Optimal control of reaction-diffusion systems

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Plan

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In this presentation we study a model for treatment of brain tumors of [Chakrabarty, Hanson 2009] :

$$\begin{cases} \partial_t y_1 = d_1 \partial_{xx} y_1 + a_1(1 - y_1/k_1)y_1 - (\alpha_{1,2} y_2 + \kappa_{1,3} y_3) y_1 \\ \partial_t y_2 = d_2 \partial_{xx} y_2 + a_2(1 - y_2/k_2)y_2 - (\alpha_{2,1} y_1 + \kappa_{2,3} y_3) y_2 \\ \partial_t y_3 = d_3 \partial_{xx} y_3 - a_3 y_3 + u \\ y_i(x,0) = y_{i,0} \ \forall\ 1 \leqslant i \leqslant 3 \\ \partial_n y_i = 0 \ \forall\ 1 \leqslant i \leqslant 3 \end{cases} \tag{1}$$

where

1. y_1 is the density of tumor cells,
2. y_2 is the density of normal cells,
3. y_3 is the drug concentration,
4. u is the rate at which the drug is being injected,
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- At first we study the existence of a unique mathematical solution of our system for every injection u.

- And in a second time, we suppose that we "control" the injection u and we want :

1. to minimize the density of tumor cells y_1 during all the treatment,
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General framework

Let $\mathcal{W}$ a Banach space. We want to study first the system

$$\begin{cases} \dfrac{\partial y(t)}{\partial t} + Ay(t) = f(y(t), t) \\ y(0) = y_0. \end{cases} \tag{2}$$

where A is a linear operator on $\mathcal{W}$, $f \in L^1(0, T; \mathcal{W})$ and $y_0 \in \mathcal{W}$.
We say that (2) is "semilinear" because :

1. A is linear,
2. f is not linear.

If $A = \partial_{xx}$, we say that (2) is a "reaction-diffusion" equation :

1. "reaction" for ∂_t,
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Definition

A one parameter family $S(t)$, $0 \leqslant t \leqslant \infty$, of bounded linear operators from $\mathcal{W}$ into $\mathcal{W}$ is a $\mathcal{C}_0$ *semigroup of linear operators on* $\mathcal{W}$ if

1. $S(0) = I$,
2. $S(s+t) = S(s)S(t)$ for every $t, s \geqslant 0$.
3. $\forall x \in \mathcal{W} \lim\limits_{t \to 0} \|S(t)x - x\|_{\mathcal{W}} = 0$.

An operator A is the *infinitesimal generator* of the semigroup $S(t)$ if

$$D(A) = \left\{ x \in \mathcal{W} : \lim_{t \to 0} \frac{S(t)x - x}{t} \text{exists} \right\} \text{ and } Ax = \lim_{t \to 0} \frac{S(t)x - x}{t}$$

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Definition (P. Meyer-Nieberg)

An ordered set $(M, \leqslant)$ is a *lattice* if for all $x, y \in M$ $\sup(x, y)$ and $\inf(x, y)$ exist and for all $x, y \in E$

$$|x|_E \leqslant |y|_E \Rightarrow \|x\|_E \leqslant \|y\|_E, \tag{3}$$

where $|y|_E = \sup(y, -y)$ $\forall y \in E$.

We suppose that $\mathcal{W}$ and $\mathcal{V} := D(A)$ are Banach lattices.

Definition

A operator A is called *positive*, if

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Condition

The function $f : \mathcal{W} \times \mathbb{R}^+ \to \mathcal{W}$ and A satisfies :

1. f is of class $\mathcal{C}^1$
2. there exists $\lambda > 0$ and $y_{min}, y_{max} \in \mathcal{W}$ with $Ay_{min} = Ay_{max} = 0$ such that:
   $(y \in \mathcal{C}^1([0,T];\mathcal{W}) \cap \mathcal{C}([0,T];D(A))$ and $y_{min} \leqslant y \leqslant y_{max})$
   $\Rightarrow (\lambda y_{min}(t) \leqslant f(y(t),t) + \lambda y(t) \leqslant \lambda y_{max}(t))$
3. $-A$ infinitesimal generator of a $\mathcal{C}_0$ positive semigroup $(S_A(t))_t$

Theorem (D. et al, 13')

For all $T > 0$, $y_{min} \leqslant y_0 \leqslant y_{max}$, the system (2) has a unique sol. in $\mathcal{C}^1([0,T];\mathcal{W}) \cap \mathcal{C}([0,T];D(A))$ and $y_{min} \leqslant y \leqslant y_{max}$.

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THEOREM (D. et al, 13')

For all $T > 0$, $y_{min} \leqslant y_0 \leqslant y_{max}$, the system (2) has a unique sol. in $\mathcal{C}^1(]0,T];\mathcal{W}) \cap \mathcal{C}([0,T];D(A))$ and $y_{min} \leqslant y \leqslant y_{max}$.

Condition

The function $f : \mathcal{W} \times \mathbb{R}^+ \to \mathcal{W}$ and A satisfies :

1. f is of class $\mathcal{C}^1$
2. there exists $\lambda > 0$ and $y_{min}, y_{max} \in \mathcal{W}$ with $Ay_{min} = Ay_{max} = 0$ such that:
   $(y \in \mathcal{C}^1(]0,T];\mathcal{W}) \cap \mathcal{C}([0,T];D(A))$ and $y_{min} \leqslant y \leqslant y_{max})$
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Proof : We consider the set

$$\Gamma := \{y \in \mathcal{C}(0,T;\mathcal{W}) : y(0) = y_0, y_{min} \leqslant y(t) \leqslant y_{max}\ \forall t \in [0,T]\}.$$

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Let $\Omega \subset \mathbb{R}^3,\ T > 0,\ Q_T := (0,T) \times \Omega$.
Our system was

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To simplify the notations, let be $\mathbf{Y} = (y_1, y_2, y_3)^\top$ and

$$\begin{cases} \dfrac{\partial \mathbf{Y}}{\partial t} = D\mathbf{A}\mathbf{Y} + b(\mathbf{Y}) + \mathbf{U} \\ \mathbf{Y}(x,0) = \mathbf{Y}_0 \end{cases} \tag{5}$$

where

$$\begin{aligned} D &= \mathrm{diag}(d_1, d_2, d_3), \\ b(\mathbf{Y}) &= (S+T)(\mathbf{Y})\mathbf{Y}, \\ S(\mathbf{Y}) &= \mathrm{diag}(a_1(1 - y_1/k_1), a_2(1 - y_2/k_2), -a_3), \\ T(\mathbf{Y}) &= \mathrm{diag}(-(\alpha_{1,2}y_2 + \kappa_{1,3}y_3), -(\alpha_{2,1}y_1 + \kappa_{2,3}y_3), 0), \\ \mathbf{U} &= (0, 0, u). \end{aligned}$$

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THEOREM (D. et al, 13')

For all $\mathbf{Y}_0 \in \mathbb{L}^2(\Omega)$ *and all* $T > 0$*, the system (5) has a unique solution in* $\mathcal{C}(0,T;\mathbb{H}^1(\Omega)) \cap \mathcal{C}^1(0,T;\mathbb{H}^1(\Omega)')$.
Moreover we have

$$0 \leqslant y_i(t,x) \leqslant k_i \tag{7}$$

almost for all $x \in Q_T$ *and* $i \in \{1,2,3\}$*, where* $k_3 = \|u\|_\infty + \|u_{3,0}\|_\infty$.

Plan

We consider the following optimal problem

$$\inf_{\mathbf{U}\in U_\partial} J(\mathbf{Y},\mathbf{U}) \tag{8}$$

where

$$\begin{cases} J(\mathbf{Y},\mathbf{U}) = \dfrac{1}{2}\displaystyle\int_{Q_T} \left(N_1 y_1^2(x,t) + Nu^2(x,t)\right) \mathrm{d}t\mathrm{d}x \\ \qquad\qquad + \displaystyle\int_\Omega \left(M_1 y_1^2(x,T) + M_3 y_3^2(x,T)\right) \mathrm{d}x \to \inf, \\ \dfrac{\partial \mathbf{Y}}{\partial t} + DA\mathbf{Y} = b(\mathbf{Y}) + \mathbf{U} \text{ in } Q_T, \\ \mathbf{Y}(0,x) = \mathbf{Y_0} \text{ in } \Omega, \\ \mathbf{U} \in U_\partial = \{(u_1,u_2,u_3) \in L^2(Q_T) : u_1 = u_2 = 0, 0 \leqslant u_3 \leqslant u_{max}\}. \end{cases} \tag{9}$$

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THEOREM (D et al, 13')

There exists a solution $(\hat{\mathbf{Y}}, \hat{\mathbf{U}}) \in \mathbb{W}(0, T) \times L^2(Q_T)^3$ *to the problem (8), where* $W(0, T) = \{y \in L^2(0, T; H^1(\Omega)); \dfrac{\partial y}{\partial t} \in L^2(0, T; H^1(\Omega)')\}$.

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Perspectives

Conlusion : we have existence and uniqueness of a solution of our system and existence of a minimum of our functional.

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1. stability and convergence of a numerical scheme for this problem
2. boundary control
3. a general study with many medicaments and cells
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Thank you for your attention ☺