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PARAMETER IDENTIFICATION OF NONLINEAR COMPARTMENTAL SYSTEMS USING ADOMIAN METHOD

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RÉSUMÉ : *The purpose of this paper is to show that Adomian method can be used to solve the problem of parameter identification of nonlinear compartmental systems. Parameter identification leads to the minimisation of an error functional given by the sum of variations between measured variables and calculated variables obtained by solving the system of differential equations. The identification was realized by applying the Adomian method for solving compartmental systems.The solution is an analytical function of time and is given in a series form explicitly dependent on the parameters of the system. The Levenberg-Marquardt method is then used for solving obtained optimization problem. Simulation results are given for illustration.*

MOTS-CLÉS : *Parameter identification, Adomian method, nonlinear compartmental system*

1. INTRODUCTION

The mathematical modelling of dynamical systems leads to nonlinear differential equations containnig parameters that must be determined from available experimental data. To perform identification we often minimize a error functional defined as the sum of the squares of the differences between experimental values (observed) and computed values obtained by resolution of the system.

In this work, we are interested in use of the Adomian Decomposition Method (ADM) (Abbaoui and Cherruault, 1994; Abbaoui *et al.*, 1995) for parameters identification of a nonlinear compartmental system. Parameter identification leads to the minimisation of an error functional given by the sum of variations between measured variables and calculated variables obtained by solving the system of differential equations

Adomian decomposition method will be used for solving the nonlinear differential system. The solution is an analytical function of time and is given in a series form explicitly dependent on the parameters of the system. Practically, an approximated solution is obtained by truncating the series.

The error functional is then explicitly dependent on the unknows parameters and the Levenberg-Marquardt method is used for solving this optimization problem.

The efficacy of this approach is proved by solving an identification problem associated to a nonlinear compartmental systems.

This paper is organized as follows : in Section 2 the identification problem is formulated. In section 3, we describe Adomian method and its application to solve nonlinear differential systems. Application of the problem to the nonlinear compartmental systems is presented in Section 4 and we give the numerical results obtained by using the combined Adomian and the Levenberg-Marquardt methods.

2. PROBLEM FORMULATION

Mathematical modelling involves identification of unknown parameters .Their determination (identification) needs the using of an optimization method.

Let us consider the model described by a nonlinear differential system :

$$\begin{cases} \dot{x}_i = f_i\left(x_1, ..., x_p, \alpha_1, ..., \alpha_q, t\right) \\ x_i\left(t=0\right) = \beta_i \quad , i = 1, .., p \end{cases} \tag{2.1}$$

where the functions f_i's are known, $x = (x_1, ..., x_p)^T$ is the state vector of the system and $\alpha_1, ..., \alpha_q$ are unkown parameters that we have to calculate from observations (measurements).

Let us consider a general observation :

$$Z = B.x \tag{2.2}$$

where B is a $(l \times p)$ constant and known matrix, called matrix of observation.

The $\alpha_1, .., \alpha_q$ are obtained by minimizing the error functional :

$$J = \sum_{j=1}^{m} \sum_{i=1}^{l} (Z_i(t_j) - Z_i^c(t_j))^2 \tag{2.3}$$

In (2.3), $Z_i(t_j)$ are the measured quantities at times t_j, Z_i^c represents the function $Z_i(t) = (B.x)_i$ calculated from the resolution of system (2.1) when $\alpha_1, .., \alpha_q$ are fixed. $(B.x)_i$ is the i th row of vector Z.

The minimisation of J according the parameters $\alpha_1, .., \alpha_q$ by an optimization method necessites the resolution of the system (2.1) at any level, because J implicitly depends on the unkown parameters.

Adomian decomposition method allows to express explicitly Z_i^c in function of unknown parameters. We obtain a functional J explicitly dependent on the parameters to identify.

3. ADOMIAN DECOMPOSITION METHOD

The decomposition method can be used for solving linear and nonlinear functional equations of various kind (differential, partial differential, integral, algebric, etc.) .

The solution is obtained in a series form, where each term is explicitly depending on the parameters arising in the equations.

Recall the main definitions and properties of the decomposition method (Cherruault,1998).

Let us consider a functional equation in the form :

$$x - N(x) = g \tag{3.1}$$

where N is the nonlinear operator (differential, partial differential, integral,...), g is a given function and we are looking for x solution of equation (3.1). Equation (3.1) is called Adomian canonical form.

The Adomian method consists in finding solution x (if it exists) in a series form :

$$x = \sum_{n=0}^{\infty} x_n \tag{3.2}$$

Then we decompose the nonlinear operator $N(x)$ as follows :

$$N(x) = \sum_{n=0}^{\infty} A_n(x_0, x_1, ..., x_n) \tag{3.3}$$

where the A_n are polynomials depending on $x_0, x_1, ..., x_n$ (Abbaoui, 1995; Cherruault, 1998) and are called Adomian polynomials. They are obtained from the relationships :

$$n!A_n = \frac{d^n}{d\lambda^n} \left[N\left(\sum_{i=0}^{n} \lambda^i x_i] \right) \right]_{\lambda=0} \quad , \; n = 0.1, 2, ... \tag{3.4}$$

where λ is a parameter introduced for convenience.

Putting expressions (3.2) and (3.3) into (3.1) leads to :

$$\sum_{n=0}^{\infty} x_n - \sum_{n=0}^{\infty} A_n = g \tag{3.5}$$

Adomian has suggested the inductive scheme:

$$\left\{ \begin{array}{c} x_0 = g \\ x_1 = A_0(x_0) \\ x_2 = A_1(x_0, x_1) \\ \vdots \\ x_{n+1} = A_n(x_0, ..., x_n), ... \end{array} \right. \tag{3.6}$$

We see that we can easily calculate the terms x_n if the Adomian polynomials A_n can be calculated.

The exact solution of equation (3.1) is now entirely determined. However it is not generally possible to calculate the series sum, so we use an approximation of the solution obtained from the truncated series :

$$\phi_s = \sum_{i=0}^{s-1} x_i$$

Y.Cherruault and K.Abbaoui (1996) have proved that the series x_n converges if the nonlinear operator N satisfies some conditions. Practical formulae for calculating these polynomials have been proposed (Cherruault, 1998).

3.1. Adomian method applied to systems of differential equations

Let us consider a system of differential equations :

$$\left\{ \begin{array}{l} \frac{dx(t)}{dt} = f(x, \alpha, t) + g \\ x_i(t = 0) = x_{i,0}^* \quad i = 1, .., p \end{array} \right. \tag{3.7}$$

where $x(t) = (x_1(t), ..., x_p(t))^T$, $f = (f_1, ..., f_p)^T$ and $g = (g_1, ..., g_p)^T$ and $\alpha = (\alpha_1, ..., \alpha_q)^T$. f_i are the nonlinear terms, g_i and parameters $x^*_{i,0}$ are given and the α_i's are the unknown parameters of the system.

Writing (3.7) in the Adomian canonical form :

$$x(t) = x(t=0) + L^{-1}f + L^{-1}g \qquad (3.8)$$

with $L^{-1}(.) = \int_0^t .dt.$

We are looking for a solution written as :

$$x_i = \sum_{n=0}^{\infty} x_{in} \quad , i = 1, .., p \qquad (3.9)$$

where the x_{in} are explicitly depending on $\alpha_1, ..., \alpha_q$.

The nonlinear terms f_i are decomposed as :

$$f_i(x_1, x_2, ..., x_p) = \sum_{n=0}^{\infty} A_{in} \quad , i = 1, .., p \qquad (3.10)$$

where A_{in} are the Adomian polynomials depending on $x_{0,1}, ..., x_{n,1}; ...; x_{0,p}, ..., x_{n,p}$. They are calculated from the formulae (Cherruault, 1998 ; Khelifa, 2002) :

$$A_{i0}(x_{0,1}, x_{0,2}, ..., x_{0,p}) = f_i(x_{0,1}, x_{0,2}, ..., x_{0,p}) \qquad (3.11)$$

For $n \neq 0$ and from $i = 1, .., p$:

$$\begin{aligned} & A_{in}(x_{0,1}, ..., x_{n,1}; ...; x_{0,p}, ..., x_{n,p}) \\ = & \sum_{sum=n} \nabla(n,k,i).Q(n,k,i) \qquad (3.12) \end{aligned}$$

where $sum = k_{11} + ... + nk_{1n} + ... + k_{p1} + ... + nk_{pn}$,

with :

$$\begin{aligned} \nabla(n,k,i) \quad = \quad & \left(\frac{\partial^{k_{1,1}+...+k_{1,n}+...+k_{p,1}+...+k_{p,n}}}{\partial x_1^{k_{1,1}+...+k_{1,n}} ... \partial x_p^{k_{p,1}+...+k_{p,n}}} \right) \\ & .f_i(x_{0,1}, x_{0,2}, ..., x_{0,p}) \qquad (3.13) \end{aligned}$$

and

$$Q(n,k,i) = \frac{x_{1,1}^{k_{1,1}}}{k_{1,1}!} ... \frac{x_{1,1}^{k_{1,n}}}{k_{1,n}!} ... \frac{x_{p,1}^{k_{p,1}}}{k_{p,1}!} ... \frac{x_{p,n}^{k_{p,n}}}{k_{p,n}!} \qquad (3.14)$$

Putting (3.9), (3.10) into the canonical form (3.8) leads to :

$$\sum_{n=0}^{\infty} x_{in} = x^*_{i.0} + L^{-1}g_i + L^{-1} \sum_{n=0}^{\infty} A_{in}, \; i = 1, .., p \quad (3.15)$$

An identification in (3.15), leads to :

$$\begin{cases} x_{i.0} = x^*_{i.0} + L^{-1}g_i \\ x_{i.n+1} = L^{-1}A_{i.n} \quad n \geq 0 \quad , i = 1, .., p \end{cases} \qquad (3.16)$$

3.2. System identification using the combined Adomian method

As we have seen in section 3.1, the solution of differential equations is given as a series where the parameters of system are explicitly expressed in the series term $x_{in}(t)$. It is the i th component of the vector solution. For practical problems, the series are generally truncated .

Usually the identification is performed by introducing an error functional :

$$J(\alpha_1, ..., \alpha_q) = \sum_{j=1}^{m} \sum_{i=1}^{p} (x_i(t_j) - x_i^c(t_j))^2 \qquad (3.17)$$

that will be minimized according to $\alpha_1, ..., \alpha_q^t$.

The $x_i(t_j)$ are the experimental data at time t_j and m is the number of measures. The x_i^c are functions x_i obtained from the resolution of the differential system by the Adomian decomposition method in form of truncated series

$$x_i^c = \sum_{j=1}^{s} v_j^i(\alpha_1, ..., \alpha_q, t) \qquad (3.18)$$

The terms v_j^i of the decomposition series explicitly depend on $\alpha_1, ..., \alpha_q$.

Putting the expressions (3.18), into the functional (3.17) leads to a functional J explicitly depending on $\alpha_1, ..., \alpha_q$.

Therefore, our identification problem (3.17), with as many parameters as it is required is reduced to a classical minimisation problem of the form :

$$\underset{\alpha_1, ..., \alpha_q}{Min} \; J(\alpha_1, ..., \alpha_q) \qquad (3.19)$$

where $J(\alpha_1, ..., \alpha_q)$ is explicitly dependent on the unkown parameters.We are required to minimize the functionnal (3.19) with respect to q unknown parameters with classical methods such as Levenberg-Marquardt

4. APPLICATION TO THE NONLINEAR COMPARTMENTAL SYSTEM

4.1. Description of the model

Let us consider the nonlinear compartimental model :

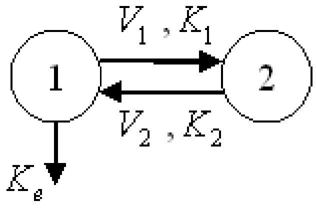

Figure 1.two compartmental model

This model with two compartments is often used in pharmacokinetic to follow the evolution of a chemical substance (drug) in a human organism (Cherruault, 1998) :

Compartment 1 is the blood compartment and compartment 2 is the compartment where the substance acts (heart, liver, lungs, tumour…).

The model with two compartments of the figure (1) is traducted by the following differential system :

$$\left\{ \begin{array}{l} \dot{x}_1 = -\left(K_e + \frac{V_1}{K_1+x_1}\right) x_1 + \frac{V_2}{K_2+x_2} x_2 \\ \dot{x}_2 = \frac{V_1}{K_1+x_1} x_1 - \frac{V_2}{K_2+x_2} x_2 \\ x_1(0) = \beta,\ x_2(0) = 0,\ \beta \text{ is fixed} \end{array} \right. \qquad (4.1)$$

where the initial conditions correspond to an instantaneous administration (injection) of a quantity of chemical substance at time 0 in the first compartment, $x_1(t)$ and $x_2(t)$ represents the concentration of the substance in compartment 1 and 2 respectively.

The kinetic type of elimination of "Michaelis- Menten" results in a quantity of matter (by unit of time) transported from compartment i to the compartment j equal to :

$$\frac{V_i x_i}{K_i + x_i} \quad , \ i = 1, 2 \qquad (4.2)$$

where V_i and K_i are the constants of Michaelis-Menten, K_e: is the constant of elimination or exchange of compartment 1 with the exterior.

4.2. *Resolution by Adomian method*

The canonical form associated to the system (4.1) is as follows:

$$x_1 = \beta - K_e L^{-1} \sum_{n=0}^{\infty} x_{1n} - L^{-1} \sum_{n=0}^{\infty} A_{1n} + L^{-1} \sum_{n=0}^{\infty} A_{2n}$$
$$x_2 = L^{-1} \sum_{n=0}^{\infty} A_{1n} - -L^{-1} \sum_{n=0}^{\infty} A_{2n} \qquad (4.3)$$

with :

$$x_1 = \sum_{n=0}^{\infty} x_{1n}, \ \ x_2 = \sum_{n=0}^{\infty} x_{2n},$$

and A_{1n}, A_{2n} are the Adomian polynomials associated to the nonlinear terms :

$$\begin{array}{rcl} f_1(x_1) & = & \dfrac{V_1 x_1}{K_1 + x_1} \\ f_2(x_2) & = & \dfrac{V_2 x_2}{K_2 + x_2} \end{array}$$

By using the simple formula presented in the section 3.1 which gives A_{in}, for i=1,2, we have :

$$\begin{array}{l} A_{i0} = f_i(x_{i0}) = \frac{V_i}{K_i+x_{i0}} x_{i0} \\ A_{i1} = x_{i1} f_i^{(1)}(x_{i0}) = x_{i1} \frac{V_i K_i}{(K_i+x_{i0})^2} \\ A_{i2} = x_{i2} f_i^{(1)}(x_{i0}) + \frac{x_{i1}^2}{2!} f_i^{(2)}(x_{i0}) \\ \quad = x_{i2} \frac{V_i K_i}{(K_i+x_{i0})^2} - x_{i1}^2 \frac{V_i K_i}{(K_i+x_{i0})^3} \\ A_{i3} = x_{i3} f_i^{(1)}(x_{i0}) + x_{i1} x_{i2} f_i^{(2)}(x_{i0}) + \frac{x_{i1}^3}{3!} f_i^{(3)}(x_{i0}) \\ \quad = x_{i3} \frac{V_i K_i}{(K_i+x_{i0})^2} - 2 x_{i1} x_{i2} \frac{V_i K_i}{(K_i+x_{i0})^3} + x_{i1}^3 \frac{V_i K_i}{(K_i+x_{i0})^4} \\ \vdots \end{array}$$

and so on

The solutions approached with the order s for $x_1(t)$ and $x_2(t)$ are given by:

$$\phi_{1,s} = \sum_{n=0}^{s-1} x_{1n}, \ \ \phi_{2,s} = \sum_{n=0}^{s-1} x_{2n}$$

where the terms x_{1n}, x_{2n} are obtained from the following recursive scheme:

$$\left\{ \begin{array}{l} x_{10} = \beta, \ \ x_{20} = 0 \\ x_{1n} = K_e L^{-1} x_{1(n-1)} - L^{-1} A_{1(n-1)} + L^{-1} A_{2(n-1)} \\ x_{2n} = L^{-1} A_{1(n-1)} - L^{-1} A_{2(n-1)}, \qquad n = 1, 2, ... \end{array} \right. , \qquad (4.4)$$

The approximate solutions $x_1(t)$ and $x_2(t)$ of the system (4.1) with order 3 are:

$$x_1(t) \approx \phi_{1,3} = \sum_{n=0}^{2} x_{1n} = x_{10} + x_{11} + x_{12}$$

$$= \beta - \left(K_e \beta + \frac{V_1}{K_1+\beta} \beta\right) t +$$
$$\left(-K_e^2 \beta + \frac{V_1 \beta}{K_1+\beta} \left(K_e - \frac{K_1 K_e}{K_1+\beta} + \frac{V_1 K_1}{(K_1+\beta)^2} + \frac{V_2 K_2}{K_2^2}\right)\right) \frac{t^2}{2}$$

and

$$x_2(t) \approx \phi_{2,3} = \sum_{n=0}^{2} x_{2n} = x_{20} + x_{21} + x_{22}$$

$$= \frac{V_1}{K_1+\beta}\beta t + \frac{V_1\beta}{K_1+\beta}\left(\frac{K_1K_e}{(K_1+\beta)} - \frac{V_1K_1}{(K_1+\beta)^2} - \frac{V_2K_2}{K_2^2}\right)\frac{t^2}{2}$$

4.3 Numerical results

Our aim consists in identifying the parameters V_1, V_2, K_1, K_2 and K_e of the model (4.1) from the initial conditions and experimental data.

We supposed that the exact parameters and the initial conditions of the model are given as follows:

$$\begin{array}{lll} x_1(0) = 1 & V_1 = 0.32 & K_1 = 0.52 \\ x_2(0) = 0 & V_2 = 0.12 & K_2 = 0.13 \\ & & K_e = 0.004 \end{array}$$

When the parameters are fixed, the truncated solutions with order 4 are :

$$\begin{aligned} \phi_{14} &= \sum_{j=0}^{3} x_{2j} = x_{20} + x_{21} + x_{22} + x_{23} \\ &= 1. - .2145t + .1053t^2 - .1391t^3 \end{aligned}$$

$$\begin{aligned} \phi_{24} &= \sum_{j=0}^{3} x_{2j} = x_{20} + x_{21} + x_{22} + x_{23} \\ &= .2105t - .10489t^2 + .1389t^3 \end{aligned}$$

It is possible to measure the concentration of the substance in the first compartment $x_1(t)$, then :

$Z_1(t_j) = x_1(t_j)$

t_j : indicate the m times of measurements.

The solutions $x_1(t)$ and $x_2(t)$ are obtained from the resolution of the system (4.1) by the Adomian method truncated at order 4. these solutions explicitly depend on the parameters V_1, V_2, K_1, K_2 , K_e and t.

Therefore, the following functional has to be minimized :

$$J = \sum_{j=0}^{m} (x_1(t_j) - x_1^c(t_j))^2 \qquad (4.5)$$

where x_1^c is calculated from the resolution of system (4.1) when V_1, V_2, K_1, K_2, K_e and t are fixed.

The results of simulation are obtained by a classical Levenberg-Marquardt.optimization method

The following table summarizes the simulation results :

Parameters	Values
V_1	.3058
V_2	.1118
K_1	.5108
K_2	.1181
K_e	.0034
Value of J	0.0000708

Table 1.Values of the identified parameters

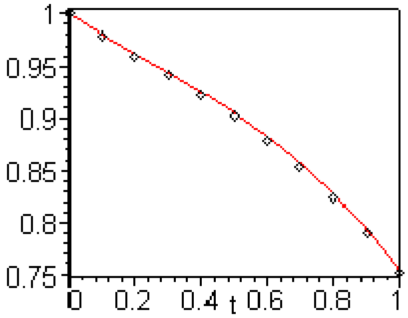

Figure 2. calculated and measured (points) 1st compartment

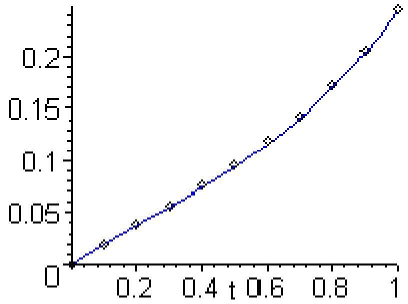

Figure 3.calculated and measured (points) 2nd compartment

We see on table 1 that the identified parameters are closed to the exact parameters. These parameters are deferred in the solutions of the compartmental model in order to compare them with the experimental data.

The comparison between the curves of the experimental data (points) and the simulated curves (lines) $x_1(t)$ and $x_2(t)$ is illustrated in Figures 2,3.

5. CONCLUSION

In this article, we have considered the problem of parameter identification in ordinary differential system. It is transformed into a classical optimization problem by the combination of the Adomian and Levenberg-Marquardt methods.

The resolution of the model by Adomian method allows to express the solution in explicit function of the unknown parameters. The error functional is then explicitly dependent on the unknows parameters and the Levenberg-Marquardt method is used for solving this optimization problem.

Application to parameter identification in an compartmental model shows that suggested methodology leads to interesting results and confirms those obtained by classical methods (Cherruault, 1998; Deeba and Khuri,1996).

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