Systems of Quasi-Linear PDEs Arising in the Modelling of Biofilms and Related Dynamical Questions

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BCAM

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Outline

Part I
Mathematical Modelling of Biofilms

Biofilms

- **Biofilms:** Microbial depositions attached to surfaces (substrata) in aqueous surroundings
- Whenever environmental conditions allow for bacterial growth cells can attach and produce a gel-like layer (EPS)
- EPS matrix yields protection against harmful exterior influences

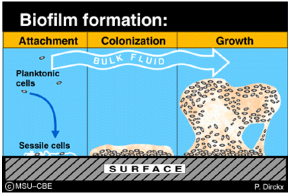

Image of the Center for Biofilm Engineering, Montana State University

- Biofilms occur in diverse applications

A Det. Continuum Biofilm Growth Model [1]

Experimental findings on the *mesoscale*: Biofilms grow in a very **irregular, heterogeneous** spatial structure

$\Longrightarrow$ Need for multi-dimensional deterministic continuum model capable to render the spatial complexity

Derived in an *ad hoc fashion* from the biofilm characteristics

(i) Existence of a threshold $m \leq m_{max}$

(ii) Spreading significant only for biomass densities $m \approx m_{max}$, negligible spreading for low densities

(iii) Sharp interface between biofilm and liquid phase

(iv) Biomass production due to reaction kinetics

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Prototype: Single-Species Model

Highly **non-linear reaction-diffusion** system [1]

$$\begin{cases} \partial_t S = d_S \Delta S - k_1 \frac{MS}{k_2 + S} \\ \partial_t M = d \nabla \cdot (D(M) \nabla M) + k_3 \frac{MS}{k_2 + S} - k_4 M \\ S|_{\partial\Omega} = 1, \quad M|_{\partial\Omega} = 0 \\ S|_{t=0} = S_0, \quad M|_{t=0} = M_0 \end{cases}$$

$\Omega \subset \mathbb{R}^n$ bounded domain

Biomass diffusion coefficient

$$D(M) := \frac{M^a}{(1-M)^b}, \qquad a, b \geq 1$$

(2-fold degenerate)

ensures sharp interface and maximal bound for M

Analytical results [2]: Well-posedness, global attractor

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[2] **Efendiev, Eberl, Zelik,** *Existence and Longtime Behavior of a Biofilm Model* (2009).

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Model Extensions: Multi-Species Biofilms

Previous analytically studied multi-species models

(i) Diffusive resistance to penetration by antibiotics [3]

(ii) Amensalistic biofilm control system [4]

$\Longrightarrow$ Existence of non-negative, bounded solutions, but uniqueness remained open: Method applied for mono-species model not applicable

[3] **Demaret, Eberl, Efendiev, Lasser,** *Analysis and Simulation of a Meso-scale Model of Diffusive Resistance of Bacterial Biofilms to Penetration of Antibiotics* (2008).

[4] **Khassehkhan, Efendiev, Eberl,** *A Degenerate Diffusion-Reaction Model of an Amensalistic Biofilm Control System: Existence and Simulation of Solutions* (2009).

Quorum-Sensing (QS)

- Quorum-sensing: Cell-cell communication mechanism to coordinate behaviour in groups
- Cells constantly produce and release low amounts of signalling molecules (autoinducers)
- When a critical value is reached, cells are rapidly induced $\Longrightarrow$ up-regulated cells, produce the molecule at a highly increased rate

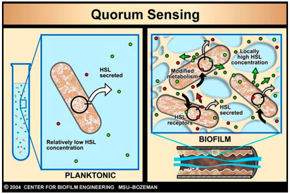

Image of the Center for Biofilm Engineering, Montana State University

Mathematical Model for QS in Biofilms [5]

X, Y volume fraction of down- and up-regulated cells

$$
\begin{cases}
\partial_t S = d_S \Delta S - k_1 \frac{MS}{k_2+S} \\
\partial_t A = d_A \Delta A - \gamma A + \alpha X + (\alpha+\beta) Y \\
\partial_t X = d \nabla \cdot (D(M) \nabla X) + k_3 \frac{XS}{k_2+S} - k_4 X - k_5 A^m X + k_5 Y \\
\partial_t Y = d \nabla \cdot (D(M) \nabla Y) + k_3 \frac{YS}{k_2+S} - k_4 Y + k_5 A^m X - k_5 Y \\
X|_{\partial\Omega} = 0, \quad Y|_{\partial\Omega} = 0, \quad S|_{\partial\Omega} = 1, \quad A|_{\partial\Omega} = 0, \\
X|_{t=0} = X_0, \, Y|_{t=0} = Y_0, \, S|_{t=0} = S_0, \, A|_{t=0} = A_0
\end{cases}
$$

$M = X + Y$ total biomass and $D(M) := \frac{M^a}{(1-M)^b}$.

Particularity: Adding X and Y we recover the prototype model

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X|_{\partial\Omega} = 0, \quad Y|_{\partial\Omega} = 0, \quad S|_{\partial\Omega} = 1, \quad A|_{\partial\Omega} = 0, \\
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Well-Posedness [6]

We assume the initial data $S_0, X_0, Y_0, A_0 \in L^\infty(\Omega)$ is non-negative, $\|X_0 + Y_0\|_{L^\infty(\Omega)} < 1$ and

$$S_0 \in H^1(\Omega),\ S_0|_{\partial\Omega} = 1,\ \ A_0, X_0, Y_0 \in H_0^1(\Omega).$$

Theorem

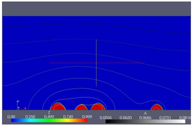
Then, there exists a unique, non-negative, global solution of the QS model, $\|X + Y\|_{L^\infty(\mathbb{R}^+\times\Omega)} < 1$*, and for any* $T > 0$

$$\begin{cases} X, Y, A, S \in C([0, T]; L^2(\Omega)) \cap L^\infty(\Omega \times (0, T)), \\ A, S \in L^2((0, T); H^1(\Omega)), \\ D_M(M)\nabla X,\ D_M(M)\nabla Y \in L^2((0, T); L^2(\Omega; \mathbb{R}^n)). \end{cases}$$

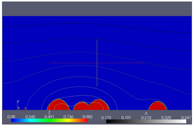
(First uniqueness result for multi-species biofilm models.)

[6] **Sonner, Efendiev, Eberl,** *On the Well-Posedness of a Mathematical Model of Quorum-Sensing in Patchy Biofilm Communities* (2011).

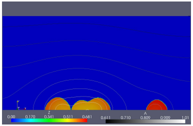
Numerical Simulations [6]



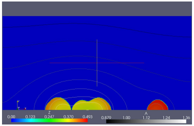
$t = 7.00$



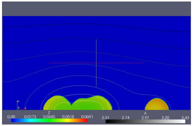
$t = 8.50$



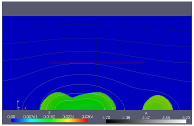
$t = 9.24$



$t = 9.28$



$t = 9.78$



$t = 11.28$

[6] **Sonner, Efendiev, Eberl,** *On the Well-Posedness of a Mathematical Model of Quorum-Sensing in Patchy Biofilm Communities* (2011).

Part II
Verifying Mathematical Models

Motivation: Positivity Preserving Models

- Many systems arising in biology, physics or engineering are modelled by systems of diffusion-convection-reaction equations.
- The solutions describe quantities such as population densities, pressure, concentrations of nutrients or chemicals, ...

$\Longrightarrow$ Natural property to require is non-negativity of solutions

Systems of Quasi-Linear Equations

We consider quasi-linear systems of the form

$$\begin{cases} \partial_t u = a(u)\cdot\Delta u - \sum_{l=1}^{n}\gamma^l(u)\cdot\partial_{x_l}u + f(u) & \Omega\times(0,T], \\ u|_{\partial\Omega} = 0 & \partial\Omega\times[0,T], \\ u|_{t=0} = u_0 & \Omega\times\{0\}, \end{cases}$$

where $u(x,t) = (u_1(x,t),\dots,u_k(x,t))$ is a vector-valued function of $(x,t)\in\overline{\Omega}\times[0,T]$, and $\Omega\subset\mathbb{R}^n$ is a bounded domain.

Aim: Necessary and sufficient conditions for the preservation of positivity

We assume there exists a **unique solution** $u(\cdot,\cdot;u_0)$ for any initial data $u_0\in K^+ := \{u:\Omega\to\mathbb{R}^k \mid u_1\geq 0,\dots,u_k\geq 0\}$.

Positivity Criterion for Quasi-Linear Systems [8]

Theorem

We assume f, the coefficient functions a_{ij} and γ_{ij}^l are sufficiently smooth and the initial data $u_0 \in K^+$ satisfies the compatibility conditions.
Then, the solution $u(\cdot, t; u_0) \in K^+$ for $t > 0$, if and only if

$$f_i\,(u_1, \ldots, \underbrace{0}_{i}, \ldots, u_k)\ \geq 0,$$

$$a_{ij}(u_1, \ldots, \underbrace{0}_{i}, \ldots, u_k) = \gamma_{ij}^l(u_1, \ldots, \underbrace{0}_{i}, \ldots, u_k) = 0,$$

for $u_1 \geq 0, \ldots, u_k \geq 0$, and $1 \leq i, j \leq k$, $i \neq j$, $1 \leq l \leq n$.

For semi-linear systems a and γ are necessarily diagonal. [7]

[7] **Efendiev, Eberl,** *On Positivity of Solutions of Semi-Linear Convection-Diffusion-Reaction Systems, with Applications in Ecology and Environmental Engineering* (2007).

[8] **Efendiev, Sonner,** *On Verifying Mathematical Models with Diffusion, Transport and Interaction* (2010).

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Systems of Semi-linear Parabolic Itô-Equations

Can we characterize the class of stochastic perturbations that preserve positivity?

$$du_i(x,t) = \Big(A^i(x,D)u_i(x,t) + f_i(x,t,u(x,t))\Big)\,dt + \underbrace{\sum_{j=1}^{\infty} q_j g_j^i(x,t,u(x,t))dW^j(t)}_{\text{stoch. perturbation}},$$

$$A^i(x,D) = \sum_{r,s=1}^{n} a^i_{rs}(x)\partial_{x_r}\partial_{x_s} - \sum_{r=1}^{n} a^i_r(x)\partial_{x_r} \text{ unif. elliptic, } dW^j \text{ Itô-differential}$$

Strategy

- Approximation by a family of random PDEs [9]
- Positivity criterion for (non-aut.) semi-linear systems

Result valid for *Itô's and Stratonovich's* interpretation [10].

[9] **Chueshov, Vuillermot,** *Non-Random Invariant Sets for Some Systems of Parabolic Stochastic PDEs* (2004).
[10] **Cresson, Efendiev, Sonner,** *On the Positivity of Solutions of Systems of Stochastic PDEs,* Accepted.

Part III
Exponential Attractors of Infinite Dimensional Dynamical Systems

Non-Autonomous Evolution Equations

$$\begin{cases} \partial_t u = \Delta u + f(t,u) & u : [s,\infty[\times\Omega \to \mathbb{R}, \\ u|_{\partial\Omega} = 0 & s \in \mathbb{R}, \Omega \subset \mathbb{R}^n \text{ bounded domain}, \\ u|_{t=s} = u_s & u_s \in X. \end{cases}$$

Assuming well-posedness

$\Longrightarrow$ generates evolution process $\{U(t,s) | \; t \geq s\}$ in Banach space X, $U(t,s) : X \to X$, $t \geq s$, family of operators s.t.

$$\begin{array}{rcll} U(t,s) \circ U(s,r) & = & U(t,r) & t \geq s \geq r \\ U(t,t) & = & Id & t \in \mathbb{R} \\ (t,s,x) & \mapsto & U(t,s)x & \text{continuous} \end{array}$$

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Non-Autonomous Attractors

Different concepts:

– skew-product flow; uniform attractors,
– pullback and forwards attractors

$\mathcal{A} = \{\mathcal{A}(t) |\ t \in \mathbb{R}\}$ global pullback attractor for $\{U(t,s) |\ t \geq s\}$

(a) $\emptyset \neq \mathcal{A}(t) \subset X$ compact for all $t \in \mathbb{R}$

(b) $U(t,s)\mathcal{A}(s) = \mathcal{A}(t)$, $t \geq s$ invariant

(c) for all bounded $D \subset X$ and $t \in \mathbb{R}$

$$\lim_{s\to\infty} \mathrm{dist}_H(U(t,t-s)D, \mathcal{A}(t)) = 0$$

(d) $\{\mathcal{A}(t) |\ t \in \mathbb{R}\}$ minimal within the family of closed subsets, that pullback attract all bounded sets

Pullback Exponential Attractors

$\{\mathcal{M}(t) \mid t \in \mathbb{R}\}$ pullback exponential attractor for $\{U(t,s) \mid t \geq s\}$

(a) $\emptyset \neq \mathcal{M}(t) \subset X$ compact for all $t \in \mathbb{R}$

(b) $\sup_{t\in\mathbb{R}} \dim_f(\mathcal{M}(t)) < \infty$ finite dimensional

(c) $U(t,s)\mathcal{M}(s) \subset \mathcal{M}(t)$, $t \geq s$ semi-invariant

(d) there exists $\omega > 0$ such that for all bounded $D \subset X$, $t \in \mathbb{R}$

$$\lim_{s\to\infty} e^{\omega s} \mathrm{dist}_H(U(t,t-s)D, \mathcal{M}(t)) = 0$$

Pullback exponential attractors **not unique**, but

- finite dimensional, robust under perturbations
- $\mathcal{A}(t) \subset \mathcal{M}(t)$: implies existence and finite dimension of the global pullback attractor !

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Assumptions

$\{U(t,s) |\ t \geq s\}_{t,s\in\mathbb{R}}$ process in Banach space V, $U = S + C$

(A1) W normed space, $V \hookrightarrow\hookrightarrow W$ compact

(A2) $\{B(t)|t \in \mathbb{R}\} \subset V$ family of bounded semi-invariant *pullback absorbing sets*:
For every bounded $D \subset V, t \in \mathbb{R}$ exists $T_{D,t} > 0$:
$U(r, r - s)D \subset B(r) \qquad \forall\ s \geq T_{D,t}, r \leq t.$

(A3) (S smoothing) There exists $\tilde{t} > 0$ and $\kappa > 0$:
$\|S(t + \tilde{t}, t)u - S(t + \tilde{t}, t)v\|_V \leq \kappa\|u - v\|_W \quad \forall u, v \in B(t)$

(A4) (C contraction) There exists $0 \leq \lambda < \frac{1}{2}$:
$\|C(t + \tilde{t}, t)u - C(t + \tilde{t}, t)v\|_V \leq \lambda\|u - v\|_V \quad \forall u, v \in B(t)$

(A5) (U Lipschitz continuous) For all $s \geq t$ there exists $L_{t,s} > 0$:
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Existence of Pullback Exponential Attractors [14]

Theorem

Let $\{U(t,s)|\ t \geq s\}$ be a process in V and $(A1)$-$(A5)$ be satisfied. If the diameter of the absorbing sets $\{B(t)|\ t \in \mathbb{R}\}$ grows at most sub-exponentially in the past, then for every $\nu \in (0, \frac{1}{2} - \lambda)$ there exists a pullback exponential attractor $\{\mathcal{M}^\nu(t)|\ t \in \mathbb{R}\}$, and the fractal dimension is uniformly bounded,

$$\dim_f^V(\mathcal{M}^\nu(t)) \leq \log_{\frac{1}{2(\nu+\lambda)}} \left(N^W_{\frac{\nu}{\kappa}}(B_1^V(0)) \right) \qquad \text{for all } t \in \mathbb{R},$$

where $N^X_\epsilon(A)$ is the minimal number of ϵ-balls in a metric space X with centres in A, needed to cover $A \subset X$.

Remark: Generalizes previous constructions [11,12,13].

[11] **Efendiev, Miranville, Zelik**, *Exp. Attractors and Finite-dim. Reduction for Nonaut. Dyn. Systems* (2005).

[12] **Langa, Miranville, Real**, *Pullback Exponential Attractors* (2010).

[13] **Czaja, Efendiev**, *Pullback Exp. Attractors for Nonaut. Equ. Part I: Semilinear Parabolic Equations* (2011).

[14] **Carvalho, Sonner**, *Pullback Exponential Attractors for Evolution Processes in Banach Spaces*, Submitted.

Applications

Non-Autonomous Damped Wave Equation

$$\begin{cases} \frac{\partial^2}{\partial t^2} u(x,t) + \beta(t) \frac{\partial}{\partial t} u(x,t) = \Delta u(x,t) + f(u(x,t)) & x \in \Omega,\ t > s, \\ u(x,t) = 0 & x \in \partial\Omega,\ t \geq s, \\ u(x,s) = u_s(x), \quad \frac{\partial}{\partial t} u(x,s) = v_s(x) & x \in \Omega, \end{cases}$$

$\Omega \subset \mathbb{R}^n$, $n \geq 3$, bounded, $u : \Omega \times [s, \infty[\to \mathbb{R}$.

Non-Autonomous Chafee Infante Equation

$$\begin{cases} \frac{\partial}{\partial t} u(x,t) = \Delta u(x,t) + \lambda u(x,t) - \beta(t) \left(u(x,t)\right)^3 & x \in \Omega,\ t > s, \\ u(x,t) = 0 & x \in \partial\Omega,\ t \geq s, \\ u(x,s) = u_s(x) & x \in \Omega, \end{cases}$$

$\Omega \subset \mathbb{R}^n$ bounded, $\lambda \in \mathbb{R}$, $u : \Omega \times [s, \infty[\to \mathbb{R}$.