Equilibration of renormalised solutions to nonlinear reaction-diffusion systems

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Introduction/Overview

Large-Time-Behaviour of Nonlinear RD systems

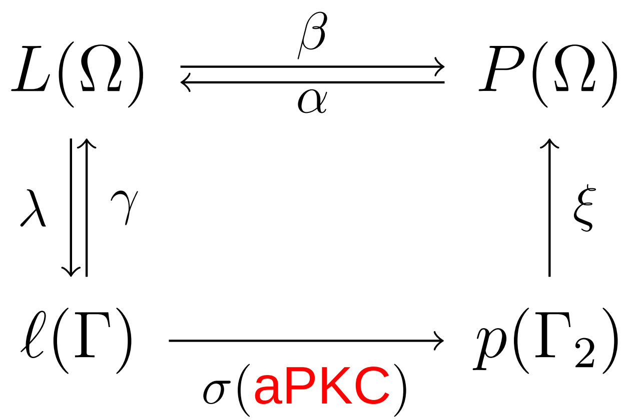
- Motivation/Application: Volume-Surface RD models
- Complex Balanced Equilibria $\longrightarrow$ Entropy (Free Energy)
- Geometry $\longrightarrow$ Non-Convex Entropy-Dissipation

- Exponential Equilibration of Renormalised Solutions
- Indirect Diffusion Effect $\longrightarrow$ Nonlinear Diffusion
- Boundary Equilibria $\longrightarrow$ Global Attractor Conjecture
- A non-complex balanced Amyloid Model

A Volume-Surface Reaction-Diffusion Model

Model Assumptions and Quantities

A complex-balanced reaction-diffusion network



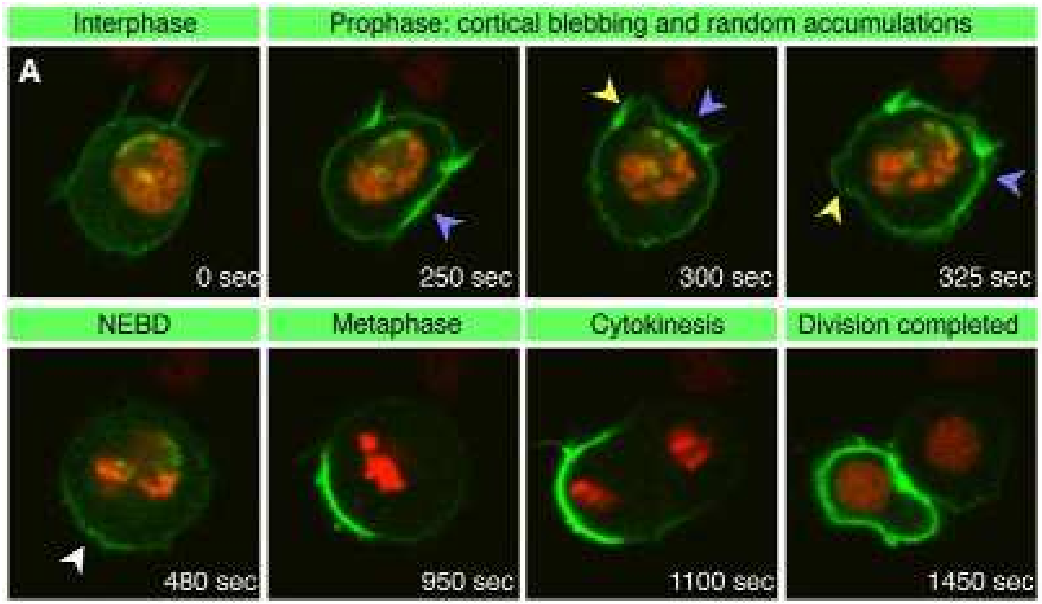
Lgl protein in cytoplasm (Ω) and cell cortex $(\Gamma = \partial\Omega)$.

aPKC kinase phosphorylates Lgl on a subpart Γ_2 of cortex.

$L(t,x)$ cytoplasmic Lgl $\leftrightarrow$ $l(t,x)$ cortical Lgl $\rightarrow$ activation of aPKC

$\rightarrow$ $p(t,x)$ cortical p-Lgl $\rightarrow$ $P(t,x)$ cytoplasmic p-Lgl $\leftrightarrow$ $L(t,x)$

A Volume-Surface Reaction-Diffusion Model



Asymmetric stem-cell division:

Cell-diversity by localisation of cell-fate determinants into one side of the cell cortex and into one of two daughter cells.[a]

[a] GFP-Pon in SOP precursor cells in living Drosophila larvae [Meyer, Emery, Berdnik, Wirtz-Peitz, Knoblich, Current Biology, 2005]

A Volume-Surface Reaction-Diffusion Model

Complex balance reaction network

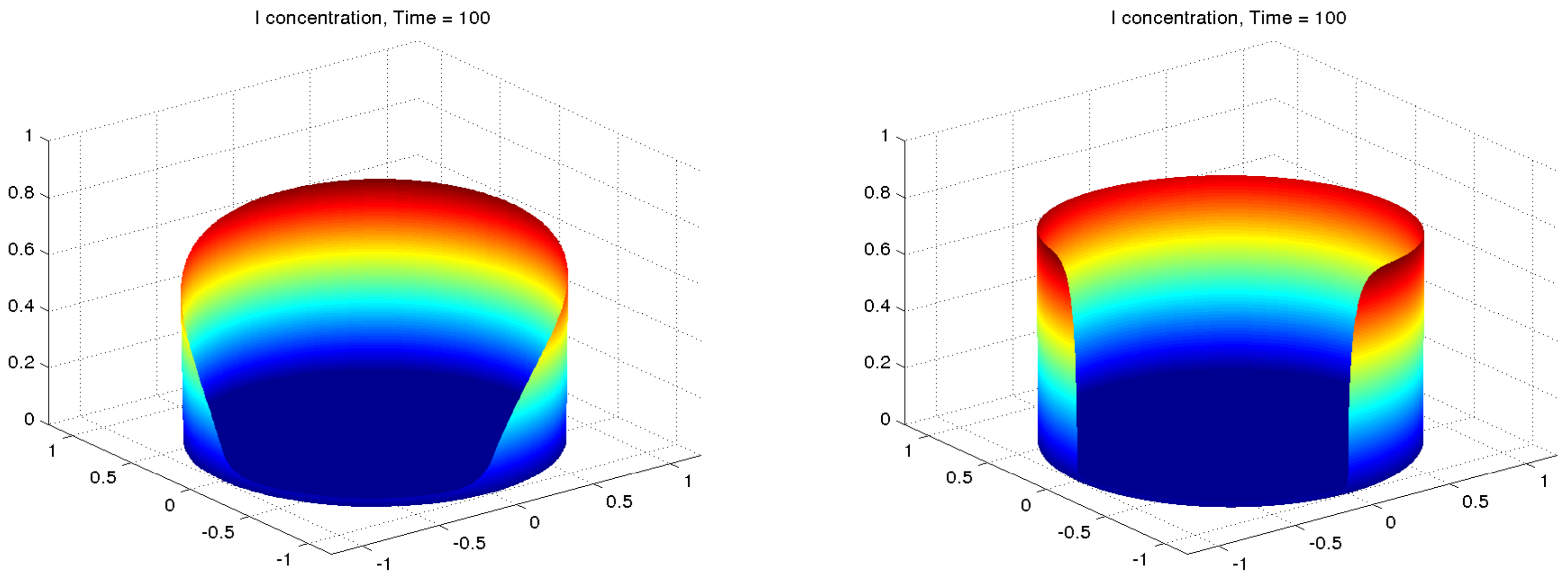


Figure 1: l-Lgl(Γ) with and without surface diffusion

Numerical analysis of VSRD models including discrete entropy structure/estimates: [a]

[a] [Egger, F., Pietschmann, Tang]

A Volume-Surface Reaction-Diffusion Model

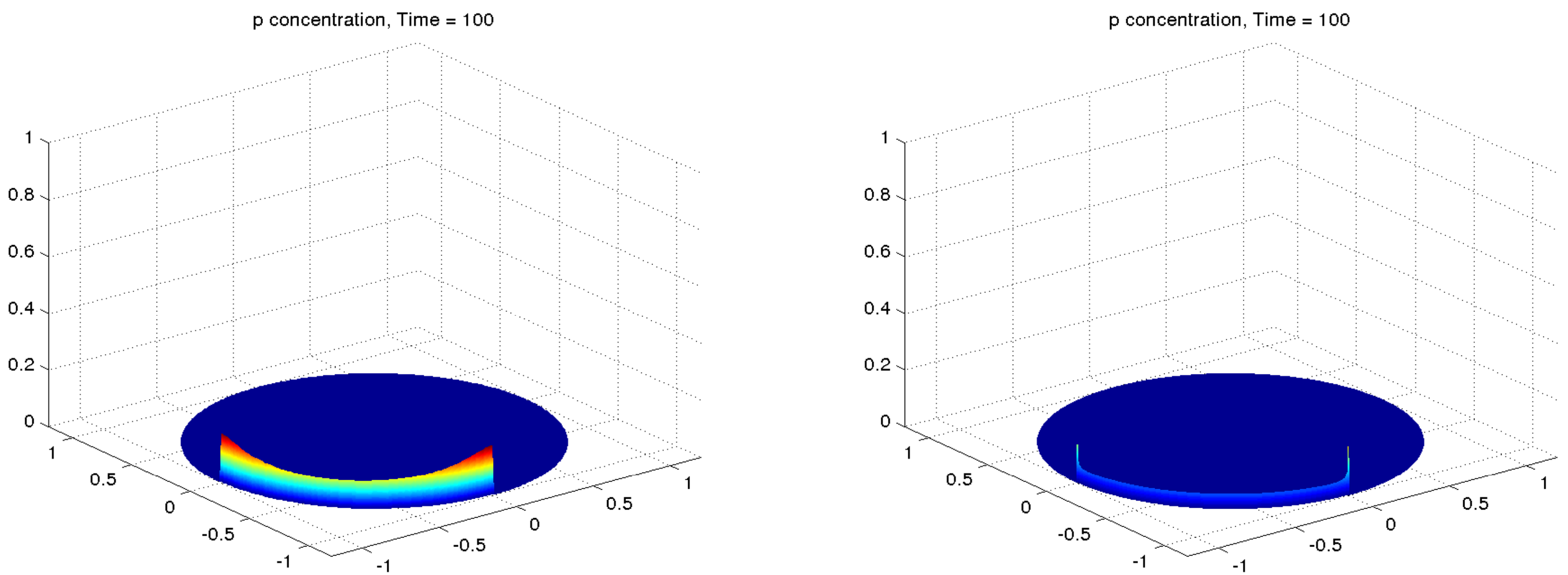


Figure 2: p-Lgl(Γ) with and without surface diffusion

Surface diffusion $O(10^{-2})$: indirect surface diffusion effect via weakly reversible reaction $O(1)$ and volume diffusion $O(10^{-2})$

A Volume-Surface Reaction-Diffusion Model

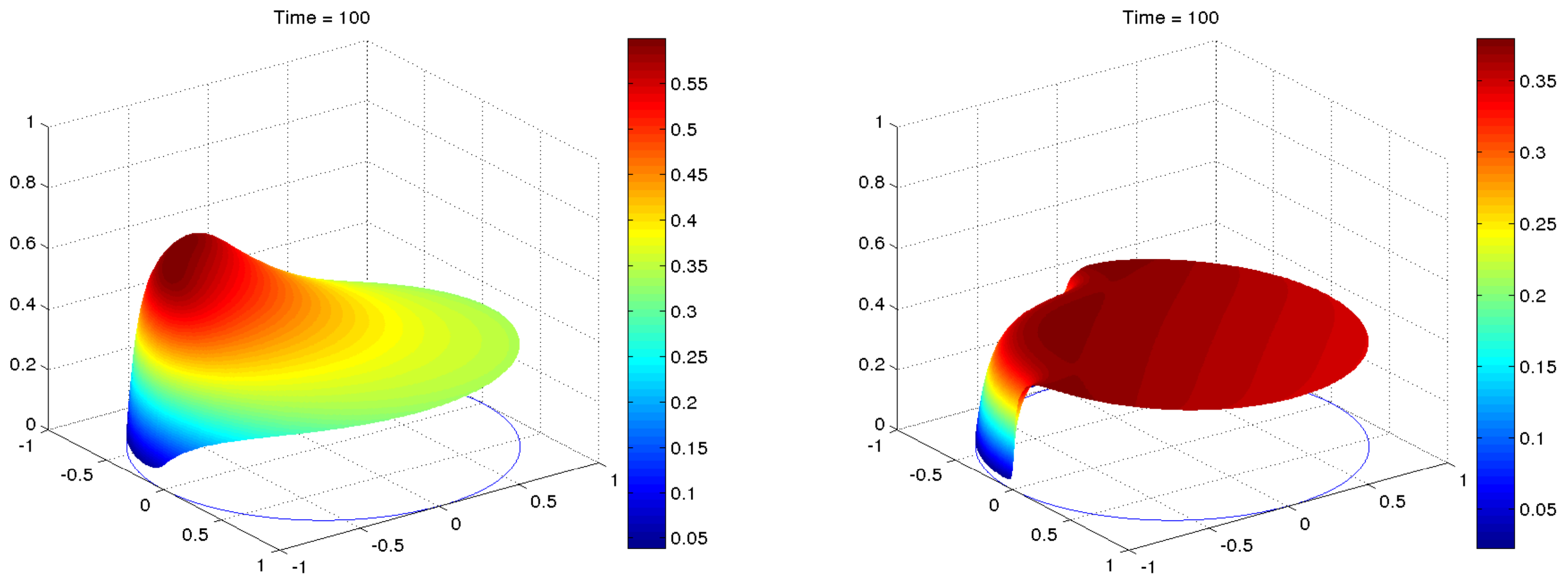


Figure 3: L-Lgl(Ω) with and without surface diffusion

Surface diffusion and weakly reversible reaction lead to stationary hump in L within Ω.

A Volume-Surface Reaction-Diffusion Model

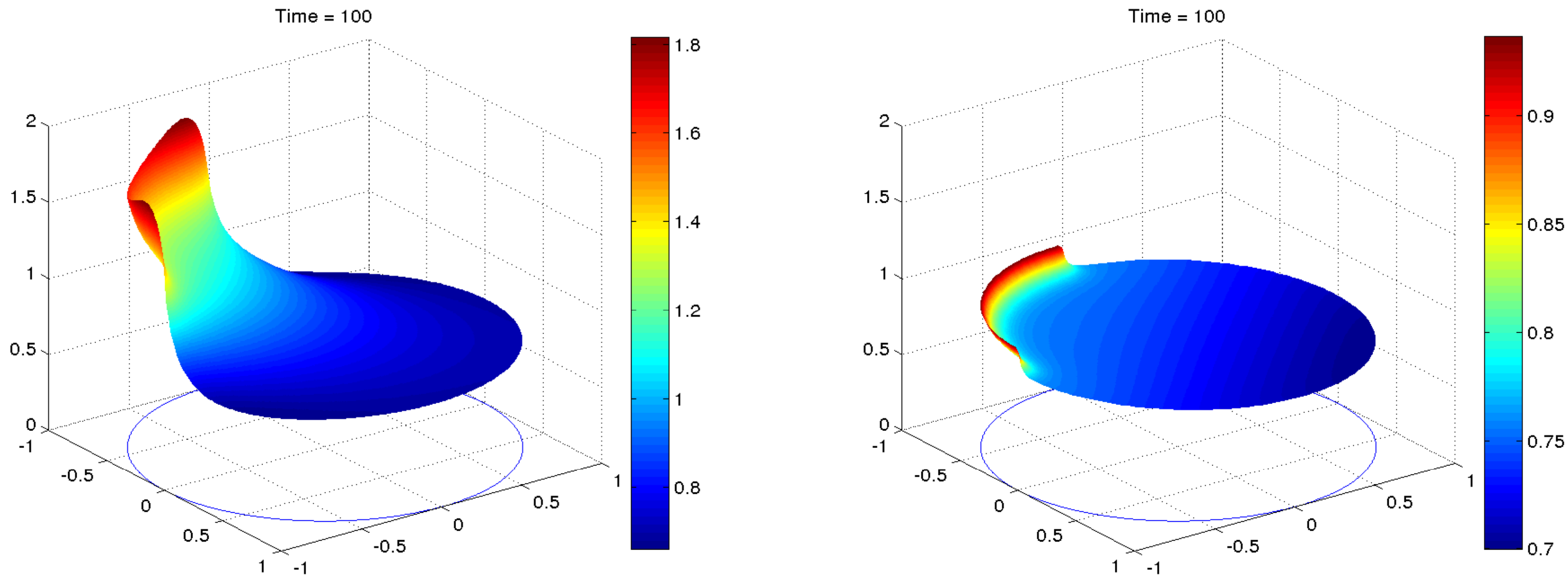
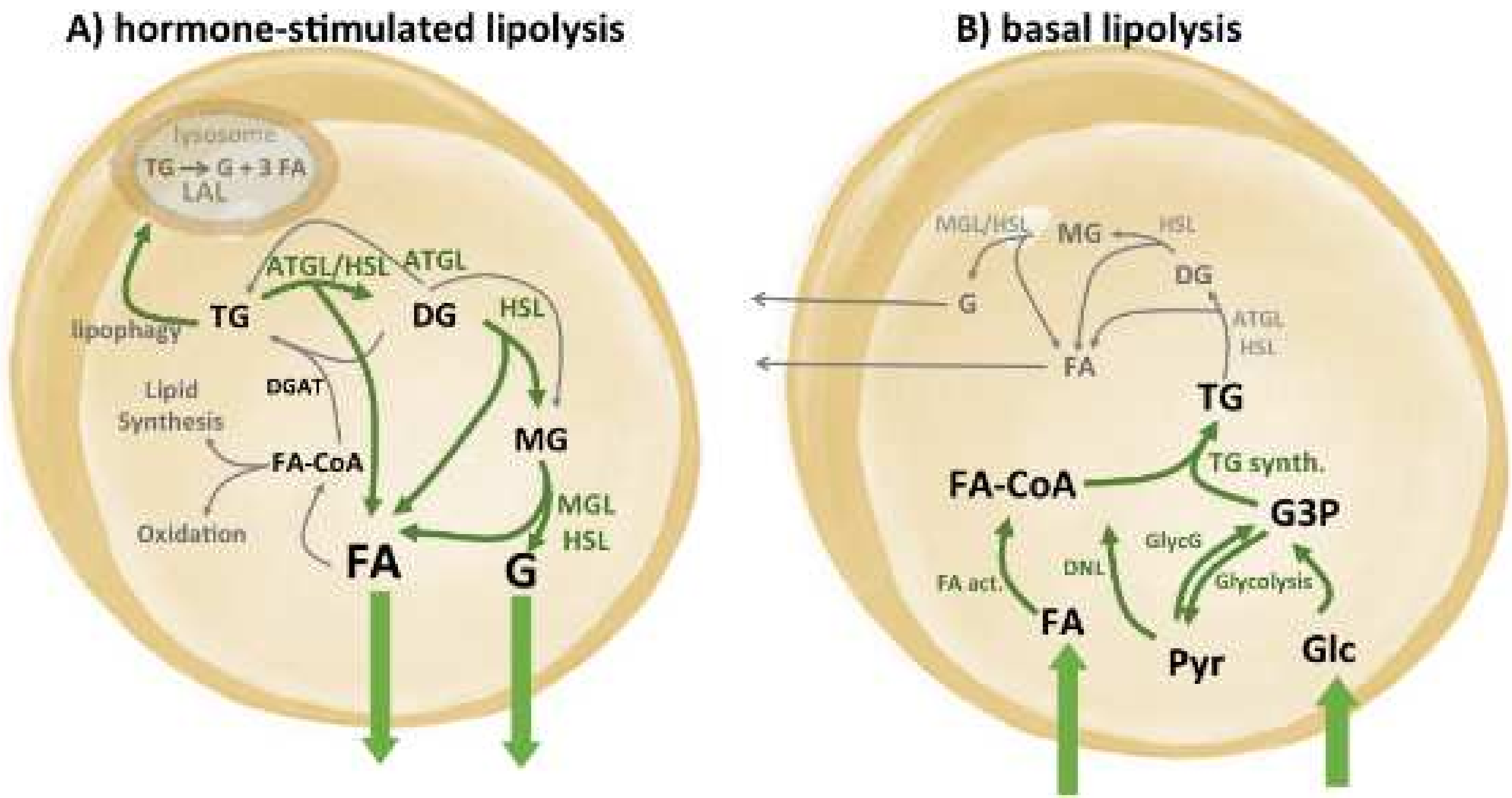


Figure 4: P-Lgl(Ω) with and without surface diffusion

Stationary hump in L as consequence of inflow from p into $P \rightarrow L$ and shape of Ω.

Another (Volume-Surface) RD Model

Lipolysis



Lipolysis: Breakdown of lipids and hydrolysis of triglycerides into glycerol and fatty acids.

Systems of Reaction-Diffusion Equations

Nonlinear Complex Balance Networks

Substances: $\mathcal{S} = \{S_1, \ldots, S_N\}$,

Complexes: $\mathcal{C} = \{\boldsymbol{y}_1, \ldots, \boldsymbol{y}_{|\mathcal{C}|}\}$ with $\boldsymbol{y}_i \in (\{0\} \cup [1, \infty))^N$,

Reactions: $\mathcal{R} = \{\boldsymbol{y} \to \boldsymbol{y}'\}$ from source $\boldsymbol{y}$ into product $\boldsymbol{y}' \in \mathcal{C}$.

Mass action law reaction rate for $\boldsymbol{y}_r \to \boldsymbol{y}_r'$: $\quad \mathbf{c}^{\boldsymbol{y}_r} = \prod_{i=1}^N c_i^{y_{r,i}}$

Reaction rate constant k_r of the reaction $\boldsymbol{y}_r \to \boldsymbol{y}_r'$.

Reaction vector: $\quad \mathbf{R}(\mathbf{c}) = \sum_{r=1}^{|\mathcal{R}|} k_r \mathbf{c}^{\boldsymbol{y}_r} (\boldsymbol{y}_r' - \boldsymbol{y}_r)$

Nonlinear Complex Balance Networks

Nonlinear reaction-diffusion network

$$\frac{\partial}{\partial t}\mathbf{c} - \mathbb{D}\Delta\mathbf{c} = \mathbf{R}(\mathbf{c}) \quad \text{for} \quad (x,t) \in \Omega \times (0, +\infty),$$

with $\mathbb{D} = \mathrm{diag}(d_1, \ldots, d_N)$.

Homogeneous Neumann BCs on Lipschitz domain Ω.

[JH72]: A complex balanced network has a unique positive equilibrium, which balances the total outflow and inflow for all complexes $\boldsymbol{y} \in \mathcal{C}$:

$$\sum_{\{r:\, \boldsymbol{y}_r = \boldsymbol{y}\}} k_r \mathbf{c}_\infty^{\boldsymbol{y}_r} = \sum_{\{s:\, \boldsymbol{y}'_s = \boldsymbol{y}\}} k_s \mathbf{c}_\infty^{\boldsymbol{y}_s}.$$

Relative (free energy) entropy functional

$$\mathcal{E}(\mathbf{c}|\mathbf{c}_\infty) = \sum_{i=1}^{N} \int_\Omega \Big(c_i \log \frac{c_i}{c_{i,\infty}} - c_i + c_{i,\infty}\Big) dx$$

Explicit (nontrivial) entropy dissipation functional with $e(x,y) = x \log{(x/y)} - x + y$

$$\begin{aligned}\mathcal{D}(\mathbf{c}) &= -\frac{d}{dt}\mathcal{E}(\mathbf{c}|\mathbf{c}_\infty) \\ &= \sum_{i=1}^{N} d_i \int_\Omega \frac{|\nabla c_i|^2}{c_i} dx + \sum_{r=1}^{|\mathcal{R}|} k_r \mathbf{c}_\infty^{y_r} e\left(\frac{\mathbf{c}^{y_r}}{\mathbf{c}_\infty^{y_r}}, \frac{\mathbf{c}^{y_r'}}{\mathbf{c}_\infty^{y_r'}}\right) \geq 0\end{aligned}$$

Nonlinear Complex Balance Networks

Theorem:[a] For complex balanced RD networks without boundary equilibria, any renormalised (Fisher [2015]) solution $\mathbf{c}(x,t)$ converges exponentially to $\mathbf{c}_\infty$ in L^1 with a rate $\lambda/2$:

$$\sum_{i=1}^{N} \|c_i(t) - c_{i,\infty}\|^2_{L^1(\Omega)} \le C_{\mathrm{CKP}}^{-1}\,\mathcal{E}(\mathbf{c}_0|\mathbf{c}_\infty)\,e^{-\lambda t} \qquad \text{for a.a. } t>0,$$

where C_{CKP} is the constant in a Csiszár-Kullback-Pinsker type inequality.

Renormalised solutions satisfy all mass/charge conservation laws and a weak entropy-dissipation law, Fisher [2017]

[a] [K.F. B.Q.Tang, to appear in ZAMP]

The Entropy Method

Quantitative large-time behaviour

$\mathcal{E}(f)$ non-increasing convex entropy functional

$\mathcal{P}(f)$ entropy production, f_∞ entropy minimising equilibrium

$$\frac{d}{dt}\mathcal{E}(f) = \frac{d}{dt}\mathcal{E}(f) - \mathcal{E}(f_\infty)) = -\mathcal{P}(f) \leq 0$$

provided conservation laws: $\mathcal{P}(f) = 0 \Longleftrightarrow f = f_\infty$

$$\mathcal{P} \geq \Phi(\mathcal{E}(f) - \mathcal{E}(f_\infty)), \quad \Phi(0) = 0, \quad \Phi \geq 0$$

$\Rightarrow$ explicit convergence in entropy, exponential if $\Phi'(0) > 0$

$\Rightarrow$ convergence in L_1 : $\|f - f_\infty\|_1^2 \leq C(\mathcal{E}(f) - \mathcal{E}(f_\infty))$

Cziszár-Kullback-Pinsker inequalities for convex entropies

Entropy Method

Advantages:

- based on functional inequalities $\rightarrow$ "robust"
- avoids linearisation $\rightarrow$ "global" results
- allows for explicit constants

nonlinear diffusion: [T], [CJMTU], [AMTU], [DV]...

inhomogeneous kinetic equations: [DV], ...

reaction-diffusion systems: [Grö83], [Grö92], [DF06], [DF08], [DF14], [MMH15], [FL16], [PSZ17], [DFT17], [FT17], [HHMM18], [FT18]   no Bakry-Emery strategy

Theorem:[a] For any complex balanced reaction networks without boundary equilibria, there exists a constant $\lambda > 0$ and the "exponential" entropy entropy-dissipation estimate

$$\mathcal{D}(\mathbf{c}(t)) \geq \lambda\,\mathcal{E}(\mathbf{c}(t)|\mathbf{c}_\infty),$$

- Proof via convexification: [MMH15] (detailed balance)
- Proof via explicit estimates using conservation laws $\mathbb{Q}\,\overline{\mathbf{c}} = \mathbf{M}$: [DFT17], [FT17]
- Proof via reduction to finite-dimensional inequality: [FT18]

[a] [L. Desvillettes, K.F., B.Q. Tang, SIMA 2017], [K.F., B.Q. Tang, Nonlinear Analysis 2017.]

Lemma:[a] For all states $\overline{\mathbf{c}} \in \mathbb{R}^N_{>0}$ satisfying $\mathcal{E}(\overline{\mathbf{c}}|\mathbf{c}_\infty) < +\infty$ and the conservation laws $\mathbb{Q}\,\overline{\mathbf{c}} = \mathbf{M}$, there exists a positive constant $H_1 = H_1(\mathbb{Q}, \mathbf{M}, \boldsymbol{y} \in \mathcal{C}, \mathcal{E}(\overline{\mathbf{c}}|\mathbf{c}_\infty))$ such that

$$\sum_{r=1}^{|\mathcal{R}|} \left[\sqrt{\frac{\overline{\mathbf{c}}}{\mathbf{c}_\infty}}^{\boldsymbol{y}_r} - \sqrt{\frac{\overline{\mathbf{c}}}{\mathbf{c}_\infty}}^{\boldsymbol{y}'_r} \right]^2 \geq H_1 \sum_{i=1}^{N} \left(\sqrt{\frac{\overline{c_i}}{c_{i,\infty}}} - 1 \right)^2 .$$

Here, $\sqrt{\frac{\overline{\mathbf{c}}}{\mathbf{c}_\infty}} = \left(\sqrt{\frac{\overline{c_1}}{c_{1,\infty}}}, \ldots, \sqrt{\frac{\overline{c_N}}{c_{N,\infty}}} \right)$.

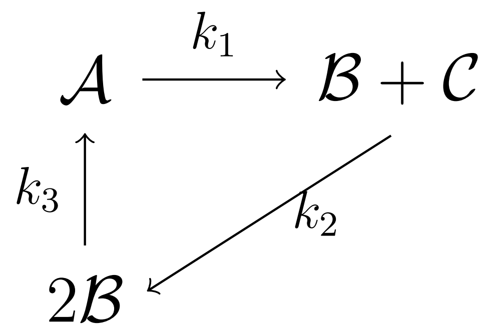
This finite-dimensional inequality implies

$$\mathcal{D}(\mathbf{c}(t)) \geq \lambda(H_1)\, \mathcal{E}(\mathbf{c}(t)|\mathbf{c}_\infty),$$

[a] [K.F., B.Q. Tang, to appear in ZAMP]

Boundary Equilibria

Example:



$$
\begin{cases}
a_t - d_a \Delta a = -k_1 a + k_3 b^2, \\
b_t - d_b \Delta b = k_1 a + k_2 bc - 2k_3 b^2, \\
c_t - d_c \Delta c = k_1 a - k_2 bc,
\end{cases}
$$

Boundary equilibrium $(a^*, b^*, c^*) = (0, 0, M)$.

Problem: $\mathcal{D}(a^*, b^*, c^*)) = 0$, but $\mathcal{E}(\mathbf{c}^* | \mathbf{c}_\infty) > 0$

No global entropy-entropy dissipation estimate possible!

Boundary Equilibria

Our approach: weaker entropy-entropy dissipation estimate along solution trajectories

$$\mathcal{D}(\mathbf{c}(t)) \geq \lambda(t)\,\mathcal{E}(\mathbf{c}(t)|\mathbf{c}_\infty)$$

Difficulty: $\lambda(t) \to 0$ near boundary equilibria.

However, if $\lambda(t)$ satisfies $\int_0^{+\infty} \lambda(s)ds = +\infty$, then

$$\mathcal{E}(\mathbf{c}(t)|\mathbf{c}_\infty) \leq \mathcal{E}(\mathbf{c}_0|\mathbf{c}_\infty)e^{-\int_0^t \lambda(s)ds} \to 0 \quad \text{as } t \to \infty.$$

$\Rightarrow$ (algebraic) instabilty of boundary equilibria

$\Rightarrow$ Exponential convergence to positive equilibrium

Boundary Equilibria

Corresponding RD system

$$\begin{cases} a_t - d_a\Delta a = -k_1 a + k_3 b^2, & x\in\Omega, \quad t>0,\\ b_t - d_b\Delta b = k_1 a + k_2 bc - 2k_3 b^2, & x\in\Omega, \quad t>0,\\ c_t - d_c\Delta c = k_1 a - k_2 bc, & x\in\Omega, \quad t>0,\\ \nabla a\cdot\nu = \nabla b\cdot\nu = \nabla c\cdot\nu = 0, & x\in\partial\Omega, \quad t>0, \end{cases}$$

$$\inf_{x\in\Omega} b(x,t) \geq \frac{1}{\left\|\frac{1}{b_0}\right\|_{L^\infty} + 2k_3 t}, \qquad \text{for all} \quad t\geq 0.$$

Solutions would need infinite initial entropy to remain close to boundary equilibria for an unbounded time interval. [a]

[a] [L. Desvillettes, K.F., B.Q. Tang, SIMA 2017]

Boundary Equilibria

Theorem:[a] Let $\mathbf{c}(t)$ be a renormalised solution of an arbitray complex balanced network. Assume that there exists $H_1 : [0, \infty) \to [0, \infty)$ such that $\int_0^\infty H_1(s)ds = +\infty$ and for a.a. $t \geq 0$

$$\sum_{r=1}^{|\mathcal{R}|} \left[\sqrt{\frac{\overline{\mathbf{c}}(t)}{\mathbf{c}_\infty}}^{\boldsymbol{y}_r} - \sqrt{\frac{\overline{\mathbf{c}}(t)}{\mathbf{c}_\infty}}^{\boldsymbol{y}'_r} \right]^2 \geq H_1(t) \sum_{i=1}^{N} \left(\sqrt{\frac{\overline{c_i}(t)}{c_{i,\infty}}} - 1 \right)^2 .$$

Then, the renormalised solution $\mathbf{c}(t)$ converges exponentially to the positive equilibrium $\mathbf{c}_\infty$.

[a] [K.F., B.Q. Tang, to appear in ZAMP]

Systems of Reaction-Diffusion Equations

Boundary Equilibria

Global Attractor Conjecture:

For any complex balanced mass action law reaction networks, all solution trajectory subject to positive initial data are conjectured to converge to the positive equilibrium $\mathbf{c}_\infty$.

Proof for ODE systems by Gheorghe Craciun in 2015?

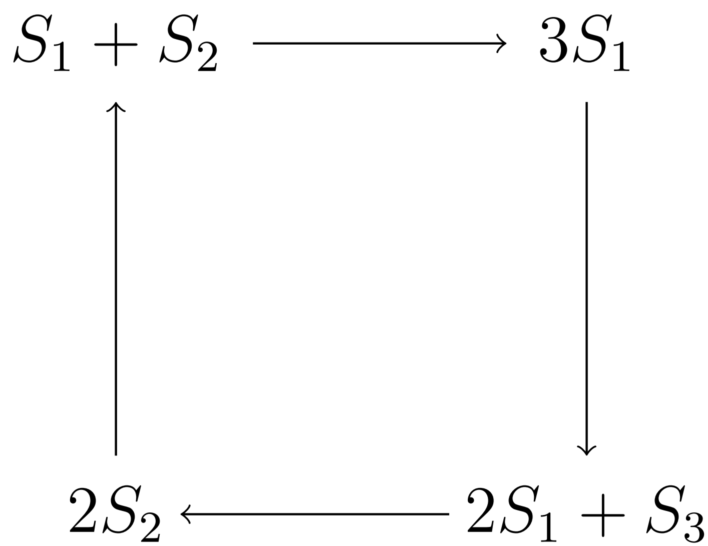
Above finite-dimensional inequality has ODE structure!?

But ODE system and averaged PDE concentrations:

$$\frac{d}{dt}\boldsymbol{u} = \mathbf{R}(\boldsymbol{u}) \neq \overline{\mathbf{R}(\mathbf{c})} = \frac{d}{dt}\overline{\mathbf{c}}(t)$$

Boundary Equilibria

Boundary equilibria for complex balanced reaction networks:



Open problem!

Systems of Reaction-Diffusion Equations

Nonlinear Diffusion

$$
\begin{cases}
\partial_t c_i - d_i \Delta(c_i^{m_i}) = f_i(\mathbf{c}), & x \in \Omega, \quad t > 0, \quad i = 1, \dots, N, \\
d_i \nabla(c_i^{m_i}) \cdot \overrightarrow{n} = 0, & x \in \partial\Omega, \quad t > 0, \quad i = 1, \dots, N, \\
c_i(x, 0) = c_{i,0}(x), & x \in \Omega, \quad i = 1, \dots, N,
\end{cases}
$$

(i) $|f_i(\mathbf{c})| \leq C(1 + |\mathbf{c}|^\nu)$, $\forall \mathbf{c} = (c_1, \dots, c_N) \in \mathbb{R}^N$, $\forall i = 1, \dots, N$

(ii) Mass dissipation: There exist positive constants $\lambda_1, \dots, \lambda_N > 0$ such that: $\sum_{i=1}^S \lambda_i f_i(u) \leq 0, \qquad \forall \mathbf{c} \in \mathbb{R}^S$

(iii) Quasi-positivity $\Rightarrow$ Propagation of non-negativity

Systems of Reaction-Diffusion Equations

Nonlinear Diffusion

- Assume $m_i > \max\{\nu - 1; 1\}$ and $m_i > \nu - \frac{4}{d+2}$ if $d \geq 3$.
  $\Rightarrow$ Existence of global weak nonnegative solutions
  $c_i \in C([0,\infty); L^1(\Omega))$, $c_i^{m_i} \in L^1(0,T; W^{1,1}(\Omega))$,
  $f_i(\mathbf{c}) \in L^1(\Omega \times [0,T])$ and

$$\|c_i\|_{L^\infty(Q_T)} \leq C_T \quad \text{for all} \quad T > 0 \quad \text{and} \quad i = 1, \ldots, N,$$

- Single reaction $\alpha_1 \mathcal{A}_1 + \cdots + \alpha_M \mathcal{A}_M \underset{k_f}{\overset{k_b}{\rightleftharpoons}} \beta_1 \mathcal{B}_1 + \cdots + \beta_N \mathcal{B}_N$.
  $\Rightarrow$ Exponential convergence to equilibrium $\forall 1 \leq p < \infty$,

$$\sum_{i=1}^{M} \|a_i(t) - a_{i\infty}\|_{L^p(\Omega)} + \sum_{j=1}^{N} \|b_j(t) - b_{j\infty}\|_{L^p(\Omega)} \leq C\, e^{-\lambda_p t}$$

Nonlinear Diffusion

Proof of existence theory extends [LP17]

- Duality estimates
- Specific bootstrap

Systems of Reaction-Diffusion Equations

Nonlinear Diffusion

A generalised version of Logarithmic Sobolev Inequality:

$$\int_\Omega \frac{|\nabla a_i|^2}{a_i^{2-m_i}} dx \geq C(\Omega, m_i)\, \overline{a}_i^{m_i-1} \int_\Omega a_i \log \frac{a_i}{\overline{a}_i} dx.$$

Degeneracy for $\overline{a}_i \sim 0$ is control by functional inequalities for indirect diffusion effect and conservation law, since not all $\overline{a}_i \sim 0$ can be small at the same time.

Setting of “slowly growing” apriori estimates:
First algebraic convergence, then exponential convergence!

Indirect diffusion effect $\sim$ “coercive hypocoercivity”

Models for amyloids and protein aggregation

with Marie Doumic, Mathieu Mézache, Human Rezaei

Model for transient oscillations in coagulation-fragmentation experiments of PrP fibrils

$$\begin{cases} \mathcal{V} + \mathcal{W} & \xrightarrow{k} & 2\mathcal{W}, & \\ \mathcal{W} + \mathcal{C}_i & \xrightarrow{a_i} & \mathcal{C}_{i+1}, & 1 \le i \le n, \\ \mathcal{C}_i + \mathcal{V} & \xrightarrow{b_i} & \mathcal{C}_{i-1} + 2\mathcal{V}, & 2 \le i \le n. \end{cases}$$

Simplest two-polymer model with normalised coefficients

$$\begin{cases} \frac{dv}{dt} = v\left[-kw + c_2\right], \\ \frac{dw}{dt} = w\left[kv - c_1\right], \end{cases} \qquad \begin{cases} \frac{dc_1}{dt} = -wc_1 + vc_2, \\ \frac{dc_2}{dt} = wc_1 - vc_2, \end{cases}$$

Models for amyloids and protein aggregation

with Marie Doumic, Mathieu Mézache, Human Rezaei

small parameter $\varepsilon = \frac{1}{k}$

$$\begin{cases} \frac{dv}{dt} = v\left[w_\infty - w\right] + \varepsilon v\left[v_\infty + w_\infty - v - w\right], \\ \frac{dw}{dt} = w\left[v - v_\infty\right] + \varepsilon w\left[v_\infty + w_\infty - v - w\right]. \end{cases}$$

Zero-order Hamiltonian $H = v_0 - v_\infty \ln v_0 + w_0 - w_\infty \ln w_0$

Full model entropy

$$\frac{d}{dt} H(v(t), w(t)) = -\varepsilon\left[(v - v_\infty) + (w - w_\infty)\right]^2.$$

$\Rightarrow$ Equilibration and oscillations for k large.

THANK YOU VERY MUCH!!