The optimal control applied to diffusion-reaction models

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Abstract

In Ecology the Diffusion-Reaction models are widely used. The term Reaction is applied in process of growth or interaction among species in absence of dispersion, and the Diffusion describe the movement of individuals. In this work, it is modelled how an inhibitor that is deposited in the surface of rat cortex spreads to avoid the massive destruction of neurones, when, for example a brain-vascular accident occurs. The solution of the resultant non-linear diffusion-reaction equation is obtained by means of the Adomian's method. The parameters of the equation of the model are identified by using a new method that uses α-dense curves. Finally, the problem of optimal control related to this model of diffusion is considered.

1 Introduction

One of the mechanisms of the cellular death in the cortex is the formation of toxic substances in the cerebral tissue. The current hypothesis is the one of the formation of peroxynitrite from nitric oxide or nitrites and radical superoxide, which are both formed by the cells as the answer to anoxia (Beckman [1]). In order to avoid this reaction of the cells, in this work we have tried to diminish the nitrites formation, which appears due to an enzymatic phenomenon. We will use a specific inhibitor of the enzyme (NO-Synthase). In our case, the more used inhibitor is the nitro-arginine (Iadecola et al. [2]).

In order to make penetrate the nitro-arginine in the brain of the rat, which is our animal model, we used the direct deposit of a nitro-arginine solution on the brain. It is the means of imposing a constant concentration of nitro-arginine on
the brain (Greenberg et al. [3], Michel et al. [4], Tabrizi-Fard y Fumy [5]). The nitro-arginine is going away to spread in the cerebral tissue, later it will have to penetrate in the cells to act. The penetration in the cells uses a transport mechanism Michaelis-Menten type (Greene et al. [6]). The nitro-arginine will inhibit the NO-Synthase, preventing the formation of nitrites. We measured the nitro-arginine, that we will denote (P), produced constantly by the enzyme in the brain, and the nitro-arginine, the inhibitor that will be denoted by (I), by micro detectors to a given depth, based on the time, we used a technique called Voltammeter Differential Pressed, applied with microelectrodes.

For example, for a depth \( x=125 \mu m =0.0125cm \), and for an initial concentration of inhibitor of \( 0.0091 \ mM/cm^3 \) in the surface of cortex the following table has been obtained by means of the Voltammeter Differential Pressed:

<table>
<thead>
<tr>
<th>Seconds</th>
<th>( I(mM/cm^3) )</th>
<th>( P(mM/cm^3) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0.00127</td>
</tr>
<tr>
<td>60</td>
<td>0.00018</td>
<td>0.00096</td>
</tr>
<tr>
<td>120</td>
<td>0.000265</td>
<td>0.0009</td>
</tr>
<tr>
<td>180</td>
<td>0.000328</td>
<td></td>
</tr>
<tr>
<td>240</td>
<td>0.000369</td>
<td>0.00084</td>
</tr>
<tr>
<td>300</td>
<td>0.000410</td>
<td></td>
</tr>
</tbody>
</table>

Once the inhibitor (the Nitro-arginine) is deposited on the brain of the rat, it spreads in the cerebral tissue and the penetration in the cells uses a transport mechanism of Michaelis-Menten type (Bradbury [7]).

2 Mathematical modelization

If we denoted by \( I(x,t) \) the extra cellular inhibitor concentration, the equation that models this chemical phenomenon is a non-linear Diffusion-Reaction equation, with two parameters, \( K \) and \( V \), to identify. This equation, in which the coefficient of diffusion has been calculated experimentally, is the following one:

\[
\frac{\partial I}{\partial t} = 0.0000038 \frac{\partial^2 I}{\partial x^2} - \frac{VI}{K + I} \quad x \geq 0, \ 0 \leq t \leq T
\]  

(1)

With the initial and contour conditions

\[
I(x,0) = C_0 \exp(-1100x),
\]  

(2)

\[
I(0,t) = C_0, \quad C_0 \ \text{constant}, \ C_0 = 0.0091 mM / cm^3.
\]  

(3)
In this equation the reaction term corresponds with the phenomenon of penetration of concentration of the inhibitor \( I(x,t) \) within the cell, and the penetration that takes place at speed of Michaelis-Menten.

This equation has a unique solution. (Rozier [8]).

3 Resolution of the non-lineal diffusion-reaction equation by the Adomian’s method

This method was proposed by the North American physicist G. Adomian (1923-1996). It is based on the search of the solution in form of series and the decomposition of the operator non-linear on series, in which the terms are calculated in a recurrent way by using some polynomials called polynomials of Adomian. Under certain conditions of convergence, the series gives the exact solution, but in practice the series is truncated, which is sufficient for obtaining a good approach. The error of truncation can be considered most of times.

More details on the method of Adomian can be found in the works made by Abbaoui [9], Cherruault and Adomian [10] and Cherruault et al. [11]. Applications to systems of non-linear differential equations appear in Grimalt and Pujol [12] and Guellal et al. [13], where there is an application to Chemistry Kinetics. For applications to partial differential equations see Guellal et al.[14].

Let us consider eqn (1) with the initial and contour conditions eqns (2) and (3). The eqn (1) is written in a canonical way as:

\[
L_t I = 0.0000038 L_{xx} I - N(I)
\]

(4)

where \( L_t I = \frac{\partial I}{\partial t} \), \( L_{xx} I = \frac{\partial^2 I}{\partial x^2} \) and \( N(I) = \frac{VI}{K + I} \).

Let us invert the operator of smaller order, \( L_t \). In this case the scheme of Adomian is written as:

\[
\forall n \geq 1 \quad I_n = 0.0000038 L_t^{-1} L_{xx} I_{n-1} - L_t^{-1} A_{n-1}
\]

where \( L_t^{-1} \) represents the integration in \( t \) and where \( A_{n,1} \) are the polynomials of Adomian corresponding to non-linearity \( N \) and depending on \( I_0, I_1, \ldots, I_{n-1} \).

The scheme of Adomian, based on Abbaoui [9] and Guellal et al. [14] is written:

\[
\sum_{n=0}^{\infty} I_n = I(x,0) + 0.0000038 L_t^{-1} L_{xx} \sum_{n=0}^{\infty} I_n - L_t^{-1} \sum_{n=0}^{\infty} A_n
\]

with \( N(I) = \sum_{n=0}^{\infty} A_n = \frac{VI}{K + I} \).
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\[ I_0 = I(x,0) = 0.0091e^{-1100x} \]
\[ I_{n+1} = 0.0000038L_i L_{ii} I_n - L_i A_n \quad (5) \]

and the \( A_n \) are calculated by the relation given in Abbaoui [9]. Therefore, applying eqn (5)

\[ I_0 = 0.0091e^{-1100x} \]
\[ I_1 = 0.0418418t e^{-1100x} - 91 \frac{t V}{10000Ke^{1100x}} + 91 \]
\[ I_2 = t^2 (0.96194298210^{11} e^{2200x} K^3 + 0.262610434110^{10} e^{1100x} K^2 + 
+ 0.238975495010^{-8} K + 0.724892334910^{5} e^{-1100x} -
- 0.41841810^{11} e^{2200x} V K^2 + 0.45510^{10} V^2 Ke^{2200x})/(10000Ke^{1100x} + 91)^3 \]

As a consequence, the add of the truncated series

\[ I = I_0 + I_1 + I_2 \quad (6) \]

allows us to give the approximate expression for \( I \).

4 Identification of the parameters of the model

The identification is carried out by means of the minimization of certain functional \( J \), called functional error. This functional expresses the difference between the experimental values and the purely mathematical ones of the model, and that is the reason why it express the approach of the reality by means of the mentioned model. So the functional \( J \) will depend on the parameters \( a_1, \ldots, a_p \).

For the identification of both parameters \( V \) and \( K \), we constructed the following functional to minimize:

\[ J = \sum_{j=0}^{m} \left( I(x_0, t_j) - I^e(x_0, t_j) \right)^2 \quad (7) \]

that represents the add of the squares of the differences between the value given by the solution of eqn (1) \( I(x_0,t_j) \) at the moment \( t_j \) to a depth \( x_0 \) and the experimental measurement \( I^e(x_0,t_j) \).

In our case \( x_0 = 125 \mu M = 0.0125 \text{ cm} \). The experimental results are given in Table 1. Therefore, if we replace in (7) the values of (6) evaluated at the same moments and in the same depth that the one in Table 1, and the values of \( I^e(x_0,t_j) \) of Table 1, we will obtain

\[ J = \sum_{j=0}^{5} \left( I(0.0125,t_j) - I^e(0.0125,t_j) \right)^2 = 
= (I(0.0125,0) - 0)^2 + (I(0.0125,60) - 0.00018)^2 + \]
The expression of this function \( J(K,V) \), calculated by MAPLE V is:

\[
J(K,V) = \\
= 0.25 \times 10^{-22} \times 1.679437706 \times 10^{60} K - 0.2129380843 \times 10^{16} V + 0.2719599266 \times 10^{31} + \\
0.5930046689 \times 10^{56} K^3 + 0.4321272385 \times 10^{48} K^2 + 0.2964542427 \times 10^{24} V^2 K \\
+ 0.4497524476 \times 10^{66} V^2 - 0.2748732538 \times 10^{55} VK^2 - 0.1095799457 \times 10^{45} V^3 K \\
- 0.8440711228 \times 10^{53} V^3 + 0.1008043646 \times 10^{29} K^4 V^2 \\
+ 0.8084757216 \times 10^{57} V^4 K^2 - 0.240712039 \times 10^{47} V^3 K^2 - 0.1169391902 \times 10^{59} V^3 K \\
- 1.488187274 \times 10^{78} V^3 K^3 + 0.9443040009 \times 10^{70} K^3 V^2 \\
+ 0.9164214033 \times 10^{62} V^2 K^2 - 0.8675392274 \times 10^{71} K^4 V \\
- 0.2974652975 \times 10^{79} K^5 V + 0.457748688999 \times 10^{64} K^4 + 0.3232595162 \times 10^{79} K^6 \\
+ 1.884494330 \times 10^{72} K^5 ) / ( 0.9365891582 \times 10^{10} K + 91)^6
\]

(8)

To obtain the minimum of this function of two variables we are going to use the Alenior Method (Cherruault [15,16]), that will allow us to replace \( J(K,V) \) by the function of a variable \( J'(\theta ) = J(h_1(\theta ), h_2(\theta ) \), where \( K= h_1(\theta ) \), \( V= h_2(\theta ) \), are the equations of the \( \alpha \)-dense curve.

Considering that our parameters appear in biochemical phenomena, their intervals of variation are \( K \in [10^{-6}, 10^{-3}] \) mM/cm\(^3\), \( V \in [10^{-8}, 10^{-4}] \) mM/cm\(^3\)/s/g. Using \( \alpha \)-dense curves (Mora & Cerruault [17,18,19]), we are going to make denser the interval \([10^{-5}, 10^{-1}] \times [10^{-8}, 10^{-4}] \) by means of the curve:

\[
K= h_1(\theta ) = \theta , \quad \theta \in [10^{-6},10^{-3}] \\
V= h_2(\theta ) = 0.000049995 + 0.000049995 \sin(2000000 \theta \pi )
\]

(9) \hspace{1cm} (10)

It becomes dense with \( \alpha < 10^{-6} \). Therefore,

\[
J'(\theta ) = J(h_1(\theta ), h_2(\theta ))= \\
= J(\theta ,0.000049995 + 0.000049995 \sin(2000000 \theta \pi ) ,
\]

function of a variable, obtained replacing in eqn (8) the eqns (9) and (10), whose minimum is reached in

\[
\theta = 0.00001074 \text{mM/cm}^3
\]

(11)

that replaced in eqn (9) gives the value of parameter \( K= h_1(\theta ) = \theta \), value that approximates quite well the presented in the specialized reference of the subject Westergaard et al.[20].
We presented the graph of $J^*(\theta)$, $\theta$ in the interval $[10^{-6}, 10^{-3}]$ in Figure 1, in logarithmic scale, where the minimum in $K=0.00001074$ is appraised.

The value of parameter $V$ is obtained by replacing eqn (11) in eqn (10), $V = 0.9865368 \times 10^{-7}$ mM/cm$^3$/s/g that also approximates suitably the one that is given in Westergaard et al.[20].

5 Optimal control problem applied to diffusion models

Let us consider this diffusion model:

$$\frac{\partial C}{\partial t} = D \frac{\partial^2 C}{\partial x^2} - V \frac{C}{K + C}, \quad C(x,0) = a e^{-1100x}$$ (12)

where $C(x,t)$ is the inhibitor concentration to a depth $x$ and in the instant $t$, and the constants $D$, $V$ and $K$ are known.

Then, to solve eqn (12) we will use the decompositional method. We will be able to truncate the series in the term 3 or 4.

We want to have a concentration $C(x_0,t_0) \equiv C_0$ with a fixed $t_0$ (biological value) in a given depth $x_0$. And we want to obtain the necessary minimum concentration of the initial inhibitor $a$ in the surface of the cortex so that $C(x_0,t_0) \equiv C_0$. 

Figure 1: Graph of $J^*(\theta)$ in logarithmic scale.
For instance, let us consider a problem in which \( D = 0.0000038 \), \( V = 10^{-7} \) and \( K = 10^{-4} \). We want to have a concentration of \( C_0 = 0.001 \) in \( t_0 = 1200 \) s with a depth \( x_0 = 0.01 \text{cm} \).

Therefore we should minimize the functional

\[
\text{Min} \left( C(x_0, t_0) - C_0 \right)^2
\]

where \( C(x_0, t_0) \) denotes the Adomian's solution of eqn (12) in the fixed instant \( t_0 \) and in a given depth \( x_0 \).

To approach a real problem we will take \( D = 0.0000038 \), \( V = 10^{-7} \) and \( K = 10^{-4} \). We want to have a concentration \( C_0 = 0.001 \) in \( t_0 = 1200 \) s. in a depth \( x_0 = 0.01 \text{cm} \).

Therefore we have to minimize:

\[
\text{Min} \left( C(0.01, 1200) - 0.001 \right)^2 \tag{13}
\]

so that \( C \) is the solution of:

\[
\frac{\partial C}{\partial t} = 0.0000038 \frac{\partial^2 C}{\partial x^2} - 10^{-7} \frac{C}{10^{-4} + C} \tag{14}
\]

\[
C(x, 0) = a e^{-1100x} \tag{15}
\]

The process to be followed is:

1. We solve with the Adomian method eqn (14) with the condition given in eqn (15). Let \( C \) be the solution.
2. We substitute in this solution \( x = 0.01 \), \( t = 1200 \), so we obtain \( C(0.01, 1200) \) that is only function of \( a \).
3. We minimize the expression of eqn (13).

The Adomian's scheme will be:

\[
\sum_{n=0}^{\infty} C_n = C(x, 0) + 0.0000038 L_t^{-1} L_{xx} \sum_{n=0}^{\infty} C_n - L_t^{-1} \sum_{n=0}^{\infty} A_n
\]

with \( N(I) = \sum_{n=0}^{\infty} A_n = \frac{10^{-7} C}{10^{-4} + C} \)

\[
C_0 = C(x, 0) = a e^{-1100x}
\]

\[
C_{n+1} = 0.0000038 L_t^{-1} L_{xx} C_n - L_t^{-1} A_n \tag{16}
\]
The $A_n$ are calculated by using the relation given in Abbaoui [9]. Then, applying eqn (16),

\[
C_0 = a e^{-1100x}
\]

\[
C_1 = 4.598 t a e^{-1100x} - 0.001 \frac{t a}{e^{1100x} + 10000a}
\]

\[
C_2 = 0.5 \times 10^{-6} a t^2 \cdot (0.2113240910^8 e^{2200x} + 0.6342481210^{12} e^{1100x} a + 0.6342481210^{16} a^2 + 0.2114160410^{20} e^{-1100x} a^3) / (e^{1100x} + 10000a)^3
\]

And the solution as a sum of a truncated series $C = C_0 + C_1 + C_2$ is:

\[
C = a e^{-1100x} + 4.598 t a e^{-1100x} - 0.001 \frac{t a}{e^{1100x} + 10000a} +
\]

\[
+ 0.5 \times 10^{-6} a t^2 \cdot (0.2113240910^8 e^{2200x} + 0.6342481210^{12} e^{1100x} a + 0.6342481210^{16} a^2 + 0.2114160410^{20} e^{-1100x} a^3) / (e^{1100x} + 10000a)^3
\]

The function to minimize is:

\[
F = (C(0.01, 1200) - 0.001)^2 =
= 0.1 \times 10^{-5} (0.8525831235 \times 10^{33} a + 0.4273740275 \times 10^{33} a^2 +
+ 0.7137876444 \times 10^{32} a^3 + 0.3973823529 \times 10^{31} a^4 - 0.3353805935 \times 10^{28})^2 /
(0.1496853543 \times 10^{10} + 0.25 \times 10^9 a)^6
\]

which has only one variable, $a$, whose minimum value is reached in

\[
a = 0.003933685.
\]

6 Conclusions

Starting of a biochemical problem that happens in the brain, we have presented a model of passive diffusion, that it tries to prevent the excess of toxic substances (Peroxynitrites) in cortex due to an enzymatic phenomenon depositing in the surface of cortex an inhibitor of the enzyme. This model takes shape in a NoLineal Partial Derived Equation with some parameters to identify.

The resolution of the equation of the model, a No-Lineal Diffusion-Reaction Equation of takes place by the method of Adomian, giving the analytical solution in truncated form of series. For the identification of parameters of the model has been used the Method of the $\alpha$-dense curves, novel technical that turns a function of several variables into another one of an only variable that makes dense the space where we worked. Applying this technique has been
obtained the values of the parameters with an excellent approach to the values published in journals specialized of the subject.

Of the obtained results it is possible to be concluded that the model is adapted sufficiently to the reality.

Lastly, we have wondered which would be the best dose, that is to say the minimum quantity that should be deposited in the surface of the córtex to obtain one given concentration at an instant and depth fixed before. This problem type belongs to the field of Control Optimal Problems, in which due to the application of the Adomian’s Method the criterium to be minimized clearly depends on the Control parameters.

References


