Control of the Flux Substrate Entering an Enzymatic Membrane

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Abstract

In this paper, we shall study an optimal control problem governed by a nonlinear partial differential equation where the system's state is a differentiable function of the control parameter.

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Let us consider a membrane which contains a certain enzyme and which separates two compartments containing solutions of the respective substrate of enzyme. In membrane occurs the reaction substrate plus enzyme to product, i.e., $E + S \Leftrightarrow ES \rightarrow E + P$.If $S(x,t)$ is the concentration of the substrate at the moment t in the point x of the unidimensional membrane then, according to Fick's law, the evolution of S in membrane is described by the equation

$$\frac{\partial S}{\partial t} - D\frac{\partial^2 S}{\partial x^2} + \frac{VS}{K+S} = 0, \quad x \in (a,b), \quad t \in [0,T]$$

where K is the constant of Michaelis and V is the reaction speed.

If in the two compartments is present an inhibitor by concentration $i = i(x,t)$ which is free to spread through membrane, then the evolution of system is described by the normalized equations (see [1], [3])

$$\text{(1)} \qquad \begin{cases} \dfrac{\partial S}{\partial t} - D\dfrac{\partial^2 S}{\partial x^2} + \dfrac{\sigma S}{1+ai+S} = 0 & \text{in} \quad (a,b)\times(0,T) \\ \dfrac{\partial i}{\partial t} - C\dfrac{\partial^2 i}{\partial x^2} = 0 & \text{in} \quad (a,b)\times(0,T) \end{cases}$$

with the initial conditions

$$\text{(2)} \qquad S(x,0) = 0, \ \ i(x,0) = 0, \ \ x \in (a,b)$$

and the boundary conditions

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$$(3)\qquad \begin{cases} S(a,t)=\alpha,\ S(b,t)=\beta,\ \forall t\in[0,T] \\ i(a,t)=u(t),\ i(b,t)=v(t). \end{cases}$$

This is a nonlinear parameter distributed system on (a,b) with the boundary controls u and v which can be manipulated for to modify the concentration S in a certain aim.

Let us consider an enzymatic membrane M which separates two compartments I and II. The memebrane is made of an inactive protein and contains an enzyme E. In the compartments I and II there are a solution which contains a substrate S (corresponding of enzyme E) and an inhibitor I, respectively, which both will spread in M. In membrane, S will begin to react (favoured by E which has a catalyst assignment), reaction which is slown down by the inhibitor I. If we consider that the membrane has the thickness equal to the unit and denote by $(y(x,y),i(x,t))$ the concentration of the substrate and of the inhibitor, respectively, in the point $x\in[0,1]$ of the membrane at the moment t, we have for (y,i) the system (see Eqs. (1)-(3))

$$(4)\qquad \begin{cases} y_t-y_{xx}+\dfrac{\sigma y}{y+i+1}=0 & \text{in}\quad (0,1)\times(0,T) \\ i_t-i_{xx}=0 & \text{in}\quad (0,1)\times(0,T) \end{cases}$$

with the initial conditions

$$(5)\qquad y(x,0)=0,\ \ i(x,0)=0,\ \ x\in(0,1)$$

and the boundary conditions

$$(6)\qquad \begin{cases} y(0,t)=\alpha,\ y(1,t)=\beta,\ \forall t\in[0,T] \\ i(0,t)=u_1(t),\ i(1,t)=u_2(t) \end{cases}$$

where α,β,σ are positive constants and $u(t)=(u_1(t),u_2(t))$ are the control functions of the process subject to the constraints $u=(u_1,u_2)\in U$, where

$$(7)\qquad \begin{aligned} &U=\{(u_1,u_2)\in L^2(0,T)\times L^2(0,T); \\ &0\le u_1(t)\le L,\ \ 0\le u_2(t)\le L,\ \ \text{a.e. } t\in[0,T]\}. \end{aligned}$$

The experimenter can modify the parameters u_1,u_2 to his liking (as part of restriction (7)) for to obtain a certain flux substrate entering to membrane. If the desired flux is defined by the functions $(y_1^0(t),y_2^0(t))$ then the problem can be mathematical formulated in this way

$$(8)\qquad \min\left\{\int_0^T((-y_x(0,t)-y_1^0(t))^2+(y_x(1,t)-y_2^0(t))^2dt;\quad (u_1,u_2)\in U\right\}$$

where (y,i) satisfy the state system (4), (5), (6).

By a *weak solution* of equation

$$(9)\qquad \begin{cases} i_t-i_{xx} \quad \text{in}\quad (0,1)\times(0,T) \\ i(x,0)=0 \end{cases}$$

with the Dirichlet boundary conditions

$$i(0,t) = u_1(t), \quad i(1,t) = u_2(t)$$

we shall mean a function $i \in L^2((0,1)\times(0,T))$ such that

$$\int_0^T \int_0^1 i(z_t - z_{xx})dxdt = \int_0^T (u_1(t)z_x(1,t) - u_2(t)z_x(0,t))dt, \quad \forall z \in Y \tag{10}$$

where

$$Y = \{z \in L^2((0,1)\times(0,T));\ z_t, z_x, z_{xx} \in L^2((0,1)\times(0,T));$$
$$z(0,t) = z(1,t) = 0;\ z(x,0) = 0\}.$$

For each $q \in L^2((0,1)\times(0,T))$ there exists one and only one solution $z^q \in Y$ to the equation $z_t - z_{xx} = q$ with the initial and Dirichlet conditions equal to zero and the application $q \to z^q$ is continuous from $L^2((0,1)\times(0,T))$ to Y. It results from this that the functional

$$q \to \int_0^T (u_1(t)z^q(1,t) - u_2(t)z^q(0,t))dt$$

is continuous on $L^2((0,1)\times(0,T))$ and therefore, for every $u \in L^2(0,T)\times L^2(0,T)$ there exists an unique $i \in L^2((0,1)\times(0,T))$ satisfying (10). Thus, we proved the existence and uniqueness of a weak solution for the problem (9).

If we redenote the unknown y, we shall can suppose that $\alpha = \beta = 0$ in the boundary conditions (6). The function $i = i^u$ being previous determined, the equation in y of the system (4) with the homogeneous boundary conditions admits an unique solution $y^u \in L^2(0,T;H_0^1(0,1))$ such that $y_t^u \in L^2(0,T;H^{-1}(\Omega))$ (see [2], p.140).

In particular, it follows that $y^u \in C([0,T];L^2(0,1))$. The existence in the problem (8) results by standard methods.

Now we shall deduce the optimality conditions (the maximum principle). We denote by $(z,q) = D_u(y^u,i^u)(v)$ the Gâteaux derivative of the application $u \to (y^u,i^u)$ from

$$L^2(0,T)\times L^2(0,T) \text{ to } (L^2((0,1)\times(0,T)))^2$$

at

$$v = (v_1,v_2) \in L^2(0,T)\times L^2(0,T).$$

Let us observe that z is the solution of the system in variation

$$\begin{cases} z_t - z_{xx} + \dfrac{\sigma(i^u+1)z}{(y^u+i^u+1)^2} = -\dfrac{\sigma y^u}{(y^u+i^u+1)^2}q = 0 & \text{in} \quad (0,1)\times(0,T) \\ q_t - q_{xx} = 0 & \text{in} \quad (0,1)\times(0,T) \\ z(x,0) = 0,\ q(x,0) = 0,\ x \in (0,1) & \\ z(0,t) = 0,\ z(1,t) = 0,\ t \in [0,T] & \\ q(0,t) = v_1(t),\ q(1,t) = v_2(t),\ t \in [0,T]. & \end{cases} \tag{11}$$

If $(u^* = (u_1^*, u_2^*), y^*, i^*)$ is optimal in Problem (8), then obviously we have

$$\int_0^T (z_x^*(0,t)(y_x^*(0,t)+y_1^0(t))+z_x^*(1,t)(y_x^*(1,t)-y_2^0(t)))dt \geq 0$$

where z^* is the solution of the system (11) with $u=u^*$, $v \in T_U(u^*)$. (Here $T_U(u^*)$ is the cone of tangents to U at $u^* \in U$).

Let us consider the dual system (suggested by the system in variation (11))

(12)

$$\begin{cases} p_t^1 + p_{xx}^1 - \dfrac{\sigma(i^*+1)}{(y^*+i^*+1)^2}p^1 = 0 & \text{in} \quad (0,1)\times(0,T) \\ p_t^2 + p_{xx}^2 + \dfrac{y^*}{(y^*+i^*+1)^2}p^1 = 0 & \text{in} \quad (0,1)\times(0,T) \\ p^1(x,T)=0,\ p^2(x,T)=0 & \text{in} \quad (0,1) \\ p^1(0,t) = -(y_x^*(0,t)+y_1^0(t)),\ p^1(1,t) = (y_x^*(1,t)-y_2^0(t)) & \text{in} \quad (0,T) \\ p^2(0,t)=0,\ p^2(1,t)=0 & \text{in} \quad (0,T) \end{cases}$$

which admits an unique solution $p^1 \in L^2((0,1)\times(0,T))$, $p^2 \in L^2(0,T);H_0^1(0,1))$ with $p_t^2 \in L^2((0,1)\times(0,T))$.

If we multiply the first equation of (11) (where $u=u^*$) with p^1, the second with p^2 and integrate on $(0,1)\times(0,T)$, finally, it follows that (the formally integration by parts is justified by the definition of weak solution $p^1 \in L^2((0,1)\times(0,T))$ of the equation (12))

$$\int_0^T (z_x^*(0,t)(y_x^*(0,t)+y_1^0(t))+z_x^*(1,t)(y_x^*(1,t)-y_2^0(t)))dt =$$

$$= \int_0^T (p_x^2(1,t)(v_2(t)-p_x^2(0,t)v_1(t))dt \geq 0, \quad \forall v \in T_U(u^*).$$

Hence

$$(p_x^2(0,t),\ -p_x^2(1,t)) \in N_U(u^*).$$

(Here $N_U(u^*)$ is the cone of normals to U at $u^* \in U$). If follows, by definition of $N_U(u^*)$, that

$$u_1^*(t) = \begin{cases} 0 & \text{if} \quad p_x^2(0,t) > 0 \\ L & \text{if} \quad p_x^2(0,t) < 0 \end{cases} \tag{13}$$

$$u_2^*(t) = \begin{cases} 0 & \text{if} \quad p_x^2(1,t) < 0 \\ L & \text{if} \quad p_x^2(1,t) > 0. \end{cases} \tag{14}$$

The system (4)∼(6), (12)∼(14) can be integrated by numerical methods.

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