Lec 1 Reaction Modeling Kinetics

Mass Action Kinetics

the rate of reaction is equal to probability of collision $\propto$ con. of the particles.

Drawbacks:

A large set of ODE to be solved

Basic Reaction

0st Order $\frac{dx}{dt} = k$ constant synthesis

1st order $\frac{dx}{dt} = -kx$ linear degradation

$x(t) = x_0 e^{-kt}$

2nd order heterodimer

$$\frac{d[XY]}{dt} = k[X][Y] = k[T_x - [XY]](T_y - [XY])$$

Rule-based modeling. Based on relational network shown in Fig 1.2A Drawbacks: sets of ODE to describe the model

Simplication Approximation

Quasis-stationary of a reaction

$X + E \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C \xrightarrow{k_2} P + E$ 4 ODE can be listed

Tofeer non dimentionlization $\begin{cases} \text{Grouping Variables} \\ \text{Normalization,} \end{cases}$

Michaelis-Menten kinetics

$$\frac{d[P]}{dt} = k_2[C] = k_2 E_T \frac{k_1[X]}{k_1[X] + k_{-1} + k_2} = V_{max}\frac{[X]}{[X]+K_m}$$

$k_2 E_T$ is the maximal rate

$K_m = \frac{k_{-1}+k_2}{k_1}$, specify

$$\frac{d[C]}{dt} = -(k_{-1}+k_2)[C] + k_1 X_T (E_T - [C])$$

$$\frac{1}{k_1(X_T+K_m)}\frac{d[C]}{dt} = -[C] + E_T\frac{X_T}{X_T+K_m}$$

This can be solved is reached exponetially fast.

Requirement / Assumption

Quasis-steady state.

Hill kinetics

$$\frac{d[P]}{dt} = V_{max}\frac{[X]^n}{K^n + [X]^n}$$

subsequent reaction when the next is triggered by one before.

第一个 low binding 其余的 $\prod$ increase

$K = (\prod K_i)^{\frac{1}{n}}$

Inhibitory

competitive

$$X + E \underset{}{\overset{k_1}{\rightleftharpoons}} C_1 \xrightarrow{k_2} P + E$$

$$\frac{dP}{dt} = V_{max}\frac{[X]}{[X] + K_m(1 + \frac{[I]}{K_I})}$$

$X + EI \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C_1I \to P + E + I$

Alloesteric

$$\frac{dP}{dt} = V = \frac{V_{max}}{1 + \frac{I}{K_I}}\frac{[X]}{K_m + [X]}$$

Goldbeter - Koshland kinetics

$$X + E_1 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C_1 \xrightarrow{k_2} X_p + E_1$$

$$X_p + E_2 \underset{p_{-1}}{\overset{p_1}{\rightleftharpoons}} C_2 \xrightarrow{p_2} X + E_2$$

Phorylation of protein.

$$\frac{d[X_p]}{dt} = -\frac{d[X]}{dt} = k_{phos} S \frac{X_T - [X_p]}{K_{m_1} + X_T - [X_p]} - k_{de} S \frac{[X_p]}{K_{m_2} + [X_p]}$$

Linear stability Analysis 与 travelling wave 结合起来看

The idea is to introduce small perturbation to a system at the steady state to study whether the perturbation grows

1. System has to be linearized around ss.
2. Based on the Jacobian matrix the stability is known.

Example $\begin{cases} \dot u = f(u,v) \\ \dot v = g(u,v) \end{cases}$ $\qquad \vec{x_s} = (u_s, v_s)^T$ is steady state

$$\frac{dx_s}{dt} = \begin{pmatrix} \dot u \\ \dot v \end{pmatrix} = 0$$

Let $w = x - x_s = \begin{pmatrix} u-u_s \\ v-v_s \end{pmatrix}$ be the small perturbation

Stable if $\vec w \to 0$ as $t \to \infty$

Linearized around $\vec{x_s}$ by Taylor Expansion

$$f(u,v) \approx \underset{0}{f(u_s, v_s)} + \frac{\partial f}{\partial u}(u-u_s) + \frac{\partial f}{\partial v}(v-v_s)$$

$$g(u,v) \sim \underset{0}{g(u_s, v_s)} + \frac{\partial g}{\partial u}\Big|_{ss} + \frac{\partial g}{\partial v}\Big|_{ss} (v$$

$$\frac{d\vec w}{dt} = \begin{pmatrix} f(\cdot,\cdot) - f(u_s, v_s) \\ g(\cdot,\cdot) - g(u_s, v_s) \end{pmatrix} = \underbrace{\begin{pmatrix} \frac{\partial f}{\partial u}\big|_{ss} & \frac{\partial f}{\partial v}\big|_{ss} \\ \frac{\partial g}{\partial u}\big|_{ss} & \frac{\partial g}{\partial v}\big|_{ss} \end{pmatrix}}_{J} \begin{pmatrix} u-u_s \\ v-v_s \end{pmatrix}$$

$J\vec w = \frac{d\vec w}{dt}$ 求 eigenvalues "因为要 decouple ODE"

For u, v

$$\lambda_{1,2} = \frac{tr(J) \pm \sqrt{tr(J)^2 - 4\det(J)}}{2}$$

$$\vec w = \sum_i w_i \vec{v_i} \Rightarrow \frac{d\vec w}{dt} = J\vec w$$

$$\sum_i \frac{d w_i \vec{v_i}}{dt} = \sum_i J w_i \vec{v_i}$$

$$\sum_i \frac{d w_i \vec v}{dt} = \sum_i w_i(t) \lambda_i \vec{v_i}$$

$$\sum_i \left[\frac{d w_i(t)}{dt} - w_i(t)\lambda_i\right]\vec{v_i} = 0$$

uncoupled since it's eigen-basis

$$\frac{d w_i(t)}{dt} = w_i(t)\lambda_i \Rightarrow w_i = w_i(0)\, e^{\lambda_i t}$$

$$\Rightarrow \vec w(t) = \sum_i w_i \vec{v_i} \exp(\lambda_i t) \qquad \lambda_i = Re(\lambda_i) + Im(\lambda_i)$$

$$= \sum_i \text{---''---} \exp[Re(\lambda_i t)] \exp[i Im(\lambda_i) t]$$

$$= \text{-------''-------} [\cos(Im(\lambda_i) t) + i\sin(\,)]$$

$\vec w(t)$ depends on $e^{Re(\lambda_i t)}$

$\Rightarrow$ { $Re(\lambda_i)$ $\forall i \le 0$, Decays to zero $\Rightarrow$ STABLE

In 2-component system

$tr(J) < 0 \quad \det(J) > 0$ 稳

如果有一个 λ_i 有 non-zero imaginary part

$$\vec w = \sum_i w_i \vec{v_i} \exp[Re_i\, t]\{\cos(\,) + i\sin(\,)\}$$

$$= \sum_i \beta_i \vec{v_i} \exp(Re_i \cdot t)(\cos(w_i t) + i\sin(w_i t))$$

Oscillations are determined by the imaginary part

Phase Plane Analysis

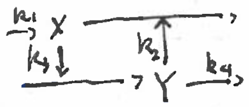
Nullclines: where the component derivative are set to zero eg. $R(I) = 0$ by $\frac{dR}{dt} = 0$

Sets of pts. in the phase plane where the state DO NOT change wrt time.

Steady State: Pts where ALL state remains stable wrt time — Intersection of nullline

Phase vectors: vectors with length — speed of change
direction — where they are going.

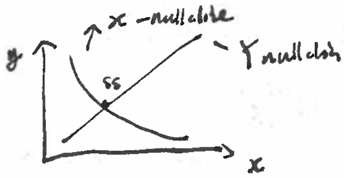
总而言之，这就是 Graphic methods to Find How the Dynamic system evolves from a initial point.
哪个像等高线带方向的图就是"风向"



$$\frac{dx}{dt} = k_1 - k_2 x y \qquad \frac{dy}{dt} = k_3 x - k_4 y.$$

当 $f(u,v) = 0 \qquad g(u,v) = 0$

$$y = \frac{k_1}{k_2 x} \qquad y = \frac{k_3 x}{k_4}$$



Lec 2 Diffusion-based Patterning

$c(x,t)$ describes the concentration given location "x" and time "t".

In 1D case: $\frac{\partial D}{\partial t} = D\frac{\partial^2 c}{\partial x^2}$ $x \in [0, L]$ where Ω is a bounded domain

How to derivate:

Fick's First Law: $J = -D\frac{\partial c}{\partial x}$ where $D = \frac{(\Delta x)^2}{2\Delta t}$ The Diffusion coeffecient.

Based on the fact Random Walk in a small interval. / h

$-\frac{1}{2}[N(x+\Delta x, t) - N(x,t)]$ $\mapsto$ $\underset{x}{|}\ \underset{x+\Delta x}{|}$ 一半向左 一半向右

$J = -\frac{1}{2}[N(x+\Delta x, t) - N(x,t)]/a\Delta t$ Flux: the amount of particles moved (流动的快慢) in a given area $\boxed{a}$

$= -\frac{1}{2}\frac{\Delta x^2}{\Delta t}\left[\frac{N(x+\Delta x, t) - N(x,t)}{a(\Delta x^2)}\right]$

$= -\frac{1}{2}D\,\frac{c(x+\Delta x, t) - c(x,t)}{\Delta x} = -D\frac{\partial c}{\partial x}$

Fick's Second Law:

Based on the conservation of mass.

$$\frac{\Delta c}{\Delta t} = -\frac{J(x+\Delta x, t) - J(x,t)}{\Delta x}$$

$$\frac{\partial c}{\partial t} = -\frac{\partial J}{\partial x} = \frac{\partial}{\partial x}D\frac{\partial c}{\partial x} = D\frac{\partial^2 c}{\partial x^2}$$

In 3D case: It's similar but $D = \frac{(\Delta L)^2}{6\Delta t}$

First Law:

$J = -D\nabla c$

Second Law

$\frac{\partial c}{\partial t} = -\nabla\cdot J = (D\Delta c)$ if D is constant

$= -\nabla(-D\nabla c)$

Solving PDE

$$\begin{cases} \frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} \\ c(t,0) = c(t,\pi) = 0 \\ c(0,x) = \sin x \end{cases}$$

这个特征模型 而是一个 madeup-

1 separation of variables

$c = T(t)X(x)$ Proposed 假设,可以分离变量 D 可以约去

$\frac{\partial T(t)X(x)}{\partial t} = D\frac{\partial^2}{\partial x^2}T(t)X(x)$

$\frac{T'}{T} = \frac{X''}{X} = \lambda$

For Temporal part $T'(t) = T(t)\cdot\lambda$

$\Rightarrow T(t) = T(0)e^{\lambda t}$

For Spatial part $X''(x) = \lambda X(x)$

$\Rightarrow X(x) = c_1 e^{\sqrt{\lambda}x} + c_2 e^{-\sqrt{\lambda}x}$

2 Boundary Condition

$c(t,0) = c(t,\pi) = 0$

$\lambda < 0 \Rightarrow \sqrt{\lambda} = i w$

$X(x) = c_1[\cos(wx) + i\sin(wx)] + c_2[\cos(-wx) + i\sin(-wx)]$

$= \cos(wx)[c_1 + c_2] + i\sin(wx)[c_1 - c_2]$

$c_1 + c_2 = 0$ $\sin c(t,\pi) = 0$

$\Rightarrow X(x) = 2ic_1\sin(wx) \Rightarrow w = n$

$\Rightarrow \lambda = -n^2$ $n = 1, 2, \ldots$

By principle of superposition

$c(t,x) = \sum_{n=1}^{\infty} A_n e^{-n^2 t}\sin(nx)$, $A_n = 2ic_1T_0$

3 Initial Condition

$c(0,x) = \sin x \Rightarrow A_n = \begin{cases} 1, & n=1 \\ 0, & \text{else} \end{cases}$

Final $c(t,x) = e^{-t^2}\sin(x)$

浓度在 Domain 边界上始终为 0 的情况

Example: IC $c(x,0) = 0$ $x > 0$

BC $c(0) = c_0$ $c(L) = 0$

i.e. 最开始浓度为 0, 有一端始终为一种浓度.

morphogen

Only Diffusion

$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2}$ $x \in [0, L]$

$c(x) = c_0\cdot\frac{L-x}{L}$ Stedy State Solution

French-Flag Model 提出的就是这种浓度梯度.

If IC: $c(0,0) = c_0$, $c(0,x) = 0$ $\forall x > 0$

This does not easily agree w/ the general solution

$c(x,t) = T(0)e^{-D\lambda t}[c_1 e^{-\sqrt{\lambda}x} + c_2 e^{\sqrt{\lambda}x}]$

这样 BC 不满足 因为

$c(0,t) = T(0)e^{-D\lambda t}(c_1 + c_2) \neq c_0$

Solution $u(x,t) = c(x,t) - c_s(x)$ where

$c_s(x) = c_0\frac{L-x}{L}$ $\boxed{\forall x > 0}$

选择的话

BC: $u(t,0) = c(t,0) - c_s(0) = 0$

$u(t,L) = 0$

IC $u(0,0) = 0$

$u(0,x) = -c_0\frac{L-x}{L}$ $\forall x \in [0, L]$

我们得到 homogenous Boundary Condition, 这个就比较好做了

Following the steps on the left

$X(x) = 2ic_1\sin\left(\frac{n\pi x}{L}\right)$

$u(x,t) = \sum_{n=1} A_n e^{-\frac{Dn^2\pi^2}{L^2}t}\sin\left(\frac{n\pi x}{L}\right)$ $A_n = 2ic_1T(0)$

IC

$u(0,x) = -c_0\frac{L-x}{L} = f(x) \stackrel{!}{=} \sum_{n=1}^{\infty} A_n e^{-\frac{Dn^2\pi^2}{L^2}t}\sin\left(\frac{n\pi x}{L}\right)$

两边乘以 $\sin\left(\frac{m\pi x}{L}\right)$ Integrate from $[0, L]$

$\int_0^L f(x)\sin\left(\frac{m\pi x}{L}\right)dx = \int_0^L \sum \# \sin\left(\frac{m\pi x}{L}\right)dx$

$\int_0^L \sin\left(\frac{n\pi x}{L}\right)\sin\left(\frac{m\pi x}{L}\right)dx = 0$ $\forall m \neq n$

$\Rightarrow$

$$\int_0^L f(x)\sin\left(\frac{n\pi x}{L}\right)dx = \frac{L}{2}A_n$$

$$\Rightarrow \quad A_n = \int_0^L f(x)\sin\left(\frac{n\pi x}{L}\right)dx \cdot \frac{2}{L}$$

$$= -\frac{2c_0}{n\pi}$$

Thus the final solution is $c(t,x) = c_s(t,x) + u(t,x)$

$$= c_0\frac{L-x}{L} + -\sum_n^{\infty} \frac{2c_0}{n\pi} e^{-D\frac{n^2\pi^2}{L^2}t}\sin\left(\frac{n\pi x}{L}\right)$$

Time to steady state

$$t = \frac{1}{k} = \frac{L^2}{Dn^2\pi^2}$$ since it reaches s.s. exponentially faster with rate k

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Example: Constant Morphogen inflow

IC : $c(x,0) = 0$

BC : $\left.\frac{\partial c}{\partial x}\right|_0 = -j \qquad \left.\frac{\partial c}{\partial x}\right|_L = 0$

~~$C_s(x) = ax+b$~~ $C_s(x) = ax+b$ 但是两个BC两个值

$\Rightarrow$ no s.s.

If BC : $\left.\frac{\partial c}{\partial x}\right|_0 = -j \qquad c(L,t) = 0$

$a = -j \quad b = Lj \qquad C_s(x,t) = -jx + Lj$

With degradation $\quad \frac{\partial c}{\partial t} = D\Delta c - kc \qquad x \in [0,1]$

IC $\quad c(x,0) = 0$

Influx $\quad$ BC $\quad \left.\frac{\partial c}{\partial x}\right|_0 = -j \qquad \left.\frac{\partial c}{\partial x}\right|_1 = 0$

$c(x) = a e^{\mu x} + b e^{-\mu x} \qquad \mu = \sqrt{\frac{k}{D}}$ is the general solution

Importance of degradation

也是一样 : Separation of variables

PDE 化为 $\quad \frac{T'}{T} + k = 6 = D\frac{X''}{X}$

这同样也是 Inhomogenous 同样也是 减去 $C_s(x)$

Without degradation $\quad \frac{\partial c}{\partial t} = D\Delta c$

BC $\quad \left.\frac{\partial c}{\partial x}\right|_0 = j \qquad c(L,t) = 0$

$\rightarrow C_s(x) = ax+b$

Standard Model : Boundary at infinity.

$\frac{\partial c}{\partial t} = D\Delta c - kc \; ; \quad 0 \le x \le \infty$

IC $\quad c(x,0) = 0$

BC $\quad c(0,t) = C_0, \quad c(x\to\infty) = 0$

Steady state solution

$c(x) = c_0\exp\left(-\frac{x}{\lambda}\right) \quad \lambda = \sqrt{\frac{D}{k}}$

Lec 3 Morphogen Gradient

SEC self-enhanced decay.

How does the system maintain robustness with morphogen gradient? How will the read out of steady state be affected by change

How does it react to changing term?

$$\frac{\partial}{\partial t} = D\Delta c - f(c)$$

BC:
1. Fixed con. at both ends $c(0,t) = c_0$ & $c(L) = 0$
2. Fix at source $c(0,t) = c_0$, $c(x \to \infty) = 0$
3. $\left.\frac{dc}{dx}\right|_0 = -j$; $\left.\frac{\partial c}{\partial x}\right|_L = 0$

IC $c(x>0, 0) = 0$

$f(c)$:

none → linear gradient

linear → exponential gradient

non-linear → powerlaw gradient

For linear degradation $c(x) = c_0 \exp\{-\frac{x}{\lambda}\}$ $\lambda = \sqrt{\frac{D}{k}}$

standard model with $c(x \to \infty) = 0$

In the seeting of the standard model:

$$\Delta x = x^*_\theta - x_\theta$$

$$c_\theta = c_0 \exp\{-\frac{x_\theta}{\lambda}\} \qquad c_\theta = c_0^* \exp\{-\frac{x_\theta^*}{\lambda}\}$$

$$\frac{c_0^*}{c_0} = \exp\{-\frac{x_\theta}{\lambda} + \frac{x_\theta^*}{\lambda}\}, \quad \boxed{\Delta x = x_\theta^* - x_\theta = \lambda \ln\left(\frac{c_0^*}{c_0}\right)}$$

Read out shift

shift

$$\Delta x = \lambda \ln \frac{c_0^*}{c_0}$$

Power-Law (Non-linear decay)

$$PDE: \frac{\partial c}{\partial t} = D\Delta c - kc^n$$

$$c(x) = \frac{1}{A(x+\varepsilon)^m}; \quad m = \frac{2}{n-1}$$

$$\boxed{\ln(x_\theta^* + \varepsilon^*) - \ln(x_\theta + \varepsilon) = \frac{1}{m} \ln\left(\frac{A^*}{A}\right)}$$

shift

Lec4. Morphogen Gradients ~~on~~ growing domain.

How do we get the Reaction-Diffusion Equations

Reasoning: Total temporal chang in Ω = change due to j (fluxes) and Reaction $R(c)$

$$\frac{d}{dt}\int_\Omega c_i(x,t)\,dx = \underbrace{\int_{\partial\Omega} j n\, dS}_{\boxed{\text{fluxes on edge}}} + \underbrace{\int_\Omega R(c)\,dx}_{\boxed{\text{Reaction}}}.$$

$$\| \qquad\qquad\qquad \|$$

$$\int_\Omega \frac{dc_i(x,t)}{dt}\,dV \qquad -\int_\Omega \nabla\cdot j\,dx \quad (\text{Divergence Thm})$$

Leibnitz Integral

$$\nabla j = -D\Delta c$$

$$\int_\Omega \frac{dc_i(x,t)}{dt}\,dV = \int_\Omega \{D_i\Delta c_i + R(c_k)\}\,dV$$

$$\int_\Omega \left[\frac{\partial c_i(x,t)}{\partial t} - D_i\Delta c_i - R(c_k)\right] dV = 0$$

$$\Rightarrow \quad \frac{\partial c_i}{\partial t} = D_i\Delta c_i + R(c_k)$$

On a growing domain

Mapping $\Omega_\xi \to \Omega_t$

$$\frac{d}{dt}\int_{\Omega_t} c_i(x,t)\,d\Omega_t = \frac{d}{dt}\int_{\Omega_\xi} c_i(x(\xi,t),t)\det J\,d\Omega_\xi$$

$$= \int_{\Omega_\xi}\left[\frac{dc_i}{dt}\det J + c_i\frac{d(\det J)}{dt}\right]d\Omega_\xi$$

$$= \int_{\Omega_\xi}\Big[\frac{\partial c_i}{\partial t} + \underbrace{u\nabla c_i}_{\text{advectio}} + \underbrace{c_i\nabla u}_{\text{dilution}}\Big]\det J\,d\Omega_\xi$$

$$= \int_{\Omega_t}\left[\frac{\partial c_i}{\partial t} + \nabla c_i u\right]d\Omega_t$$

u: $\frac{dx}{dt}$ velocity

$$\Rightarrow \quad \frac{\partial c_i}{\partial t} + \nabla c_i u = D_i\Delta c_i + R(c_i)$$

Lagrangian Framework   跟着细胞做标记

A mapping b/w ϕ is able to map from Euler to Lagrain

(x,t) (X,t)

Euler.

Material Derivative

$F = F(X,t)$: the value of F experienced at time t by the particle initially at X

$$\frac{dF}{dt} = \frac{dF(x(X,t),t)}{dt} = \frac{dF(X,t)}{dt}$$

$$\underbrace{\frac{dF(X,t)}{dt}}_{\text{Lag}} = \frac{\partial F}{\partial t}\Big|_x + \frac{\partial F}{\partial x_k}\frac{\partial x_k(X,t)}{\partial t} = \underbrace{\frac{\partial F}{\partial t}\Big|_x + u\nabla F}_{\text{Euler}}$$

In the case of uniform growth, stays the same in lag.

ALE

$$\frac{\partial c_i}{\partial t}\Big|_z + \underbrace{w\nabla c_i}_{\text{advection}} + \underbrace{c_i\nabla u}_{\text{dilution}} = D_i\Delta c_i + R(c_i)$$

$w = u - v$ [the velocity b/w materials and ALE]

u: material velocity; v: mesh velocity

Example Uniform Growth

X ~ starting dom

$x(t) = L(t)X$ ~ Euler

把Euler坐标 → Lag坐标

$$\frac{\partial X}{\partial x} = \frac{1}{L(t)} \qquad u = \frac{dx}{dt} = \dot L(t)X \qquad \frac{\partial u}{\partial X} = \dot L(t)$$

$$\frac{\partial c}{\partial t} + \nabla(cu) = D\frac{\partial^2 c}{\partial x^2} + R(c)$$

$$\frac{dc}{dt} + c\frac{\partial u}{\partial x} = D\frac{\partial^2 c}{\partial x^2} + R(c)$$

$$\frac{\partial c}{\partial t} + c\cdot\frac{\partial u}{\partial X}\cdot\frac{\partial X}{\partial x} = D\frac{\partial^2 c}{\partial X^2}\left(\frac{\partial X}{\partial x}\right)^2 + R(c)$$

$$\frac{\partial c}{\partial t} + c\cdot\dot L(t)\cdot\frac{1}{L(t)} = D\frac{\partial^2 c}{\partial X^2}\left(\frac{1}{L(t)}\right)^2 + R(c)$$

Lec 5 Turing Pattern

Patterns: SS (in time) solution of sets of equations

$$\dot{u} = f(u,v) + \boxed{D_1 \Delta u}$$
$$\dot{v} = g(u,v) + \boxed{D_2 \Delta v}$$
Diffusion term

IC: $u(x,0) = U_0(x)$
$v(x,0) = V_0(x)$

$\vec{w} = \begin{pmatrix} u-u^* \\ v-v^* \end{pmatrix}$ $\quad \dot{\vec{w}} = J\vec{w}$

$w(x,t) = \sum_{i=1} a_i \vec{v}_i \exp(\lambda_i t)$

$\lambda_i = \dfrac{tr(J) \pm \sqrt{tr(J)^2 - 4\det J}}{2}$

$\lim_{t\to\infty} w(x,t) \to 0$ we have a stable system

$\Rightarrow \lambda_i < 0 \quad \forall i = 1,2$

$\Rightarrow tr(J) < 0 \quad \det(J) > 0$

With Diffusion

$\dot{\vec{w}} = J\vec{w} + D\Delta\vec{w} \qquad D = \begin{bmatrix} D_1 & 0 \\ 0 & D_2 \end{bmatrix}$ $\quad D_1 > 0, D_2 > 0$ "Biological"

1. By separatation of variables

$\vec{w} = \phi(t) W(x)$

$\phi(t) = \sum_i a_i \vec{v}_i \exp(\lambda_i t)$ $\quad \dot{\phi} = J\phi$

$W(x) = \sum_i \alpha_i \vec{v}_i \exp(ikx)$ $\quad JW = -D\Delta W$

$w = \sum_i a_i \vec{v}_i \exp\{\lambda_i t + ikx\}$

$\dot{\vec{w}} = \lambda \vec{w}$ 因为 那个从表达式看出来

$J\vec{w} + D\Delta\vec{w} = J\vec{w} - k^2 D\vec{w}$

$\Rightarrow \lambda\vec{w} = J\vec{w} - k^2 D\vec{w}$

$(H - \lambda I)\vec{w} = 0 \qquad H = J - k^2 D$

2. 满足 Non-trivial solution 条件

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

$\det(H) + \lambda^2 - \lambda\, tr(H) = 0$

$\circ\ tr(H) = tr(J) - k^2(D_1 + D_2)$

$\det(H) = D_1 D_2 k^4 - (D_2 f_u + D_1 g_v)k^2 + \det(J)$

instability requires $\det(H) < 0$

$\Rightarrow \quad D_2 f_u + D_1 g_v > D_1 D_2 k^2 + \dfrac{\det(J)}{k^2} > 0$

$\det(H) = h(k^2)$ 二次方程

$k^2_{min} = \dfrac{D_2 f_u + g_v D_1}{2 D_1 D_2}$

$\Rightarrow \det(H) = h_{min}^2 = -\dfrac{(D_2 f_u + D_1 g_v)^2}{4 D_1 D_2} + \det(J)$
< 0

$-(D_2 f_u + D_1 g_v)^2 + 4 D_1 D_2 \det(J) < 0.$

要让 $D_2 f_u + D_1 g_v > 0$ 因为 $g_v + f_u = tr(J) < 0$

$\Rightarrow D_1\ D_2$ 不同 且 $g_u + f_v$ 不同 方向

If $\Omega = [0, L]$ zero flux

$\sum a_n \vec{v}_n \exp(\lambda_i k^2 t) \cos\left(\frac{n\pi x}{L}\right)$

Zero-flux $(\vec{n}\cdot\nabla)\vec{w} = 0$ on $\partial\Omega$,

$W(x) = \sum_n \alpha_n \cos\left(\frac{n\pi x}{L}\right)$, $\quad k^2 = \dfrac{n^2\pi^2}{L^2}$

因为 $\sin(kL) = 0 \Rightarrow kL = n\pi$

$W(x) = \sum_n \alpha_n \exp\{ikx\} = \cancel{\sum \alpha_n \exp}$

$= \sum_n \alpha_n(\cos(kx) + i\sin(kx))$ $\quad \sin kL = 0$

$= \sum_n \alpha_n \cos\left(\frac{n\pi x}{L}\right)$

Summary. 2-component system

$\dfrac{\partial u}{\partial t} = D_1 \nabla^2 u + f(u,v)$

$\dfrac{\partial v}{\partial t} = D_2 \nabla^2 v + g(u,v)$

Turing Instability iff

$f_u + g_v < 0 \Leftrightarrow tr(J) < 0$
$\det(J) > 0$
STABLE solution w/o Diffusion

$D_1 g_v + D_2 f_u > 2\sqrt{D_1 D_2 (\det J)}$
This is unstable w/o diffusion

Lec 9 Travelling wave.

$u(x,t)$ represents a travelling wave
it will travells without change of shape.] speed of propagation is a const. c

$u(x,t) = u(x-ct) = u(z)$ $z = x - ct$

z is the wave variables,

Example Logistics growth

general solution:

$$u(x,t) = \frac{c\exp(t)}{1+c\exp(t)}$$

If IC: $u(x,0) = \frac{1}{1+\exp(x)}$

$\Rightarrow u(x,t) = \frac{\exp(t-x)}{1+\exp(t-x)}$ $z = x-t$

如果 z 是 const. then the shape does NOT change

i.e. $\frac{dx}{dt} = 1$

PDE $\Rightarrow$ Sets of ODEs

$u(x,t) = u(x-ct) = u(z)$

$$\begin{cases} \frac{\partial u}{\partial t} = -c\frac{du}{dz} \\ \frac{\partial u}{\partial x} = \frac{du}{dz} \end{cases}$$

Diffusion

$\frac{\partial u}{\partial t} = D\frac{\partial^2 u}{\partial x^2}$

$\Leftrightarrow u_t = D u_{xx}$ 简写

对 x 求导 两次

$\Rightarrow D U'' + cU' = 0$ since we have $u_t = -c\frac{du}{dz}$

$\Rightarrow U(z) = A + B\exp(-cz/D)$ has to be bounded and non-negative.

const.

$\Rightarrow B = 0$ There's no physically realistic travelling solution for linear parabolic PDEs.

An additional term $f(u)$

$u_t = f(u) + D u_{xx}$

$DU'' + cU' + f(u) = 0$

① Fisher equation $f(u) = ku(1-u)$

$u_t = ku(1-u) + D u_{xx}$

non-dimensionalized $\Rightarrow$

$u_t = u(1-u) + u_{xx}$

$U'' + cU' + U(1-U) = 0$ ODE $\Rightarrow$ $\begin{cases} U' = V \\ V' = -cV - U(1-U) \end{cases}$

Determine the linear stability of the system

$\vec{w} = (U-U_s, V-V_s)^T$

$\frac{dw}{dt} = (\quad)\vec{w} = Jw$ $\lambda_{1,2} = \frac{tr(J) \pm \sqrt{[tr(J)]^2 - 4\det(J)}}{2}$

然后我们可以观察 Nullline ..

$U' = V$

$V' = -cV - U(1-U)$

(1,0) saddle node

(0,0) stable pt.

For Travelling waves to exist we require one stable node and one saddle node.

Ca^+ stimulated calcium release mechanism

$u_t = f(u) + D u_{xx}$ $\Rightarrow$ $DU'' + cU' + f(U) = 0$

kinetics for Ca^{2+}: $u_t = A(u) - r(u) + L = f(u)$

$= \frac{k_1 u^2}{k_2 + u^2} - k_3 u + L$ 有三个根

$= A(u-u_1)(u-u_2)(u-u_3)$

By looking at the graph of $f(u)$

$\Rightarrow \{ \; u' = \frac{du}{dz} = \alpha(U-U_1)(U-U_3)$

Ca^{2+} wave in Amphibian Eggs

Wave pining

If a travelling wave eventually halts. the phenomenon is reffered as wave pining.

$U' = \frac{du}{dz} = \alpha(U-U_1)(U-U_3)$ 因为 $U' = 0$ at U_1 U_3

$\Rightarrow U'' = \alpha(2U - U_1 - U_3)U'$

$\Rightarrow$ 代入 $D\alpha(2U-U_1-U_3)U' + \alpha(U-U_1)(U-U_3) + A(U-U_1)\cdots = 0$

$(U-U_1)(U-U_3)[D\alpha^2(2U-U_1-U_3) + c\alpha + A(U-U_2)] = 0$

To be zero for all U

Lec 10 chemotaxis

the presence of a gradient in a chemoattraction give rise to movement up the con. gradient

Continuum Model

cell density $n(x,t)$

chemo $r(x,t)$

1. Random Walk Diffusion
2. Chemical Flux

$$J_c = -\chi n \frac{\partial r}{\partial x} \qquad r: \text{repell}$$

$$J_c = \chi n \frac{\partial a}{\partial x} \qquad a: \text{attrant.}$$

Keller-Segel Model

$$\left.\begin{aligned} J_c &= n\chi(a)\nabla a \\ J_D &= -D\nabla n \end{aligned}\right| \begin{aligned} &\text{chem} \\ &\text{Diffu} \end{aligned} \qquad J = J_c + J_D$$

General Model

cells: $\frac{\partial u}{\partial t} = D_u \nabla^2 u - \alpha \underbrace{\nabla (u\chi(v)\nabla v)}^{\text{chemo flux}} + f(u,v)$

Attractant: $\frac{\partial v}{\partial t} = D_v \nabla^2 v + g(u,v)$

Parameter: α, χ, D_u, D_v

To have patterns: Unstable steady state => Linear stability analysis.

$\vec{w} = \varepsilon \begin{pmatrix} u_i \\ v_i \end{pmatrix}$ around the steady state

$$\frac{\partial \vec{w}}{\partial t} = D\Delta\vec{w} + J\vec{w} \qquad D = \begin{pmatrix} D_u & -\alpha u^* \chi(v^*) \\ 0 & D_v \end{pmatrix}$$

Also using separation of variable.

$$J = \begin{pmatrix} f_u^* & f_v^* \\ g_u^* & g_v^* \end{pmatrix}$$

$$\Rightarrow w_i = \phi_i(t) W_i(x) = \exp(\lambda_i t) \cdot \exp(ik_i x)$$

与Turing Pattern 那套相似

$$\frac{\partial w}{\partial t} = \lambda w = J\vec{w} + D\Delta\vec{w} = J\vec{w} - k^2 D\vec{w}$$

对谁求导

$$\Rightarrow H\vec{w} = \lambda\vec{w} \qquad H = J - k^2 D$$

$$H = \begin{pmatrix} f_u^* - D_u k^2 & f_v^* + \alpha\chi u^* k^2 \\ g_u^* & g_v^* - D_v k^2 \end{pmatrix}$$

学也有用

Real part of $\lambda(0) < 0 \Rightarrow tr(J) = (f_u^* + g_v^*) < 0$

what is a Ising model and MWC model ?

the energy functions of this system $\vec{s} = \{s_1 \ldots\}$

$$H(\vec{s}) = -\sum_{\langle ij \rangle} \underbrace{J s_i s_j}_{\text{interaction}} - \sum_i \underbrace{h s_i}_{\text{external affect}}$$

$\vec{s} \sim$ Boltzmann dist.

MWC - subclusters divided but in the same configure

~~Sam~~ Special case of the cluster.

$$\begin{cases} J = \infty & \text{在同个clu} \\ J = 0 & \text{不同} \end{cases}$$

粗粒化模拟 protein subunit interaction.

E.coli chemotaxis signal

加多 signal / ligand 的形状还都保持大致不变

<u>Negative Feedback with a buffer node</u>

Lec 6 Tissue Simulation Framework.

Continuous Tissue Models

和统不太适合 先看 cell-based 的吧

Cell-based modelling

why? since various cellular activities can be easily represented via this method

1. Cellular Potts Model. (On lattice)
   从 Ising Model 那里 来的.
   - spin $\sigma(x) \in \mathbb{Z}^{+,0}$
   - value: cell identity

Hamiltonian. Energy function describes how it evolves over time

$$H = \underbrace{H_v}_{\text{volume constraction}} + \underbrace{H_a}_{\text{adhesion}}$$

Using Metropolis algo. to calculate the spin value and how it progress over time.

- Initialization { Random / Real data.

2. Spheroid Model
   - Represent cells as particles $\boxed{\text{spherical}}$
   - Determined all the ~~sum~~ of the force → Movement

eg

3. Subcellular Model.
   Using potential function (Morse potential)
   ⇒ Force acting on each subcellular components
   ⇒ Movement.

4. Vertex Model.
   - Polygons / sharing edges
   - Forces derived from potentials. at each vertex

$$E(R_i) = \underbrace{\sum_{\alpha} \frac{K_\alpha}{2}(A_\alpha - A_\alpha^0)^2}_{\text{Elastic compared to resting area.}} + \underbrace{\sum_{\langle ij \rangle} \Lambda_{ij} l_{ij}}_{\text{Tension}} + \underbrace{\sum_{\alpha} \frac{\Gamma_\alpha}{2} L_\alpha^2}_{\text{contractility}}$$

5. Immerse Boundary Cell Model
   比 Vertex 更加细致
   - cell-cell junction also approximated.

	Pros	Cons
Cellular Potts	Simples, high abstr	Expensive as you have to calculate at each time step.
Spherical	~~No~~ Cheap.	No cellular details. Only spherical. No signally / restricted
Subcellular	Shape details.	expensive
Vertex	details ⇑ efficient	Shared edges.
IBCM	junction 细节	2D, Expensive.

Lec 15 Organization of Epithelial tissue.

- Epithelia cells are well connected via a ring of Intercellular junctions.
- Usually the boundary are well-defined as a "polygonal" shape

why on average we only have 6 neighbours.

- Aboav–Weaire Law
  $m_n = 5 + \frac{8}{n}$ it's average no. of neighbo

- Lewis's Law: cell Area related to Polygon class

$$A_n = \frac{A_0}{N} \frac{(n-2)}{4} \quad \text{edge.}$$

N: Total Number of cells

- Euler's Theorem — Averaging Neighbour Number.

$$F - E + V = \chi$$

F: Faces, E: Edge, V: vertices, χ: global character of the manifold

$$\sum n F_n = 2E$$

每个 Edge separate 两个面.

每个 vertex 分开多少个

$$\sum \alpha V_\alpha = 2E$$

每个 Edge 把两个 vertex 连接起来.

$$\sum_{1 \dots \infty} n F_n = F \sum n P_n = F\langle n \rangle \quad \text{Average number}$$

$$F + \frac{2-\alpha}{\alpha} E = \chi \Rightarrow F + \frac{2-\alpha}{\alpha} \sum_n F_n = \chi$$

$$\Rightarrow \langle n \rangle = \frac{2\alpha}{\alpha - 2} + \frac{2\alpha\chi}{(\alpha-2)F}$$

limit of $\langle n \rangle$ goes to $\frac{2\alpha}{\alpha-2}$. 在细胞 $\alpha = 3$ ⇒

1. Impact of cellular distrim.
   MC Theory I guess
2. Tissue Mechanics
   Modelled by vertex models.

$$F - E + V = \chi$$

$$V = \frac{2E}{\alpha} \qquad E = \frac{\sum}{2} n F_n.$$