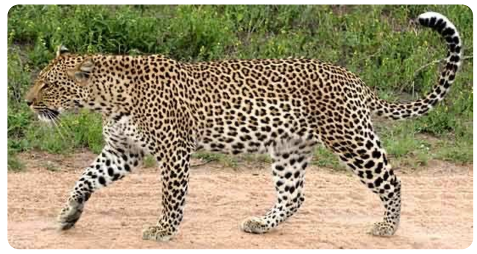
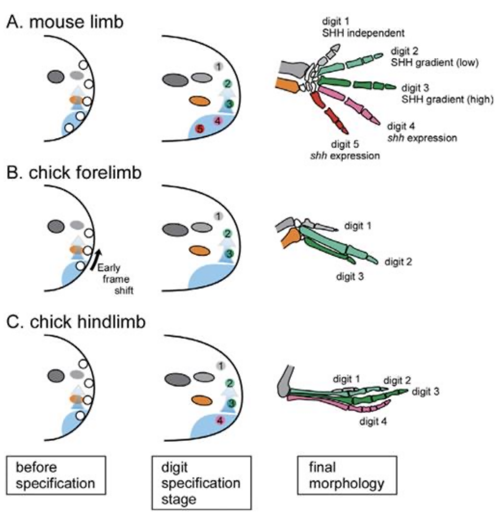
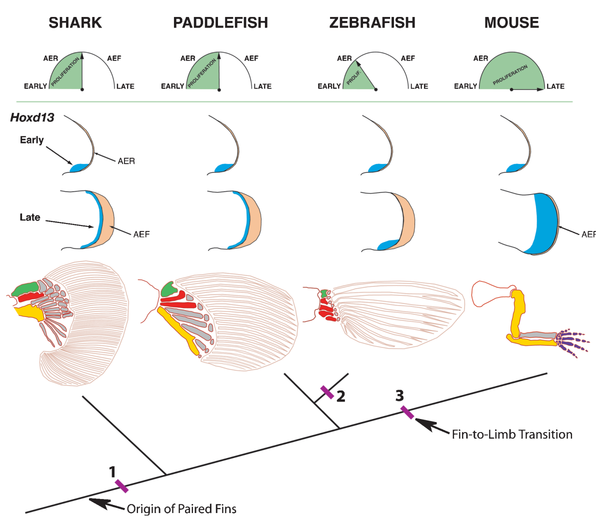
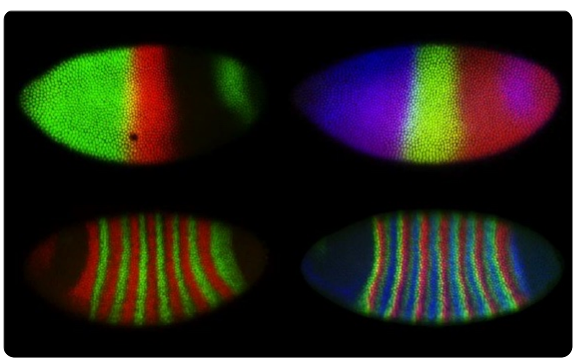
III C. Turing instability + pattern formation

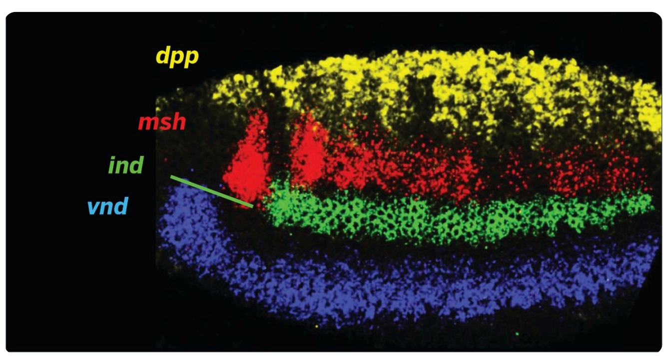
1. Background on biological patterns





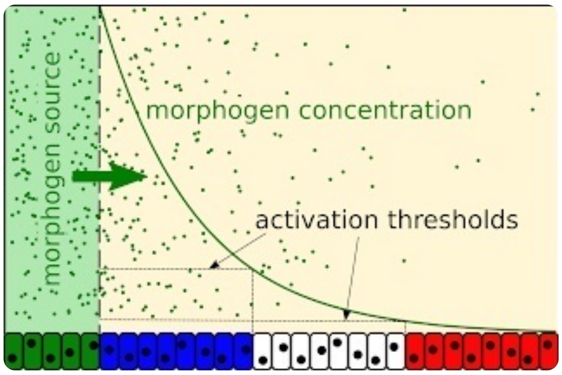


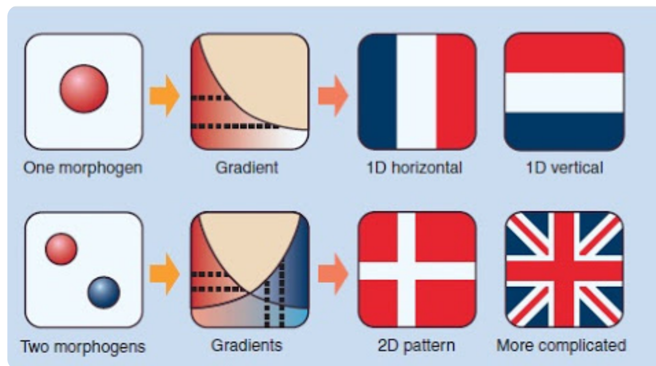




Two general strategies to form biological pattern

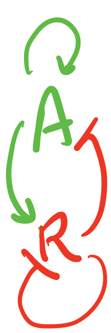
* Morphogen gradient (Lewis Wolpert)
  - positional information laid out externally
  - cells respond passively (gene expression & movement)

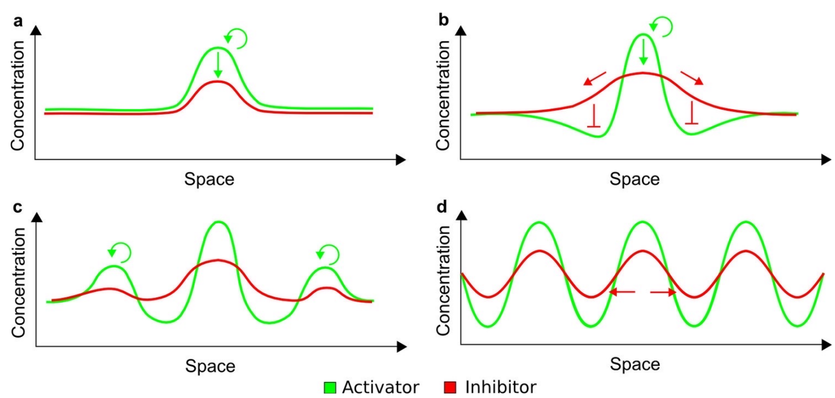




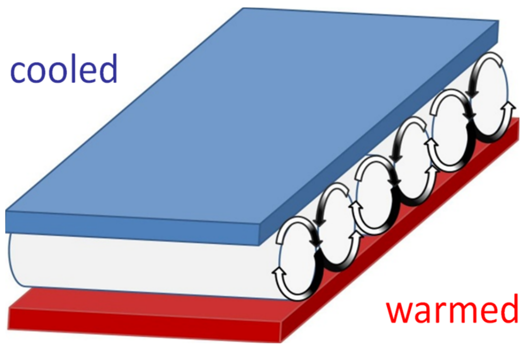
* Reaction-diffusion systems (Alan Turing)
  - pattern formation autonomous (self-organized)
  - typically involve mutual signaling

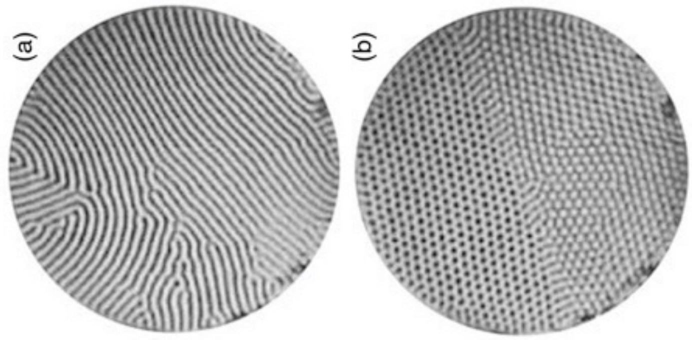
⇒ Turing patterns: 2 diffusing species (A + R)
  - slow diffusion of activator (short-range activation)
  - fast diffusion of inhibitor (long-range inhibition)





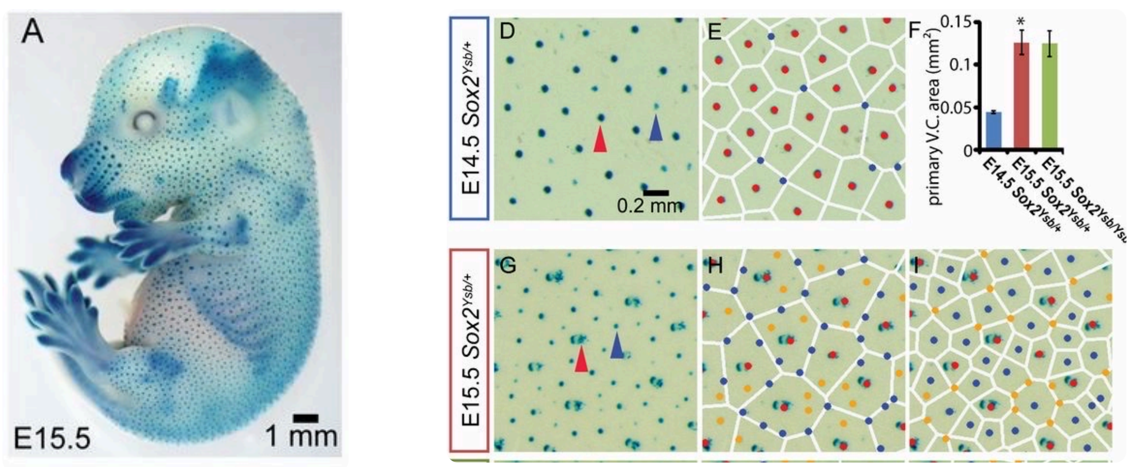
* pattern formation dynamics best studied in exemplary physical & chemical systems
e.g. Rayleigh-Benard convection

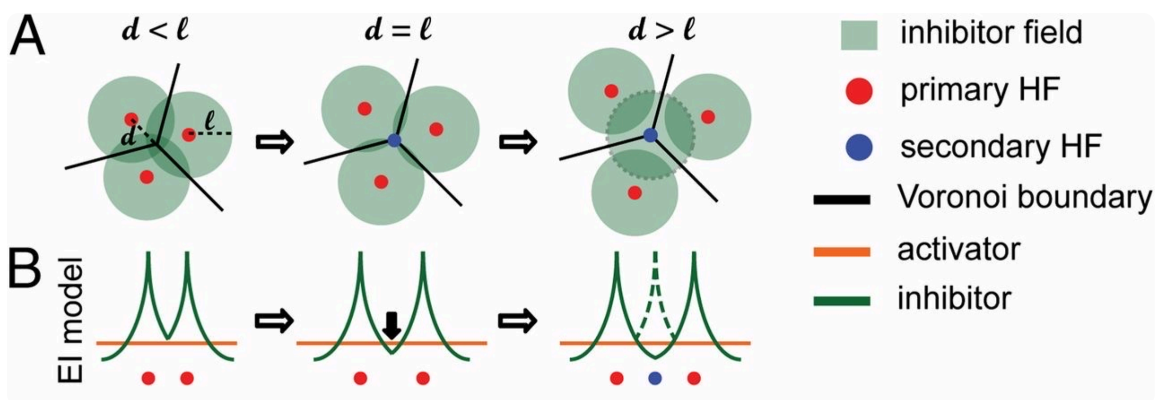




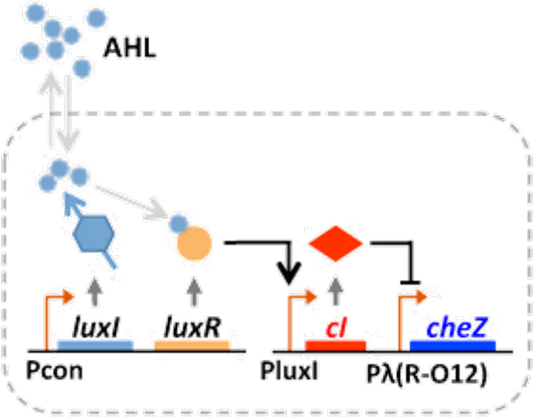
* origins of biological pattern often hard to elucidate
→ early failures

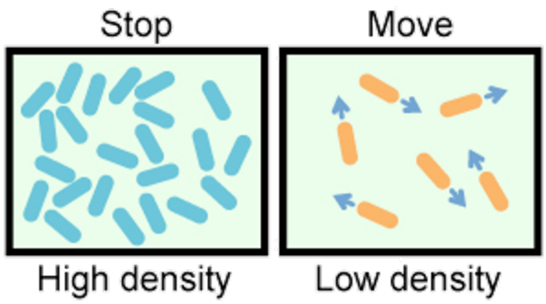
* Some real-life (not-quite-Turing) examples.
- hair follicles in developing mice (Cheung et al, 2012)





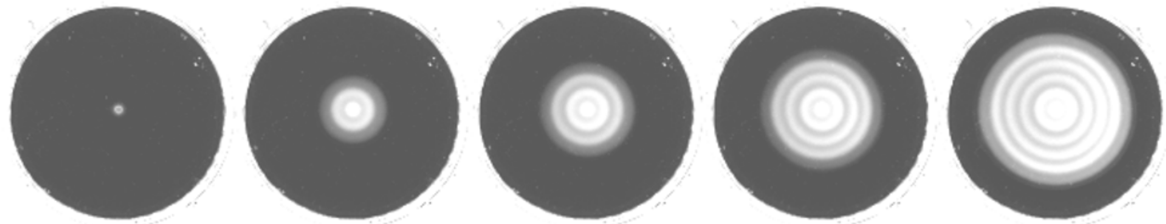
— Synthetic pattern from engineered bacteria (Lin et al, 2011)



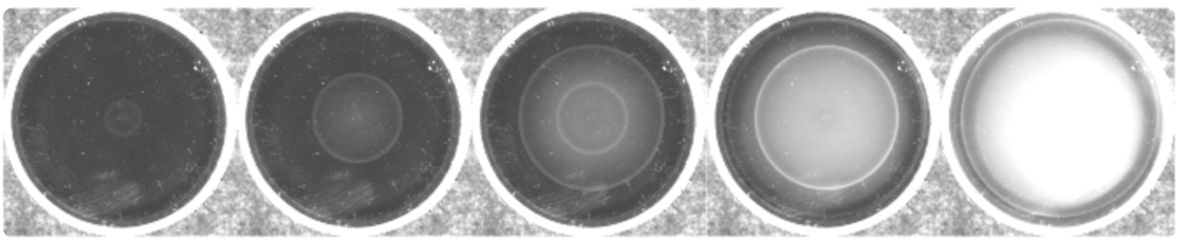


time

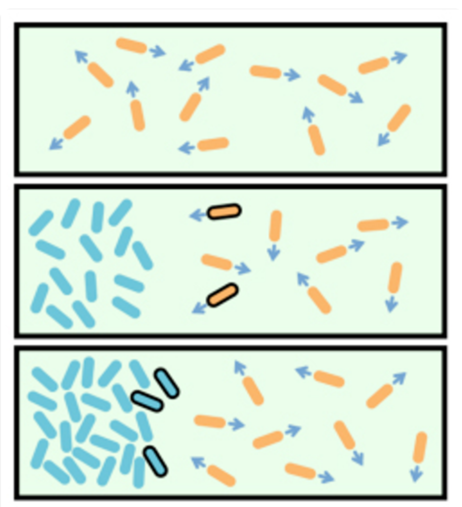
engr strain



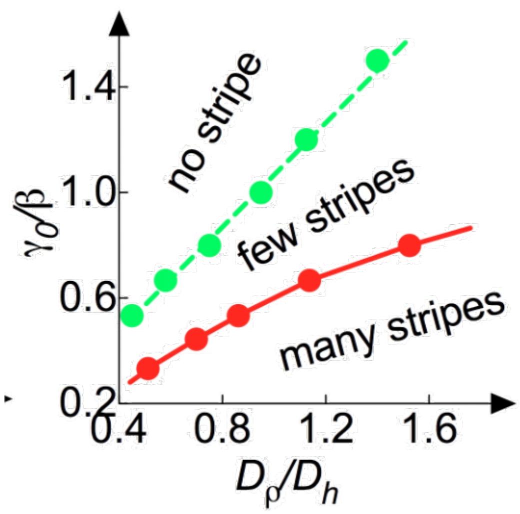
WT



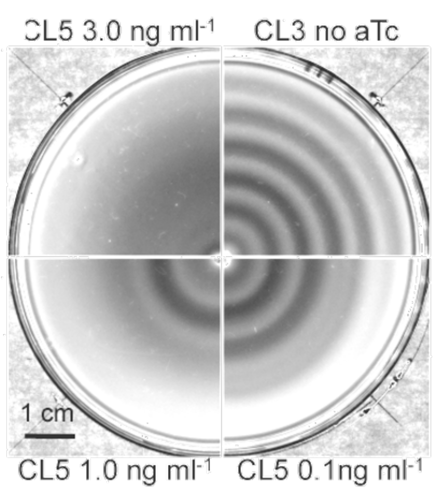
Mechanism:



Phase diagram:

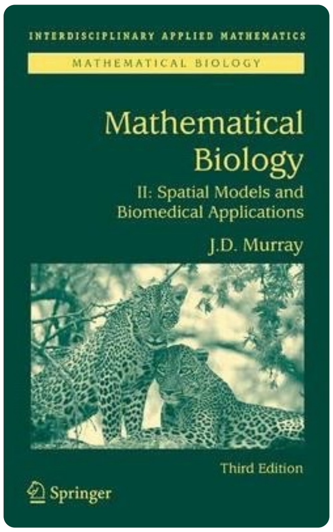


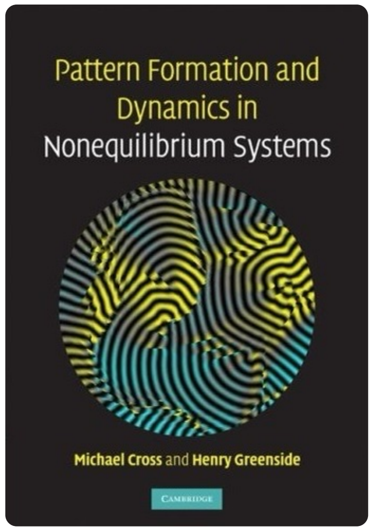
vary D_ρ



Outline for this section:

- describe the math of Turing instability
- pattern formation for simple dynamical system
- Turing space: mode selection
  and system size dependence





- Amplitude eqn: Stripe vs spots
  secondary instability

⇒ bio applications (team projects)

2. Turing instability

Recall $N=2$ dynamical system

$$\begin{cases} \dot{u} = f(u,v) \\ \dot{v} = g(u,v) \end{cases} \xrightarrow[v = v^* + \delta v]{u = u^* + \delta u} \begin{pmatrix} \delta\dot{u} \\ \delta\dot{v} \end{pmatrix} = M \begin{pmatrix} \delta u \\ \delta v \end{pmatrix}$$

Community matrix M:

$$M = \begin{pmatrix} f_u & f_v \\ g_u & g_v \end{pmatrix};$$

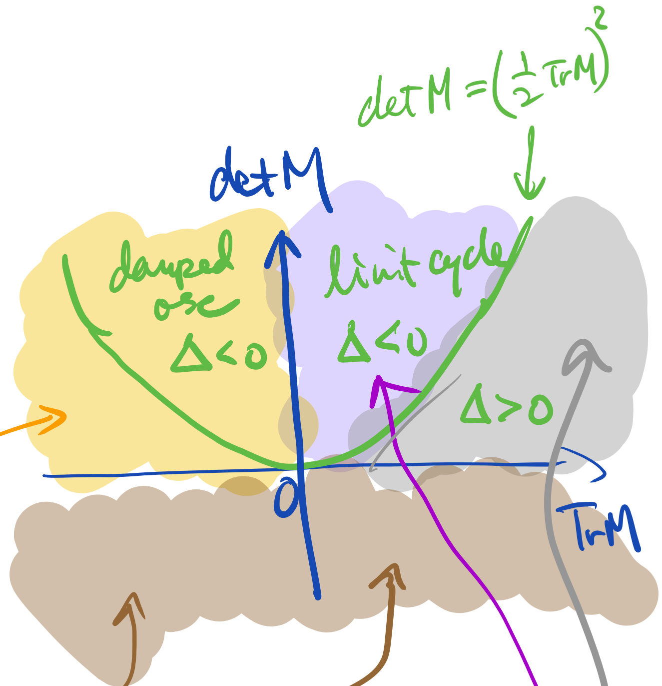
$$\det(M - \lambda I) = 0$$

$$\to (f_u - \lambda)(g_v - \lambda) - f_v g_u = 0$$

$$\lambda^2 - \lambda \underbrace{(f_u + g_v)}_{\mathrm{Tr}\,M} + \underbrace{f_u g_v - f_v g_u}_{\det M} = 0$$

(Note derivatives evaluated at u^*, v^*)

$$\lambda = \frac{1}{2}\mathrm{Tr}\,M \pm \sqrt{\underbrace{\left(\tfrac{1}{2}\mathrm{Tr}\,M\right)^2 - \det M}_{\Delta}}$$



→ Condition for stability:

$\left.\begin{array}{l}\mathrm{Tr}\,M < 0 \\ \det M > 0\end{array}\right\}$ $\lambda_\pm < 0$

→ bistability (saddle pt)

$\det M < 0$: $\lambda_+ > 0,\ \lambda_- < 0$

→ unstable spiral: $\mathrm{Tr}\,M > 0$, $\det M > \left(\frac{1}{2}\mathrm{Tr}\,M\right)^2$

→ unstable node: $\left.\begin{array}{l}\mathrm{Tr}\,M > 0 \\ \det M < \left(\frac{1}{2}\mathrm{Tr}\,M\right)^2\end{array}\right\}$ $\lambda_\pm > 0$

from the stable state ($\mathrm{Tr}\,M<0$, $\det M>0$)

- transition across $\mathrm{Tr}\,M=0$: Hopf bifurcation
- transition across $\det M=0$ (for finite k): Turing instability (1952)

(1912 - 1954)

* Consider diffusive spatial coupling:

$$\partial_t u = f(u,v) + D_u \partial_x^2 u$$
$$\partial_t v = g(u,v) + D_v \partial_x^2 v.$$

Finite wavelength perturbation (k = wave #)

let $u(x,t) = u^* + \delta u(t)\, e^{ikx}$

$v(x,t) = v^* + \delta v(t)\, e^{ikx}$

$$\frac{\partial}{\partial t}\begin{pmatrix}\delta u\\ \delta v\end{pmatrix} = \begin{pmatrix} f_u & f_v \\ g_u & g_v\end{pmatrix}\begin{pmatrix}\delta u\\ \delta v\end{pmatrix} + \begin{pmatrix}-D_u k^2 \delta u\\ -D_v k^2 \delta v\end{pmatrix}$$

$$\Rightarrow \underbrace{\begin{pmatrix} f_u - D_u k^2 & f_v \\ g_u & g_v - D_v k^2\end{pmatrix}}_{M(k)} - \lambda I = 0$$

Stability at k: $\det\left[M(k) - \lambda I\right] = 0$

$$\rightarrow \lambda^2 - \lambda\, \underbrace{\mathrm{Tr}(M(k))}_{T(k)} + \underbrace{\mathrm{Det}(M(k))}_{\Delta(k)} = 0$$

$$\lambda(k) = \frac{T(k)}{2} \pm \sqrt{\left(\frac{T(k)}{2}\right)^2 - D(k)}$$ (dispersion relation)

* Express $T(k)$ and $D(k)$ in terms of $T(0)$, $D(0)$

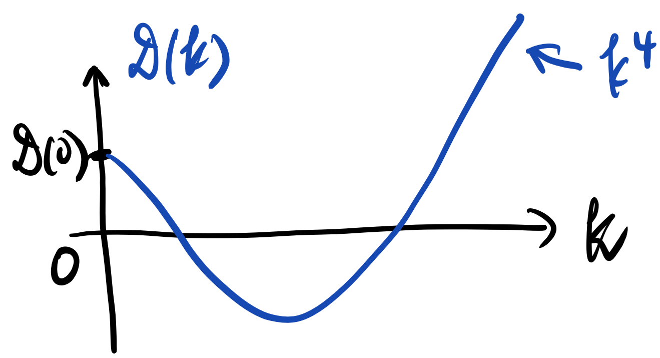
$$T(k) = f_u - D_u k^2 + g_v - D_v k^2$$
$$= T(0) - D_u k^2 - D_v k^2$$

→ since $k=0$ state stable, $T(0) < 0$, → $T(k) < 0 \ \forall k$.

$$D(k) = f_u g_v - f_v g_u + D_u D_v k^2$$
$$- (g_v D_u k^2 + f_u D_v k^2)^4$$
$$= D(0) - (g_v D_u + f_u D_v) k^2 + D_u D_v k^4$$

Since $k=0$ state stable, then $D(0) > 0$.

→ possible for $D(k)$ to be $-$ve for some k.



- requires $g_v D_u + f_u D_v > 0$

but since $f_u + g_v = T(0) < 0$,

→ must have $D_u \neq D_v$

and f_u, g_v have opposite sign.

Without loss of generality, take $f_u > 0 > g_v$

i.e., v is auto-inhibiting,

u is auto-activating

Since $f_u + g_v < 0 \quad \to \quad |g_v| > |f_u|$

for $f_u D_v + g_v D_u > 0$,

must have $D_v > D_u$

$\Rightarrow$ Inhibitor diffuses more rapidly than activator!

Note: Since $\Delta(0) = f_u g_v - f_v g_u > 0$.

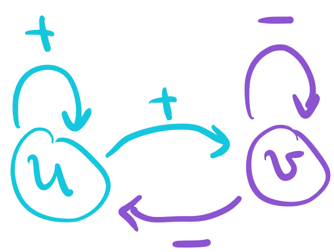
and $f_u g_v < 0$

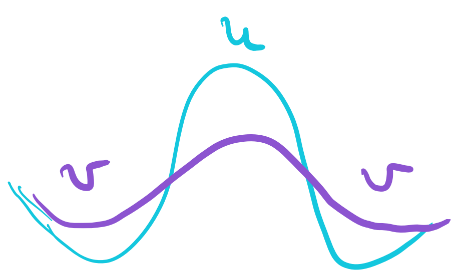
we must also have $f_v g_u < 0$

two scenarios:

i) $f_v < 0, \quad g_u > 0$.

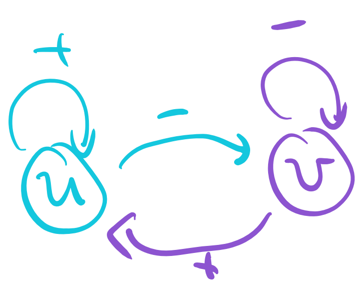
$$M = \begin{pmatrix} + & - \\ + & - \end{pmatrix}$$

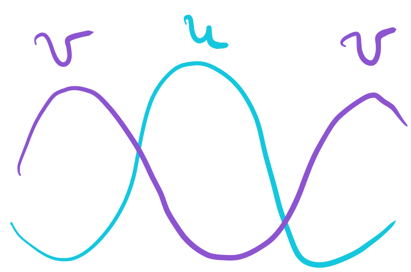




ii) $f_v > 0 \quad g_u < 0$

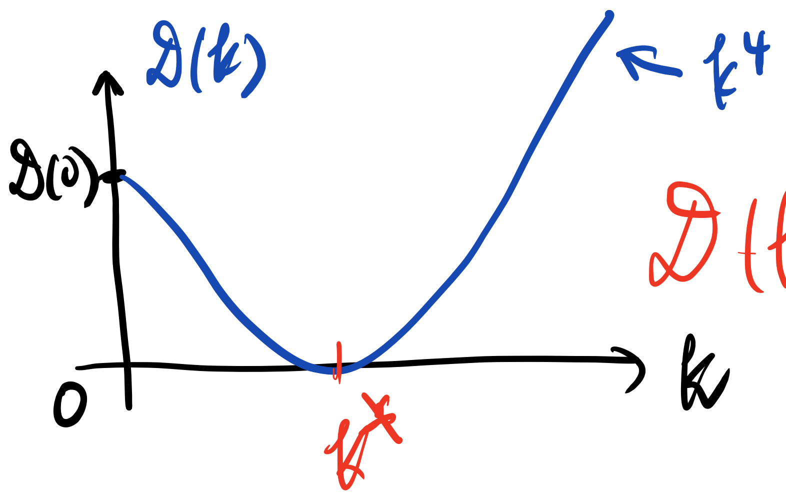
$$M = \begin{pmatrix} + & + \\ - & - \end{pmatrix}$$





* quantitative criterion for Turing instability:

$$\mathcal{D}(k) = \mathcal{D}(0) - (g_v D_u + f_u D_v)\,k^2 + D_u D_v\, k^4$$



$\mathcal{D}(k^*) \le 0$

minimum: $\quad \frac{d}{dk}\mathcal{D}(k)\Big|_{k^*} = 0 = -2k^*(g_v D_u + f_u D_v) + 4(k^*)^3 D_u D_v$

$$(k^*)^2 = \frac{g_v D_u + f_u D_v}{2 D_u D_v}.$$

$$\mathcal{D}(k^*) = \mathcal{D}(0) - \frac{(g_v D_u + f_u D_v)^2}{2 D_u D_v} + \cancel{D_u D_v}\,\frac{(g_v D_u + f_u D_v)^2}{4 D_u^{\cancel{2}} D_v^{\cancel{2}}}$$

$$= \mathcal{D}(0) - \frac{(g_v D_u + f_u D_v)^2}{4 D_u D_v}$$

$\Rightarrow$ quantitative criterion for Turing instability:

$\mathcal{D}(k^*) \le 0: \quad f_u D_v + g_v D_u \ge 2\sqrt{\mathcal{D}(0)\, D_u \cdot D_v}$

at threshold, unstable mode is

$$(k^*)^2 = \frac{g_v D_u + f_u D_v}{2 D_u D_v} = \frac{2\sqrt{\mathcal{D}(0) D_u D_v}}{2 D_u D_v} = \sqrt{\frac{\mathcal{D}(0)}{D_u D_v}}$$