On a volume-surface reaction-diffusion system modeling asymmetric stem cell division: quasi-steady-state approximation and convergence to equilibrium

Tang Quoc Bao
(*joint work with* Klemens Fellner, Evangelos Latos *and* Stefan Rosenberger)

University of Graz, Austria

Mini-workshop "PDEs: Analysis and Applications"

HUST, August 19, 2014

Section 1

Motivation: Asymmetric stem cell division

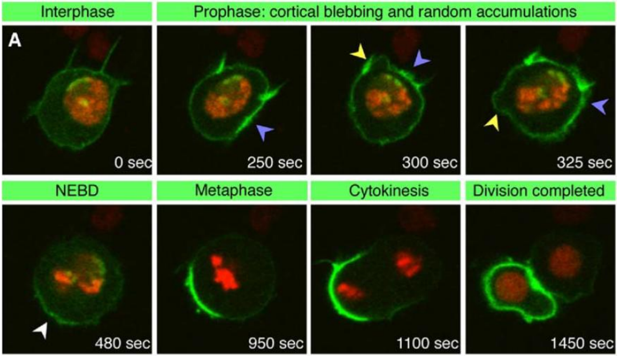


Figure: Asymmetric stem cell division. [1]

[1] Mayer *et al.*, *Current Biology*, **15** (2005)

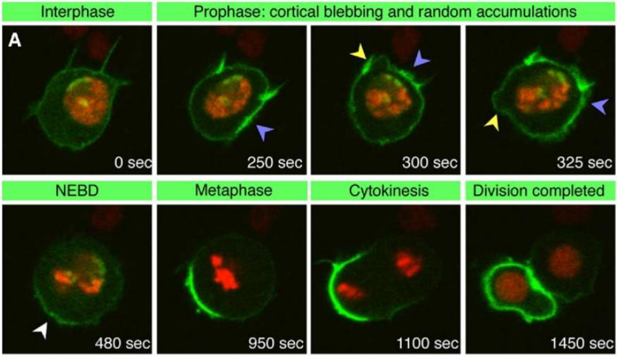


Figure: Asymmetric stem cell division. [1]

Observed processes:

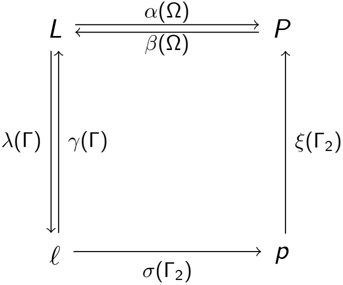
- Volume diffusions;
- Surface diffusions;
- Chemical reactions;

[1] Mayer *et al.*, *Current Biology*, **15** (2005)

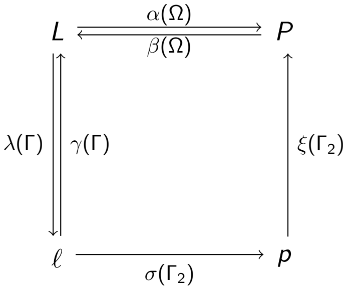
Section 2

Linear models: Quasi-steady-state approximation

Reaction Dynamics and the System

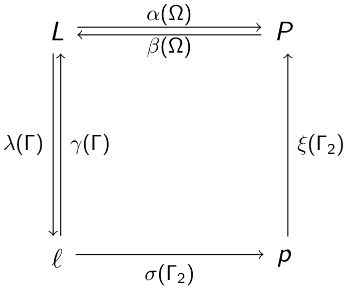


Reaction Dynamics and the System



(Volume) $$\begin{cases} L_t = d_L \Delta L - \beta L + \alpha P, \\ d_L \partial_\nu L = -\lambda L + \gamma \ell \end{cases}$$

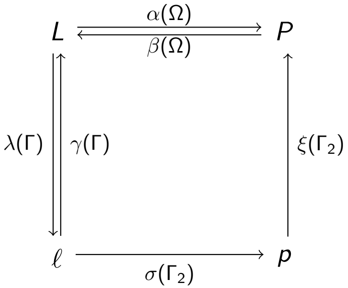
Reaction Dynamics and the System



(Volume) $\begin{cases} L_t = d_L \Delta L - \beta L + \alpha P, \\ d_L \partial_\nu L = -\lambda L + \gamma \ell \end{cases}$

(Volume) $\begin{cases} P_t = d_P \Delta P + \beta L - \alpha P, \\ d_P \partial_\nu P = \chi_{\Gamma_2} \xi p \end{cases}$

Reaction Dynamics and the System

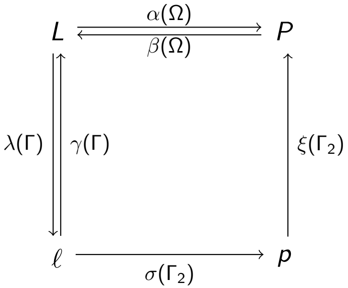


(Volume) $\begin{cases} L_t = d_L \Delta L - \beta L + \alpha P, \\ d_L \partial_\nu L = -\lambda L + \gamma \ell \end{cases}$

(Volume) $\begin{cases} P_t = d_P \Delta P + \beta L - \alpha P, \\ d_P \partial_\nu P = \chi_{\Gamma_2} \xi p \end{cases}$

(Surface) $\ell_t = d_\ell \Delta_\Gamma \ell + \lambda L - \gamma \ell - \chi_{\Gamma_2} \sigma \ell$

Reaction Dynamics and the System



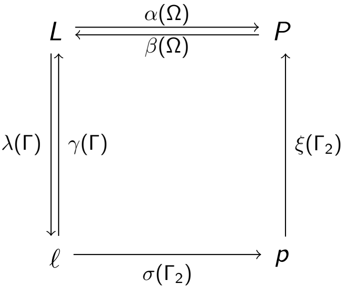
(Volume) $\begin{cases} L_t = d_L \Delta L - \beta L + \alpha P, \\ d_L \partial_\nu L = -\lambda L + \gamma \ell \end{cases}$

(Volume) $\begin{cases} P_t = d_P \Delta P + \beta L - \alpha P, \\ d_P \partial_\nu P = \chi_{\Gamma_2} \xi p \end{cases}$

(Surface) $\ell_t = d_\ell \Delta_\Gamma \ell + \lambda L - \gamma \ell - \chi_{\Gamma_2} \sigma \ell$

(Surface) $\begin{cases} p_t = d_p \Delta_{\Gamma_2} p - \xi p + \sigma \ell, \\ d_p \partial_\nu p = 0 \end{cases}$

Reaction Dynamics and the System



(Volume) $\begin{cases} L_t = d_L \Delta L - \beta L + \alpha P, \\ d_L \partial_\nu L = -\lambda L + \gamma \ell \end{cases}$

(Volume) $\begin{cases} P_t = d_P \Delta P + \beta L - \alpha P, \\ d_P \partial_\nu P = \chi_{\Gamma_2} \xi p \end{cases}$

(Surface) $\ell_t = d_\ell \Delta_\Gamma \ell + \lambda L - \gamma \ell - \chi_{\Gamma_2} \sigma \ell$

(Surface) $\begin{cases} p_t = d_p \Delta_{\Gamma_2} p - \xi p + \sigma \ell, \\ d_p \partial_\nu p = 0 \end{cases}$

$+$ Non-negative initial data.

Goals:

1. Global existence of weak solutions
2. Asymptotic analysis (Quasi-stead-state approximation)

Subsection 1

Global existence of weak solutions

Localized method

(L) $\begin{cases} L_t = d_L \Delta L - \beta L + \alpha P, \\ d_L \partial_\nu L = -\lambda L + \gamma \ell \end{cases}$	(P) $\begin{cases} P_t = d_P \Delta P + \beta L - \alpha P, \\ d_P \partial_\nu P = \chi_{\Gamma_2} \xi p \end{cases}$
(l) $\ell_t = d_\ell \Delta_\Gamma \ell + \lambda L - \gamma \ell - \chi_{\Gamma_2} \sigma \ell$	(p) $\begin{cases} p_t = d_p \Delta_{\Gamma_2} p - \xi p + \sigma \ell, \\ d_p \partial_\nu p = 0 \end{cases}$

Localized method

(L) $\begin{cases} L_t = d_L \Delta L - \beta L + \alpha P, \\ d_L \partial_\nu L = -\lambda L + \gamma \ell \end{cases}$	(P) $\begin{cases} P_t = d_P \Delta P + \beta L - \alpha P, \\ d_P \partial_\nu P = \chi_{\Gamma_2} \xi p \end{cases}$
(l) $\ell_t = d_\ell \Delta_\Gamma \ell + \lambda L - \gamma \ell - \chi_{\Gamma_2} \sigma \ell$	(p) $\begin{cases} p_t = d_p \Delta_{\Gamma_2} p - \xi p + \sigma \ell, \\ d_p \partial_\nu p = 0 \end{cases}$

Localized method

(L) $\begin{cases} L_t = d_L \Delta L - \beta L + \alpha P, \\ d_L \partial_\nu L = -\lambda L + \gamma \ell \end{cases}$	(P) $\begin{cases} P_t = d_P \Delta P + \beta L - \alpha P, \\ d_P \partial_\nu P = \chi_{\Gamma_2} \xi p \end{cases}$
(l) $\ell_t = d_\ell \Delta_\Gamma \ell + \lambda L - \gamma \ell - \chi_{\Gamma_2} \sigma \ell$	(p) $\begin{cases} p_t = d_p \Delta_{\Gamma_2} p - \xi p + \sigma \ell, \\ d_p \partial_\nu p = 0 \end{cases}$

Localized method

(L) $\begin{cases} L_t = d_L \Delta L - \beta L + \alpha P, \\ d_L \partial_\nu L = -\lambda L + \gamma \ell \end{cases}$	(P) $\begin{cases} P_t = d_P \Delta P + \beta L - \alpha P, \\ d_P \partial_\nu P = \chi_{\Gamma_2} \xi p \end{cases}$
(l) $\ell_t = d_\ell \Delta_\Gamma \ell + \lambda L - \gamma \ell - \chi_{\Gamma_2} \sigma \ell$	(p) $\begin{cases} p_t = d_p \Delta_{\Gamma_2} p - \xi p + \sigma \ell, \\ d_p \partial_\nu p = 0 \end{cases}$

Localized method

(L) $\begin{cases} L_t = d_L \Delta L - \beta L + \alpha P, \\ d_L \partial_\nu L = -\lambda L + \gamma \ell \end{cases}$	(P) $\begin{cases} P_t = d_P \Delta P + \beta L - \alpha P, \\ d_P \partial_\nu P = \chi_{\Gamma_2} \xi p \end{cases}$
(l) $\ell_t = d_\ell \Delta_\Gamma \ell + \lambda L - \gamma \ell - \chi_{\Gamma_2} \sigma \ell$	(p) $\begin{cases} p_t = d_p \Delta_{\Gamma_2} p - \xi p + \sigma \ell, \\ d_p \partial_\nu p = 0 \end{cases}$

$$S = \{\ell \in C([0,T]; L^2(\Gamma)), p \in C([0,T]; L^2(\Gamma_2)) : \ell(0) = \ell_0,\ p(0) = p_0\}.$$

$$(\ell_1, p_1) \in S \xrightarrow{\text{insert to } (L), (P)} (L_1, P_1) \xrightarrow{\text{insert to } (l), (p)} (\ell_2, p_2) \in S$$

Localized method

(L) $\begin{cases} L_t = d_L \Delta L - \beta L + \alpha P, \\ d_L \partial_\nu L = -\lambda L + \gamma \ell \end{cases}$	(P) $\begin{cases} P_t = d_P \Delta P + \beta L - \alpha P, \\ d_P \partial_\nu P = \chi_{\Gamma_2} \xi p \end{cases}$
(l) $\ell_t = d_\ell \Delta_\Gamma \ell + \lambda L - \gamma \ell - \chi_{\Gamma_2} \sigma \ell$	(p) $\begin{cases} p_t = d_p \Delta_{\Gamma_2} p - \xi p + \sigma \ell, \\ d_p \partial_\nu p = 0 \end{cases}$

$$S = \{\ell \in C([0,T]; L^2(\Gamma)), p \in C([0,T]; L^2(\Gamma_2)) : \ell(0) = \ell_0,\ p(0) = p_0\}.$$

$$(\ell_1, p_1) \in S \xrightarrow{\text{insert to } (L),(P)} (L_1, P_1) \xrightarrow{\text{insert to } (l),(p)} (\ell_2, p_2) \in S$$

$$(\ell_1, p_1) \longrightarrow (\ell_2, p_2) \longrightarrow (\ell_3, p_2) \longrightarrow \ldots \xrightarrow{????} (\ell^*, p^*)$$

$$(\ell^*, p^*) \xrightarrow{\text{insert to} (EqL),(EqP)} (L^*, P^*) \Longrightarrow (L^*, P^*, \ell^*, p^*) \text{ is a solution to the system}$$

Localized method

Lemma

Let $\mathcal{A}(\ell_1, p_1) = (\ell_2, p_2)$. Then $\mathcal{A}$ is a contraction mapping when T is small enough. As a corollary, the system $(L) - (P) - (l) - (p)$ has a unique **local weak solution**.

Proof. For all (ℓ, p) and (ℓ_1, p_1) in S, we have

$$\|\mathcal{A}(\ell, p) - \mathcal{A}(\ell_1, p_1)\| \leq \underbrace{\left(\frac{\lambda^2}{2\gamma} + \frac{\lambda^2\sigma^2}{4\gamma\xi}T\right)\frac{2k}{\beta\lambda}T(2d_P Te^{2d_P T} + 1)}_{<1 \text{ when } T \text{ is small enough}}\|(\ell, p) - (\ell_1, p_1)\|$$

with $k = \max\{\beta\gamma^2/2\lambda, C_P\alpha\xi^2/4d_P\}$.

Theorem

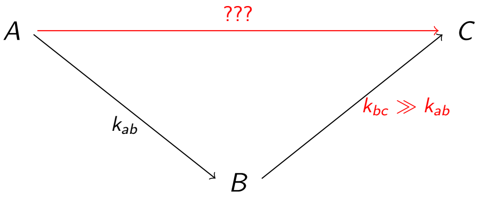
For any $(L_0, P_0, \ell_0, p_0) \in L^2(\Omega) \times L^2(\Omega) \times L^2(\Gamma) \times L^2(\Gamma_2)$, *there exists a unique* **global weak solution** *to the system (L)-(P)-(l)-(p). Moreover, if the initial data is non-negative then the weak solution is non-negative.*

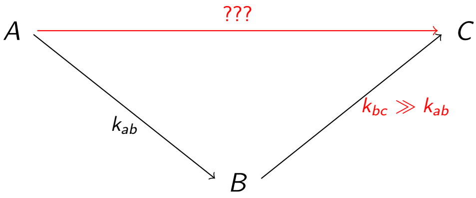
Proof: Some *a priori* estimates of an L^2-functional.
Remark:

- General initial data: The L^2-growth of the solution is **exponentially bounded** in time;
- Non-negative initial data: The L^2-growth of the solution is **uniformly bounded** in time;

Subsection 2

Quasi-steady-state approximation


???
A
C
k_{ab}
$k_{bc} \gg k_{ab}$
B



A system with 3 substances: A, B and C

$\xrightarrow{k_{ab} \gg k_{bc}}$ A **reduced** system with 2 substabces: A and C

Quasi-steady-state approximation (QSSA):

A complex, complicated reaction system

$$\xrightarrow{\text{fast reaction rates}}$$ A **simpler, reduced** system.

Quasi-steady-state approximation (QSSA):

A complex, complicated reaction system

$\xrightarrow{\text{fast reaction rates}}$ A **simpler, reduced** system.

QSSA is done routinely in chemical engineering but **mathematical proofs** often are missing!

Some references:

- In Desvillettes *et al.* (2007 - Bull. Inst. Math. Acad. Sin.)and Bothe *et al.* (2010 - JMAA):

$$A + B \underset{k_2 \gg k_1, k_4}{\overset{k_1}{\rightleftharpoons}} C \underset{k_4}{\overset{k_3 \gg k_1, k_4}{\rightleftharpoons}} E + F$$

becomes

$$A + B \underset{\beta}{\overset{\alpha}{\rightleftharpoons}} E + F$$

Some references:

- In Desvillettes *et al.* (2007 - Bull. Inst. Math. Acad. Sin.)and Bothe *et al.* (2010 - JMAA):

$$A + B \underset{k_2 \gg k_1, k_4}{\overset{k_1}{\rightleftharpoons}} C \underset{k_4}{\overset{k_3 \gg k_1, k_4}{\rightleftharpoons}} E + F$$

  becomes

$$A + B \underset{\beta}{\overset{\alpha}{\rightleftharpoons}} E + F$$

- Bothe *et al.* (2003 - JMAA)

$$mA \underset{k_2}{\overset{k_1}{\rightleftharpoons}} nE$$

$\xrightarrow{k_1+k_2 \longrightarrow +\infty}$ A **nonlinear diffusion** problem!

Some references:

- In Desvillettes *et al.* (2007 - Bull. Inst. Math. Acad. Sin.)and Bothe *et al.* (2010 - JMAA):

$$A + B \underset{k_2 \gg k_1, k_4}{\overset{k_1}{\rightleftharpoons}} C \underset{k_4}{\overset{k_3 \gg k_1, k_4}{\rightleftharpoons}} E + F$$

  becomes

$$A + B \underset{\beta}{\overset{\alpha}{\rightleftharpoons}} E + F$$

- Bothe *et al.* (2003 - JMAA)

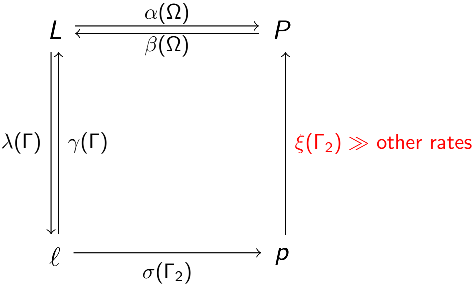
$$mA \underset{k_2}{\overset{k_1}{\rightleftharpoons}} nE$$

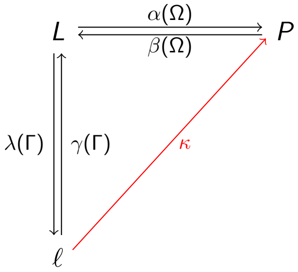
  $\xrightarrow{k_1+k_2 \longrightarrow +\infty}$ A **nonlinear diffusion** problem!

- Bothe and Pirre (2010 - DCDS, Comm. PDEs)

$$A + B \xrightarrow{k} C$$

  $\xrightarrow{k \longrightarrow +\infty}$ A **free surface** problem!


L
P
α(Ω)
β(Ω)
λ(Γ)
γ(Γ)
ξ(Γ2) ≫ other rates
ℓ
p
σ(Γ2)


L
$\alpha(\Omega)$
$\beta(\Omega)$
P
$\lambda(\Gamma)$
$\gamma(\Gamma)$
κ
ℓ

Denote by $(L^\xi, P^\xi, \ell^\xi, p^\xi)$ the solution of the original system depending on ξ.

Theorem

Let $\xi \to +\infty$. We have

$$(L^\xi, P^\xi, \ell^\xi, p^\xi) \longrightarrow (L, P, \ell, 0)$$

in $L^2([0,T]\times\Omega) \times (L^1([0,T]\times\Omega)) \times L^2([0,T]\times\Gamma) \times L^2([0,T]\times\Gamma_2)$, where (L, P, ℓ) is the solution to the QSSA.

Denote by $(L^\xi, P^\xi, \ell^\xi, p^\xi)$ the solution of the original system depending on ξ.

Theorem

Let $\xi \to +\infty$. We have

$$(L^\xi, P^\xi, \ell^\xi, p^\xi) \longrightarrow (L, P, \ell, 0)$$

in $L^2([0,T]\times\Omega) \times (L^1([0,T]\times\Omega)) \times L^2([0,T]\times\Gamma) \times L^2([0,T]\times\Gamma_2)$, where (L, P, ℓ) is the solution to the QSSA.

Proof.

- $\{L^\xi\}_{\xi>0}, \{P^\xi\}_\xi, \{\ell_\xi\}_{\xi>0}$ are bounded in $L^2([0,T]\times\Omega)$ (or $L^2([0,T]\times\Gamma)$) uniformly in ξ: **duality method**;
- $p^\xi \longrightarrow 0$ in $L^2([0,T]; L^2(\Gamma_2))$ as $\xi \longrightarrow +\infty$;
- $\{L^\xi\}_{\xi>0}$ is relatively compact in $L^2([0,T]; L^2(\Omega))$, thus $L^\xi \to L$;
- $\{\ell^\xi\}_{\xi>0}$ is relatively compact in $L^2([0,T]; L^2(\Gamma))$, thus $\ell^\xi \to \ell$;
- $\{P^\xi\}_{\xi>0}$ is relatively compact in $L^1([0,T]; L^1(\Omega))$, thus $P^\xi \to P$;
- Verify that (L, P, ℓ) is the solution to the QSSA.

□

Why does P^{ξ} only converges in $L^1([0,T];L^1(\Omega))$?

Because of the singular boundary flux $d_P\partial_\nu P^{\xi} = \chi_{\Gamma_2}\xi p$!!!

Why does P^ξ only converges in $L^1([0, T]; L^1(\Omega))$?

Because of the singular boundary flux $d_P \partial_\nu P^\xi = \chi_{\Gamma_2} \xi p$!!!

Conjecture: We can get the convergence in $L^2(L^2)$ (at least for large time) **if** we know that the solution of the original system converges to the equilibrium!

This is non-trivial due to:

- Complexity of the reaction dynamics;
- The volume-surface coupling.

Section 3

Nonlinear models: Convergence to equilibrium

$\mathcal{U}$: volume substance; $\mathcal{V}$: surface substance.
$\mathcal{U}$ and $\mathcal{V}$ react on the boundary as

$$\alpha\mathcal{U} \underset{k_u(t,x)}{\overset{k_v(t,x)}{\rightleftarrows}} \beta\mathcal{V}$$

Denote by $u(t,x)$ and $v(t,x)$ the concentrations of $\mathcal{U}$ and $\mathcal{V}$ respectively. We have a surface-volume reaction diffusion system:

$$\begin{cases} u_t - \delta_u \Delta u = 0, & x \in \Omega, \\ \quad \delta_u \partial_\nu u = -\alpha(k_u u^\alpha - k_v v^\beta), & x \in \partial\Omega, \\ v_t - \delta_v \Delta_{\partial\Omega} v = \beta(k_u u^\alpha - k_v v^\beta), & x \in \partial\Omega, \\ u(0,x) = u_0(x), \quad v(0,x) = v_0(x). \end{cases} \tag{1}$$

$\mathcal{U}$: volume substance; $\mathcal{V}$: surface substance.
$\mathcal{U}$ and $\mathcal{V}$ react on the boundary as

$$\alpha\mathcal{U} \underset{k_u(t,x)}{\overset{k_v(t,x)}{\longleftrightarrows}} \beta\mathcal{V}$$

Denote by $u(t,x)$ and $v(t,x)$ the concentrations of $\mathcal{U}$ and $\mathcal{V}$ respectively. We have a surface-volume reaction diffusion system:

$$\begin{cases} u_t - \delta_u \Delta u = 0, & x \in \Omega, \\ \quad \delta_u \partial_\nu u = -\alpha(k_u u^\alpha - k_v v^\beta), & x \in \partial\Omega, \\ v_t - \delta_v \Delta_{\partial\Omega} v = \beta(k_u u^\alpha - k_v v^\beta), & x \in \partial\Omega, \\ u(0,x) = u_0(x), \quad v(0,x) = v_0(x). \end{cases} \tag{1}$$

Two goals:

1. Global existence of solutions.
2. Explicit convergence to equilibrium.

$$\begin{cases} u_t - \delta_u \Delta u = 0, & x \in \Omega, \\ \quad \delta_u \partial_\nu u = -\alpha(k_u u^\alpha - k_v v^\beta), & x \in \partial\Omega, \\ v_t - \delta_v \Delta_{\partial\Omega} v = \beta(k_u u^\alpha - k_v v^\beta), & x \in \partial\Omega, \\ u(0,x) = u_0(x), \;\; v(0,x) = v_0(x). \end{cases}$$

Assumptions:

- Stoichiometric coefficients $\alpha, \beta \geq 1$ (not necessarily integers);
- Reaction rates
  - Existence of solutions: $k_{\min} \leq k_u(t,x), k_v(t,x) \leq k_{\max}$.
  - Convergence to equilibrium: $k_u, k_v \equiv$ constants.
- Non-negative initial data $u_0 \in L^\infty(\Omega)$ and $v_0 \in L^\infty(\partial\Omega)$.

Subsection 1

Existence of a unique global solution

Difficulties:

- General polynomial nonlinearities;
- Volume-surface coupling.

Difficulties:

- General polynomial nonlinearities;
- Volume-surface coupling.

Methods: Upper and lower solutions.
Consider a general PDEs:

$$\mathbf{u}_t = \mathbf{F}(\mathbf{u}), \quad \mathbf{u}(0) = \mathbf{u}_0. \tag{2}$$

- Upper solution $\overline{\mathbf{u}}$: $\overline{\mathbf{u}}_t \geq \mathbf{F}(\overline{\mathbf{u}})$ and $\overline{\mathbf{u}}(0) \geq \mathbf{u}_0$;
- Lower solution $\underline{\mathbf{u}}$: $\underline{\mathbf{u}}_t \leq \mathbf{F}(\underline{\mathbf{u}})$ and $\underline{\mathbf{u}}(0) \leq \mathbf{u}_0$.

Comparison principle: For any solution $\mathbf{u}$ to (2):

$$\overline{\mathbf{u}} \geq \mathbf{u} \geq \underline{\mathbf{u}}.$$

General framework

$$\mathbf{u}_t = \mathbf{F}(\mathbf{u}), \quad \mathbf{u}(0) = \mathbf{u}_0. \tag{2}$$

Concept of the proof:

$(\overline{\mathbf{u}}^{(0)}, \overline{\mathbf{v}}^{(0)})$

$(\overline{\mathbf{u}}^{(1)}, \overline{\mathbf{v}}^{(1)})$

$(\overline{\mathbf{u}}^{(2)}, \overline{\mathbf{v}}^{(2)})$

$\cdots$ $(\mathbf{u}^*, \mathbf{v}^*)$

$(\underline{\mathbf{u}}^{(2)}, \underline{\mathbf{v}}^{(2)})$

$(\underline{\mathbf{u}}^{(1)}, \underline{\mathbf{v}}^{(1)})$

$(\underline{\mathbf{u}}^{(0)}, \underline{\mathbf{v}}^{(0)})$

General framework

$$\mathbf{u}_t = \mathbf{F}(\mathbf{u}), \quad \mathbf{u}(0) = \mathbf{u}_0. \tag{2}$$

Concept of the proof:

$(\overline{\mathbf{u}}^{(0)}, \overline{\mathbf{v}}^{(0)})$

$(\overline{\mathbf{u}}^{(1)}, \overline{\mathbf{v}}^{(1)})$

$(\overline{\mathbf{u}}^{(2)}, \overline{\mathbf{v}}^{(2)})$

$\cdots$ $(\mathbf{u}^*, \mathbf{v}^*)$

$(\underline{\mathbf{u}}^{(2)}, \underline{\mathbf{v}}^{(2)})$

$(\underline{\mathbf{u}}^{(1)}, \underline{\mathbf{v}}^{(1)})$

$(\underline{\mathbf{u}}^{(0)}, \underline{\mathbf{v}}^{(0)})$

General framework

$$\mathbf{u}_t = \mathbf{F}(\mathbf{u}), \quad \mathbf{u}(0) = \mathbf{u}_0. \tag{2}$$

Concept of the proof:

$(\overline{\mathbf{u}}^{(0)}, \overline{\mathbf{v}}^{(0)})$

$(\overline{\mathbf{u}}^{(1)}, \overline{\mathbf{v}}^{(1)})$

$(\overline{\mathbf{u}}^{(2)}, \overline{\mathbf{v}}^{(2)})$

$\cdots$ $(\mathbf{u}^*, \mathbf{v}^*)$

$(\underline{\mathbf{u}}^{(2)}, \underline{\mathbf{v}}^{(2)})$

$(\underline{\mathbf{u}}^{(1)}, \underline{\mathbf{v}}^{(1)})$

$(\underline{\mathbf{u}}^{(0)}, \underline{\mathbf{v}}^{(0)})$

General framework

$$\mathbf{u}_t = \mathbf{F}(\mathbf{u}), \quad \mathbf{u}(0) = \mathbf{u}_0. \tag{2}$$

Concept of the proof:

$$(\overline{\mathbf{u}}^{(0)}, \overline{\mathbf{v}}^{(0)}) \longrightarrow (\overline{\mathbf{u}}^{(1)}, \overline{\mathbf{v}}^{(1)}) \longrightarrow (\overline{\mathbf{u}}^{(2)}, \overline{\mathbf{v}}^{(2)})$$

$$\cdots \qquad (\mathbf{u}^*, \mathbf{v}^*)$$

$$(\underline{\mathbf{u}}^{(2)}, \underline{\mathbf{v}}^{(2)})$$

$$(\underline{\mathbf{u}}^{(0)}, \underline{\mathbf{v}}^{(0)}) \longrightarrow (\underline{\mathbf{u}}^{(1)}, \underline{\mathbf{v}}^{(1)})$$

General framework

$$\mathbf{u}_t = \mathbf{F}(\mathbf{u}), \quad \mathbf{u}(0) = \mathbf{u}_0. \tag{2}$$

Concept of the proof:

$$(\overline{\mathbf{u}}^{(0)}, \overline{\mathbf{v}}^{(0)}) \to (\overline{\mathbf{u}}^{(1)}, \overline{\mathbf{v}}^{(1)}) \to (\overline{\mathbf{u}}^{(2)}, \overline{\mathbf{v}}^{(2)})$$

$$\cdots \qquad (\mathbf{u}^*, \mathbf{v}^*)$$

$$(\underline{\mathbf{u}}^{(0)}, \underline{\mathbf{v}}^{(0)}) \to (\underline{\mathbf{u}}^{(1)}, \underline{\mathbf{v}}^{(1)}) \to (\underline{\mathbf{u}}^{(2)}, \underline{\mathbf{v}}^{(2)})$$

General framework

$$\mathbf{u}_t = \mathbf{F}(\mathbf{u}), \quad \mathbf{u}(0) = \mathbf{u}_0. \tag{2}$$

Concept of the proof:

$$(\overline{\mathbf{u}}^{(0)}, \overline{\mathbf{v}}^{(0)}) \to (\overline{\mathbf{u}}^{(1)}, \overline{\mathbf{v}}^{(1)}) \to (\overline{\mathbf{u}}^{(2)}, \overline{\mathbf{v}}^{(2)}) \to \cdots$$

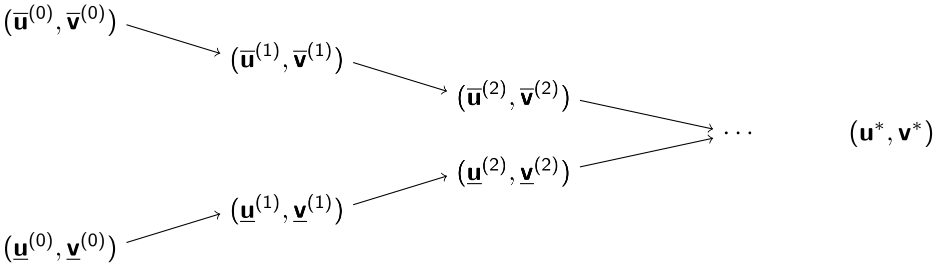
$$(\mathbf{u}^*, \mathbf{v}^*)$$

$$(\underline{\mathbf{u}}^{(0)}, \underline{\mathbf{v}}^{(0)}) \to (\underline{\mathbf{u}}^{(1)}, \underline{\mathbf{v}}^{(1)}) \to (\underline{\mathbf{u}}^{(2)}, \underline{\mathbf{v}}^{(2)})$$

General framework

$$\mathbf{u}_t = \mathbf{F}(\mathbf{u}), \quad \mathbf{u}(0) = \mathbf{u}_0. \tag{2}$$

Concept of the proof:



General framework

$$\mathbf{u}_t = \mathbf{F}(\mathbf{u}), \quad \mathbf{u}(0) = \mathbf{u}_0. \tag{2}$$

Concept of the proof:

$$(\overline{\mathbf{u}}^{(0)}, \overline{\mathbf{v}}^{(0)}) \longrightarrow (\overline{\mathbf{u}}^{(1)}, \overline{\mathbf{v}}^{(1)}) \longrightarrow (\overline{\mathbf{u}}^{(2)}, \overline{\mathbf{v}}^{(2)}) \longrightarrow \cdots$$

$$(\underline{\mathbf{u}}^{(0)}, \underline{\mathbf{v}}^{(0)}) \longrightarrow (\underline{\mathbf{u}}^{(1)}, \underline{\mathbf{v}}^{(1)}) \longrightarrow (\underline{\mathbf{u}}^{(2)}, \underline{\mathbf{v}}^{(2)}) \longrightarrow \cdots$$

$$\cdots \longrightarrow (\mathbf{u}^*, \mathbf{v}^*)$$

$$\begin{cases} u_t - \delta_u \Delta u = 0, & x \in \Omega, \\ \quad \delta_u \partial_\nu u = -\alpha(k_u u^\alpha - k_v v^\beta), & x \in \partial\Omega, \\ v_t - \delta_v \Delta_{\partial\Omega} v = \beta(k_u u^\alpha - k_v v^\beta), & x \in \partial\Omega, \\ u(0,x) = u_0(x), \;\; v(0,x) = v_0(x). \end{cases} \tag{1}$$

Theorem

Assume that

- $\Omega \subset \mathbb{R}^n$ *is bounded with smooth boundary* $\partial\Omega$ *(e.g.* $\partial\Omega \in C^{2+\epsilon}$*);*
- *Stoichiometric coefficients* $\alpha, \beta \geq 1$*;*
- *Reaction rates are uniform bounded:* $k_{min} \leq k_u(t,x), k_v(t,x) \leq k_{max}$*;*
- *Non-negative initial data* $u_0 \in L^\infty(\Omega)$ *and* $v_0 \in L^\infty(\partial\Omega)$*.*

Then the system (1) *has a unique weak solution which satisfies the system in weak sense.*

Subsection 2

Convergence to equilibrium

When $k_u = k_v = 1$ (we write $\Gamma = \partial\Omega$)

$$\begin{cases} u_t - \delta_u \Delta u = 0, & x \in \Omega, \\ \quad \delta_u \partial_\nu u = -\alpha(u^\alpha - v^\beta), & x \in \Gamma, \\ v_t - \delta_v \Delta_\Gamma v = \beta(u^\alpha - v^\beta), & x \in \Gamma, \\ u(0,x) = u_0(x), \quad v(0,x) = v_0(x). \end{cases}$$

Conservation of mass:

$$\beta \int_\Omega u(t,x)dx + \alpha \int_\Gamma v(t,x)dS$$
$$= \beta \int_\Omega u_0(x)dx + \alpha \int_\Gamma v_0(x)dS =: M \quad \text{for all } t > 0.$$

Constant equilibrium: (u_∞, v_∞) satisfies

$$\begin{cases} u_\infty^\alpha = v_\infty^\beta & \text{(balance of reactions)}, \\ \beta|\Omega|u_\infty + \alpha|\Gamma|v_\infty = M & \text{(conservation of mass)}. \end{cases}$$

Convergence to equilibrium: $(u(t), v(t)) \longrightarrow (u_\infty, v_\infty)$ as $t \to +\infty$?

Why consider constant rates k_u and k_v?

- If $k_u \equiv k_u(x), k_v \equiv k_v(x)$, then **no explicit equilibrium!**

$$\begin{cases} -\delta_u \Delta u_\infty = 0, & x \in \Omega, \\ \delta_u \partial_\nu u_\infty = -\alpha(k_u(x)u_\infty^\alpha - k_v(x)v_\infty^\beta), & x \in \Gamma, \\ -\delta_v \Delta_\Gamma v_\infty = \beta(k_u(x)u_\infty^\alpha - k_v(x)v_\infty^\beta), & x \in \Gamma. \end{cases}$$

Why consider constant rates k_u and k_v?

- If $k_u \equiv k_u(x), k_v \equiv k_v(x)$, then **no explicit equilibrium!**

$$\begin{cases} -\delta_u \Delta u_\infty = 0, & x \in \Omega, \\ \delta_u \partial_\nu u_\infty = -\alpha(k_u(x) u_\infty^\alpha - k_v(x) v_\infty^\beta), & x \in \Gamma, \\ -\delta_v \Delta_\Gamma v_\infty = \beta(k_u(x) u_\infty^\alpha - k_v(x) v_\infty^\beta), & x \in \Gamma. \end{cases}$$

- If $k_u \equiv k_u(t,x), k_v \equiv k_v(t,x)$, then **no equilibrium is defined!** It may arise

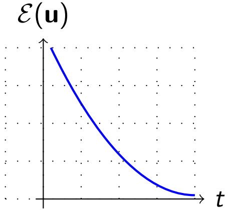
$$k_u(t,x) \longrightarrow k_{u,\infty}(x), \qquad k_v(t,x) \longrightarrow k_{v,\infty}(x)$$

General framework

Consider a general flow $\mathbf{u}_t = \mathbf{F}(\mathbf{u}(t))$ with equilibrium $\mathbf{u}_\infty$ satisfying $\mathbf{F}(\mathbf{u}_\infty) = 0$.

General framework

Consider a general flow $\mathbf{u}_t = \mathbf{F}(\mathbf{u}(t))$ with equilibrium $\mathbf{u}_\infty$ satisfying $\mathbf{F}(\mathbf{u}_\infty) = 0$.
A functional $\mathcal{E}(\mathbf{u})$ is called an **entropy** if:

$\dfrac{d\mathcal{E}}{dt} \leq 0$ or $\mathcal{D}(\mathbf{u}) = -\dfrac{d\mathcal{E}}{dt} \geq 0$	
$\dfrac{d\mathcal{E}}{dt} = 0 +$ conservation laws $\Leftrightarrow \mathbf{u} \equiv \mathbf{u}_\infty$	$\mathcal{E}(\mathbf{u})(t) \longrightarrow \mathcal{E}(\mathbf{u}_\infty)$?
$\mathcal{E}(\mathbf{u}) - \mathcal{E}(\mathbf{u}_\infty) \geq \kappa \|\mathbf{u} - \mathbf{u}_\infty\|$	$\mathcal{E}(\mathbf{u})(t) \longrightarrow \mathcal{E}(\mathbf{u}_\infty) \Longrightarrow \mathbf{u}(t) \longrightarrow \mathbf{u}_\infty$

General framework

Gronwall's inequality

$$y'(t) \leq -\lambda y(t), \quad t > 0 \Longrightarrow y(t) \leq e^{-\lambda t} y(0), \quad t > 0.$$

General framework

Gronwall's inequality

$$y'(t) \leq -\lambda y(t), \quad t > 0 \Longrightarrow y(t) \leq e^{-\lambda t} y(0), \quad t > 0.$$

If we have an $\boxed{entropy - entropy\ estimate}$

$$\mathcal{D}(\mathbf{u}) \geq \lambda(\mathcal{E}(\mathbf{u}) - \mathcal{E}(\mathbf{u}_\infty))$$

then

$$\underbrace{\frac{d}{dt}(\mathcal{E}(\mathbf{u}) - \mathcal{E}(\mathbf{u}_\infty))}_{y'(t)} = \frac{d}{dt}\mathcal{E}(\mathbf{u}) = \mathcal{D}(\mathbf{u}) \leq \underbrace{-\lambda(\mathcal{E}(\mathbf{u}) - \mathcal{E}(\mathbf{u}_\infty))}_{-\lambda y(t)},$$

thus

$$\mathcal{E}(\mathbf{u})(t) - \mathcal{E}(\mathbf{u}_\infty) \leq e^{-\lambda t}(\mathcal{E}(\mathbf{u})(0) - \mathcal{E}(\mathbf{u}_\infty)).$$

Advantages of the method

- Explicit, computable rates of convergence;

Advantages of the method

- Explicit, computable rates of convergence;
- Rely on functional inequalities $\longrightarrow$ robust to various problems;

Advantages of the method

- Explicit, computable rates of convergence;
- Rely on functional inequalities $\longrightarrow$ robust to various problems;
- Obtain functional inequalities as by-product;

Explicit convergence to equilibrium for reaction-diffusion systems by entropy method

- In Fellner & Desvillettes 2006 (JMAA) (**first result on system!**)

$$2\mathcal{U} \rightleftharpoons \mathcal{W} \quad \text{and} \quad \mathcal{U} + \mathcal{V} \rightleftharpoons \mathcal{W}$$

- In Fellner & Desvillettes 2007 (DCDS Supplements)

$$2\mathcal{U} \rightleftharpoons \mathcal{W}$$

  with degenerate diffusions.
- In Fellner & Desvillettes 2008 (RMI)

$$\mathcal{U} + \mathcal{V} \rightleftharpoons \mathcal{W} + \mathcal{Z}$$

- In A. Mielke *et al.* 2013 (preprint)

$$\sum_{i=1}^{n} \alpha_i \mathcal{A}_i \rightleftharpoons \sum_{j=1}^{m} \beta_j \mathcal{A}_j$$

  But, this doesn't provide explicit rates and is not applicable to surface-volume reaction-diffusion systems.

$$\begin{cases} u_t - \delta_u \Delta u = 0, & x \in \Omega, \\ \quad \delta_u \partial_\nu u = -\alpha(u^\alpha - v^\beta), & x \in \Gamma, \\ v_t - \delta_v \Delta_\Gamma v = \beta(u^\alpha - v^\beta), & x \in \Gamma, \\ u(0,x) = u_0(x), \quad v(0,x) = v_0(x). \end{cases}$$

We consider Boltzmann-type entropy

$$\mathcal{E}(u,v) = \int_\Omega (u \log u - u + 1)dx + \int_\Gamma (v \log v - v + 1)dS$$

and its entropy dissipation

$$\mathcal{D}(u,v) = \delta_u \int_\Omega \frac{|\nabla u|^2}{u} dx + \delta_v \int_\Gamma \frac{|\nabla_\Gamma v|^2}{v} dS + \int_\Gamma (u^\alpha - v^\beta) \log \frac{u^\alpha}{v^\beta} dS.$$

Theorem

There exists explicit constants $C_0 > 0$ and $\lambda > 0$ such that

$$\|u(t) - u_\infty\|^2_{L^1(\Omega)} + \|v(t) - v_\infty\|^2_{L^1(\Gamma)} \le C_0 e^{-\lambda t}$$

for all $t \ge 0$.

Lemma

There exists an **explicit** *constant* $\lambda = \lambda(\alpha, \beta, M, |\Omega|, |\Gamma|) > 0$ *such that*

$$\mathcal{D}(u, v) \geq \lambda(\mathcal{E}(u, v) - \mathcal{E}(u_\infty, v_\infty)).$$

Lemma

There exists an **explicit** *constant* $\lambda = \lambda(\alpha, \beta, M, |\Omega|, |\Gamma|) > 0$ *such that*

$$\mathcal{D}(u, v) \geq \lambda(\mathcal{E}(u, v) - \mathcal{E}(u_\infty, v_\infty)).$$

Remarks:

- Global estimate;
- Fully nonlinear technique without any linearization.

$$\mathcal{D}(u,v) \geq \lambda(\mathcal{E}(u,v) - \mathcal{E}(u_\infty, v_\infty)).$$

Proof: Sorry, it is too long!

$$\mathcal{D}(u,v) \geq \lambda(\mathcal{E}(u,v) - \mathcal{E}(u_\infty, v_\infty)).$$

Proof: Sorry, it is too long!

- Non-degenerate case $\delta_v > 0$:

$$\mathcal{D}(u,v) = \delta_u \int_\Omega \frac{|\nabla u|^2}{u} dx + \delta_v \int_\Gamma \frac{|\nabla_\Gamma v|^2}{v} dS + \int_\Gamma (u^\alpha - v^\beta) \log \frac{u^\alpha}{v^\beta} dS.$$

The proof is based on only **mass conservation**.

$$\mathcal{D}(u,v) \geq \lambda(\mathcal{E}(u,v) - \mathcal{E}(u_\infty, v_\infty)).$$

Proof: Sorry, it is too long!

- Non-degenerate case $\delta_v > 0$:

$$\mathcal{D}(u,v) = \delta_u \int_\Omega \frac{|\nabla u|^2}{u} dx + \delta_v \int_\Gamma \frac{|\nabla_\Gamma v|^2}{v} dS + \int_\Gamma (u^\alpha - v^\beta) \log \frac{u^\alpha}{v^\beta} dS.$$

The proof is based on only **mass conservation**.

- Degenerate case $\delta_v = 0$:

$$\mathcal{D}(u,v) = \delta_u \int_\Omega \frac{|\nabla u|^2}{u} dx + \int_\Gamma (u^\alpha - v^\beta) \log \frac{u^\alpha}{v^\beta} dS.$$

The proof uses the L^∞-bounds of solutions. Moreover, there exists $\kappa > 0$ such that

$$\|\nabla U\|_\Omega^2 + \|U^\alpha - V^\beta\|_\Gamma^2 \geq \kappa \|V - \overline{V}\|_\Gamma^2.$$

Diffusion of u + reaction of u and v $\Longrightarrow$ diffusion-type of v

$$\mathcal{D}(u,v) \geq \lambda(\mathcal{E}(u,v) - \mathcal{E}(u_\infty, v_\infty)).$$

Proof: Sorry, it is too long!

- Non-degenerate case $\delta_v > 0$:

$$\mathcal{D}(u,v) = \delta_u \int_\Omega \frac{|\nabla u|^2}{u} dx + \delta_v \int_\Gamma \frac{|\nabla_\Gamma v|^2}{v} dS + \int_\Gamma (u^\alpha - v^\beta) \log \frac{u^\alpha}{v^\beta} dS.$$

The proof is based on only **mass conservation**.

- Degenerate case $\delta_v = 0$:

$$\mathcal{D}(u,v) = \delta_u \int_\Omega \frac{|\nabla u|^2}{u} dx + \int_\Gamma (u^\alpha - v^\beta) \log \frac{u^\alpha}{v^\beta} dS.$$

The proof uses the L^∞-bounds of solutions. Moreover, there exists $\kappa > 0$ such that

$$\|\nabla U\|_\Omega^2 + \|U^\alpha - V^\beta\|_\Gamma^2 \geq \kappa \|V - \overline{V}\|_\Gamma^2.$$

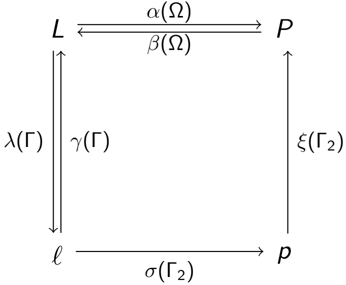
Diffusion of u + reaction of u and $v \Longrightarrow$ diffusion-type of v

Can we relax the use of the uniform bound of the solution in the degenerate case? **Yes**, if $\alpha = \beta = 1$ (linear case).

Section 4

Chemical reaction networks

Linear models:



Nonlinear models:

$$\alpha\mathcal{U} \underset{k_u(t,x)}{\overset{k_v(t,x)}{\rightleftharpoons}} \beta\mathcal{V}$$

For more complex reaction systems (reaction networks), the

- Explicit convergence to equilibrium; and
- Quasi-steady-state approximation

are **completely open!**

A conjecture for a linear system!

Conjecture

Consider n substances $A_1, \ldots, A_n$ with reactions:

$$A_i \leftrightharpoons A_j$$

with the rates k_{ij} and k_{ji} respectively. Assume that the reaction network is **weakly reversible**, *that is, for any $i \neq j$, there exists a reaction chain*

$$A_i \to A_{k_1} \to \ldots \to A_{k_r} \to A_j.$$

Then, the solution to the system **converges exponentially fast** *to equilibrium with computable rates.*

Section 5

Conclusion and further works

Conclusion

- Linear models: Existence and QSSA;
- Nonlinear models: Existence and convergence to equilibrium.

Conclusion

- Linear models: Existence and QSSA;
- Nonlinear models: Existence and convergence to equilibrium.

Further works

- Linear models: Convergence to equilibrium?
- Nonlinear models: QSSA?
- General chemical reaction systems?

THANK YOU VERY MUCH!