ORIGINAL ARTICLE

Determination of parameters for Cauchy's problem for systems of ODEs with application to biological modelling

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Abstract—An inverse numerical method that estimates parameters of dynamic mathematical models given some information about unknown trajectories at some time is applied to examples taken from Biology and Ecology. The method consists of determining an overdetermined system of algebraic equations using the experimental data. The solution of the overdetermined system is then obtained using, for example the least-square method. To illustrate the effectiveness of the method an analysis of examples and a numerical example for the model that monitors the dynamics of HIV is presented.

Keywords-Inverse problem; least squares methods; parameter estimation; dymamic systems; predator-prey system;

I. INTRODUCTION

Function approximation on a fixed interval by means of an initial value problem of an ordinary differential equation with unknown coefficients and unknown initial values as presented by M Shatalov, I. Fedotov and S.V. Joubert in [7], is central to this study. In their paper al method to determine both the unknown coefficients and initial values of a dynamic system by minimizing a certain goal function is presented. In earlier collaborations Shatalov and Fedotov suggested the use of such an approach in identifying dynamic systems' parameters from experimental data, see [6].

Several other parameter estimation methods are presented in literature, for instance the stochastic models; the Bayesion approach, the Monte Carlo technique, the numerical method with combined Adomain/Alienor approach, the differential evolution (DE) and the hybrid Taguchi-differential evolution algorithm.

The method used is based on integrating both sides of equations of a dynamic system, and applying regression methods to the overdetermined system of linear algebraic equations with possible constraints. The unknown parameters and initial values can then be obtained using the method of least squares. In this paper, the proposed method gives parameter estimates that have a percentage relative error that is mostly less than 0.4% for artificially generated data and parameters that are in the expected range for real data.

As an illustration of the method of identifica-

tion, we present the analysis for problems from Biology and Ecology. The following mathematical models are taken as examples: model of a free population (with negligible mortality and with mortality different from zero), population with negligible mortality and unknown initial conditions, interspecies modifications of the Lotka-Voltera model and a model that monitors the dynamics of HIV. Numerical results with artificially generated data and real data is then given for the model that monitors the dynamics of HIV.

A. Inverse methods

The general approach to the inverse system identification of a n –dimensional parameter $\mathbf{a} \in \mathcal{A} \subset \mathbb{R}^n$, where $\mathcal{A}$ can coincide with $\mathbb{R}^n$ (no constrains between entries of $\mathbf{a}$) and $\mathcal{A}$ can be subset of $\mathbb{R}^n$ (there are constrains) in a system of ordinary differential equations of the following form

$$\dot{\mathbf{x}} = \mathbf{f}(t, \mathbf{x}, \mathbf{a}), \qquad (1)$$

where $\mathbf{x}$ is vector-function $[0, T] \ni t \longrightarrow \mathbf{x}(t) \in \mathbb{R}^m$ subject to experimental information concerning the values $\mathbf{x}(t_j)$ at the point $t_j \in [0, T]$ is known:

t_0	$\cdots$	t_j	$\cdots$	t_N
$\mathbf{x}_0 = \mathbf{x}(t_0)$	$\cdots$	$\mathbf{x}_j = \mathbf{x}(t_j)$	$\cdots$	$\mathbf{x}_N = \mathbf{x}(t_N)$

$$(2)$$

The general approach to find a solution of the formulated problem (1) consists of determining an overdetermined system of algebraic equations using the experimental data (2)

$$\mathbb{A}\mathbf{a} = \mathbf{h}, \qquad (3)$$

with respect to unknown vector $\mathbf{a}$. The solution of the system (3) is then obtained using any method of solution of the overdetermined system, for example the least-square method which minimize the difference $\mathbb{A}\mathbf{a} - \mathbf{h}$ using Euclidean metric. It is known that in this case (see, for example [5]), the solution of (3) can be obtained by solving the following system

$$\mathbb{A}^\top \mathbb{A}\mathbf{a} = \mathbb{A}^\top \mathbf{h}, \qquad (4)$$

to obtain $\mathbf{a}$.

II. MATHEMATICAL MODELS

1) Problem 1: Free population: Consider a single species that grows by sexual reproduction. Assume that the individuals move in the population like Brownian motion particles (or that the population is colonial), then the frequency of contact between the individuals is proportional to the squared population density [1]. Further assuming that mortality is different from zero and is independent of the population size, the scalar function $\mathbf{f}(t, x, \mathbf{a})$ is given by

$$\mathbf{f}(t, x, \mathbf{a}) = \frac{a_1 x^2}{x + a_2} - a_3 x, \qquad (5)$$

with the unknown vector $\mathbf{a} = (a_1, a_2, a_3)^\top \in \mathbb{R}^3$, $n = 3$, $m = 1$ and $a_1 > a_3$. The parameters a_1 and a_2 represent per capita birth rate (fecundity) and the population at which half of the females are able to reproduce, respectively. The mortality rate of the population is represented by a_3. The parameters a_1, a_2 and a_3 are positive and $\mathbf{x}(t) = x(t) \in \mathbb{R}$ is a scalar function. We also assume that x_0 is specified.

A special case arises if we assume that the population is of negligible mortality. That is, if $a_3 = 0$ the scalar function $\mathbf{f}(t, x, \mathbf{a})$ is then given as

$$\mathbf{f}(t, x, \mathbf{a}) = \frac{a_1 x^2}{x + a_2}. \qquad (6)$$

2) Problem 2: Population with negligible mortality and x_0 unknown: Here we consider the special case of Problem 1 (that is, if $a_3 = 0$) but with the value x_0 considered as an incorrect value which must be corrected. The statement of such a problem naturally appears since the initial value $x_0 = x(t_0)$ plays an important role, namely; it defines the Cauchy's problem for equation (1) and, secondly x_0 is included widely in computations below. Therefore if x_0 given from an experiment has low accuracy, it would be desirable to define this value with more accuracy.

3) Problem 3:Nonlinear predation at small prey population: In this problem we consider an interspecies modification of the Lotka-Voltera model

where there is a nonlinear predation at small prey population. Consider the system

$$\left.\begin{aligned}\dot{x} &= -a_1 \frac{x^2 y}{x^p + a_2} + a_3 x, \\ \dot{y} &= a_4 \frac{x^2 y}{x^p + a_2} - a_5 y,\end{aligned}\right\} \quad (7)$$

where $p = 1, 2$, $a_1, a_2, a_4 > 0$, $a_3, a_5 \geq 0$ and $n = 5$, $m = 2$. The prey and predator densities are represented by $x(t)$ and $y(t)$, respectively. In this model, the parameters a_1 represent the rate of the consumption of prey by the predator population, a_2 the prey population density at which the predator's consumption is half the maximum value [1], a_3 the prey's growth rate, a_4 is rate at which the prey contributes to the predator's growth rate and a_5 is the predator's death rate.

4) Problem 4: A model that monitors the dynamics of HIV: Consider the following two-dimensional model that monitors the dynamics of HIV. The model considers two sub-populations: HIV susceptible (x), the HIV infected population (y). The total population size is given by $N = x + y$. The model is described by

$$\left.\begin{aligned}\dot{x} &= -a_1 \frac{xy}{N} - a_2 x + a_3, \\ \dot{y} &= a_1 \frac{xy}{N} - a_4 y,\end{aligned}\right\} \quad (8)$$

where a_1, a_2, a_3 and a_4 are all positive constants model parameters. The parameter a_1 and a_2 denotes the average rate of infection by HIV, a_2 the natural cessation of sexual activity, a_3 the recruitment rate of susceptible and a_4 denotes the death rates of the infected population due to HIV. This model is a modified version of the three dimensional one by Gumel (see, [3]). The vector $\mathbf{a} = (a_1, a_2, a_3, a_4)^\mathsf{T} \in \mathbb{R}^4$ is unknown. Note that in this case $n = 4$ and $m = 2$.

III. CONSTRUCTION OF OVERDETERMINED SYSTEMS

Consider equation (1) where $\mathbf{f}$ is defined by

$$\mathbf{f}(t, x, \mathbf{a}) = \frac{a_1 x^2}{x + a_2}, \quad (9)$$

The resultant equation can be rewritten as

$$\dot{x}x + a_2 \dot{x} = a_1 x^2, \quad (10)$$

Integration of (10) with respect to t from t_0 to t_j $(j = 1, 2, \ldots, N)$ gives

$$-a_1 P_j + a_2 \Delta x_j = -\Delta h_j, \quad (11)$$

where

$$\left.\begin{aligned}\Delta x_j &= x(t_j) - x(t_0), \\ P_j &= \int_{t_0}^{t_j} x^2 dt, \\ \Delta h_j &= \left[\frac{1}{2}x^2(t_j) - \frac{1}{2}x^2(t_0)\right].\end{aligned}\right\} \quad (12)$$

The integral P_j can be calculated by using a quadrature rule, for example trapezoidal rule. Thus, System (3) is solved with

$$\mathbb{A} = \begin{pmatrix} -P_1 & \Delta x_1 \\ \vdots & \vdots \\ -P_N & \Delta x_N \end{pmatrix},$$

$$\mathbf{a} = \begin{pmatrix} a_1 \\ a_2 \end{pmatrix} \text{ and } \mathbf{h} = \begin{pmatrix} \Delta h_1 \\ \vdots \\ \Delta h_N \end{pmatrix}.$$

Now, suppose that (1) is defined as in (10) and the initial condition is unknown. Let us replace in (11) Δx_j and Δh_j by those given in (12):

$$-a_1 P_j + a_2 x_j - \left(a_2 x_0 + \frac{1}{2}x_0^2\right) = -h_j, \quad (13)$$

where $h_j = \frac{1}{2}x_j^2$ under the assumption that for P_j we use the old values of x_0 defined by (2) for $j = 1$ and for $j \geq 2$ the values of P_j are evaluated by an open quadrature rule. Formally speaking system (13) is nonlinear but setting

$$-\left(a_2 x_0 + \frac{1}{2}x_0^2\right) = a_3, \quad (14)$$

we obtain the linear system of the form (3) with

$$\mathbb{A} = \begin{pmatrix} -P_1 & x_1 & 1 \\ \vdots & \vdots & \vdots \\ -P_N & x_N & 1 \end{pmatrix},$$

$$\mathbf{a} = \begin{pmatrix} a_1 \\ a_2 \\ a_3 \end{pmatrix}, h = \begin{pmatrix} -h_1 \\ \vdots \\ -h_N \end{pmatrix}.$$

The value of x_0 can then be obtained from Equation (14).

Equation (1) with $\mathbf{f}$ defined by (5) can be written in the form

$$x\dot{x} + a_2\dot{x} = a_1x^2 - a_3x^2 - a_2a_3x, \qquad (15)$$

In contrast to (10) two supplementary terms $-a_3x^2$ and $-a_2a_3x$ arise. Integrating (15) we obtain

$$(a_1 - a_3)P_j - a_2x_j + \left(\frac{1}{2}x_0^2 + a_2x_0\right) - a_2a_3X_j = h_j, \quad (16)$$

where $X_j = \int_{t_0}^{t_j} xdt$. Introducing the new vector $\mathbf{b} = (b_1, b_2, b_3, b_4)$ where $b_1 = a_1 - a_2$, $b_2 = a_2$, $b_3 = \frac{1}{2}x_0^2 + a_2x_0$ and $b_4 = a_2a_3$ the system can be written in the form (3) where

$$\mathbb{A} = \begin{pmatrix} P_1 & -x_1 & 1 & -X_1 \\ \vdots & \vdots & \vdots & \vdots \\ P_N & -x_N & 1 & -X_N \end{pmatrix},$$

$$\mathbf{b} = \begin{pmatrix} b_1 \\ b_2 \\ b_3 \\ b_4 \end{pmatrix} \text{ and } h = \begin{pmatrix} h_1 \\ \vdots \\ h_N \end{pmatrix}$$

In other words, we obtain the following system

$$b_1P_j - b_2x_j + b_3 - b_4X_j = h_j, \ (j = 1, \ldots N) \quad (17)$$

Since the Jacobian is $\frac{\partial b}{\partial a} = a_2 + x_0 \neq 0$, we can find the vector $\mathbf{b}$ and hence the unknown vector $\mathbf{a}$.

The system (7) of an interspecies modification of the Lotka–Voltera model for nonlinear predation at small prey population can be written as

$$\left.\begin{array}{c} \dot{x}x^p + a_2\dot{x} = -a_1x^2y + a_3x^{p+1} + a_2a_3x \\ \dot{y}x^p + a_2\dot{y} = a_4x^2y - a_5yx^p - a_2a_5y \end{array}\right\} \quad (18)$$

where $p = 1, 2$, $a_1, a_2, a_4 > 0$ and $a_3, a_5 \geq 0$. Integrating (18) we obtain

$$\left.\begin{array}{c} \Delta h_j = -a_1Z_j - a_2\Delta x_j + a_3P_j + a_2a_3X_j \\ S_j = -a_2\Delta y_j + a_4Z_j - a_5Q_j - a_2a_5Y_j \end{array}\right\} \quad (19)$$

where, using the same notation as in (12):

$$\left.\begin{array}{c} \Delta x_j = x(t_j) - x(t_0), \\ P_j = \int_{t_0}^{t_j} x^2dt, \\ \Delta h_j = \left[\frac{1}{2}x^2(t_j) - \frac{1}{2}x^2(t_0)\right]. \end{array}\right\} \quad (20)$$

and

$$X_j = \int_{t_0}^{t_j} x(t)dt, Y_j = \int_{t_0}^{t_j} y(t)dt, \quad (21)$$

$$Z_j = \int_{t_0}^{t_j} y(t)x^2(t)dt, Q_j = \int_{t_0}^{t_j} x^p(t)y(t)dt,$$

$$S_j = \int_{t_0}^{t_j} x^p(t)dt, \quad (22)$$

with $j = 1\ldots N$. Introducing the new vector $\mathbf{b} = (b_1, b_2, b_3, b_4, b_5, b_6, b_7)^\top$ where $b_1 = a_1$, $b_2 = a_2$, $b_3 = a_3$, $b_4 = a_4$, $b_5 = a_5$, $b_6 = a_2a_3$ and $b_7 = a_2a_5$, we write the System (19) in the form (3) where

$$\mathbb{A} = \begin{pmatrix} -Z_1 & -\Delta x_1 & P_1 & 0 & 0 & X_1 & 0 \\ -Z_2 & -\Delta x_2 & P_2 & 0 & 0 & X_2 & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ -Z_N & -\Delta x_N & P_N & 0 & 0 & X_N & 0 \\ 0 & -\Delta y_1 & 0 & Z_1 & -Q_1 & 0 & -Y_1 \\ 0 & -\Delta y_2 & 0 & Z_2 & -Q_2 & 0 & -Y_2 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ 0 & -\Delta y_N & 0 & Z_N & -Q_N & 0 & -Y_N \end{pmatrix}$$

and

$$\mathbf{h} = (\Delta h_1, \ldots, \Delta h_N, S_1, \ldots, S_N).$$

In other words, we obtain the following system of $2N$ equations with seven unknowns:

$$\left.\begin{array}{c} \Delta h_j = -b_1Z_j - b_2\Delta x_j + b_3P_j + b_6X_j, \\ S_j = -b_2\Delta y_j + b_4Z_j - b_5Q_j - b_7Y_j, \end{array}\right\} \quad (23)$$

subject to

$$\left.\begin{array}{c} -b_6 + b_2b_3 = 0, \\ -b_7 + b_2b_5 = 0. \end{array}\right\} \quad (24)$$

To evaluate numerically the right hand side of S_j can be considered as the Riemann–Stietjes integral $S_j = \int_0^{t_j} x^p(t)dy(t)$, (see, for example Dragomir and Fedotov [3]). Otherwise this integral can be computed using numerical differentiation.

Another approach to construct the over deter-mined system is generally appealing since the system obtained is simpler than (19). This method is possible due to the special form of the system (7); namely the system can be written as

$$\left.\begin{array}{l} \dot{x} = -a_1 g(x, y, a_2) + a_3 x, \\ \dot{y} = a_4 g(x, y, a_2) - a_5 y, \end{array}\right\} \quad (25)$$

where $g(x, y, a_2) = \frac{x^2 y}{x^p + a_2}$. Eliminating $g(x, y, a_2)$ we get

$$\dot{y} + c_1 y + c_2 \dot{x} - c_3 x = 0, \quad (26)$$

where

$$a_5 = c_1, \frac{a_4}{a_1} = c_2 \text{ and } \frac{a_4 a_3}{a_1} = c_3. \quad (27)$$

Using the integration techniques that we discussed earlier, we determine the vector $\mathbf{c} = (c_1, c_2, c_3)^\top$ and hence $\frac{c_3}{c_2} = a_3$, which will be considered as unknown in the next step.

Multiplying the first equation of (7) by $(x^p + a_2)$, we obtain

$$x^p \dot{x} + a_2 \dot{x} = -a_1 x^2 y + a_3 x^{p+1} + a_2 a_3 x. \quad (28)$$

After integration of (28) the overdetermined system can be written as

$$a_1 Z_j + a_2 (\Delta x_j - a_3 X_j) = -\Delta h_j + a_3 P_j, \quad (29)$$

where $j = 1, \ldots, N$, and Z_j, P_j, X_j, Δh_j, Δx_j were defined in (20) and (22). The unknown parameters a_1 and a_2 may then be determined from equation (29) and a_4 and a_5 from (27).

A. A model that monitors the dynamics of HIV

The system (8) can be written as

$$\left.\begin{array}{l} \dot{x} = -a_1 P_j - a_2 X_j + a_3, \\ \dot{y} = a_1 P_j - a_4 Y_j. \end{array}\right\} \quad (30)$$

where

$$\Delta x_j = x(t_j) - x(t_0), \ \Delta y_j = y(t_j) - y(t_0),$$

$$P_j = \int_0^{t_j} \frac{x(t) y(t)}{x(t) + y(t)} dt,$$

$$X_j = \int_0^{t_j} x(t) dt \text{ and } Y_j = \int_0^{t_j} y(t) dt.$$

The system (30) can be written in the form (3) with

$$\mathbb{A} = \begin{pmatrix} -P_1 & -X_1 & 1 & 0 \\ -P_1 & -X_2 & 1 & 0 \\ \vdots & \vdots & \vdots & \vdots \\ P_1 & 0 & 0 & -Y_1 \\ P_1 & 0 & 0 & -Y_2 \\ \vdots & \vdots & \vdots & \vdots \end{pmatrix}$$

and

$$\mathbf{h} = (\Delta x_1, \Delta x_2, \ldots, \Delta y_1, \Delta y_2, \ldots)^\top$$

IV. NUMERICAL EXTRACTION OF MODEL PARAMETERS

In order to illustrate the effectiveness of the method the parameter identification of the system (8) is presented. Using parameter values from Gumel [4], we generate points of solutions of the system (8) by the adaptive Runge-Kutta method. A mathematical software *Mathcad* was used for the adaptive Runge-Kutta method and for the in-tegration by quadratue rules. These solutions are then perturbed by a normal distribution with mean $\bar{x}$ and standard deviation $\delta = 0.5$ and further taken as "experimental data".

Furthermore, system (8) is studied in the context of the Gauteng Province, South Africa. Data used in the numerical simulation is obtained from the Acturial Society of South Africa (ASSA) (see [2]) HIV prevalence estimates. The data is compiled from the population sensus, antenatal survey and registered deaths [2]. The ASSA 2003 tables gives the population N and the number infected with HIV y. From the relationship

$$N = x + y, \quad (31)$$

we obtain the susceptible population x as

$$x = N - y. \quad (32)$$

The results given in Table 2 below, show a comparison of the parameters used (from Gumel [4]), the estimated parameters and the percentage error given by $||\alpha - \tilde{\alpha}||/||\alpha|| \times 100$.

Table 2: Problem 4: The parameter estimates and errors.

Parameter	Actual value α	Estimated value $\tilde{\alpha}$	% Error
a_1	0.24	0.2404	0.375
a_2	0.03125	0.0313	0.16
a_3	2000	2000	0.000
a_4	0.531	0.532	0.16

Applying the parameter estimation method in the case of the transmission dynamics of HIV in the Gauteng Province, South Africa the following estimates are obtained:

$$\begin{pmatrix} a_1 \\ a_2 \\ a_3 \\ a_4 \end{pmatrix} = \begin{pmatrix} 0.393 \\ 0.049 \\ 565143 \\ 0.149 \end{pmatrix}.$$

Figures 1 and 2 below show the comparison of the estimated solutions with the "experimental data" and the absolute error in the decimal logarithmic scale. The initial value problem was solved with the new coefficients and old initial conditions.
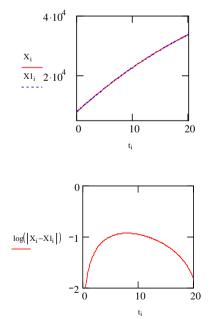

Fig. 2.   Comparison of the estimated solutions, Y_i, with the "experimental data" and the absolute error in the decimal logarithmic scale.
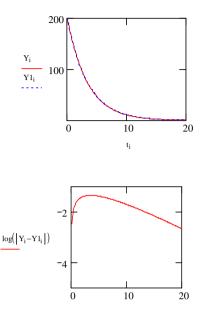

Fig. 1.   Comparison of the estimated solutions, X_i, with the "experimental data" and the absolute error in the decimal logarithmic scale.

From the comparison of the parameters in Table 2, Figures 1 and 2, it can be seen that the estimated parameters are close enough to the actual values. The estimated parameters of dynamic HIV mathematical models for the Gauteng Province are all nonnegative and also in the expected ranges.

V. CONCLUSION AND SUGGESTIONS FOR FURTHER RESEARCH

A method for estimating parameters of dynamic mathematical models given some information about unknown trajectories at some time, by Shatalov, Fedotov and Joubert [7], was applied to problems from Biology and Ecology. In Problem 2 where the initial value was assumed to be unknown with accuracy, the method was applied to find this value. To illustrate the efficiency of the method, a numerical example for the model that monitors the dynamics of HIV was presented. The estimated parameters for the artificially generated data are close enough to the actual parameter values and for the Gauteng Province the estimated parameters

are in the expected ranges.

The method for estimating parameters values could be improved by incorporating a suitable penalty term that minimizes the error caused by numerical quadrature and high observational noise levels in the real data. An improvement of the method will be investigated in future studies.

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