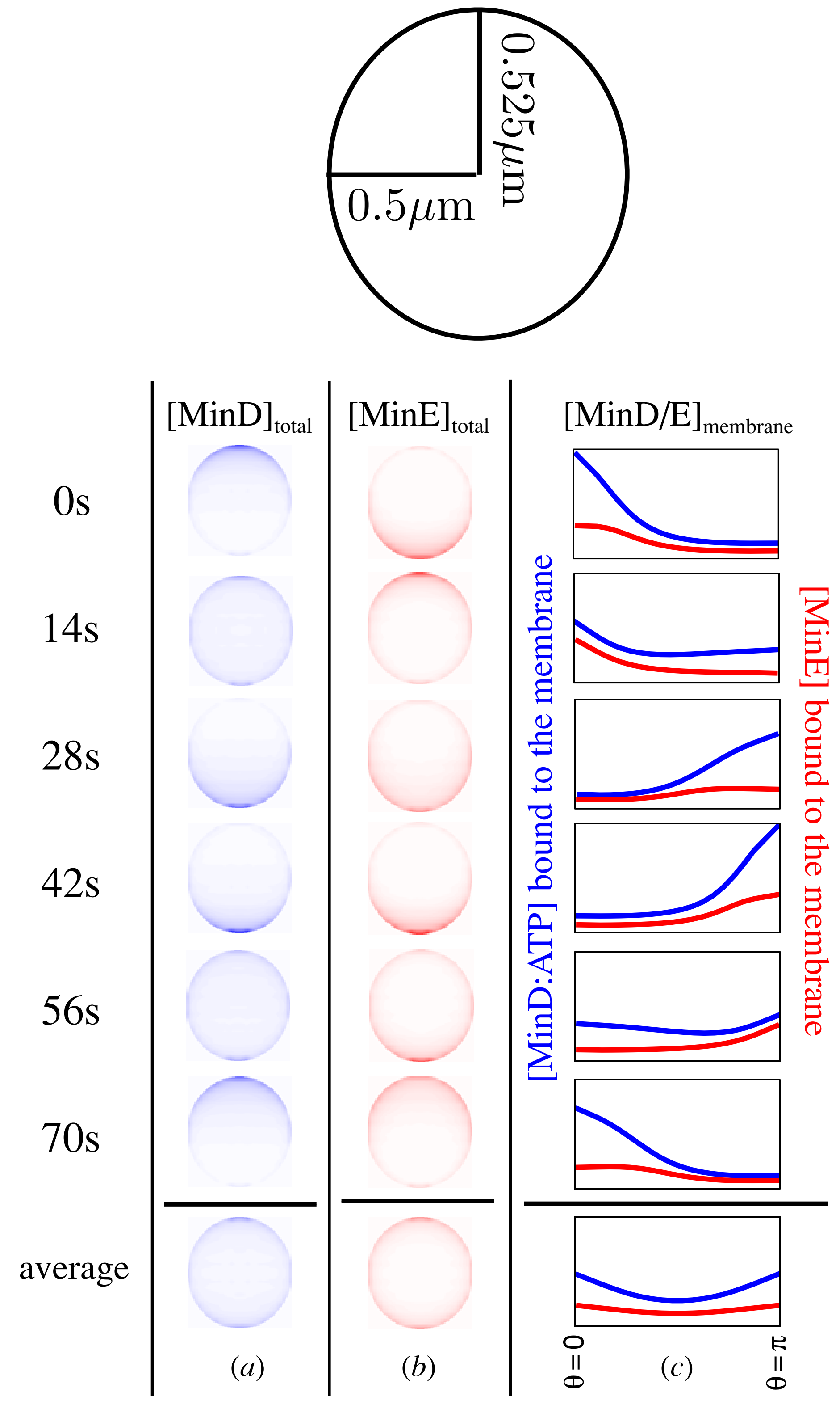
Oscillations possible only for sufficiently large cells



K.C. Huang and N.S. Wingreen, Phys. Biol. 1, 229 (2004)

Finding midline is not enough to divide properly in spherical bacteria

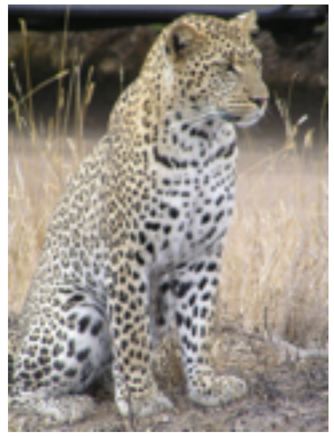




Slight deformation of the cell due to chromosomes could be enough to properly align Min oscillations

Patterns in nature

zebra



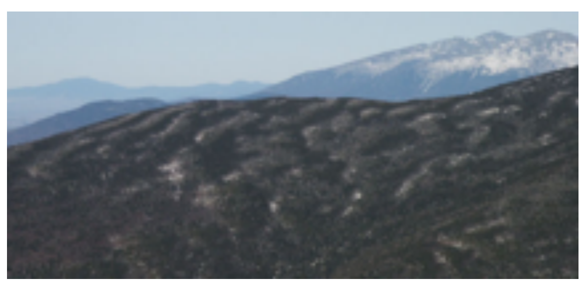
leopard

royal angelfish

peacock

giant pufferfish

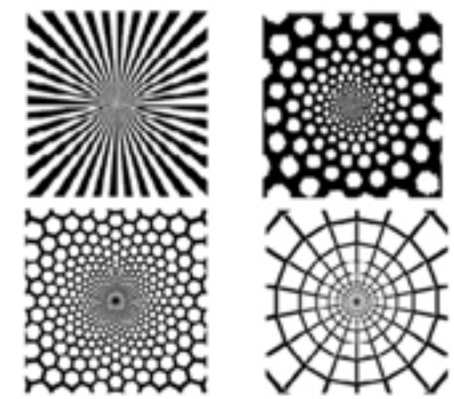
tiger bush



fir waves

mussels

clouds



hallucination patterns

1952: Alan Turing wrote “The Chemical Basis of Morphogenesis”

Many of these patterns can be constructed with reaction-diffusion models.

What are the minimal requirements that produce such patterns?

Reaction-diffusion equations

$$\frac{\partial C_i(\vec{r},t)}{\partial t} = F_i\left(\{C_j(\vec{r},t)\}\right) + D_i \nabla^2 C_i(\vec{r},t)$$

$i = 1, 2, \cdots, N$ **N interacting components**

In the absence of diffusion find stable fixed points

$$F_i\left(\{C_j^*\}\right) = 0$$

Can diffusion destabilize such fixed points?

Linearize the PDE around the fixed point

$$c_i(\vec{r},t) = C_i(\vec{r},t) - C_i^*$$

$$\frac{\partial c_i(\vec{r},t)}{\partial t} = \sum_{j=1}^{N} M_{ij}^0 c_j(\vec{r},t) + D_i \nabla^2 c_i(\vec{r},t) \qquad M_{ij}^0 = \left.\frac{\partial F_i}{\partial C_j}\right|_{C^*}$$

$\Big\downarrow$ **Fourier transform**

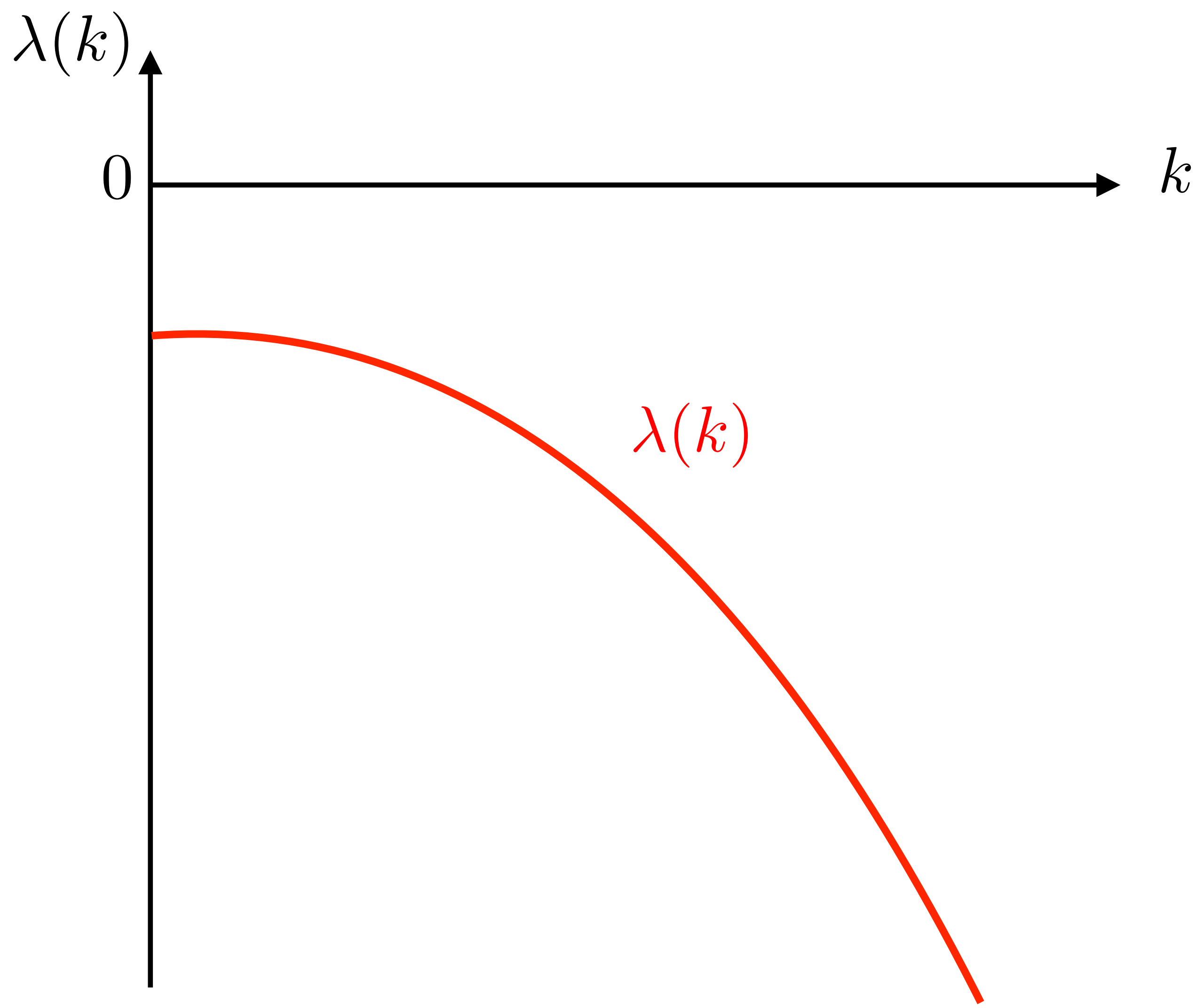
$$\frac{\partial \tilde{c}_i\left(\vec{k},t\right)}{\partial t} = \sum_{j=1}^{N} \left(M_{ij}^0 - \delta_{ij} k^2 D_i\right) \tilde{c}_j\left(\vec{k},t\right)$$

What are the eigenvalues for such system?

One component system (*N*=1)

$$\frac{\partial \tilde{c}_1\left(\vec{k},t\right)}{\partial t} = \left(M_{11}^0 - k^2 D_1\right)\tilde{c}_1\left(\vec{k},t\right) \equiv \lambda(k)\tilde{c}_1\left(\vec{k},t\right)$$

Because fixed point is stable in the absence of diffusion, we must have $M_{11} < 0$.



There are no diffusion induced instabilities for one component system!

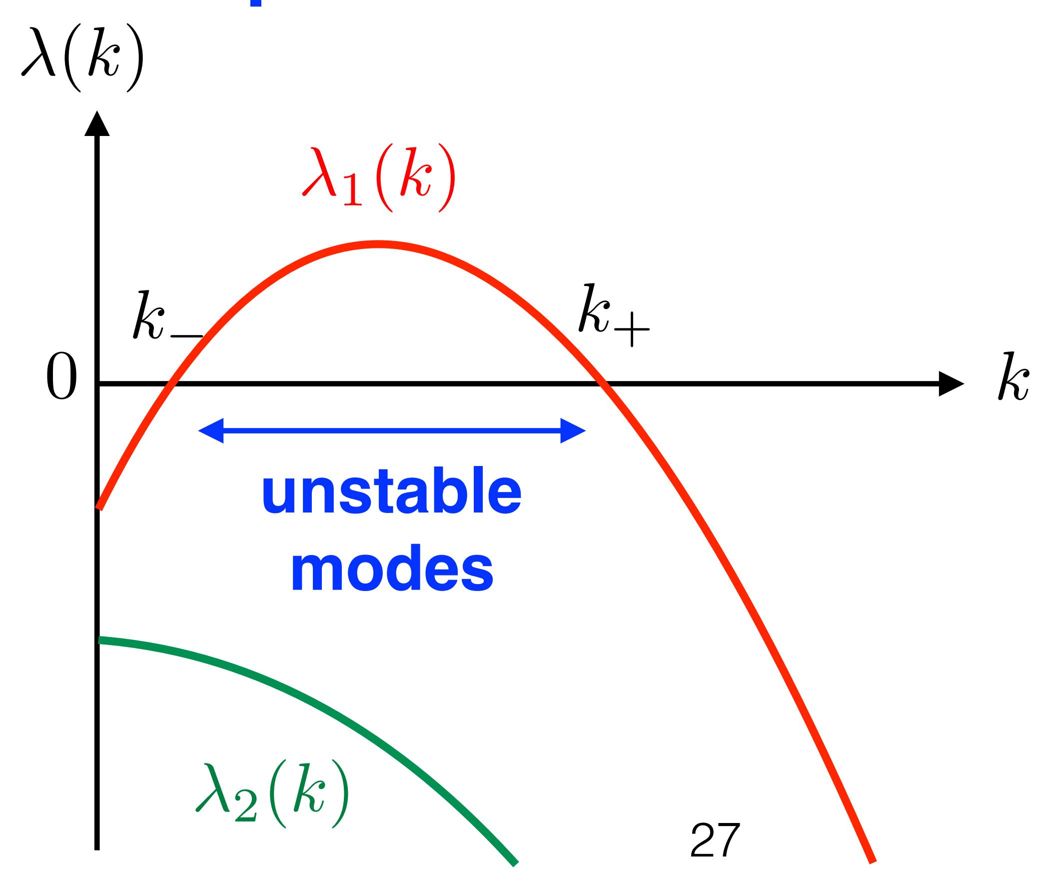
Two component system (N=2)

$$\frac{\partial}{\partial t}\begin{pmatrix} \tilde{c}_1(\vec{k},t) \\ \tilde{c}_2(\vec{k},t) \end{pmatrix} = \begin{pmatrix} M_{11}^0 - k^2 D_1, & M_{12}^0 \\ M_{21}^0, & M_{22}^0 - k^2 D_2 \end{pmatrix} \begin{pmatrix} \tilde{c}_1(\vec{k},t) \\ \tilde{c}_2(\vec{k},t) \end{pmatrix}$$

Relation between eigenvalues and trace of the matrix

$$\boxed{\begin{aligned} \lambda_1(0) + \lambda_2(0) &= M_{11}^0 + M_{22}^0 < 0 \\ \lambda_1(k) + \lambda_2(k) &= M_{11}^0 + M_{22}^0 - k^2(D_1 + D_2) < 0 \end{aligned}}$$

Therefore we must have one positive and one negative eigenvalue for Turing instability!
No temporal oscillations are possible!



What are the conditions for matrix M_{ij}^0 that lead to Turing instability?

Two component system (N=2)

$$\frac{\partial}{\partial t}\begin{pmatrix}\tilde{c}_1(\vec{k},t)\\ \tilde{c}_2(\vec{k},t)\end{pmatrix} = \begin{pmatrix} M_{11}^0 - k^2 D_1, & M_{12}^0 \\ M_{21}^0, & M_{22}^0 - k^2 D_2\end{pmatrix}\begin{pmatrix}\tilde{c}_1(\vec{k},t)\\ \tilde{c}_2(\vec{k},t)\end{pmatrix}$$

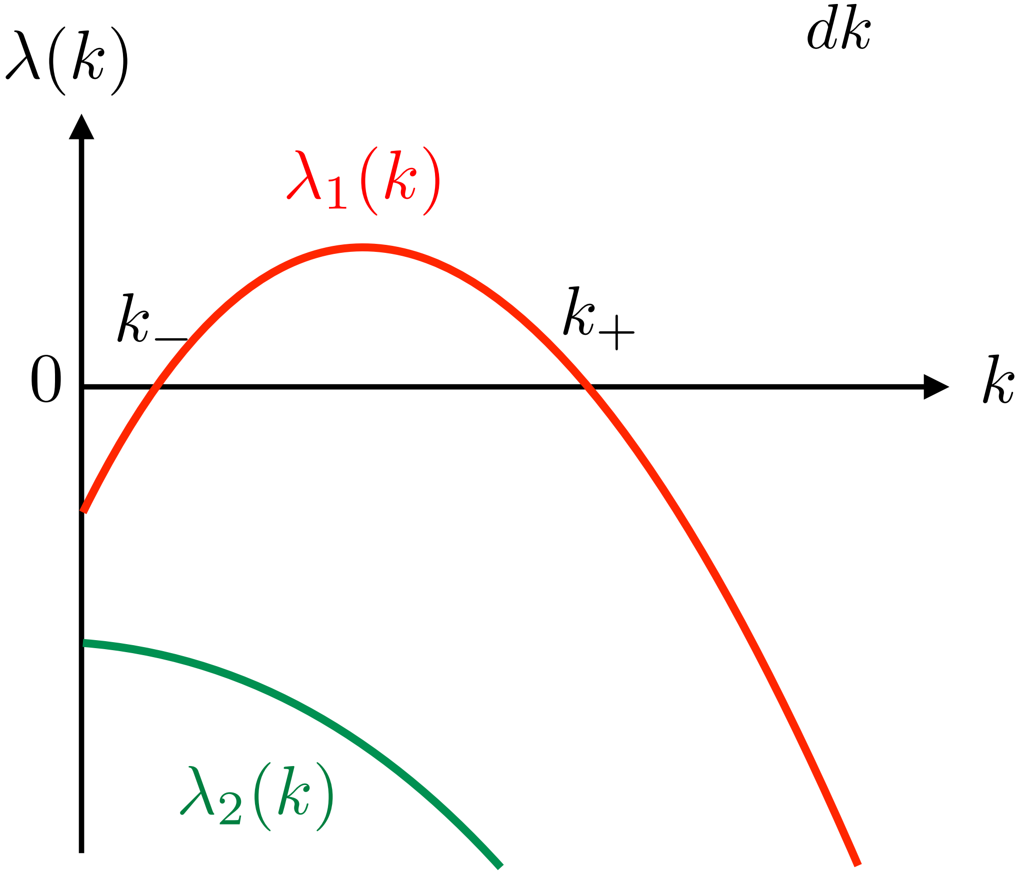
Relation between eigenvalues and determinant of the matrix

$$\lambda_1(k)\lambda_2(k) = (M_{11}^0 - k^2 D_1)(M_{22}^0 - k^2 D_2) - M_{12}^0 M_{21}^0$$

$$\lambda_1(k)\lambda_2(k) = M_{11}^0 M_{22}^0 - M_{12}^0 M_{21}^0 - k^2(M_{11}^0 D_2 + M_{22}^0 D_1) + k^4 D_1 D_2$$

Determinant becomes negative and reaches minimal value at $k^* \in (k_-, k_+)$.

$$\frac{d(\lambda_1(k)\lambda_2(k))}{dk} = 0 \longrightarrow \boxed{k^{*2} = \frac{M_{11}^0 D_2 + M_{22}^0 D_1}{2D_1 D_2} > 0}$$



$$\Big\downarrow \; \lambda_1(0) + \lambda_2(0) < 0$$

$$\boxed{M_{11}^0 M_{22}^0 < 0}$$

$$\Big\downarrow \; \lambda_1(0)\lambda_2(0) > 0$$

$$\boxed{M_{12}^0 M_{21}^0 < 0}$$

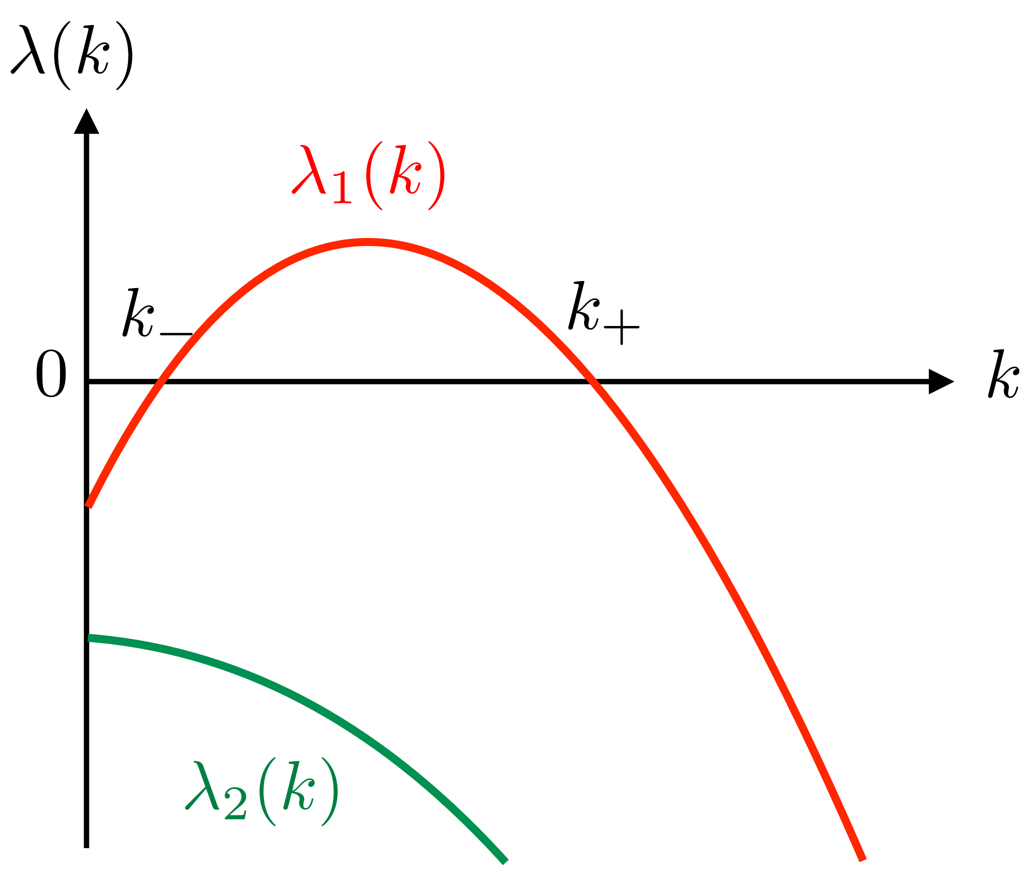
Two component system (N=2)

$$\frac{\partial}{\partial t}\begin{pmatrix}\tilde{c}_1(\vec{k},t)\\ \tilde{c}_2(\vec{k},t)\end{pmatrix}=\begin{pmatrix}M_{11}^0-k^2D_1, & M_{12}^0\\ M_{21}^0, & M_{22}^0-k^2D_2\end{pmatrix}\begin{pmatrix}\tilde{c}_1(\vec{k},t)\\ \tilde{c}_2(\vec{k},t)\end{pmatrix}$$

Without loss of generality we can assume $M_{11}^0<0$ **,** $M_{22}^0>0$

$$M_{11}^0+M_{22}^0<0 \longrightarrow \boxed{|M_{11}^0|>|M_{22}^0|}$$

$$\frac{M_{11}^0D_2+M_{22}^0D_1}{2D_1D_2}>0 \longrightarrow \boxed{D_1>\frac{|M_{11}^0|}{|M_{22}^0|}D_2>D_2}$$



Finite wavelength Turing instabilities arise by long-ranged inhibition and short-range excitation. The resulting patterns are fixed in time.

In the system with 3 or more components oscillating patterns in time are also possible.