多種の相互作用

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7．数理モデリングの基礎

微分方程式

$$\frac{dx}{dt} = f(x), \ x|_{t=0} = x_0$$ autonomous

$$\frac{dx}{dt} = Ax, \ x|_{t=0} = x_0$$ linear system

$$\frac{dx}{dt} = x^2, \ x|_{t=0} = T^{-1} \Longrightarrow x(t) = (T-t)^{-1}, \ \lim_{t \uparrow T} x(t) = +\infty$$ blowup

$$\frac{dx}{dt} = \sqrt{x}, \ x \geq 0, \ x|_{t=0} = 0 \Longrightarrow x(t) = \begin{cases} 0, & 0 \leq t \leq T \\ \frac{1}{4}(t-T)^2, & t \geq T \end{cases}$$ uniqueness

Fundamental theorem (Lipschitz continuity)
・local wellposedness
・extension of the solution

normalization $$\frac{dx}{dt} = kx^2, \ \bar{t} = kt, \ \frac{dx}{d\bar{t}} = x^2$$

integration $$\frac{dx}{dt} = f(x), \ \int \frac{dx}{f(x)} = \int dt = t + c$$

exponential function $$e^x = \sum_{n=0}^{\infty} \frac{x^n}{n!}, \ \frac{d}{dx} e^x = e^x$$

Euler relation $$e^{\imath\theta} = \cos\theta + \imath \sin\theta, \ \theta \in \mathbf{R}$$ theory of linearized stability

3つの応用

resolution of isotope

physical constant (known)

$$\frac{dx}{dt} = -\lambda x, \; x(0) = x_0$$

$$\Rightarrow \quad x(t) = x_0 e^{-\lambda t}$$

$$\frac{1}{2} = \frac{x(t_2)}{x(t_1)} = \frac{x_0 e^{-\lambda t_2}}{x_0 e^{-\lambda t_1}} = e^{-\lambda(t_2 - t_1)}$$

$$\log 2 = \lambda(t_2 - t_1)$$

$$\Delta t \equiv t_2 - t_1 = \frac{\log 2}{\lambda}$$

half-life

absolute dating

$t = 0$ starting of the resolution of C14

$$R_0 = -\left.\frac{dx}{dt}\right|_{t=0}$$

resolution rate of the plant
known

$$R_0 = \lambda x_0$$

$$R = -\left.\frac{dx}{dt}\right|_{t=t}$$

Resolution rate of the buried material
measurable

$$R = \lambda x_0 e^{-\lambda t}$$

$$\frac{R_0}{R} = \frac{\lambda x_0}{\lambda x_0 e^{-\lambda t}} = e^{\lambda t} \quad \Rightarrow \quad t = \frac{1}{\lambda} \log \frac{R_0}{R}$$

computable

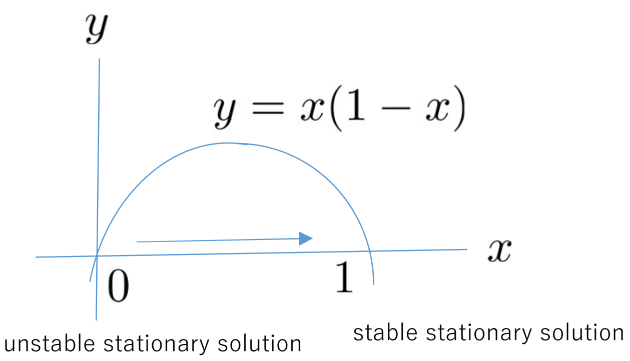
saturation

$$\frac{dx}{dt} = x(1-x), \; x|_{t=0} = x_0 \in (0,1)$$

logistic equation

$$x(t) = \frac{x_0}{x_0 + (1 - x_0)e^{-t}}$$

sigmoid function

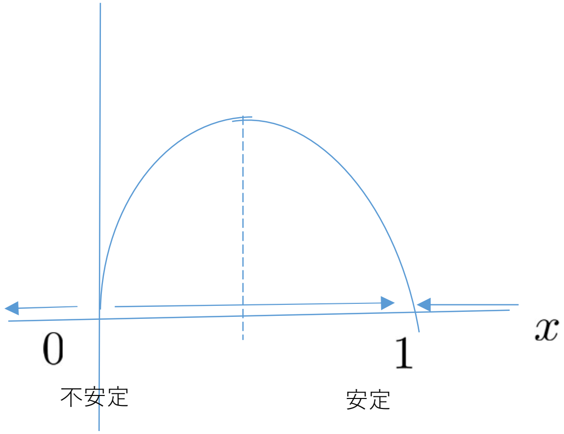


1次元力学系

$$\dot{x} = f(x)$$

$y = f(x)$ $\quad$ $f(x_0) = 0,\ x(0) = x_0$ $\xrightarrow{\text{解の一意性}}$ $x(t) \equiv x_0$

定常解（定常状態）



$$f(0) = f(1) = 0$$
$$f(x) > 0,\ 0 < x < 1$$
$$f(x) < 0,\ x < 0, x > 1$$

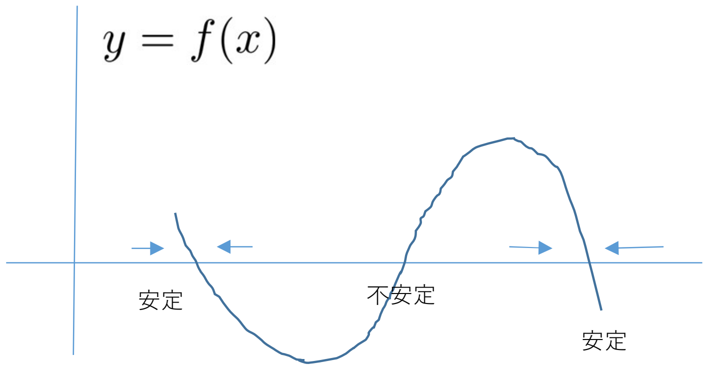
$\Longrightarrow$ $x = 0, 1$ 定常解

線形化理論 $f'(1) < 0$ $\Longrightarrow$ 安定

漸近安定

$f'(0) > 0$ $\Longrightarrow$ 不安定

局所理論



大域理論

モース理論

2次元力学系

$$\dot{x} = f(x,y),\ \dot{y} = g(x,y) \qquad \underset{\text{stationary state}}{f(x_0,y_0) = g(x_0,y_0) = 0} \qquad \underset{\text{perturbation}}{X = x - x_0,\ Y = y - y_0}$$

$$f(x,y) = f(x_0,y_0) + f_x(x_0,y_0)(x-x_0) + f_y(x_0,y_0)(y-y_0) + o(\sqrt{(x-x_0)^2+(y-y_0)^2})$$

$$g(x,y) = g_x(x_0,y_0) + g_x(x_0,y_0)(x-x_0) + g_y(x_0,y_0)(y-y_0) + o(\sqrt{(x-x_0)^2+(y-y_0)^2})$$

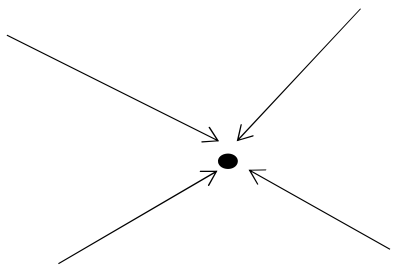
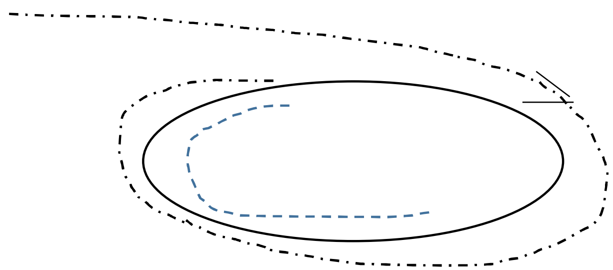
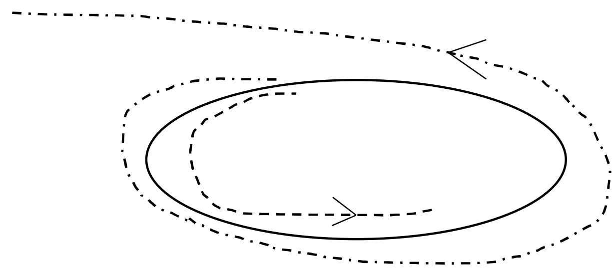
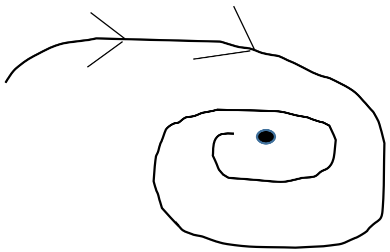
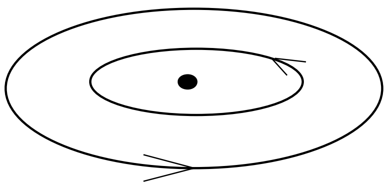
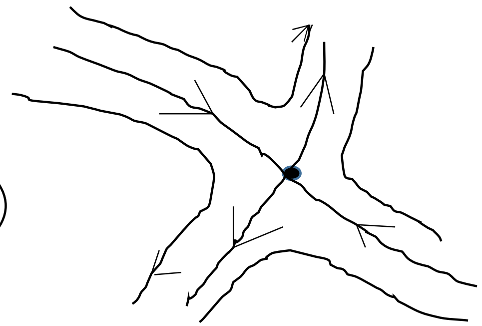
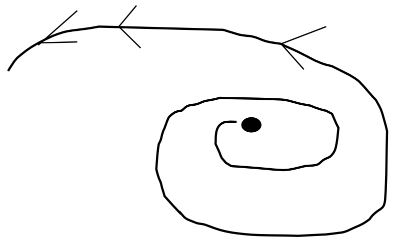
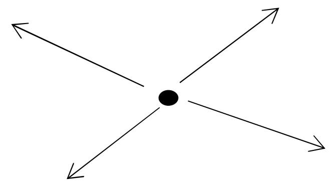
$$\frac{d}{dt}\begin{pmatrix} X \\ Y \end{pmatrix} = \begin{pmatrix} f_x(x_0,y_0) & f_y(x_0,y_0) \\ g_x(x_0,y_0) & g_y(x_0,y_0) \end{pmatrix}\begin{pmatrix} X \\ Y \end{pmatrix}$$

linearized equation

nodes（stable, unstable）
forcus (stable, unstable)
cebter
saddle

sub-critical Hopf bifurcation
super-critical Hopf bifurcation

caos

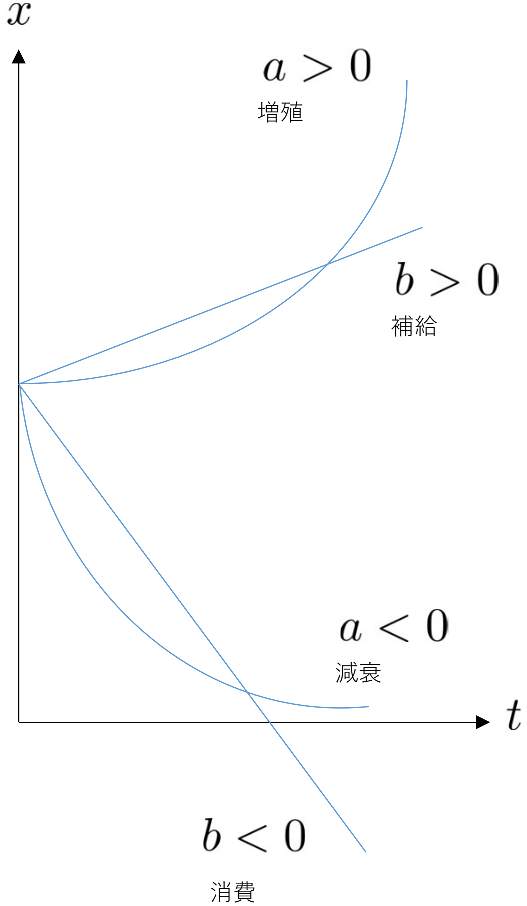
反応の次数

状態量の時間変化

$$x = x(t)$$

$$\frac{dx}{dt} = b$$ 0 次反応

$$\frac{dx}{dt} = ax$$ 1次反応

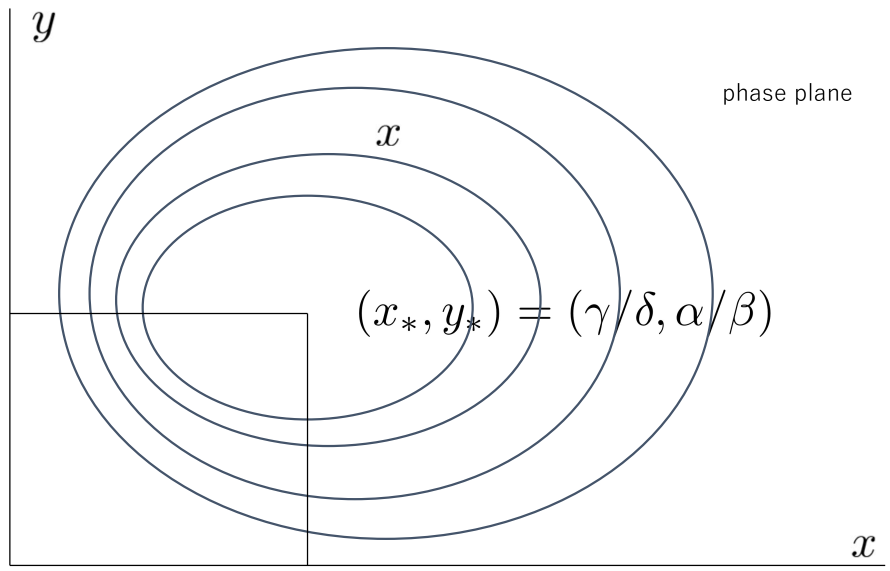


Prey-predator model

$$\frac{dx}{dt} = (\alpha - \beta y)x, \quad x|_{t=0} = x_0 > 0$$ prey

growth rate

$$\frac{dy}{dt} = (-\gamma + \delta x)y, \quad y|_{t=0} = y_0 > 0$$ predator



質量作用の法則

$$x + y \to y\ (\beta),\ \ y \to z\ (\gamma)$$

SIR model

$$\frac{dx}{dt} = -\beta x y,\ \ \frac{dy}{dt} = \beta x y - \gamma y,\ \ \frac{dz}{dt} = \gamma y$$

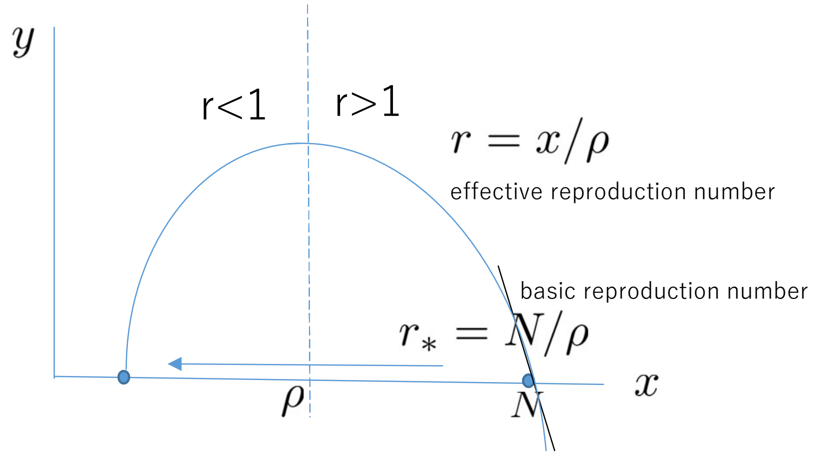
x uninfected

y infected

z excluded

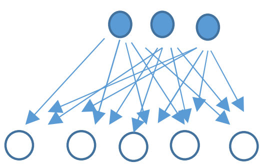
$$\frac{d}{dt}(x+y+z) = 0 \qquad x + y + z = N$$

$$\frac{dy}{dx} = \frac{dy/dt}{dx/dt} = \frac{\beta x y - \gamma y}{-\beta x y} = -1 + \frac{\rho}{x} \qquad \rho = \frac{\gamma}{\beta}$$

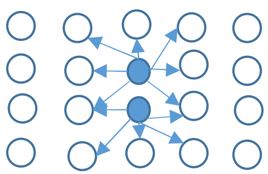


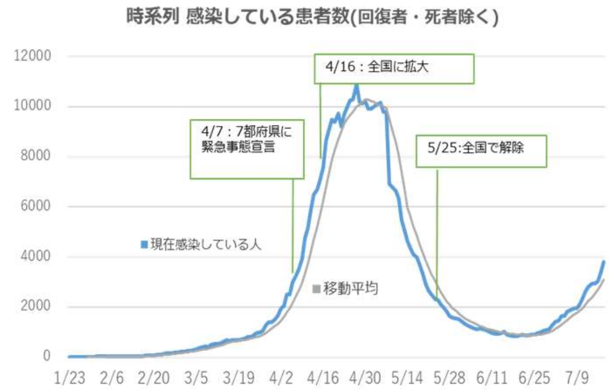
3×5＝15

2nd order reaction



spatial distribution





重合の規則

1. 分子の衝突によって定率で化学反応が発生する
2. 分子の衝突確率は濃度の積に比例する

質量作用の法則

素過程（基本モデル）

$$A + B \to AB \ (k)$$
$$AB \to A + B \ (\ell)$$

$$\frac{d}{dt}[A] = -k[A][B] + \ell[AB]$$
$$\frac{d}{dt}[B] = -k[A][B] + \ell[AB]$$
$$\frac{d}{dt}[AB] = k[A][B] - \ell[AB]$$

変形2

$$A + AB \to ABA \ (k)$$
$$ABA \to A + AB \ (2\ell)$$

$$\frac{d}{dt}[A] = -k[A][AB] + 2\ell[ABA]$$
$$\frac{d}{dt}[AB] = -k[A][AB] + 2\ell[ABA]$$
$$\frac{d}{dt}[ABA] = k[A][BB] - 2\ell[ABA]$$

$$A + AB \to AAB \ (k)$$
$$AAB \to A + AB \ (\ell)$$

$$\frac{1}{2}N_A(N_A - 1) \approx \frac{N_A^2}{2}$$

変形1

$$A + BB \to ABB \ (2k)$$
$$ABB \to A + BB \ (\ell)$$

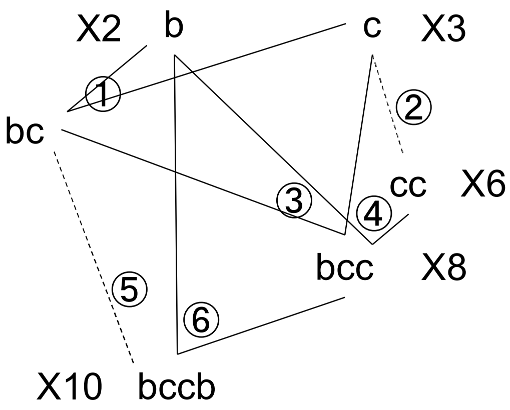
$$\frac{d}{dt}[A] = -2k[A][BB] + \ell[ABB]$$
$$\frac{d}{dt}[BB] = -2k[A][BB] + \ell[ABB]$$
$$\frac{d}{dt}[ABB] = 2k[A][BB] - \ell[ABB]$$

変形3

$$A + A \to AA \ (k/2)$$
$$AA \to A + A \ (\ell)$$

$$\frac{d}{dt}[A] = 2\left(-\frac{k}{2}[A]^2 + \ell[AA]\right)$$
$$\frac{d}{dt}[AA] = \frac{k}{2}[A]^2 - \ell[AA]$$

反応ネットワークの構築



$$b + c \to bc \quad (k_2), \qquad bc \to b + c \quad (\ell_2)$$
$$c + c \to cc \quad (k_3), \qquad cc \to c + c \quad (\ell_3)$$

b - c 簡略化モデル

$$\frac{dX_2}{dt} = \text{①} -k_2X_2X_3 + \ell_2X_5 \; \text{④} - 2k_2X_2X_6 + \ell_2X_8 - k_2X_2X_8 + 2\ell_2X_{10} \; \text{⑥}$$

$$\frac{dX_3}{dt} = \text{①} -k_2X_2X_3 + \ell_2X_5 \; \text{②} - k_3X_3^2 + 2\ell_3X_6 \; \text{③} - k_3X_3X_5 + \ell_3X_8$$

$$\frac{dX_5}{dt} = \text{①} \; k_2X_2X_3 - \ell_2X_5 - k_3X_5X_3 + \ell_3X_8 \; \text{③} - k_3X_5^2 + 2\ell_3X_{10} \; \text{⑤}$$

$$\frac{dX_6}{dt} = \frac{k_3}{2}X_3^2 \; \text{②} - \ell_3X_6 - 2k_2X_6X_2 + \ell_2X_8 \; \text{④}$$

$$\frac{dX_8}{dt} = 2k_2X_2X_6 - \ell_2X_8 \; \text{④} + k_3X_3X_5 \; \text{③} - \ell_3X_8 - k_2X_2X_8 + 2\ell_2X_{10} \; \text{⑥}$$

$$\frac{dX_{10}}{dt} = k_2X_2X_8 \; \text{⑥} - 2\ell_2X_{10} + \frac{k_3}{2}X_5^2 - \ell_3X_{10} \; \text{⑤}$$

重合の規則

2X6.. ...b, c 結合
2X10…b, c 解離

単体粒子の質量保存
反応のグルーピング

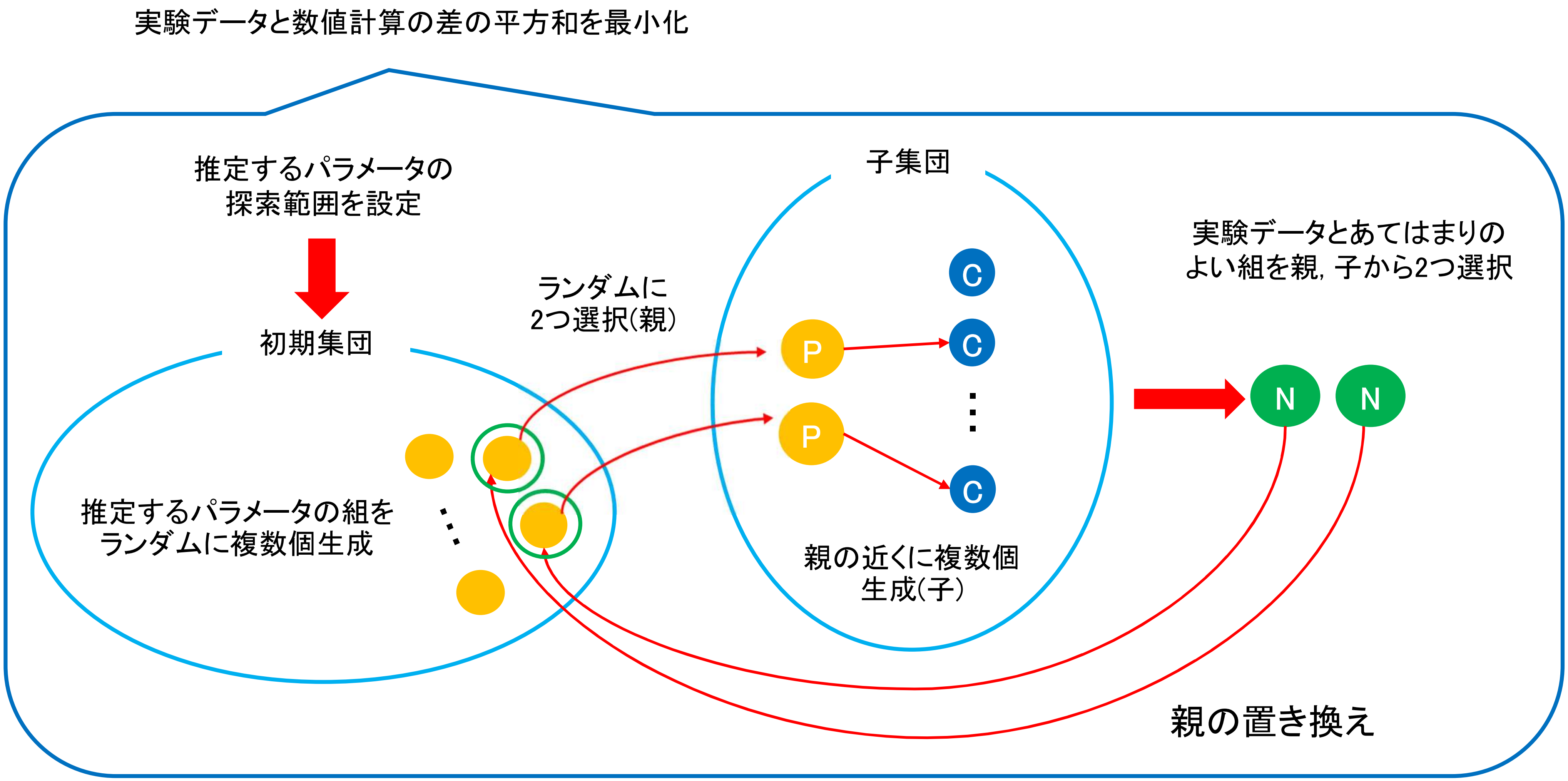
安定化

小数パラメータ
データベース（システム生物学）

ロバスト性

遺伝アルゴリズム

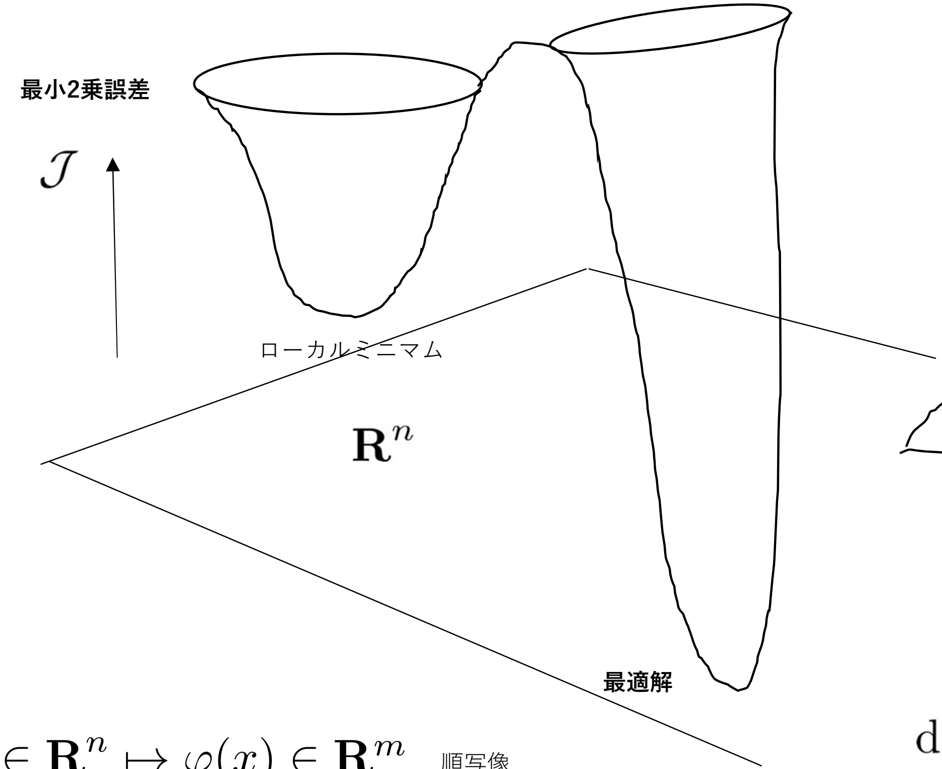
反応速度、初期濃度の推定

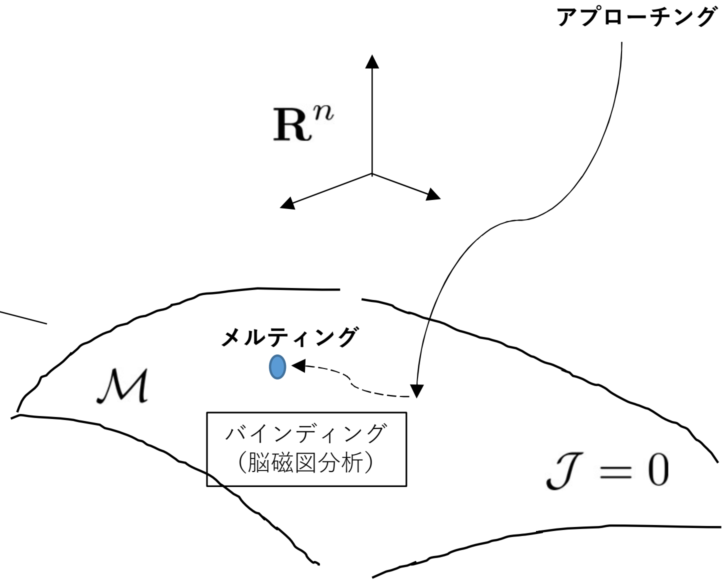


最適化の基礎概念

$m > n$ **過剰決定系** 解の存在

$m < n$ **不足決定系** 解の一意性





平行最適化の理論

フリージングゾーン

$$|\varphi'(x_\ell)\Delta x_\ell| \approx J(x_\ell)^{1/2}$$

擬解の多様体（非線形の場合）

$$\dim \mathcal{M} = n - m \qquad \mathcal{M} = \{x \in \mathbf{R}^n \mid \varphi(x) = z\}$$

$x \in \mathbf{R}^n \mapsto \varphi(x) \in \mathbf{R}^m$ 順写像

$z \in \mathbf{R}^m$ 観測データ

$\varphi(x) = z,\ x \in \mathbf{R}^n$ 未知源

$J(x) = \frac{1}{2}|\varphi(x) - z|^2$ 誤差

$\Delta x_\ell = x_{\ell+1} - x_\ell$ 反復列

$\sqrt{2J(x_\ell)}$

$$\Delta J_\ell \equiv J(x_{\ell+1}) - J(x_\ell) = (\varphi'(x_\ell)\Delta x_\ell, \varphi(x_\ell) - z) + o(|\Delta x_\ell|)$$

次元解析の方法

t: 1, X1:10^{-12}, X2:10^{-12}

c, d attachment-detachment

k1+: **10^{12} (X1),** k1-: 1 (X3)
X3: 10^{-12} (X3), k-:1 (X4)
X4: 10^{-12} (X1)
k+: 10^{12} (X2)

k2-: 1 (X5), X5: 10^{-12} (X2)
K2+: 10^{12} (X5)

event on plasma membrane

event time scale and mean number of molecules determine the chemical rate

unit system
attachment: / Ds
detachment: /s
molecular concentration: D (mol/dm^2)
Time (second): s

Experimental data
equilibrium: k1+/k1-=**5.3X10^{11}** [/D]
detachment k1-=**0.724** [/s]
attachment: k1+=**3.8X10^{11}** [/Ds]

attachment-detachment time scale= 1s
→ 2k1×(X1)^2=2×10^{-12}
(3.8×10^{11})×(2.64×10^{-12})^2
=**2.65×10^{-12}**

次元解析

$$\frac{dX_1}{dt} = -2k_1^+X_1^2 + 2k_1^-X_3 - k_+X_1X_2 + k_-X_4$$

$$\frac{dX_2}{dt} = -k_+X_1X_2 + k_-X_4 - 2k_2^+X_2^2 + 2k_2^-X_5$$

$$\frac{dX_3}{dt} = k_1^+X_1^2 - k_1^-X_3$$

$$\frac{dX_4}{dt} = k_+X_1X_2 - k_-X_4$$

$$\frac{dX_5}{dt} = k_2^+X_2^2 - k_2^-X_5$$

X1=[c]
X2=[d]
X3=[cc*]
X4=[c*d]
X5=[dd]

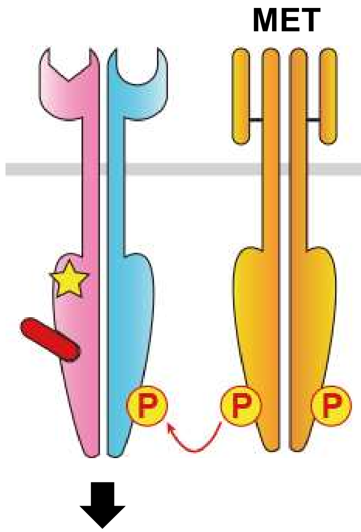
Volume of one cell : V=10^-15 [m^3] = 10^-12 [L]
cell radius: 5×10^{-5} [m]
surface area 4¥pi (5×10^{-5})^2×10^2= 3.14×10^{-8} [dm^2]
50,000 molecules
5×10^4 / 6×10^23 = 8.3×10^-20 [mol]
molecular concentration on plasma membrane
2.64×10^{-12} [D (mol/dm^2)] 2.64=8.3/3.14 no raft

$$c+c \underset{k1-}{\overset{k1+}{\rightleftarrows}} cc^* \qquad c+d \underset{k-}{\overset{k+}{\rightleftarrows}} c^*d$$

$$d+d \underset{k2-}{\overset{k2+}{\rightleftarrows}} dd$$

MET amplification

4～20%

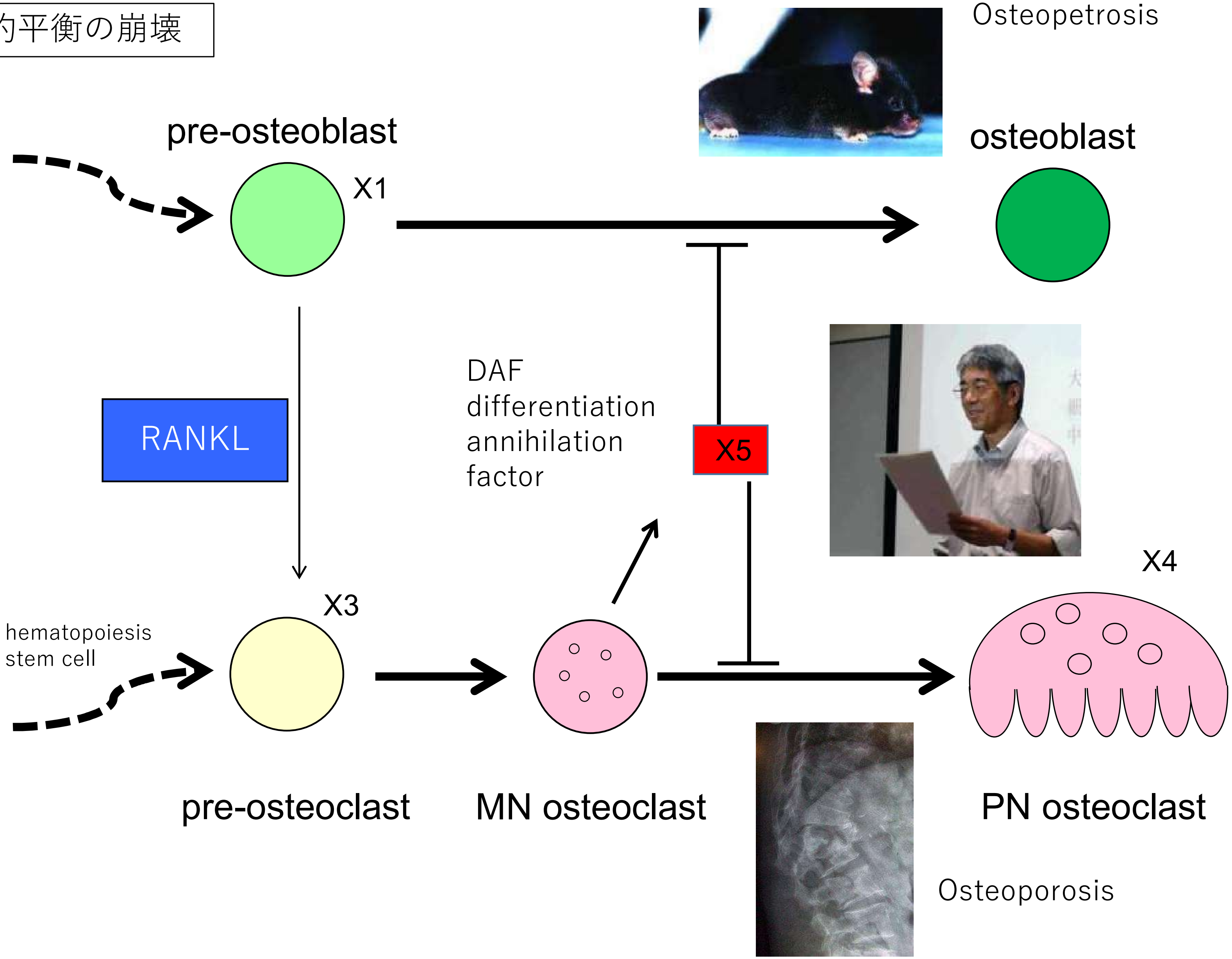


Survival

薬剤耐性

数理モデルは反応速度のオーダーを規定する

骨代謝 – 動的平衡の崩壊


Osteopetrosis
pre-osteoblast
X1
osteoblast
RANKL
DAF
differentiation
annihilation
factor
X5
X4
X3
hematopoiesis
stem cell
pre-osteoclast
MN osteoclast
PN osteoclast
Osteoporosis

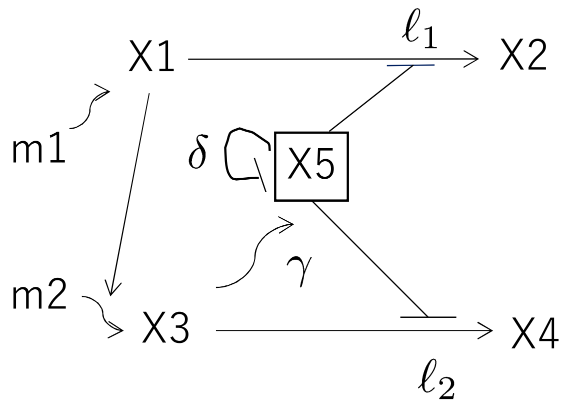
The Model

X1 pre-osteoblast
X2 osteoblast
X3 pre-osteoclast
X4 osteoclast
X5 DAF

cell

molecule

bottom up model – molecular level



top down model – tissue level

$$m_2 = m_2(X_1) = aX_1 + b$$

$$\ell_1 = \ell_1(X_5) = \frac{c}{dX_5 + e}$$

$$\ell_2 = \ell_2(X_5) = \frac{f}{gX_5 + h}$$

Tissue
Cell
Molecule

multiscale model

$$\frac{dX_1}{dt} = -\ell_1 X_1 + m_1$$

$$\frac{dX_2}{dt} = \ell_1 X_1$$

$$\frac{dX_3}{dt} = -\ell_2 X_3 + m_2$$

$$\frac{dX_4}{dt} = \ell_2 X_3$$

$$\frac{dX_5}{dt} = \gamma X_3 - \delta X_5$$

The simplest response function which can be generalized in later mathematical analysis. Lack of the precise data evidence is compensated by the standard recipe in biology.

dynamical equilibrium
X1, X3, X5⋯ stationary

Dynamical Equilibrium $\frac{dX_1}{dt} = \frac{dX_3}{dt} = \frac{dX_5}{dt} = 0$

$\Longleftrightarrow$

$$\ell_1 X_1 = m_1, \quad \ell_2 X_3 = m_2, \quad \gamma X_3 = \delta X_5$$

$\Longleftrightarrow$

$$X_1 = \frac{m_1}{\ell_1(X_5)}, \quad X_3 = \frac{m_2(X_1)}{\ell_2(X_5)}, \quad X_3 = \frac{\delta}{\gamma} X_5$$

$\Longleftrightarrow$

$$\boxed{\frac{\delta}{\gamma} X_5 = \varphi(X_5),} \quad X_1 = \frac{m_1}{\ell_1(X_5)}, \quad X_3 = \varphi(X_5)$$

$$\begin{aligned} \varphi(X_5) &= m_2\left(\frac{m_1}{\ell_1(X_5)}\right) \cdot \frac{1}{\ell_2(X_5)} \\ &= \frac{1}{f}\left(\frac{am_1}{c}(dX_5 + e) + b\right)(gX_5 + h) \end{aligned}$$

tissue level

$$\frac{dX_1}{dt} = -\ell_1 X_1 + m_1$$
$$\frac{dX_2}{dt} = \ell_1 X_1$$
$$\frac{dX_3}{dt} = -\ell_2 X_3 + m_2$$
$$\frac{dX_4}{dt} = \ell_2 X_3$$
$$\frac{dX_5}{dt} = \gamma X_3 - \delta X_5$$

molecular level

$$m_2 = aX_1 + b$$
$$\ell_1 = \frac{c}{dX_5 + e}$$
$$\ell_2 = \frac{f}{gX_5 + h}$$

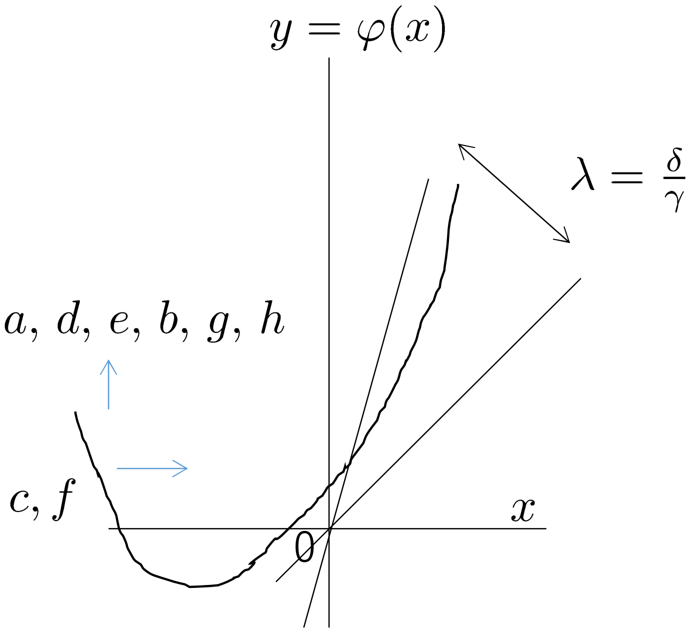
$$m_2 = m_2(X_1), \ \ell_1 = \ell_1(X_5), \ \ell_2 = \ell_2(X_5)$$

Existence of Dynamical Equilibrium

$$x \in [0, +\infty) \ \mapsto \ \varphi(x) \in (0, +\infty)$$

strictly convex

$$\varphi(x) = \frac{1}{f}\left(\frac{am_1}{c}(dx+e)+b\right)(gx+h)$$

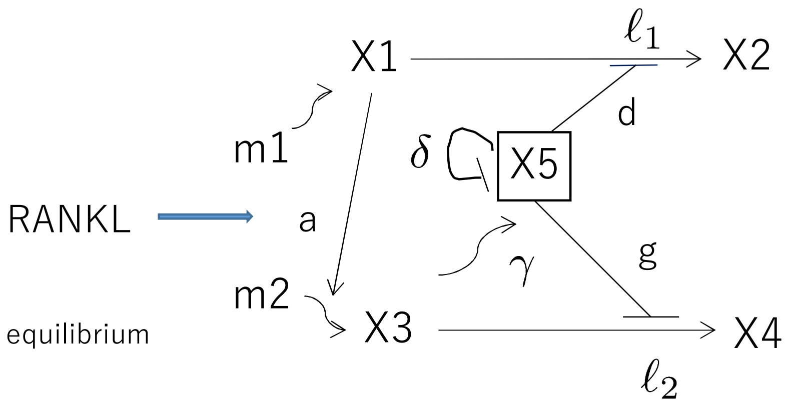


Examples of controllable parameters

$$\boxed{\frac{\delta}{\gamma} X_5 = \varphi(X_5)}$$

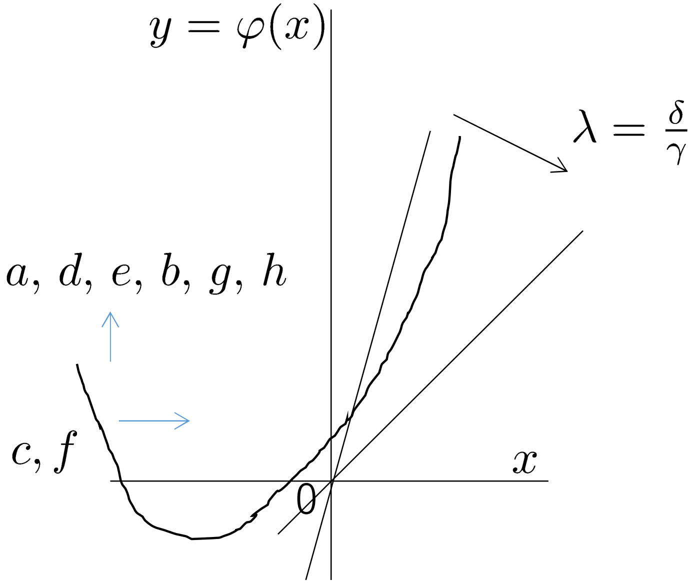
$$X_1 = \frac{m_1}{\ell_1(X_5)},\ \ell_1(X_5) = \frac{f}{dX_5 + e}$$

$$X_3 = \varphi(X_5)$$



DAF(X5) activation
RANKL injection → breaking down of dynamical equilibrium

Breaking Down of Dynamical Equilibrium



where unstable dynamical equilibrium takes a role.

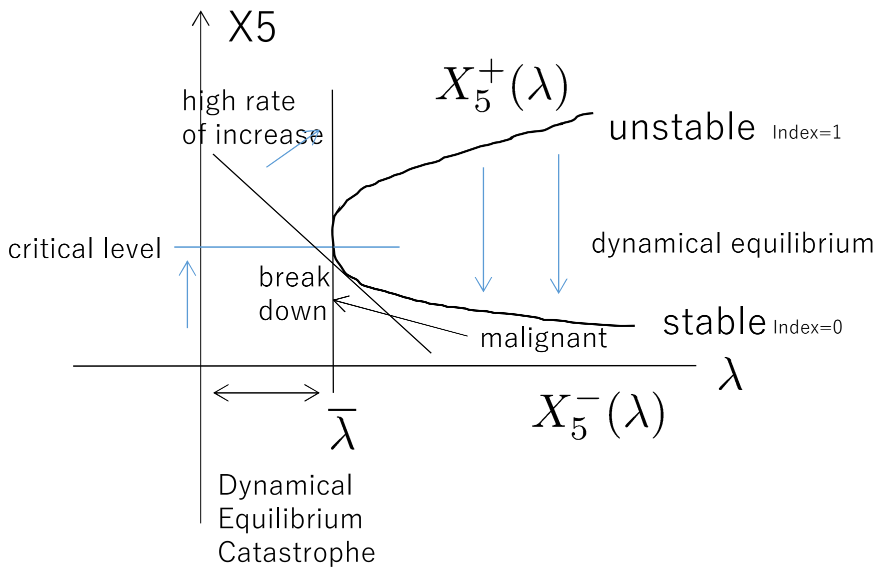
$$\frac{dX_5}{dt} = \gamma X_3 - \delta X_5$$
$$\approx \gamma\varphi(X_5) - \delta X_5$$

around linearly non-degenerate dynamical equilibrium

osteoporosis?

osteopetrosis?

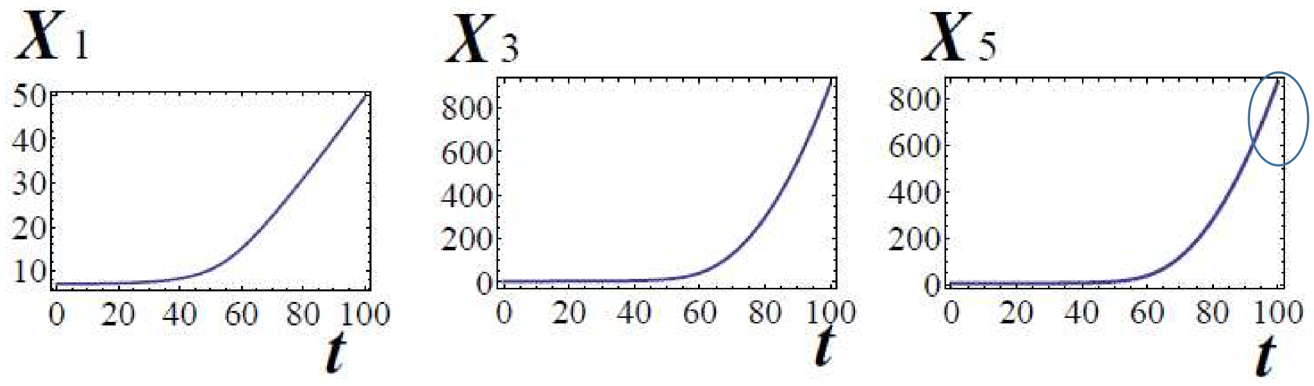
It occurs with the change of environment (parameters)



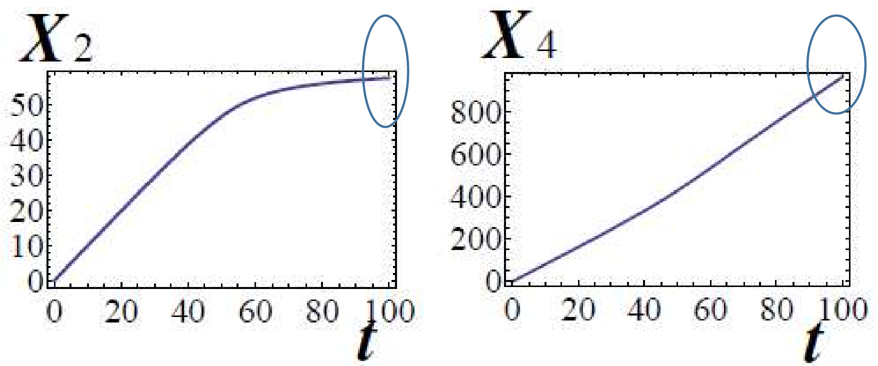
$(X_5^0 = 4)$ ➡ $X_1^0 = 7,\ X_3^0 = 4$

$X_1(0) = 7(1+0.01),\ X_3(0) = 4(1+0.01),$ $X_5(0) = 4(1+0.01),\ X_2(0) = 0,\ X_4(0) = 0$

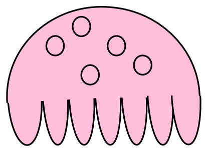
around the unstable dynamical equilibrium



$$\frac{d}{dt}\left(\frac{dX_4}{dX_2}\right) \approx \frac{dX_5}{dt} > 0$$



keep to stay in near from dynamical equilibrium

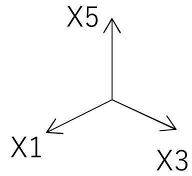


osteoporosis

catastrophe around the unstable dynamical equilibrium

Dynamics Near from Dynamical Equilibrium

dynamics around the unstable dynamical equilibrium



Near from dynamical equilibrium contains unstable manifold

quasi-dynamical equilibrium

$$X_1 = \frac{m_1}{\ell_1(X_5)}$$

$$X_3 = \varphi(X_5)$$

near from equilibrium

$$X_1 \approx \frac{m_1}{\ell_1(X_5)}$$

$$X_3 \approx \varphi(X_5)$$

a cube containing the quasi-dynamical equilibrium curve independent of λ

non-compact orbit

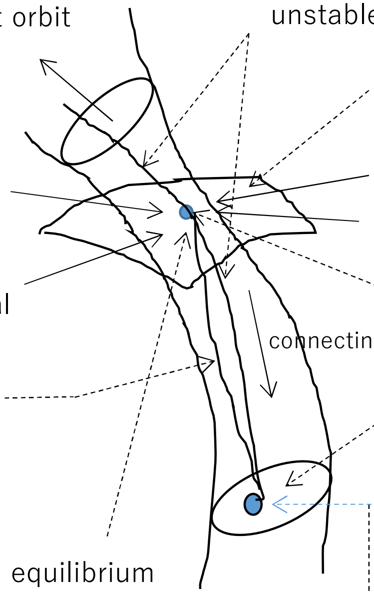
unstable manifold

stable manifold

Morse index 1

connecting orbit

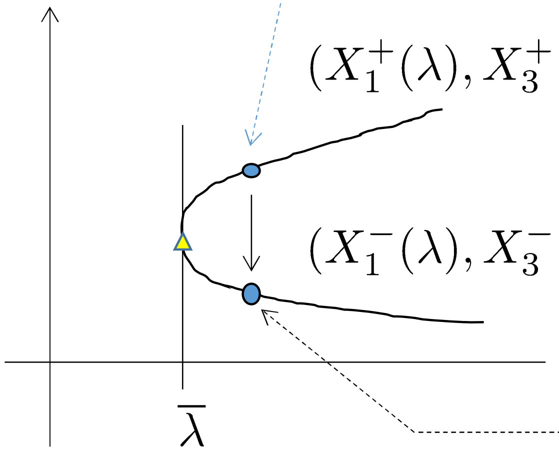
Morse index 0



unstable dynamical equilibrium

$$\frac{dX_5}{dt} \approx \gamma\varphi(X_5) - \delta X_5$$

dynamical component of near from dynamical equilibrium



$$(X_1^+(\lambda), X_3^+(\lambda), X_5^+(\lambda))$$

$$(X_1^-(\lambda), X_3^-(\lambda), X_5^-(\lambda))$$

$$\bar{\lambda}$$

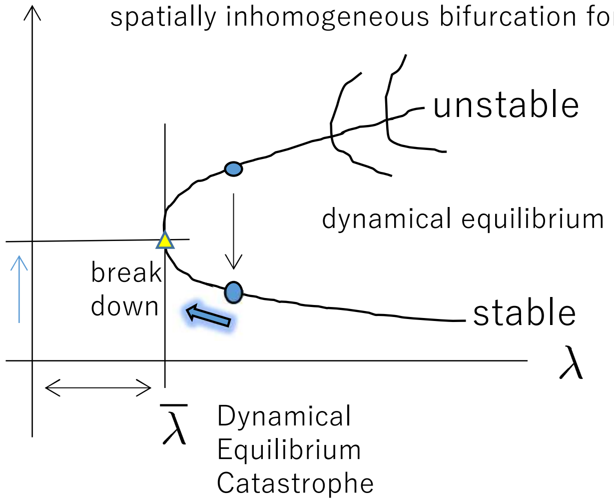
stable dynamical equilibrium

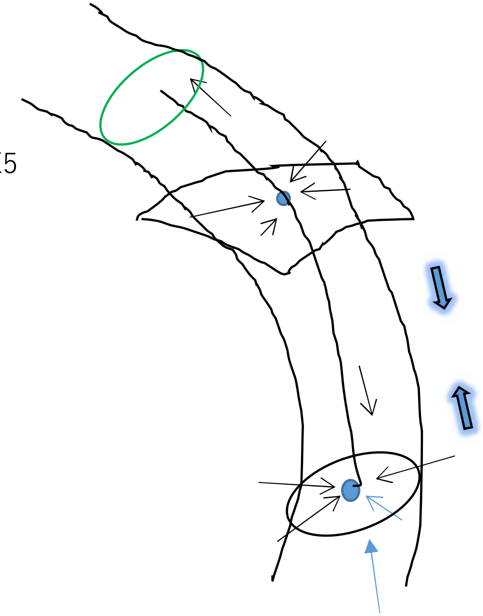
$$\frac{d}{dt}\begin{pmatrix} X_1 \\ X_3 \end{pmatrix} = \begin{pmatrix} m_1 \\ m_2(X_1) \end{pmatrix} - \begin{pmatrix} \ell_1(X_5) & 0 \\ 0 & \ell_2(X_5) \end{pmatrix}\begin{pmatrix} X_1 \\ X_3 \end{pmatrix}$$

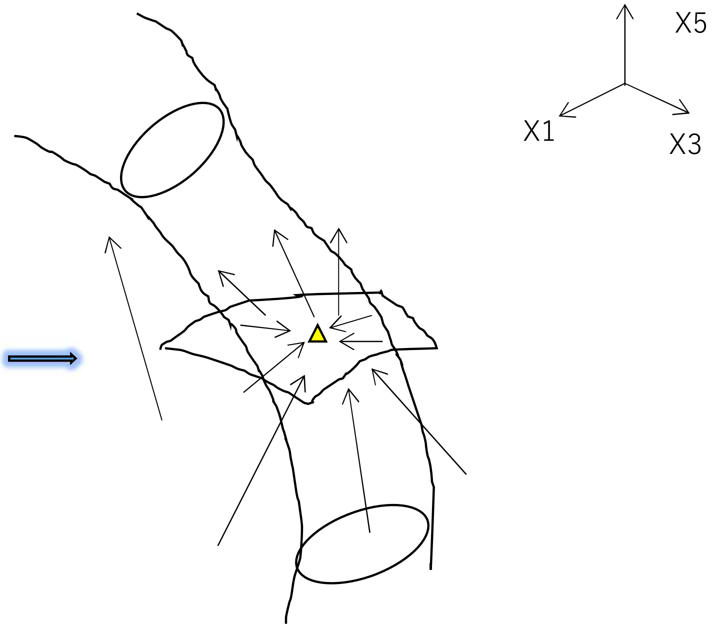
stable components

complicated transient dynamics

spatially inhomogeneous bifurcation for diffusion of X5



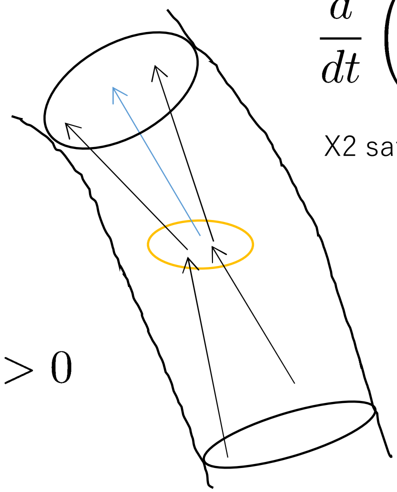




$$\frac{d}{dt}\left(\frac{dX_4}{dX_2}\right) > 0$$

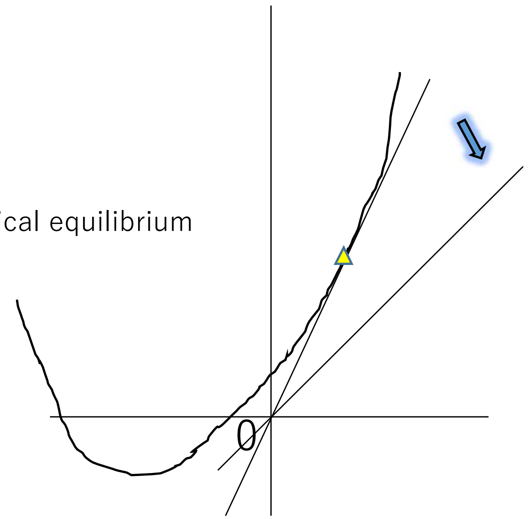
X2 saturate at the breaking down of dynamical equilibrium

$$\frac{dX_5}{dt} > 0$$



relatively long in time stay near
from dynamical equilibrium

osteoporosis



8．反応拡散系

$$\tau_j \frac{\partial u_j}{\partial t} - d_j \Delta u_j = f_j(u) \text{ in } Q_T$$
$$\left.\frac{\partial u_j}{\partial \nu}\right|_{\partial\Omega} = 0, \quad u_j|_{t=0} = u_{j0}(x)$$

$\Omega \subset \mathbf{R}^n$ bounded domain, $\partial\Omega$ smooth

$Q_T = \Omega \times (0,T) \qquad 1 \leq j \leq N$

ν outer unit normal

$\tau = (\tau_j) > 0, \ d = (d_j) > 0$

$u_0 = (u_{j0}) \geq 0$ smooth

[local. Lipschitz cont.]

$f_j : \mathbf{R}^N \to \mathbf{R}, \ 1 \leq j \leq N$

loc. Lipschitz cont.

⟹

$\exists 1$ classical solution local-in-time

$T \in (0, +\infty]$ maximal existence time

[quasi-positive]

$f_j(u_1, \cdots, u_{j-1}, 0, u_{j+1}, \cdots, u_n) \geq 0, \ \forall j$

$0 \leq u_0 = (u_{j0}) \in \mathbf{R}^N$ ⟹

$u = (u_j(\cdot, t)) \geq 0$

[mass dissipation]

$$\sum_{j=1}^N f_j(u) \leq 0, \ u = (u_j) \geq 0$$

⟹ $$\frac{\partial}{\partial t}(\tau \cdot u) - \Delta(d \cdot u) \leq 0$$
$$\left.\frac{\partial u}{\partial \nu}\right|_{\partial\Omega} = 0$$

$\|\tau \cdot u(t)\|_1 \leq \|\tau \cdot u_0\|_1$

[quadratic]

$|\nabla f_j(u)| \leq C(1 + |u|), \ \forall j$

Theorem (Fellner-Morgan-Tang 20, 21)

$T = +\infty \qquad \|u(\cdot, t)\|_\infty \leq C$

Examples

chemical reaction $A_1 + \cdots + A_m \rightleftharpoons A_{m+1} + \cdots + A_N$

$$\tau_j \frac{\partial u_j}{\partial t} - d_j \Delta u_j = \chi_j f(u), \quad \left.\frac{\partial u_j}{\partial \nu}\right|_{\partial\Omega} = 0$$

micro-canonical ensemble

$$f(u) = \prod_{j=1}^{m} u_j - \prod_{j=m+1}^{N} u_j, \ \chi_j = \begin{cases} -1, & 1 \leq j \leq m \\ 1, & m+1 \leq j \leq N \end{cases}$$

spatially homogeneous stationary state $\quad \overline{w} = \frac{1}{|\Omega|}\int_\Omega w$

$$0 \leq \exists 1 z = (z_j) \in \mathbf{R}^N, \ f(z) = 0$$

$$z_i + z_k = \overline{u}_{i0} + \overline{u}_{k0}, \ 1 \leq i \leq m, \ m+1 \leq k \leq N$$

$\Longrightarrow \quad z = (z_j) > 0$

Theorem $\quad m = 2, \ N = 4 \quad$ (quadratic)

$\Longrightarrow \quad T = +\infty \qquad \|u(\cdot,t) - z\|_\infty \leq Ce^{-\delta t}$

Devillettes-Fellner 08, Pierre-S.-Zou 17, Pierre-S.-Umakoshi 18

$$\Phi(s) = s(\log s - 1) + 1 \geq 0$$

relative entropy (diversity) $\qquad$ entropy

$$E(w \mid v) = \int_\Omega v \ \Phi\left(\frac{w}{v}\right), \ E(w) = \int_\Omega \Phi(w)$$

$$E(u) = \sum_{j=1}^{N} \tau_j E(u_j), \ E(u \mid z) = \sum_{j=1}^{N} \tau_j E(u_j \mid z_j)$$

$\Longrightarrow \quad E(u|z) = E(u) - E(z)$

$$\boxed{\frac{d}{dt}E(u) = -D(u)}$$

$$D(u) = 4\sum_{j=1}^{N} d_j \|\nabla\sqrt{u_j}\|_2^2 + \int_\Omega f(u) \log \frac{\prod_{j=m+1}^{N} u_j}{\prod_{j=1}^{m} u_j}$$

[logarithmic Sobolev] $\quad D(u) \geq 2\delta E(u|z)$

[Csiz'ar-Kullback] $\quad \|v - \overline{v}\|_1^2 \leq 4\overline{v}E(v|\overline{v})$

ロトカ・ボルテラ系

$$\tau_j \frac{\partial u_j}{\partial t} = d_j \Delta u_j + (e_j + \sum_k a_{jk} u_k) u_j$$

$$\left.\frac{\partial u_j}{\partial \nu}\right|_{\partial\Omega} = 0, \ \ u_j|_{t=0} = u_{j0}(x) \geq 0$$

$$(Au, u) \leq 0, \ \forall u \geq 0 \qquad A = (a_{jk})$$

$\longrightarrow$ $T = +\infty$

$e = (e_j) \leq 0$ $\longrightarrow$ $\|u(\cdot, t)\|_\infty \leq C$

Masuda-Takahashi 94 (n=1) S.-Yamada 15 (n=2)

scaling invariance (e=0)

$$u_j^\mu(x,t) = \mu^2 u_j(\mu x, \mu^2 t), \ \ \mu > 0$$

rigidness (n=2, quadratic growth by L^1 control)

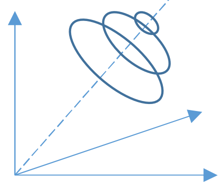
$$\|u_0\|_1 \ll 1 \ \Rightarrow \ T = +\infty, \ \sup_{t \geq 0} \|u(\cdot,t)\|_\infty < +\infty$$

entropy $\longrightarrow$ asymptotic spatially homogenization (S.-Yamada 15)

$E = L \cap \mathbf{R}_+^N, \ \exists L$ affine space of co-dimension 2

Any non-stationary solution is periodic-in-time with the orbit $\mathcal{O} \cong S^1$ contractible to a stationary solution in $\mathbf{R}_+^N \setminus E$

Any distinct two orbits $\mathcal{O}_1, \mathcal{O}_2 \cong S^1$ do not link in $\mathbf{R}_+^N$



spatially homogeneous part

$$\begin{pmatrix} 0 & a_{12} & a_{13} & a_{14} & \cdots & a_{1N} \\ a_{21} & 0 & a_{23} & a_{24} & \cdots & a_{2N} \\ a_{31} & a_{32} & 0 & a_{34} & \cdots & a_{3N} \\ \vdots & \vdots & \ddots & \ddots & \ddots & \vdots \\ \vdots & \vdots & & \ddots & \ddots & a_{N-1N} \\ a_{N1} & a_{N2} & \cdots & \cdots & a_{NN-1} & 0 \end{pmatrix}$$

free

2N-3 dimension

$$a_{kl} = \frac{a_{1k}a_{2l} - a_{1l}a_{2k}}{a_{12}}$$

$$3 \leq k < l \leq N$$

$$a_{12} \neq 0, \ \ e = (e_j) = 0$$

Kobayashi-S.-Yamada 19

Smoluchowski-Poisson equation – a model in statistical mechanics

$\Omega \subset \mathbf{R}^2$ bounded domain, $\partial\Omega$ smooth

1. Smoluchowski Part

$$u_t = \nabla \cdot (\nabla u - u\nabla v)$$

$$\left. \frac{\partial u}{\partial \nu} - u\frac{\partial v}{\partial \nu} \right|_{\partial\Omega} = 0$$

2. Poisson Part

$$-\Delta v = u, \ \ v|_{\partial\Omega} = 0$$

canonical ensemble

1. total mass conservation $\frac{d}{dt}\|u(t)\|_1 = 0$

2. free energy decreasing

$$\mathcal{F}(u) = \int_\Omega u(\log u - 1) - \frac{1}{2}\int\int_{\Omega\times\Omega} G(x,x')u \otimes u$$

$$\frac{d}{dt}\mathcal{F}(u) = -\int_\Omega u|\nabla(\log u - v)|^2 \le 0$$

$G(x,x') = G(x',x)$ Green's function

2D is critical for blowup of the solution to quadratic nonlinearity under the total mass control

self-similar transformation due to the quadratic growth

$$u_\mu(x,t) = \mu^2 u(\mu x, \mu^2 t), \ \mu > 0$$

$\|u\|_1 = \|u_\mu\|_1 \equiv \lambda \ \Leftrightarrow \ n = 2$ *critical dimension*

$$\mathcal{F}(u) = \int_{\mathbf{R}^2} u(\log u - 1) - \frac{1}{2}\langle \Gamma * u, u\rangle, \ \ \Gamma(x) = \frac{1}{2\pi}\log\frac{1}{|x|}$$

$\mathcal{F}(u_\mu) = \left(2\lambda - \frac{\lambda^2}{4\pi}\right)\log\mu + \mathcal{F}(u)$ *critical mass* $\lambda = 8\pi$

quantized blowup mechanism with Hamiltonian control
1. stationary 2. finite time 3. infinite time

Former results (1) any space dimension

entropy dissipation $\sum_{j=1}^{N} f_j(u) \log u_j \leq 0$

Capto-Goudon-Vasseur 09 $\Omega = \mathbf{R}^n$

loc. Lipschitz cont. quasi-positive
mass dissipation, entropy dissipation
quadratic growth

Souplet 18 $\Omega = \mathbf{R}^n$ or $\Omega \subset \mathbf{R}^n$

$$\sum_{j=1}^{N} f_j(u)(1 + \log u_j) \leq C \sum_{j=1}^{N} u_j \log(1 + u_j)$$

loc. Lipschitz cont. quasi-positive, quadratic growth

Fellner-Tang

1. Sobolev inequality in space-time
2. Parabolic Giorgi-Nash-Moser regularity
3. Regularity interpolation
4. Souplet's trick by semigroup estimate

Former results (2) without entropy dissipation

Pierre-Rolland 15

$$0 \leq \exists u = (u_j(\cdot,t)) \in C([0,+\infty), L^1(\Omega)^N)$$

global-in-time weak solution

Pierre-S.-Yamada 19

$\mathcal{O} = \{u(\cdot,t)\} \subset L^1(\Omega)^N$ pre-compact

1. Mechanism to protect the solution from the measure?
2. Why 2D is thought to be critical?

L1解の方法

Pierre-Rolland 15 $0 \leq \exists u = (u_j(\cdot, t)) \in C([0, +\infty), L^1(\Omega)^N)$ global-in-time weak solution

Pierre-S.-Yamada 19 $\mathcal{O} = \{u(\cdot, t)\} \subset L^1(\Omega)^N$ pre-compact

weak solution to $0 \leq u = (u_j(\cdot, t)) \in L^\infty_{loc}([0, T), L^1(\Omega)^N)$

$$\tau_j \frac{\partial u_j}{\partial t} - d_j \Delta u_j = f_j(u), \quad \left.\frac{\partial u_j}{\partial \nu}\right|_{\partial\Omega} = 0, \quad u_j|_{t=0} = u_{j0}(x) \geq 0$$

⟺ (def.)

$$f_j(u) \in L^1_{loc}(\overline{\Omega} \times (0, T))$$

as distributions

$$\frac{d}{dt}\int_\Omega u_j \varphi - d_j \int_\Omega u_j \Delta\varphi = \int_\Omega f_j(u)\varphi, \ \forall \varphi \in W^{2,\infty}(\Omega), \ \left.\frac{\partial \varphi}{\partial \nu}\right|_{\partial\Omega} = 0$$

$u_j|_{t=0} = u_{j0}(x)$ in the sense of measures

L2-L1 estimate

$$\tau_j \frac{\partial u_j}{\partial t} - d_j \Delta u_j = f_j(u)$$

$$\left.\frac{\partial u_j}{\partial \nu}\right|_{\partial\Omega} = 0, \ \ u_j|_{t=0} = u_{j0}(x) \geq 0$$

$$\sum_{j=1}^{N} f_j(u) \leq 0 \quad \Longrightarrow$$

$$\tau = (\tau_j), \ \ d = (d_j) > 0$$

$$\frac{\partial}{\partial t}(\tau \cdot u) - \Delta(d \cdot u) \leq 0, \ \ u = (u_j) \geq 0$$

$$\left.\frac{\partial}{\partial \nu}(d \cdot u)\right|_{\partial\Omega} \leq 0, \ \ u|_{t=0} = u_0 = (u_{j0})$$

$$\tau \cdot u(\cdot, t) - \tau \cdot u_0 \leq \int_0^t \Delta(d \cdot u(\cdot, s)) \ ds$$

$$\frac{d}{dt} \int_\Omega \tau \cdot u \leq 0 \ \Longrightarrow \ \boxed{\sup_{0 \leq t < T} \|u(\cdot, t)\|_1 \leq C}$$

$$\Longrightarrow \quad (\tau \cdot u(\cdot, t), d \cdot u(\cdot, t)) - (\tau \cdot u_0, d \cdot u(\cdot, t)) \leq -(\nabla d \cdot u(\cdot, t), \nabla \int_0^t d \cdot u(\cdot, s) \ ds)$$

$$= -\frac{1}{2} \frac{d}{dt} \|\nabla \int_0^t d \cdot u(\cdot, s) \ ds\|_2^2$$

$$\Longrightarrow$$

$$\int_0^T (\tau \cdot u(\cdot, t), d \cdot u(\cdot, t)) \ dt \leq \|\tau \cdot u_0\|_2 \cdot \int_0^T \|d \cdot u(\cdot, t)\|_2 \ dt$$

$$\leq CT^{\frac{1}{2}} \|\tau \cdot u_0\|_2 \cdot \{\int_0^T \|d \cdot u(\cdot, t)\|_2^2 \ dt\}^{\frac{1}{2}} \ \Longrightarrow \ \boxed{\|u\|_{L^2(Q_T)} \leq CT^{\frac{1}{2}} \|u_0\|_2}$$

L1 pre-compactness

1. semi-group reduction   Baras-Pierre 84

$$\frac{\partial w}{\partial t} - \Delta w = H \in L^1(Q_T)$$

$$\left.\frac{\partial w}{\partial \nu}\right|_{\partial\Omega} = 0, \ \ w|_{t=0} = w_0(x) \in L^1(\Omega)$$

$$w = w(\cdot,t) \in L^\infty(0,T;L^1(\Omega)) \bigcap L^1_{loc}(0,T;W^{1,1}(\Omega))$$

weak solution

i.e.   as distributions

$$\frac{d}{dt}\int_\Omega w\varphi + \int_\Omega \nabla w \cdot \nabla \varphi = \int_\Omega H\varphi, \ \forall \varphi \in W^{1,\infty}(\Omega)$$

$w|_{t=0} = w_0$ in the sense of measures

$$\Longrightarrow \quad w(\cdot,t) = e^{t\Delta}w_0 + \int_0^t e^{(t-s)\Delta}H(\cdot,s)\ ds$$

in particular $w \in C([0,T],L^1(\Omega))$

$$\mathcal{F} : (w_0,H) \in L^1(\Omega)\times L^1(Q_T) \mapsto w \in C([0,T],L^1(\Omega))$$

continuous

2. compactness   c.f. Baras 78

$$\mathcal{F} : (w_0,H) \in L^1(\Omega)\times L^1(Q_T) \mapsto w \in L^1(Q_T)$$

compact

Proof $\mathcal{F}^* : L^\infty(Q_T) \to L^\infty(\Omega)\times L^\infty(Q_T)$

$$\mathcal{F}^*(h) = (\theta|_{t=0}, \theta)$$

$$\frac{\partial \theta}{\partial t} + \Delta\theta = h, \ \left.\frac{\partial \theta}{\partial \nu}\right|_{\partial\Omega} = 0, \ \ \theta|_{t=T} = 0$$

compact from the parabolic regularity

---

pre-compactness of the orbit in L1

$$0 \ \leq \ u_k(\cdot,t) = u(\cdot,t+t_k)$$

$$\leq \ \exists w_k(\cdot,t) \in L^2(\Omega\times(-1,1))$$

comparison theorem   compact   dominated convergence theorem alternative argument applicable to other systems (S.-Yamada)

L2 estimate in space and time

quasi-positive
mass dissipation
quadratic growth

$\Longrightarrow$ $$\sum_{j=1}^{N} f_j(u)\log u_j \leq C(1+|u|^2)$$

singularity relaxation

$\Longrightarrow$ $$\sup_{0\leq t<T}\int_\Omega \Phi(u_j(\cdot,t)) \leq C_T$$

$$\Phi(s) = s(\log s - 1) + 1 \geq 0, \ \ s>0$$

global GN inequality

$\Longrightarrow$ T=+∞ if n=1, 2

monotonicity formula $$\int_{-1}^{1}\left|\frac{d}{dt}\int_\Omega u_j(\cdot,t+t_k)\varphi\right| dt \leq C_\varphi$$

$$\forall\varphi\in C^2(\overline{\Omega}), \ \ \left.\frac{\partial\varphi}{\partial\nu}\right|_{\partial\Omega}=0$$

by L2 control in space-time

evokes the measure-valued continuation (very weak solution)

Smoluchowski-Poisson equation

2D case – time control

Corollary $n=2 \;\Rightarrow\; T=+\infty,\;\; \|u(\cdot,t)\|_\infty \le C$

loc. Lipschitz cont.
quasi-positive
mass dissipation
quadratic growth

semi-group theory $$T\in(0,+\infty],\;\; \limsup_{t\uparrow T}\|u(t)\|_2<+\infty \;\Rightarrow\; \limsup_{t\uparrow T}\|u(t)\|_\infty<+\infty$$

Gagliardo-Nirenberg $$\frac{d}{dt}\|u\|_2^2+\delta\|\nabla u\|_2^2\le C\|u\|_3^3$$

$$C\|u\|_3^3\le C'\|u\|_2^{\frac{6-n}{2}}\|u\|_{H^1}^{\frac{n}{2}}\le\frac{\delta}{2}\|u\|_{H^1}^2+C''\|u\|_2^{\frac{6-n}{2}\cdot\frac{4}{4-n}}$$

$$\frac{1}{\frac{4}{n}}+\frac{1}{\frac{4}{4-n}}=1$$

$n\le 6$ $\qquad$ $n\le 3$

$\|u\|_1\le C$ Poincare-Wirtinger $$-\frac{2}{4-n}-1=-\frac{6-n}{4-n}$$

$$\frac{d}{dt}\|u\|_2^2\le C(\|u\|_2^2+1)^{\frac{6-n}{4-n}} \;\Longrightarrow\; -\frac{d}{dt}(\|u\|_2^2+1)^{-\frac{2}{4-n}}\le C$$

$$t_k \uparrow T \in (0,+\infty],\ u^k(t) = u(t+t_k)$$

$$-\frac{d}{dt}(\|u^k\|_2^2+1)^{-\frac{2}{4-n}} \le C$$

$$(\|u^k(-t)\|_2^2+1)^{-\frac{2}{4-n}} \le (\|u^k(0)\|_2^2+1)^{-\frac{2}{4-n}} + Ct, \quad 0<t<T$$

Pierre-S.-Yamada

assume $\lim_{k\to\infty} \|u^k(0)\|_2 = +\infty$ ⟹ subsequence

$$u^k \to \exists u^\infty \text{ in } C_{loc}((-\infty,0],L^1(\Omega)),\ L^2_{loc}(\overline{\Omega}\times(-\infty,0])$$

$$(\|u^\infty(-t)\|_2^2+1)^{-\frac{2}{4-n}} \le Ct$$

n=2 ⟹ $\|u^\infty(t)\|_2^2+1 \ge \delta(-t)^{-1},\ -T<t<0$

$$\|u^\infty(-t)\|_2^2+1 \ge \delta t^{-\frac{4-n}{2}}, \quad 0<t<T$$

$u^\infty \notin L^2_{loc}(\overline{\Omega}\times(-T,0])$ contradiction

反応拡散系（続き）

$$\tau_j \frac{\partial u_j}{\partial t} - d_j \Delta u_j = f_j(u) \text{ in } Q_T$$

$$\left.\frac{\partial u_j}{\partial \nu}\right|_{\partial\Omega} = 0, \ \left.u_j\right|_{t=0} = u_{j0}(x)$$

$\Omega \subset \mathbf{R}^n$ bounded domain, $\partial\Omega$ smooth

$Q_T = \Omega \times (0,T) \qquad 1 \leq j \leq N$

ν outer unit normal

$\tau = (\tau_j) > 0, \ d = (d_j) > 0$

$u_0 = (u_{j0}) \geq 0$ smooth

[local. Lipschitz cont.]

$f_j : \mathbf{R}^N \to \mathbf{R}, \ 1 \leq j \leq N$

loc. Lipschitz cont.

⟶

$\exists 1$ classical solution local-in-time

$T \in (0, +\infty]$ maximal existence time

[quasi-positive]

$f_j(u_1, \cdots, u_{j-1}, 0, u_{j+1}, \cdots, u_n) \geq 0, \ \forall j$

$0 \leq u_0 = (u_{j0}) \in \mathbf{R}^N$ ⟶

$u = (u_j(\cdot, t)) \geq 0$

[mass dissipation]

$$\sum_{j=1}^N f_j(u) \leq 0, \ u = (u_j) \geq 0$$

⟶ $\frac{\partial}{\partial t}(\tau \cdot u) - \Delta(d \cdot u) \leq 0$

$$\left.\frac{\partial u}{\partial \nu}\right|_{\partial\Omega} = 0$$

$$\|\tau \cdot u(t)\|_1 \leq \|\tau \cdot u_0\|_1$$

[quadratic]

$|\nabla f_j(u)| \leq C(1 + |u|), \ \forall j$

Theorem (Fellner-Morgan-Tang 20, 21)

$T = +\infty \qquad \|u(\cdot, t)\|_\infty \leq C$

Pierre-Rolland 15 $0 \leq \exists u = (u_j(\cdot,t)) \in C([0,+\infty), L^1(\Omega)^N)$ global-in-time weak solution

Pierre-S.-Yamada 19 $\mathcal{O} = \{u(\cdot,t)\} \subset L^1(\Omega)^N$ pre-compact

alternative proof of $T = +\infty$ $\|u(\cdot,t)\|_\infty \leq C$ for n=2 via space control $(L^{1,\infty}_{x,t})$

$$\frac{1}{2}\frac{d}{dt}\int_\Omega \sum_j \tau_j u_j^2 \, dx + \sum_j d_j \|\nabla u_j\|_2^2 \leq C(1 + \|u\|_3^3)$$

Gagliardo-Nirenberg $\|u\|_3^3 \leq C\|u\|_1\|u\|_{H^1}^2 \ (n=2)$ semigroup estimate

⟶ $\|u_0\|_1 \ll 1 \ \Rightarrow \ T = +\infty, \ \|u(t)\|_\infty \leq C$ (epsilon regularity)

Localization ⟶ $\lim_{R\downarrow 0} \limsup_{t\uparrow T} \|u(t)\|_{L^1(\Omega\cap B(x_0,R))} < \exists\varepsilon_0 \quad \Rightarrow \quad x_0 \notin \mathcal{S}$ blowup set

while $\lim_{R\downarrow 0} \limsup_{t\uparrow T} \|u(t)\|_{L^1(\Omega\cap B(x_0,R))} \geq \varepsilon_0$ impossible

because pre-compactness of $\mathcal{O} = \{u(\cdot,t)\} \subset L^1(\Omega)^N$ c.f. Smoluchowski-Poisson equation

⟶ $\mathcal{S} = \emptyset$

多項式増大の一般論

$$\tau_j \frac{\partial u_j}{\partial t} - d_j \Delta u_j = f_j(u) \text{ in } Q_T$$

$$\left.\frac{\partial u_j}{\partial \nu}\right|_{\partial\Omega} = 0, \ \ u_j|_{t=0} = u_{j0}(x)$$

$\Omega \subset \mathbf{R}^n$ bounded domain, $\partial\Omega$ smooth

$Q_T = \Omega \times (0, T)$ $\quad 1 \leq j \leq N$

ν outer unit normal

$\tau = (\tau_j) > 0, \ d = (d_j) > 0$

$u_0 = (u_{j0}) \geq 0$ smooth

[local. Lipschitz cont.]

$f_j : \mathbf{R}^N \to \mathbf{R}, \ 1 \leq j \leq N$

loc. Lipschitz cont.

⟶

$\exists 1$ classical solution local-in-time

$T \in (0, +\infty]$ maximal existence time

[quasi-positive]

$f_j(u_1, \cdots, u_{j-1}, 0, u_{j+1}, \cdots, u_n) \geq 0, \ \forall j$

$0 \leq u_0 = (u_{j0}) \in \mathbf{R}^N$ ⟶

$u = (u_j(\cdot, t)) \geq 0$

[mass dissipation]

$$\sum_{j=1}^N f_j(u) \leq 0, \ \ u = (u_j) \geq 0$$

⟶

$$\frac{\partial}{\partial t}(\tau \cdot u) - \Delta(d \cdot u) \leq 0$$

$$\left.\frac{\partial u}{\partial \nu}\right|_{\partial\Omega} = 0$$

$$\|\tau \cdot u(t)\|_1 \leq \|\tau \cdot u_0\|_1$$

[polynomial growth rate]

$$|\nabla f_j(u)| \leq C(1 + |u|^{q-1}), \ \ 1 \leq j \leq N$$

Theorem 1 (S. 20) $\forall n, \ \forall q > 1$

$$\exists \lim_{t \uparrow T} \left(\frac{d \cdot u}{\tau \cdot u} \right) (\cdot, t) \text{ in } C(\overline{\Omega}) \ \Rightarrow \ T = +\infty, \ \|u(t)\|_\infty \leq C$$

Remark 1 Pierre-Schmitt 97 N=2

$\exists$ nonlinearity (fifth-order polynomials) inhomogeneous boundary conditions $T < +\infty,\ n = 10$

$$\frac{d \cdot u}{\tau \cdot u} = \frac{d_1 + d_2 v}{\tau_1 + \tau_2 v},\ v \equiv u_2/u_1 = \frac{c + d|x|^2/(T-t)}{a + b|x|^2/(T-t)}$$

$\exists$ the other example even for n=1

Problem 1 classification of self-similar blowup to v

c.f. N=2 $T < +\infty \quad \Rightarrow \quad \limsup_{t \uparrow T} \|u_j(t)\|_\infty = +\infty,\ j = 1, 2$

$$\frac{d \cdot u}{\tau \cdot u} = \frac{d_1 u_2^{-1} + d_2 u_1^{-1}}{\tau_1 u_2^{-1} + \tau_2 u_1^{-1}} \in C(\overline{\Omega} \times [0, T])?$$

obstruction - collision of blowup points

blowup profile?

$$\frac{\partial u}{\partial t} - \Delta u = u^2 \qquad \left.\frac{\partial u}{\partial \nu}\right|_{\partial\Omega} = 0$$

$$\frac{du}{dt} = u^2,\ u|_{t=0} = T^{-1} \quad \Rightarrow \ u(t) = (T-t)^{-1}$$

$v = u^{-2} \geq 0$ viscosity solution?

$$\frac{\partial v}{\partial t} - \Delta v = -\frac{3}{2} v^{-1} |\nabla v|^2 - 2v^{1/2},\ \left.\frac{\partial v}{\partial \nu}\right|_{\partial\Omega} = 0$$

locally uniformly in backward parabolic region

$$n \leq 2 \ \Rightarrow \ u(x,t) = (T-t)^{-1} + o(1)$$

$\Longrightarrow$ $u(\cdot, T)^{-1} = v(\cdot, T)^{1/2} \in [0, +\infty)$ blowup pattern

爆発解析

Proof of Theorem 1

uniqueness of the classical solution … OK

$$\sup_{0\le t<T}\|u(t)\|_\infty \le C$$ ⟹ existence of global in time uniformly bounded classical solution

assume the contrary (subsequence) $\exists x_k \to x_0 \in \overline{\Omega},\ \exists t_k \uparrow T,\ |u(x_k,t_k)| \to +\infty$

$$0<r\ll 1,\ \tilde{u}^k(x,t)=r^\alpha u(rx+x_k, r^2t+t_k),\ \alpha=\frac{2}{q-1}$$

⟹ $$\tau_j\frac{\partial \tilde{u}_j^k}{\partial t}-d_j\Delta\tilde{u}_j^k=\tilde{f}_j(\tilde{u}^k),\ \tilde{u}^k=(\tilde{u}_j^k)\ge 0 \text{ in } \Omega_k\times(T_k^1,T_k^2),\ \left.\frac{\partial \tilde{u}_j^k}{\partial \nu}\right|_{\partial\Omega_k}=0$$

$$\tilde{f}_j(u)=r^{2+\alpha}f_j(r^{-\alpha}u),\ \Omega_k=r^{-1}(\Omega-\{x_k\}),\ T_k^1=-t_k/r^2,\ T_k^2=(T-t_k)/r^2$$

drop k, large $\exists\gamma\subset\mathbf{R}^n$ hyper-plane, $B_2\cap\gamma\neq\emptyset$ or $=\emptyset$ $0\in\tilde{B}_2=$ one-side of B_2 cut by γ

$$\tau_j\frac{\partial \tilde{u}_j}{\partial t}-d_j\Delta\tilde{u}_j=\tilde{f}_j(\tilde{u}),\ \tilde{u}=(\tilde{u}_j)\ge 0 \text{ in } \tilde{Q}_2,\ \left.\frac{\partial \tilde{u}_j}{\partial \nu}\right|_{\gamma\cap B_2}=0$$ $$\tilde{Q}_2=\tilde{B}_2\times(-4,0),\ \tilde{Q}_1=\tilde{B}_1\times(-1,0)$$

⟹ derive uniform estimate in $0<r\ll 1$

Lemma 1 (c.f. Capto-Vasseur)

Moser's iteration scheme

$$\forall p > (\frac{n}{2}+1)(q-1), \ \exists \varepsilon_0 > 0$$

$$\|\tilde{u}\|_{L^p(\tilde{Q}_1)} < \varepsilon_0 \ \Rightarrow \ 0 \leq \tilde{u}_j(0,0) \leq 1, \ 1 \leq j \leq N$$

mass conservation by a suspend unknown

$$\sum_j f_j(u) = 0, \ u = (u_j) \geq 0$$

$$\tilde{M} = \tau \cdot \tilde{u}, \ v = \tilde{M}\zeta, \ \zeta(x,t) = \varphi(x)\eta(t) \ \text{cut-off} \qquad \varphi \in C_0^\infty(B_2), \ \left.\frac{\partial \varphi}{\partial \nu}\right|_\gamma = 0, \ \eta \in C_0^\infty(-4,0]$$

⟹

$$\frac{\partial v}{\partial t} - \Delta(\tilde{d}v) = f \ \text{in} \ \tilde{Q}_2, \ \left.\frac{\partial}{\partial \nu}(\tilde{d}v)\right|_{B_2 \cap \gamma} = 0 \qquad \tilde{d} = \frac{d \cdot \tilde{u}}{\tau \cdot \tilde{u}}$$

$$f = M\zeta_t - 2\nabla \cdot (\tilde{d}M\nabla\zeta) + \tilde{d}M\Delta\zeta$$

$$0 < d_* = \frac{\min_j d_j}{\max_j \tau_j} \leq \tilde{d}(x,t) \equiv \frac{d \cdot \tilde{u}}{\tau \cdot \tilde{u}} \leq d^* = \frac{\max_j d_j}{\min_j \tau_j} < +\infty \qquad \tilde{u} = (\tilde{u}_j)$$

VMO

Apply parabolic L^p maximal regularity uniform on compact set of coefficients in VMO to the dual system

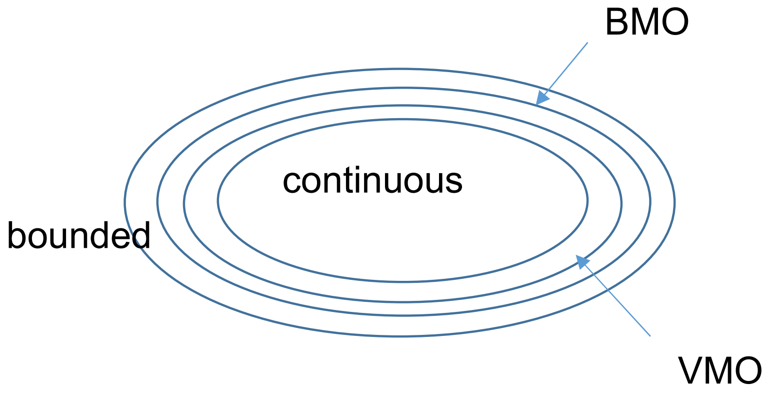
uniform estimate for coefficients in a compact set in VMO

Remark 5 $f \in \mathrm{VMO},\ \varepsilon > 0,\ x_0 \in \Omega \ \Rightarrow\ \exists g \in \mathrm{BMO},\ \exists r > 0$

$\|g\|_{BMO(B)} < \varepsilon,\ f = g \text{ in } B(x_0, r)$

local smallness of the BMO norm

VMO:BMO ~ continuous: bounded



Lemma 2 (maximal regularity, Weidemaier 05)

$$w_t + \tilde{d}\Delta w = -\theta \geq 0 \text{ in } \omega \times (-4, 0),\ \left.\frac{\partial w}{\partial \nu}\right|_{\partial\omega} = 0,\ w|_{t=0} = 0 \quad \Longrightarrow$$

$$\int_{-4}^{0} \|w(t)\|^p_{W^{2,p}(\tilde{Q}_1)} dt \leq C\|\theta\|^p_{L^p(\tilde{Q}_2)},\ 1 < p < \infty,\ p \neq 3$$

$$\tilde{B}_1 \subset \text{supp } \varphi \subset \omega \subset \tilde{B}_2,\ \partial\omega \text{ smooth}$$

duality argument between $v = \tilde{M}\zeta,\ \tilde{M} = \tau \cdot u$

Lemma 3 $$\|\tilde{M}\|_{L^q(\tilde{Q}_2)} \leq C \sup_{-16<t<0} \|\tilde{M}(t)\|_{L^1(\tilde{B}_4)},\ 1 < q < n$$

$$\Longrightarrow \quad \|\tilde{M}\|_{L^{p'}(\tilde{Q}_1)} \leq C \sup_{-16<t<0} \|\tilde{M}(t)\|_{L^1(\tilde{B}_4)},\ \frac{1}{p'} = \frac{1}{q} - \frac{1}{n},\ p' > \frac{n}{n-1},\ p' \neq \frac{3}{2}$$

Dual Alexandroff – Bakelman - Pucci estimate (Caputo-Goudon-Vasseiur)

Lemma 4 (FMT) $\|\tilde{M}\|_{L^{1+\frac{1}{n}}(\tilde{Q}_2)} \leq C \sup_{-16<t<0} \|\tilde{M}(t)\|_{L^1(\tilde{B}_4)}$ ABP… $L^\infty - L^{n+1}$

Lemma 3+ Lemma 4 ⟹ $\forall p > 1,\ \exists \rho > 4,\ \|\tilde{M}\|_{L^p(\tilde{Q}_1)} \leq C \sup_{-\rho^2<t<0} \|\tilde{M}(t)\|_{L^1(\tilde{B}_\rho)}$

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pre-scaled analysis ⟹ duality argument (CGV) Lemma 5 $\sup_{-\rho^2<t<0} \|\tilde{M}(t)\|_{L^1(\tilde{B}_\rho)} \leq Cr^\theta$

$$M = \tau \cdot u,\ \hat{d} = \frac{d \cdot u}{\tau \cdot u} \qquad \exists \Phi,\ -\Delta\Phi = M,\ \left.\frac{\partial \Phi}{\partial \nu}\right|_{\partial\Omega} = 0$$

$$\frac{\partial \Phi}{\partial t} = \hat{d}\Delta\Phi,\ \left.\frac{\partial \Phi}{\partial \nu}\right|_{\partial\Omega} = 0$$ ⟹ (Krylov-Safonov)

$$[\Phi]_{C^\theta(\Omega\times(t_0,t_0+1))} \leq C\|\Phi\|_{L^\infty(\Omega\times(t_0-1,t_0+1))}$$

Lemma 5+ Lemma 1 ⟹

$$0 \leq u_j(x_k,t_k) \leq Cr^{-\alpha},\ 1 \leq j \leq N,\ 0 < r \ll 1$$

contradiction

consequences derived from this argument

Theorem 2

$$n = 3$$

$$1 < q < 9/5 \quad \Rightarrow \quad T = +\infty, \ \|u(t)\|_\infty \leq C$$

$$q = \sigma \downarrow$$

Theorem 3 [entropy inequality]

$$\sum_j f_j(u) \log u_j \leq C(1 + |u|^\sigma), \ 1 < \sigma \leq 1 + \frac{2}{n}$$

$$n = 2, 3, \ 1 < q < 2 + \frac{2}{n}, \quad \sigma = 1 + \frac{2}{n}$$

n=2, critical dimension in this context

or $$n \geq 4, \ 1 < q < 2 + \frac{1}{n}, \ \sigma = 1 + \frac{1}{n} \quad \Rightarrow \quad T = +\infty, \ \|u(t)\|_\infty \leq C$$

(especially, n=2, q=2) S.-Yamada 15

1. n>3 → dual ABP
   n=3 → L^2 duality argument is efficient

2. entropy inequality → local epsilon regularity in space-time