Patterns via diffusion: A general framework

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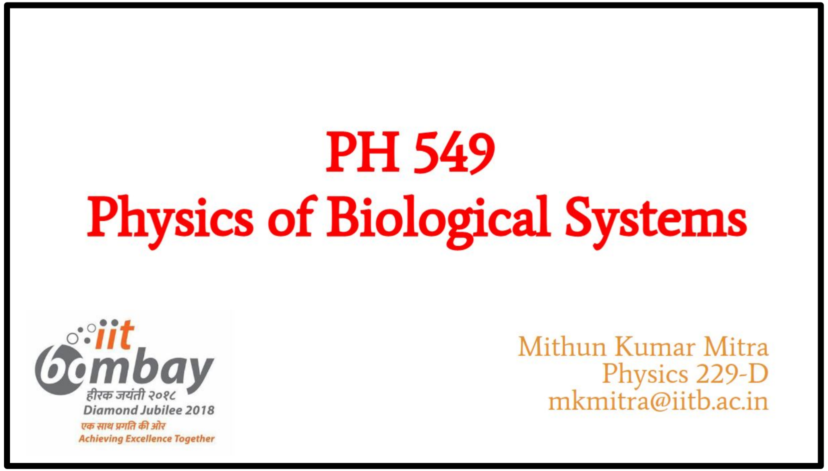
Workshop on Flags, Landscapes, and Signalling,

IMSc, 2024

"How can events in space and time which take place within the boundaries of a living organism, be accounted for by physics and chemistry?"

What is life? Erwin Schrodinger (1943)

Online lectures



https://bit.ly/physicsofbio

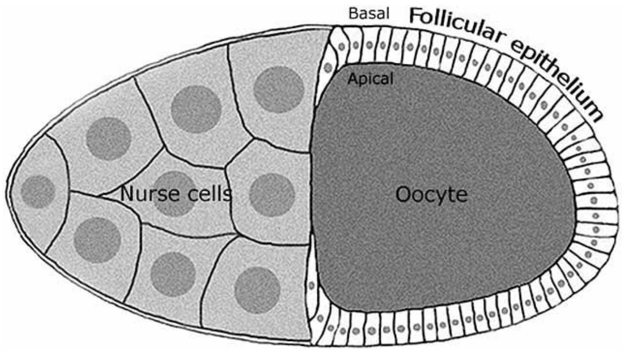
https://bit.ly/stochasticbio

Design / Patterns

Isotropic + homogenous single cell

Symmetry breaking

Positional information



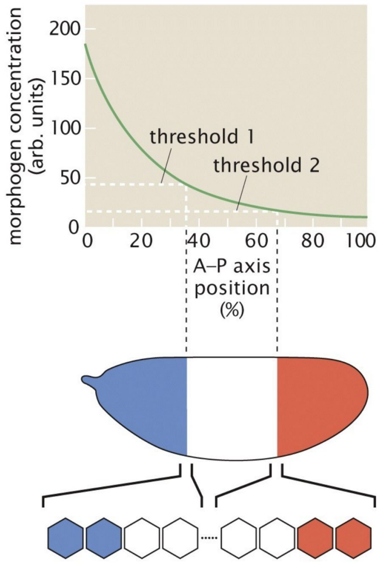


Figure 20.3 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

The minimal model

Reaction + Diffusion

Reactions occur with specific reactions rates. The reactants and products can also diffuse spatially. Together this can give rise to spatial patterns.

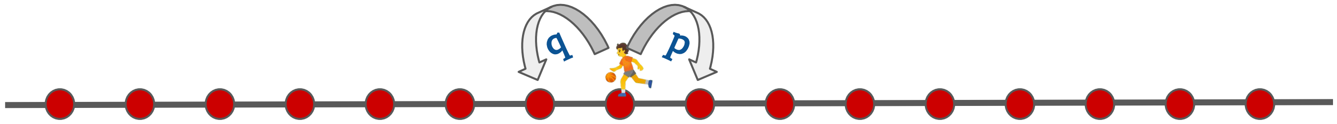
Gene regulatory networks

Feedback loops of proteins

Motion of proteins / morphogens

The Statistical Mechanics of Random Walks

Microscopic particle description $\longrightarrow$ Probabilistic macroscopic description



Microscopic $\quad x(t+\Delta t) = x(t) + l(t) \qquad P(l) = p\,\delta(l-\Delta x) + q\,\delta(l+\Delta x)$

Macroscopic $\quad P(x,t) = p\,P(x-\Delta x, t-\Delta t) + q\,P(x+\Delta x, t-\Delta t)$

Continuum Limit

$p = q$

$$\frac{\partial P(x,t)}{\partial t} = D\frac{\partial^2 P(x,t)}{\partial x^2}$$

$p \neq q$

$$\frac{\partial P(x,t)}{\partial t} = -v\frac{\partial P(x,t)}{\partial x} + D\frac{\partial^2 P(x,t)}{\partial x^2}$$

The Statistical Mechanics of Random Walks

Microscopic particle description $\longrightarrow$ Probabilistic macroscopic description

Random Walks $\longrightarrow$ Diffusion equation

$$\frac{\partial P(x,t)}{\partial t} = D\frac{\partial^2 P(x,t)}{\partial x^2}$$

$$P(x,t) = \frac{1}{\sqrt{4\pi Dt}}e^{-\frac{x^2}{4Dt}}$$

$$\langle x(t)\rangle = \int xP(x,t)dx = 0$$

$$\langle x^2(t)\rangle = \int x^2P(x,t)dx = 2Dt$$

UNIVERSALITY

$$\langle x^2(t)\rangle \propto t^1$$

The Statistical Mechanics of Random Walks

An entropic approach

$$P(x,t) = \frac{\Omega(x,t)}{\int \Omega(x,t)\, dx}$$

$$\Omega(x,t) = \Omega(n_R, N) = \frac{N!}{n_R!(N-n_R)!}$$

$$P(x,t) = \frac{1}{2^N} \frac{N!}{(\frac{N}{2} + \frac{x}{2\Delta x})!(\frac{N}{2} - \frac{x}{2\Delta x})!}$$

$$n_R + n_L = N = T/\Delta t$$

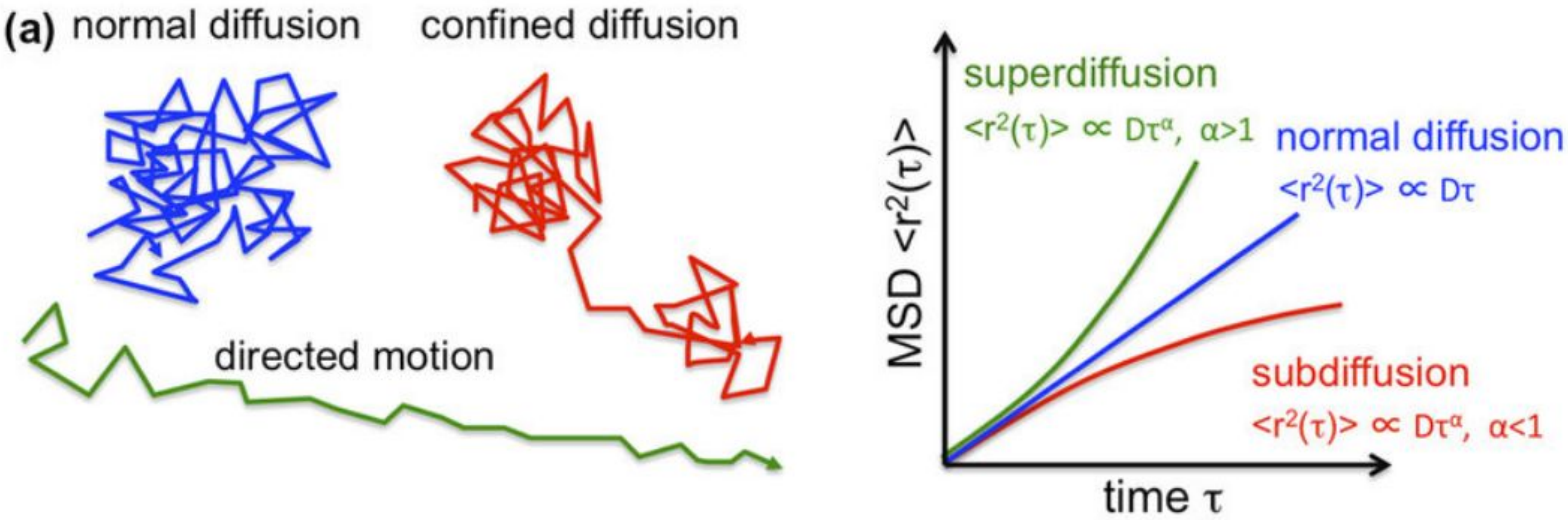
$$(n_R - n_L)\Delta x = x$$

$\downarrow$ Stirling's approx.

$$P(x,t) = \frac{1}{\sqrt{2\pi N \Delta x^2}} e^{-\frac{x^2}{2N\Delta x^2}} = \frac{1}{\sqrt{4\pi D t}} e^{-\frac{x^2}{4Dt}}$$

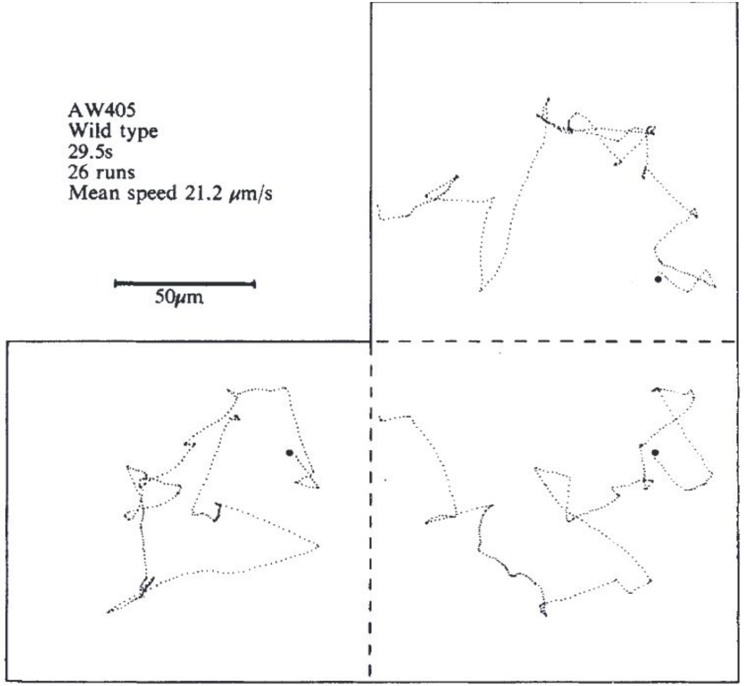
CLT: The probability distribution of the sum of N i.i.d. random variables converges to a gaussian as N → ∞, if the mean and variance of each individual random variable is finite.

Random Walks in biology

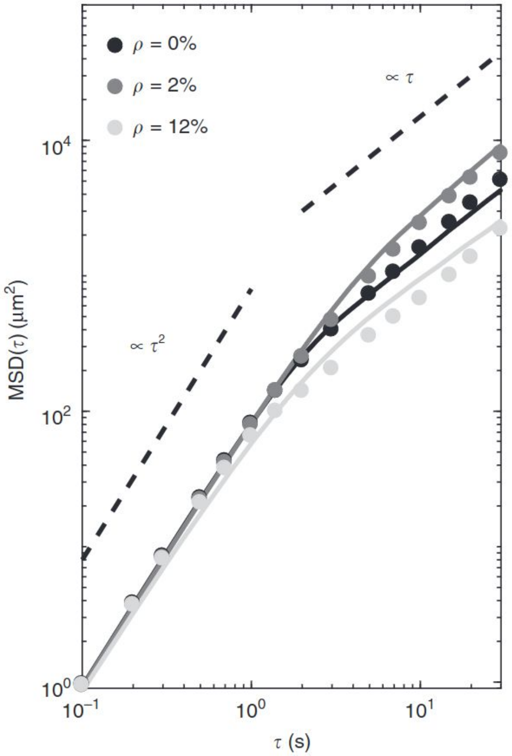


Kapanidis et. al. 2018

Random Walks in biology

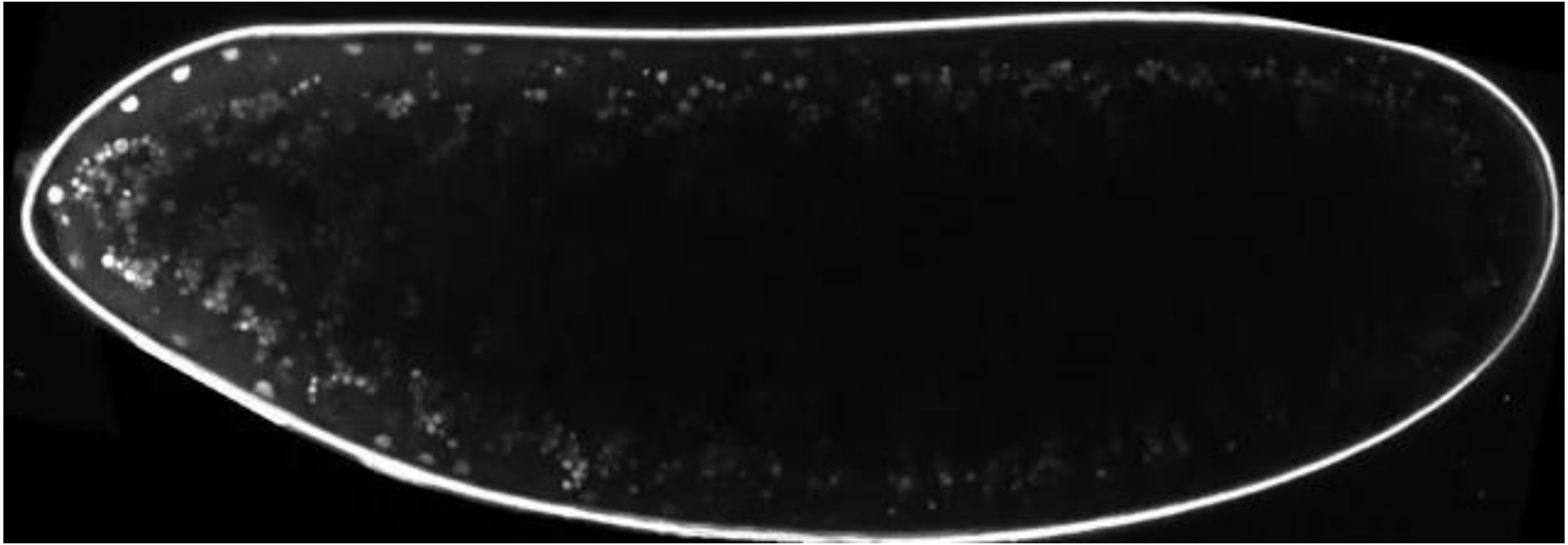


Berg & Brown, Nature, 1972

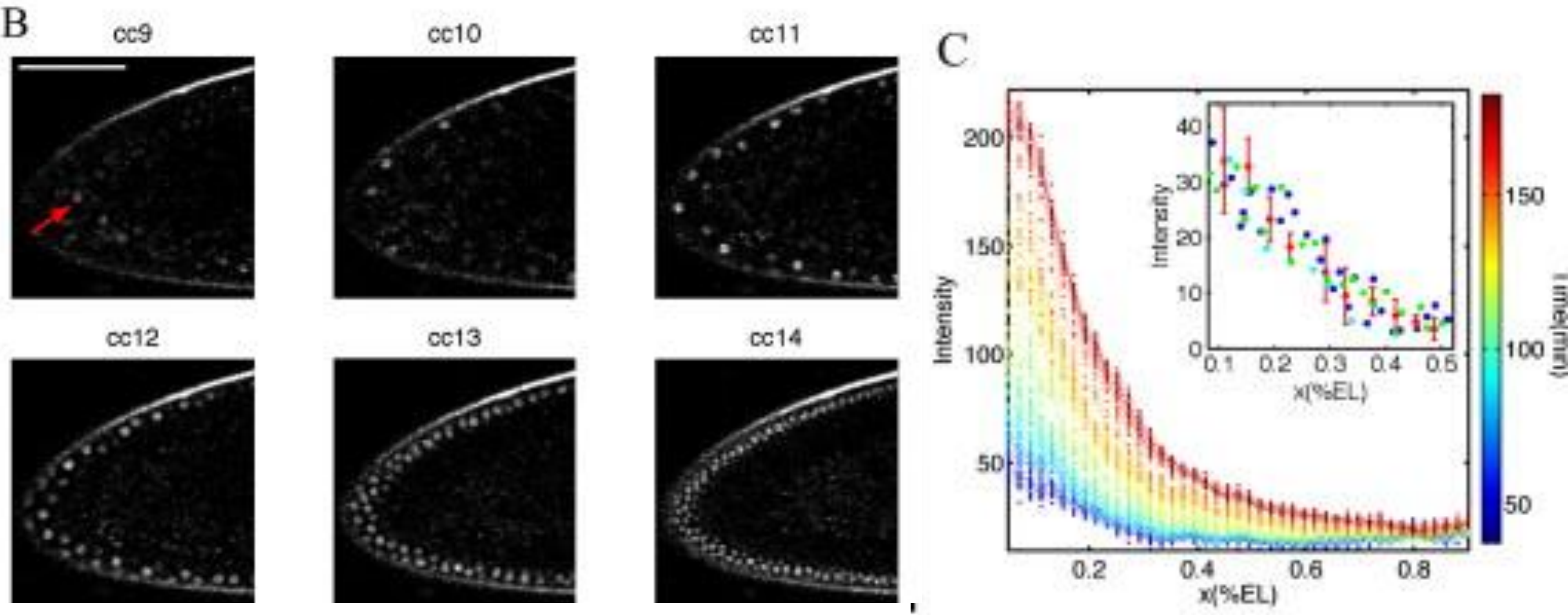


Makarchuk , ... , Volpe, Nature Communications, 2019

The Bicoid gradient in Drosophila



The Bicoid gradient in Drosophila



Gregor et. al. (2007)

The Bicoid gradient in Drosophila

The bicoid proteins degrades with a typical lifetime t and simultaneously also diffuses along the AP axis of the embryo

$$\frac{\partial[Bcd]}{\partial t} = D\frac{\partial^2[Bcd]}{\partial x^2} - \frac{1}{\tau}[Bcd]$$

At all times, there is protein production from the maternally deposited mRNA at the anterior end of the embryo.

$$[Bcd](x=0,t) = [Bcd]_{\mathrm{max}}$$

Synthesis - Diffusion - Degradation (SDD Model)

What is the steady state concentration profile of Bicoid?

The Bicoid gradient in Drosophila

Steady state: $$D\frac{\partial^2[Bcd]}{\partial x^2} = \frac{1}{\tau}[Bcd]$$

$$[Bcd](x) = [Bcd]_{\max} e^{-x/\lambda}$$

$$\lambda^{ex}_{D.\,melanogaster} \sim 100\,\mu m$$

$$D_{bicoid} \sim 5\,\mu m^2/s \qquad \tau_{bicoid} \sim 3000\,s$$

$$\lambda^{th.}_{D.\,melanogaster} \sim 120\,\mu m$$

The Bicoid gradient in Drosophila

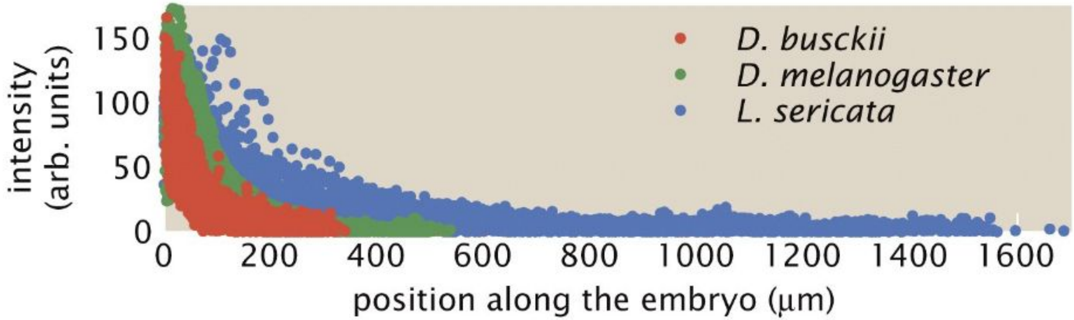
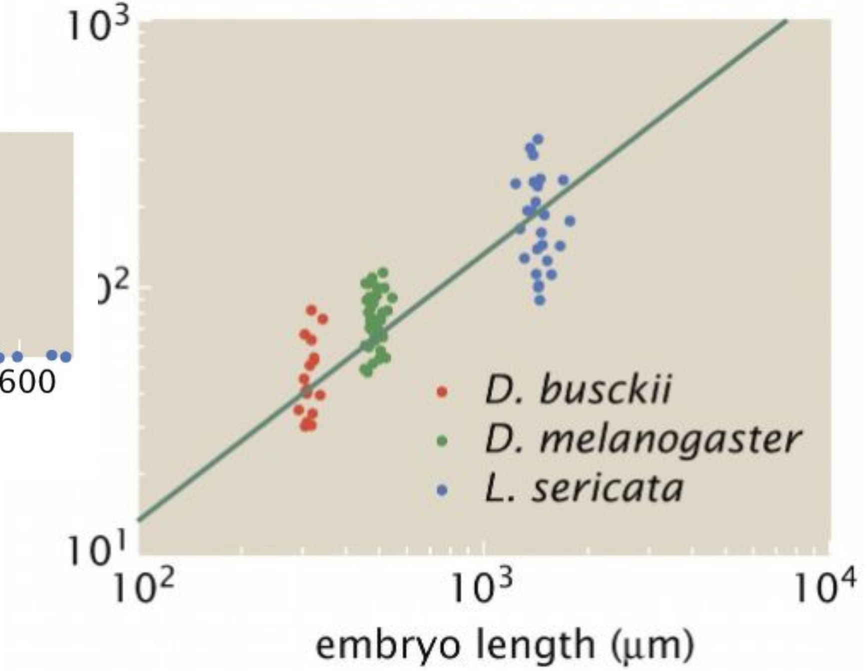
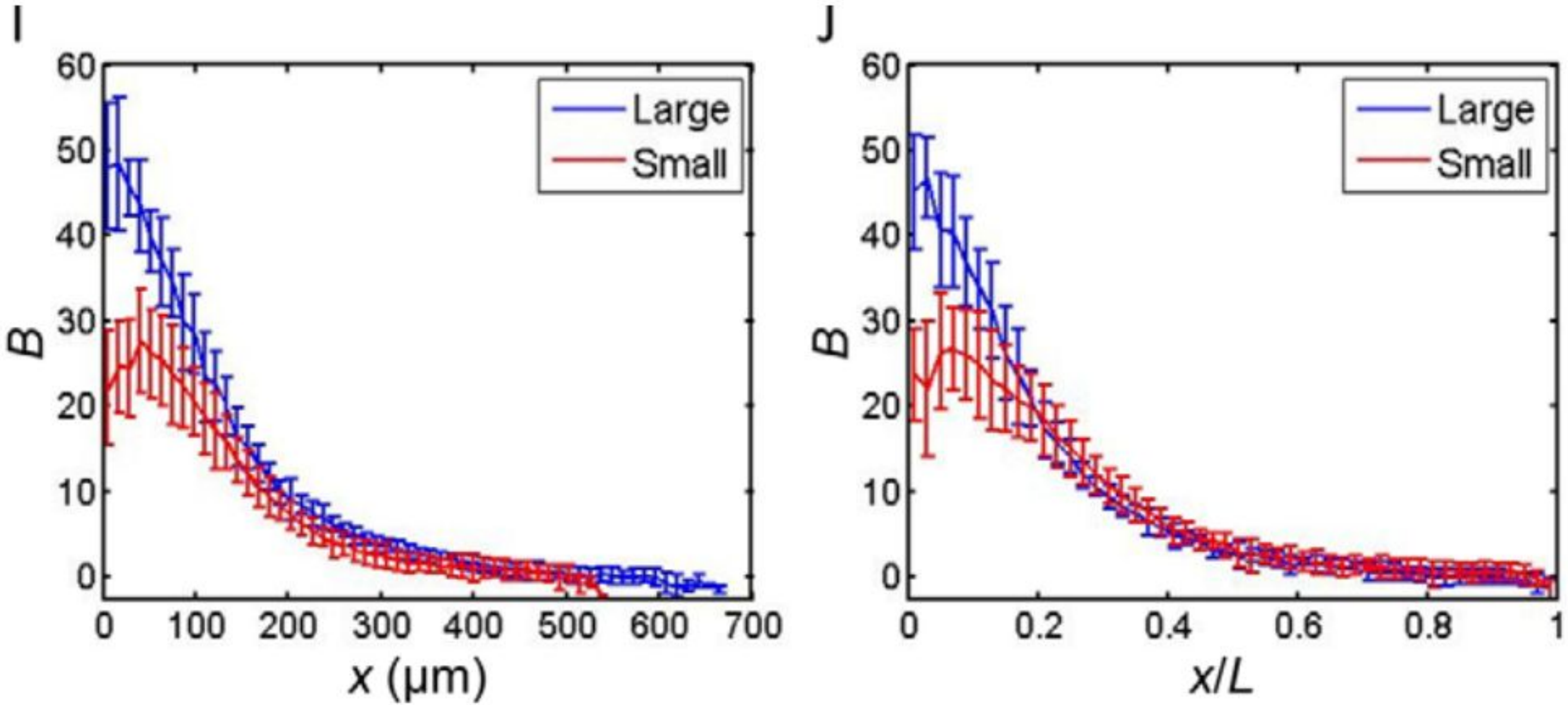


Figure 20.4b Physical Biology of the Cell, 2ed. (© Garland Science 2013)



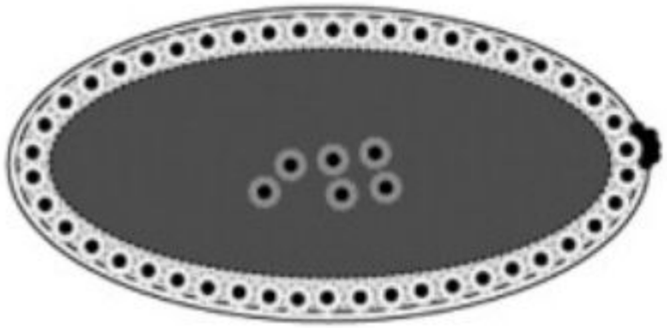
The Bicoid gradient in Drosophila

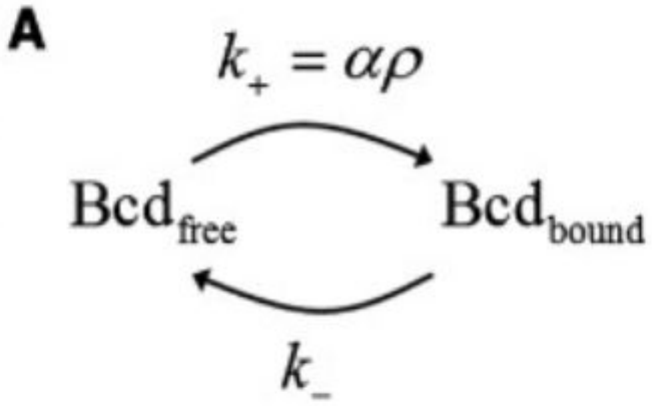


Cheung et. al. Development (2011)

The Bicoid gradient in Drosophila

Nucleocytoplasmic shuttling





$$C_{tot}(x,t) = \frac{Q}{D}\left(\frac{\lambda(t)}{\sqrt{\pi}}e^{-\frac{x^2}{\lambda(t)^2}} - x\,.\,erfc\left(\frac{x}{\lambda(t)}\right)\right),$$

Coppey et. al. Dev. Biol. (2007)

The Bicoid gradient in Drosophila

mRNA gradient

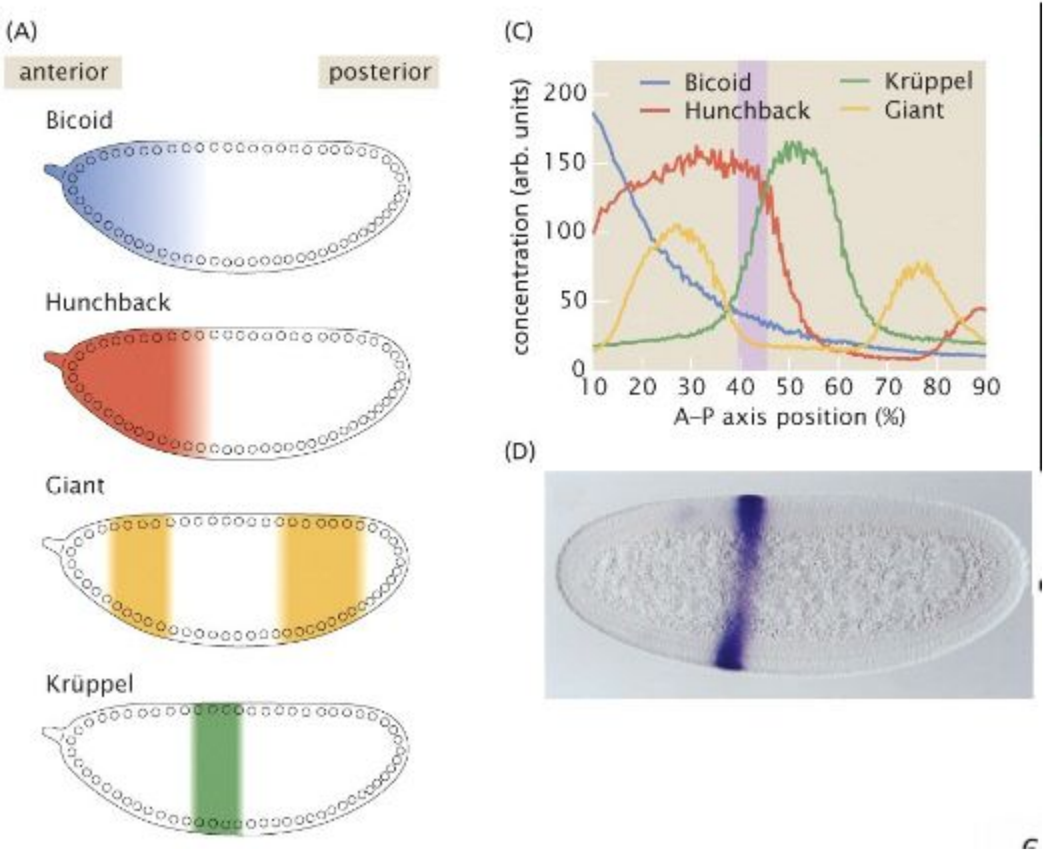
bcd mRNA

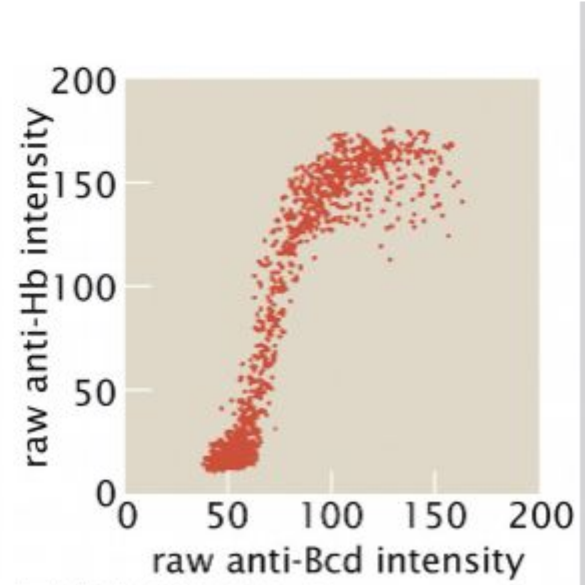
$$j(x,t) = \frac{Q}{\sqrt{2\pi}\sigma} e^{-\frac{x^2}{2\sigma^2}},$$

$$C_{ss}(x) = \frac{Q}{2\alpha\lambda_{eq}} e^{\frac{\sigma^2}{2\lambda_{eq}^2}}\left(e^{-\frac{x}{\lambda_{eq}}} erfc\left(\frac{\sigma^2 + \lambda_{eq}x}{\sqrt{2}\lambda_{eq}\sigma}\right) + e^{-\frac{x}{\lambda_{eq}}} erfc\left(\frac{\sigma^2 - \lambda_{eq}x}{\sqrt{2}\lambda_{eq}\sigma}\right)\right).$$

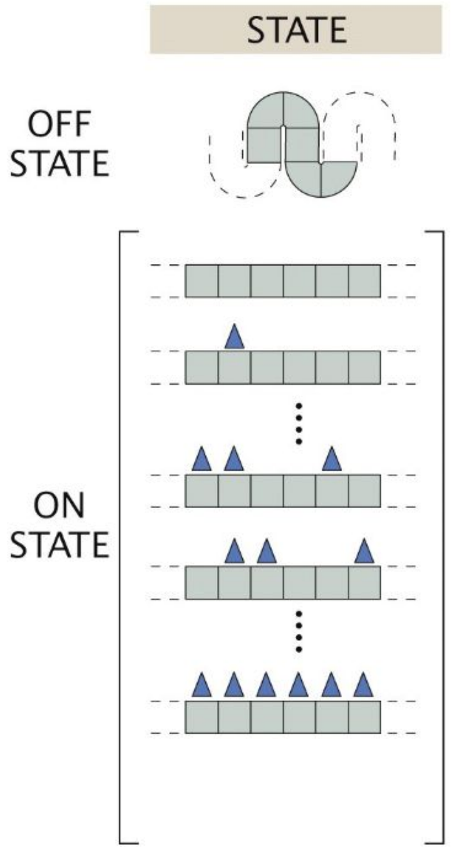
Berezhovskii et. al. (2009)

The patterning cascade

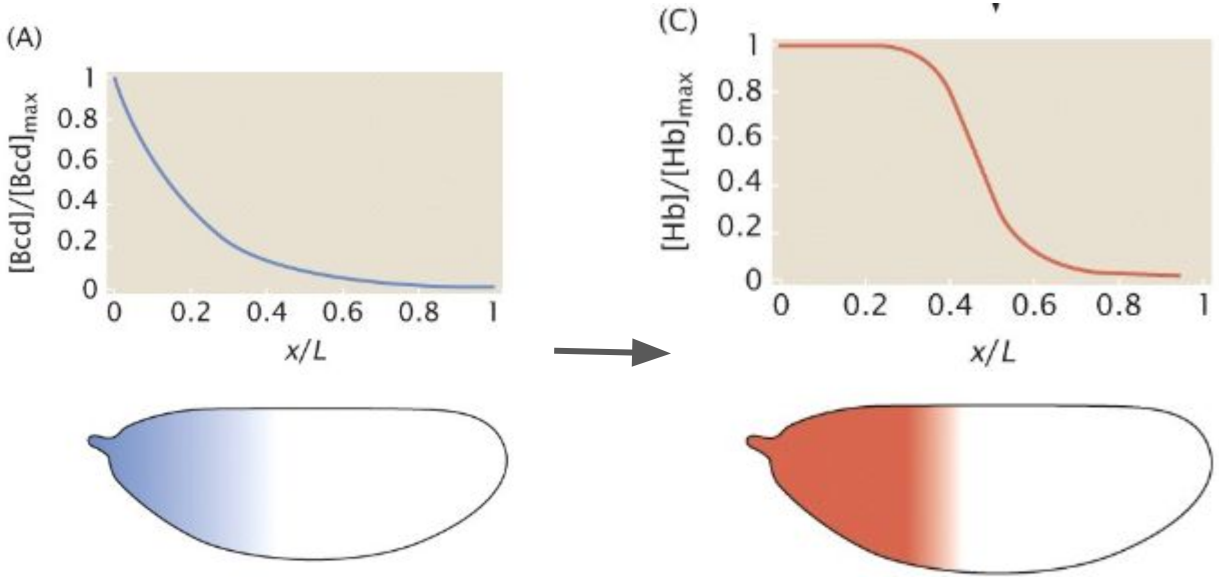




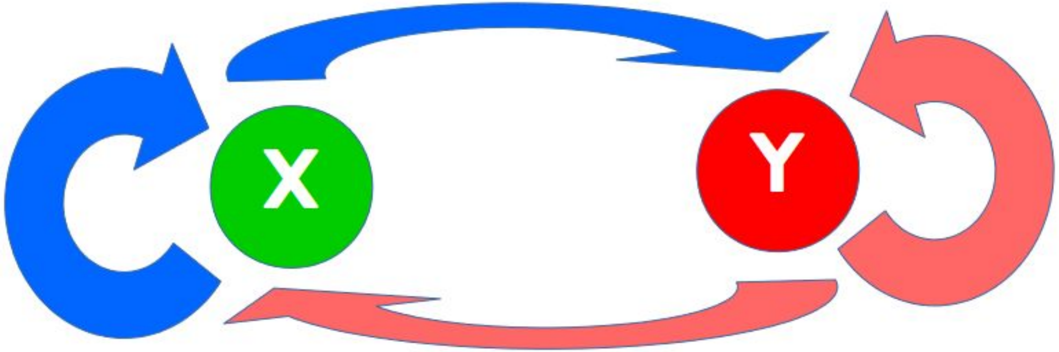
The patterning cascade



$$[Hb](x) = [Hb]_{max} \frac{e^{-\beta\varepsilon_{on}}\left(1+[Bcd]_{max}e^{-x/\lambda}/K_d^{on}\right)^6}{e^{-\beta\varepsilon_{on}}\left(1+[Bcd]_{max}e^{-x/\lambda}/K_d^{on}\right)^6+e^{-\beta\varepsilon_{off}}}$$



Reaction diffusion and spatial patterns



$$\frac{dX}{dt} = 5X - 6Y + 1$$

$$\frac{dY}{dt} = 6X - 7Y + 1$$

Steady state: $X = Y = 1$

Reaction diffusion and spatial patterns

Is the steady state X = Y = 1 a stable steady state?

Consider the deviations from the steady state: $x = X - 1$

$y = Y - 1$

$$\frac{d}{dt}\begin{pmatrix} x \\ y \end{pmatrix} = \begin{pmatrix} 5 & -6 \\ 6 & -7 \end{pmatrix}\begin{pmatrix} x \\ y \end{pmatrix}$$

$$\lambda = \lambda_{1/2} = -1$$

$$x(t) = x_0 e^{\lambda t} \qquad y(t) = y_0 e^{\lambda t}$$

The steady state is stable against perturbations

Reaction diffusion and spatial patterns

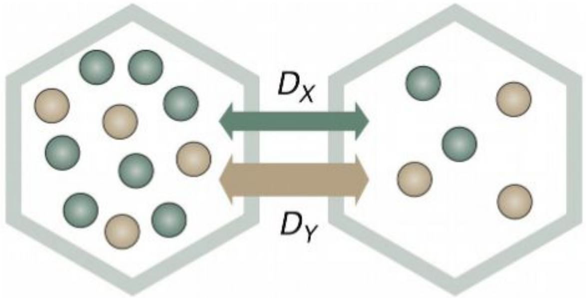


Figure 20.11a Physical Biology of the Cell, 2ed. (© Garland Science 2013)

$$\frac{dX_1}{dt} = 5X_1 - 6Y_1 + 1 + D_X(X_2 - X_1)$$

$$\frac{dY_1}{dt} = 6X_1 - 7Y_1 + 1 + D_Y(Y_2 - Y_1)$$

$$\frac{dX_2}{dt} = 5X_2 - 6Y_2 + 1 + D_X(X_1 - X_2)$$

$$\frac{dY_2}{dt} = 6X_2 - 7Y_2 + 1 + D_Y(Y_1 - Y_2)$$

Reaction diffusion and spatial patterns

$$\frac{d}{dt}\begin{pmatrix} x_1 \\ y_1 \\ x_2 \\ y_2 \end{pmatrix} = \begin{pmatrix} 5-D_X & -6 & D_X & 0 \\ 6 & -7-D_Y & 0 & D_Y \\ D_X & 0 & 5-D_X & -6 \\ 0 & D_Y & 6 & -7-D_Y \end{pmatrix}\begin{pmatrix} x_1 \\ y_1 \\ x_2 \\ y_2 \end{pmatrix}$$

Let, $D_X = 0.5$

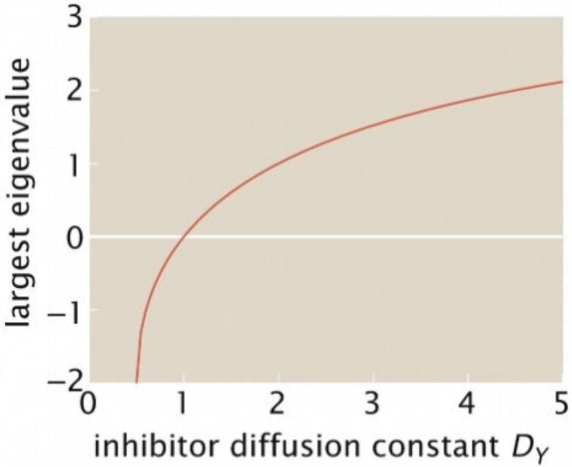


Figure 20.11b Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Reaction diffusion and spatial patterns

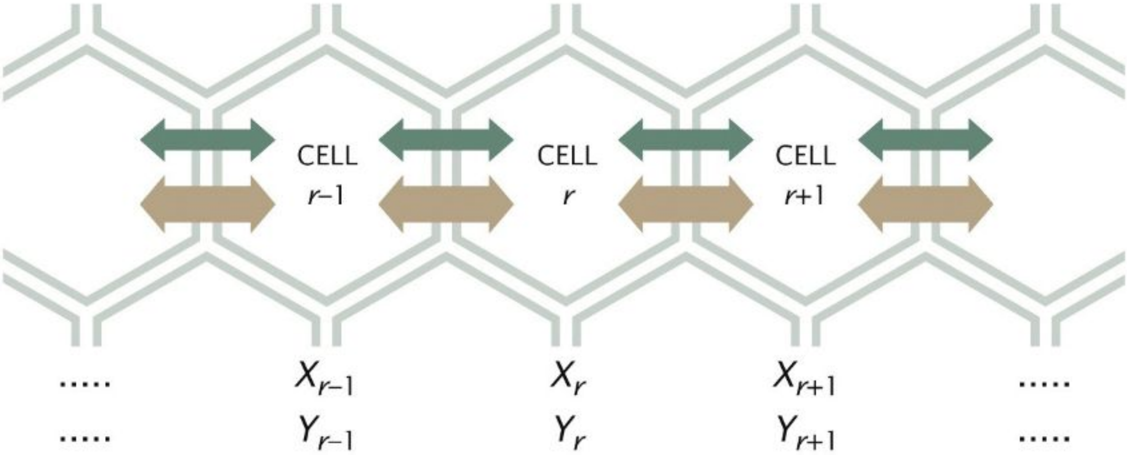


Figure 20.12a Physical Biology of the Cell, 2ed. (© Garland Science 2013)

$$\frac{dX_r}{dt} = f(X_r, Y_r)$$

$$\frac{dY_r}{dt} = g(X_r, Y_r)$$

Steady state: $(X_r, Y_r) = (h, k)$

Reaction diffusion and spatial patterns

$$\frac{dX_r}{dt} = f(X_r, Y_r) + D_X(X_{r+1} + X_{r-1} - 2X_r)$$

$$\frac{dY_r}{dt} = g(X_r, Y_r) + D_Y(Y_{r+1} + Y_{r-1} - 2Y_r)$$

Consider perturbations from the steady state:

$$(X_r, Y_r) = (h + x_r, k + y_r)$$

Linear stability analysis:

$$\frac{dx_r}{dt} = A_1 x_r + B_1 y_r + D_X(x_{r+1} + x_{r-1} - 2x_r)$$

$$\frac{dy_r}{dt} = A_2 x_r + B_2 y_r + D_Y(y_{r+1} + y_{r-1} - 2y_r)$$

Reaction diffusion and spatial patterns

$$A_1 = \left.\frac{\partial f}{\partial X}\right|_{(h,k)} \qquad B_1 = \left.\frac{\partial f}{\partial Y}\right|_{(h,k)}$$

$$A_2 = \left.\frac{\partial g}{\partial X}\right|_{(h,k)} \qquad B_2 = \left.\frac{\partial g}{\partial Y}\right|_{(h,k)}$$

Consider a trial solution of the form:

$$x_r(t) = x(t)e^{i(2\pi r/\lambda)}$$

$$\frac{dx}{dt} = \left[A_1 + D_X\left(e^{i(2\pi/\lambda)} + e^{-i(2\pi/\lambda)} - 2\right)\right]x + B_1 y$$

$$\frac{dy}{dt} = A_2 x + \left[B_2 + D_Y\left(e^{i(2\pi/\lambda)} + e^{-i(2\pi/\lambda)} - 2\right)\right]y$$

Reaction diffusion and spatial patterns

$$\frac{dx}{dt} = \left[A_1 - D_X\left(\frac{2\pi}{\lambda}\right)^2\right]x + B_1 y$$

$$\frac{dy}{dt} = A_2 x + \left[B_2 - D_Y\left(\frac{2\pi}{\lambda}\right)^2\right]y$$

$$\frac{d}{dt}\begin{pmatrix} x \\ y \end{pmatrix} = \begin{pmatrix} A_1 - D_X\left(\frac{2\pi}{\lambda}\right)^2 & B_1 \\ A_2 & B_2 - D_Y\left(\frac{2\pi}{\lambda}\right)^2 \end{pmatrix}\begin{pmatrix} x \\ y \end{pmatrix}$$

Reaction diffusion and spatial patterns

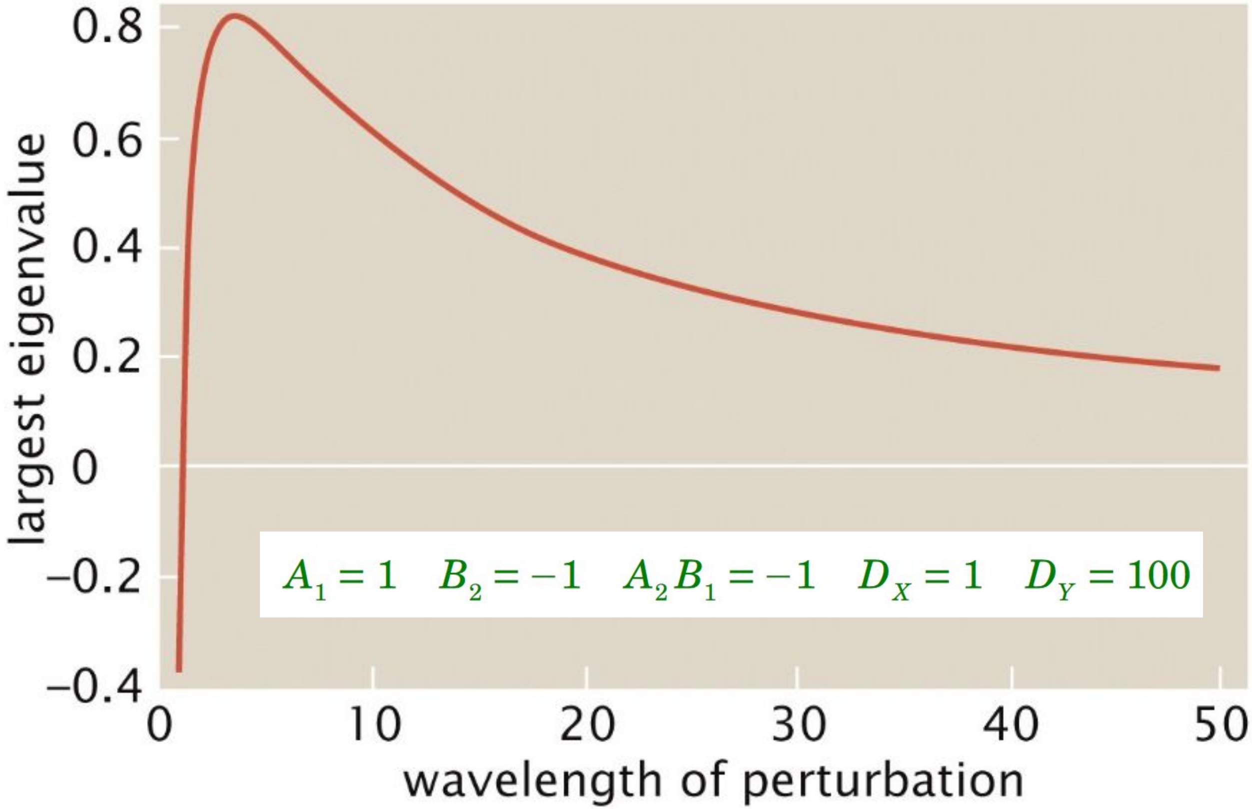
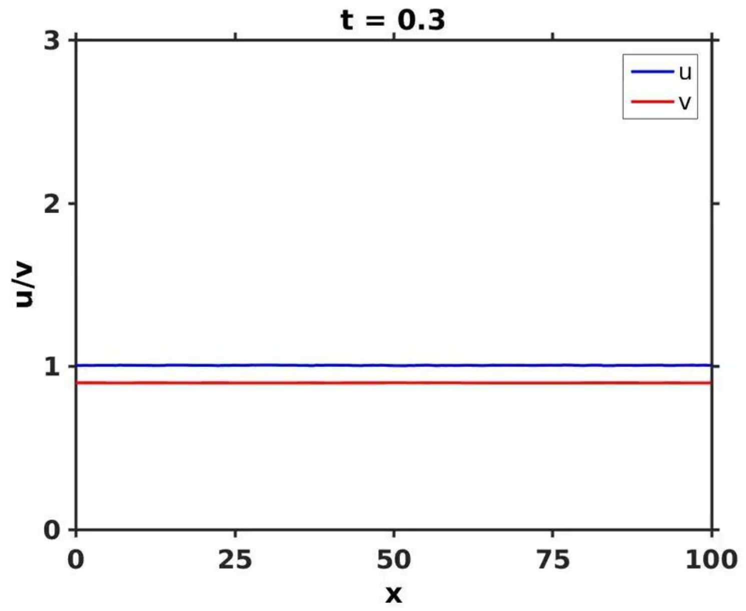


Figure 20.12b Physical Biology of the Cell, 2ed. (© Garland Science 2013)

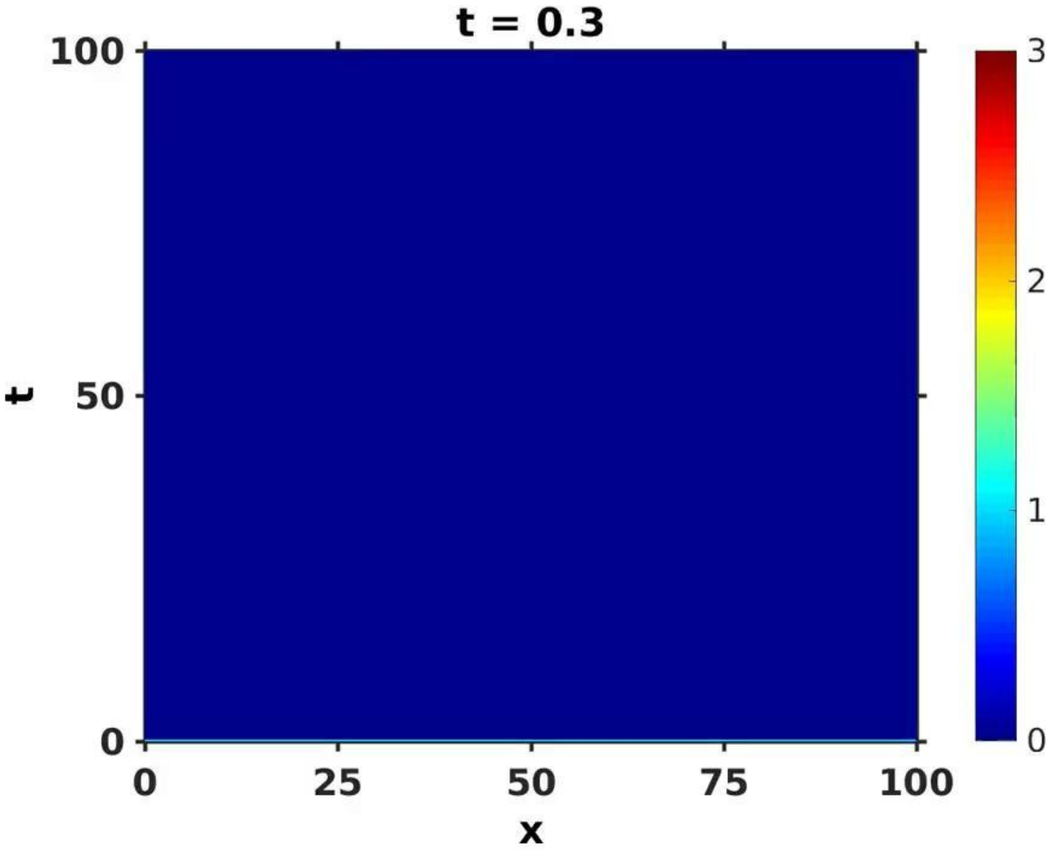
Reaction diffusion and spatial patterns

$$f(u,v) = c_1 - c_{-1}u + c_3 u^2 v$$
$$g(u,v) = c_2 - c_3 u^2 v$$

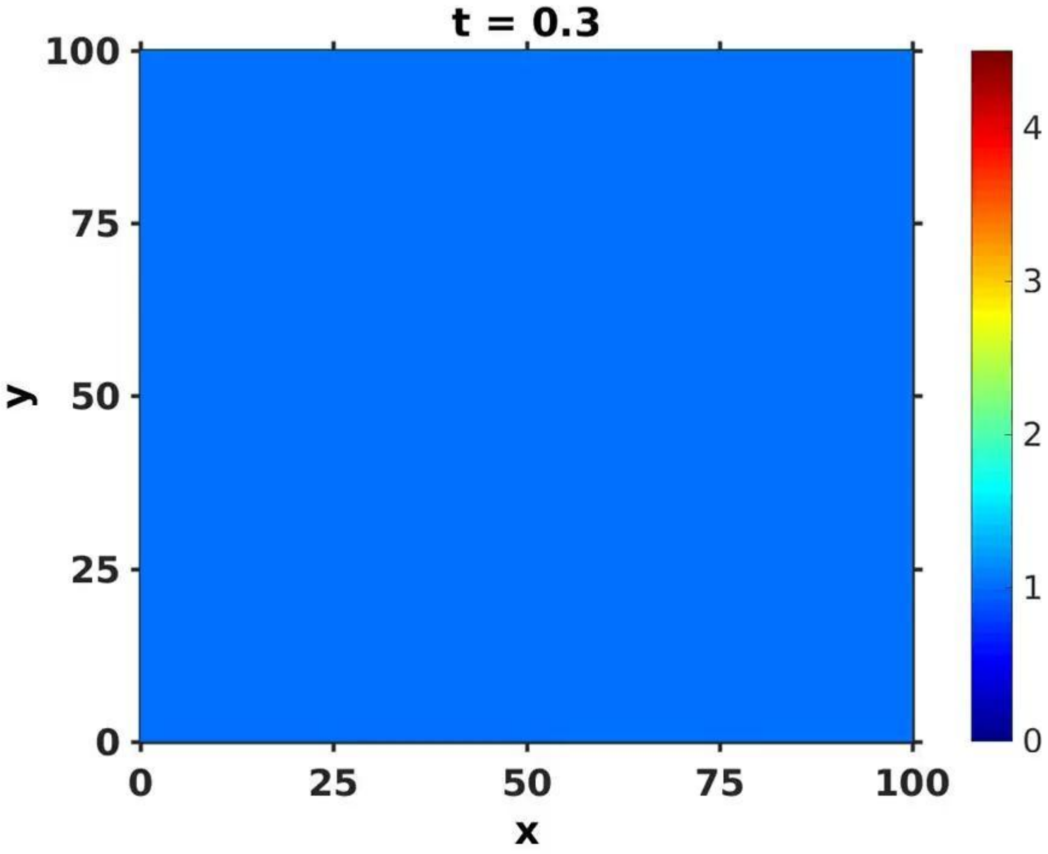
Schnakenberg, J. Theor. Biol. 81, 389 (1979)



Reaction diffusion and spatial patterns



Reaction diffusion and spatial patterns



Reaction diffusion and spatial patterns

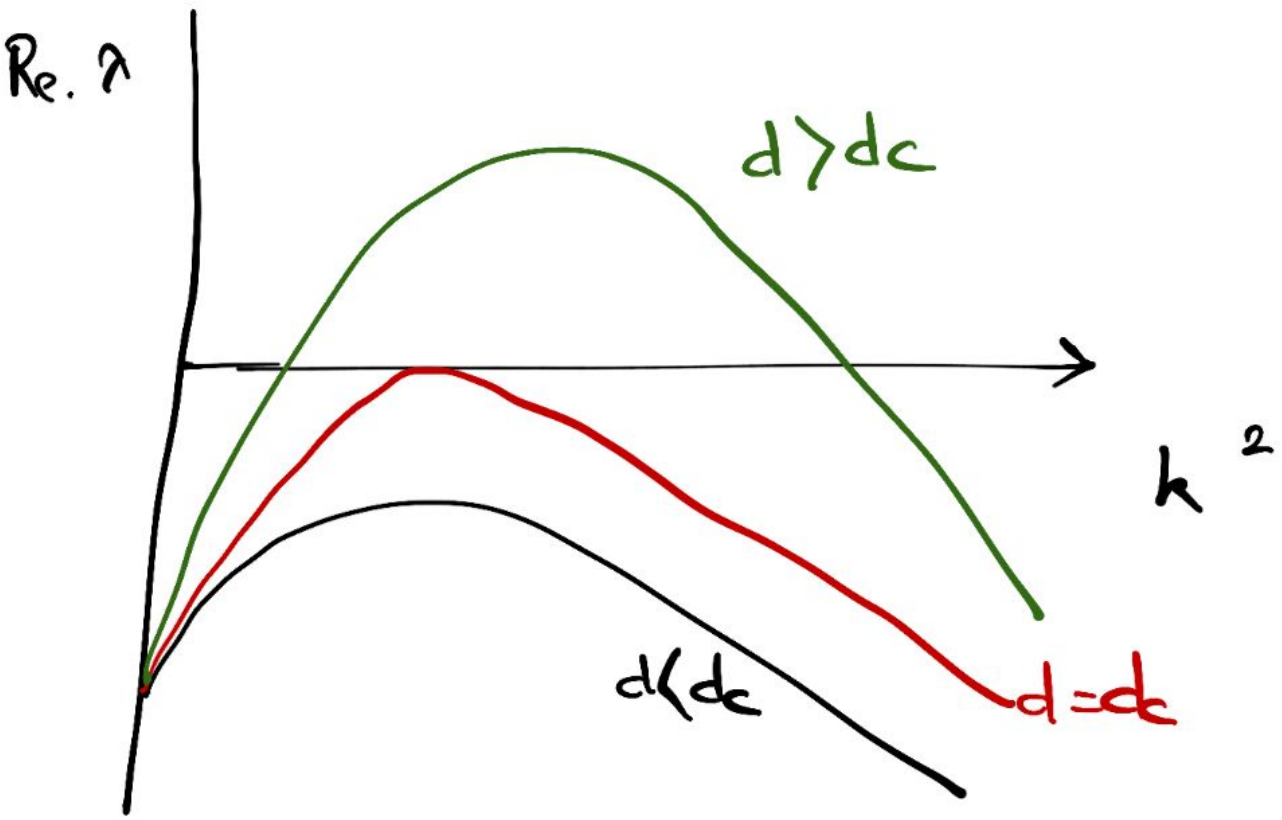
$$f_u + g_v < 0$$

$$f_u g_v - f_v g_u > 0$$

$$d f_u + g_v > 0$$

$$(d f_u + g_v)^2 - 4d(f_u g_v - f_v g_u) > 0$$

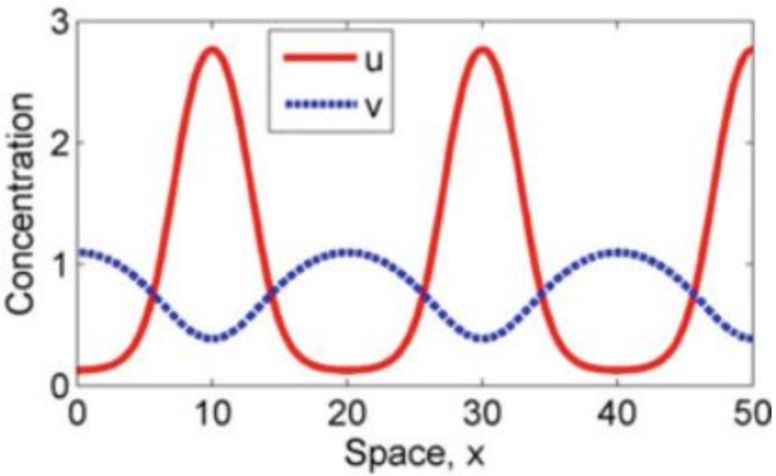
Reaction diffusion and spatial patterns



Reaction diffusion and spatial patterns

Schnakenberg Kinetics

$$f(u, v) = a - u + u^2 v; \;\; g(u, v) = b - u^2 v,$$

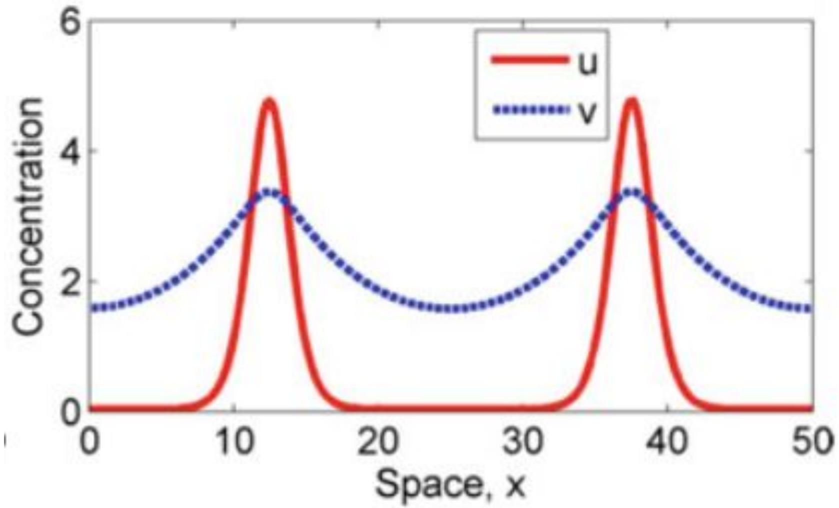


Mainey and Woolley (2019)

Reaction diffusion and spatial patterns

Gierer Meinhardt Kinetics

$$f(u,v) = a - bu + \frac{u^2}{v}; \;\; g(u,v) = u^2 - v,$$



Mainey and Woolley (2019)

Reaction diffusion and spatial patterns

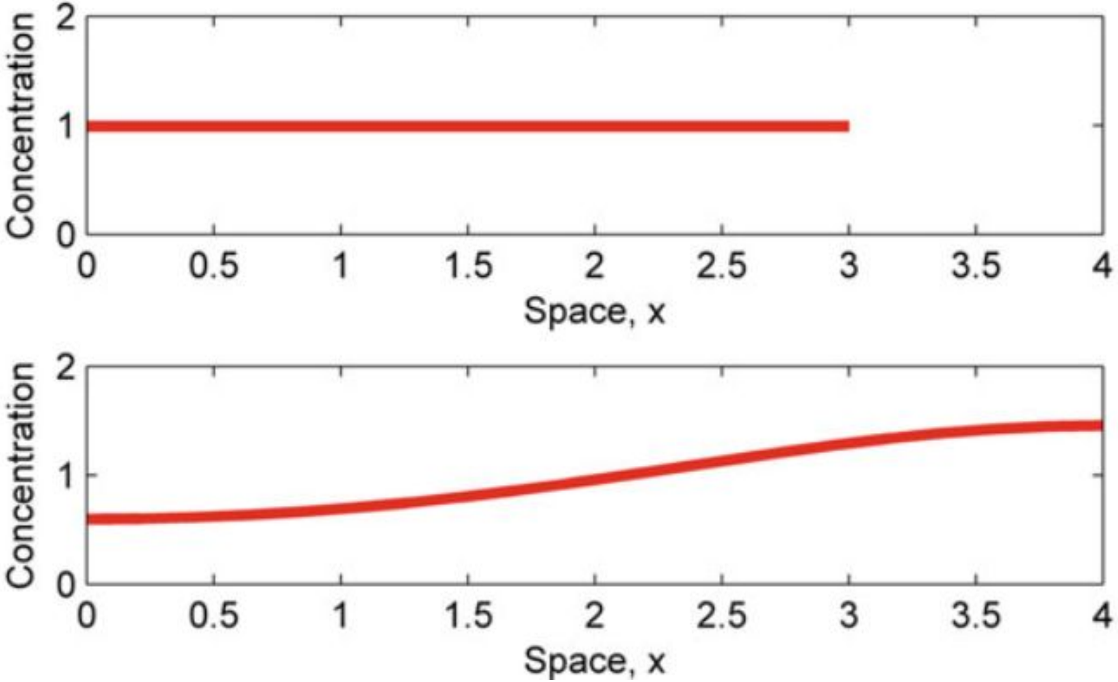
What motifs of chemical kinetics admit Turing patterns?

$$J_p = \begin{pmatrix} + & - \\ + & - \end{pmatrix} \text{ or } J_c = \begin{pmatrix} - & - \\ + & + \end{pmatrix}.$$

$$J'_p = \begin{pmatrix} - & + \\ - & + \end{pmatrix} \text{ and } J'_c = \begin{pmatrix} + & + \\ - & - \end{pmatrix}$$

Reaction diffusion and spatial patterns

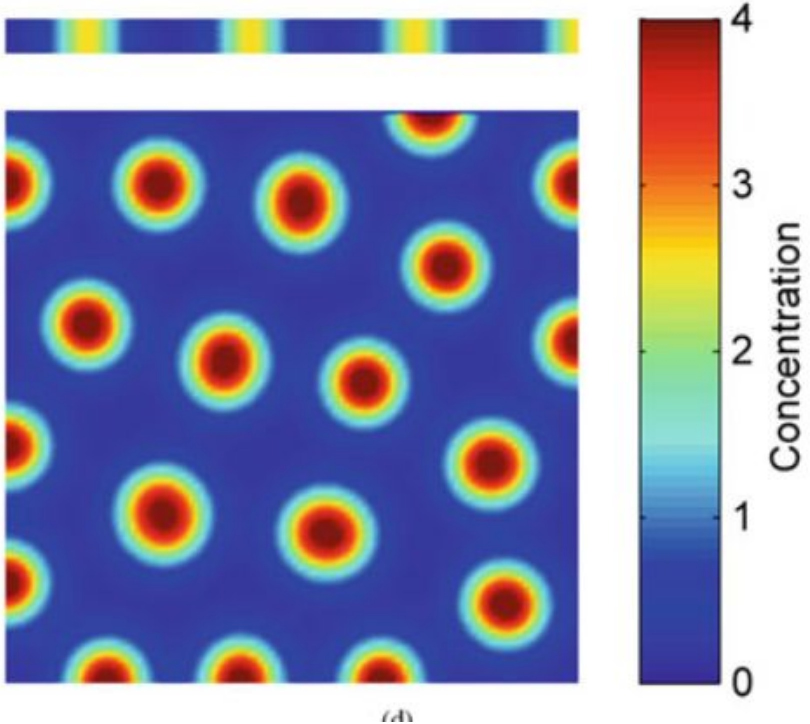
Length control of Turing patterns



Mainey and Woolley (2019)

Reaction diffusion and spatial patterns

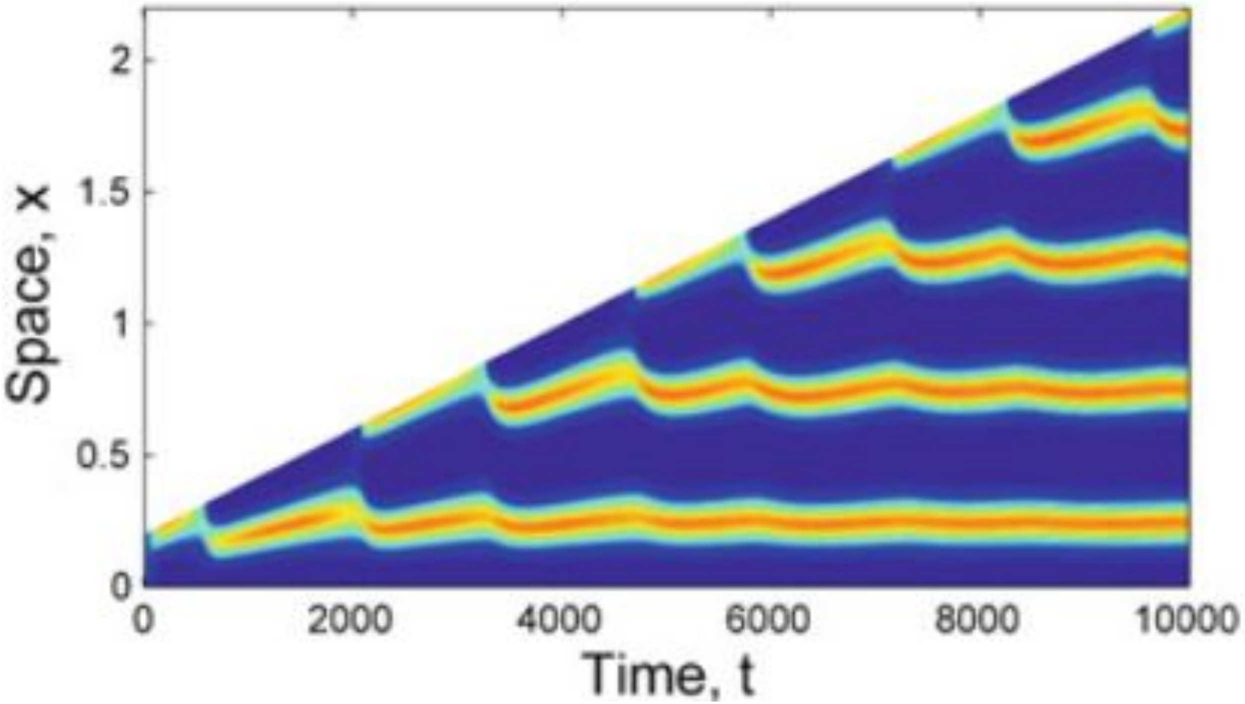
Length control of Turing patterns



Mainey and Woolley (2019)

Reaction diffusion and spatial patterns

Turing patterns on growing domains



Mainey and Woolley (2019)

Reaction diffusion and spatial patterns

- ❑ Unequal diffusion coefficients
- ❑ Increasing complexity of components
- ❑ Patterns in growing systems
- ❑ Robustness of patterns