

Identification of HIV Dynamic System in the Case of Incomplete Experimental Data

P. Mathye*, I. Fedotov* and M. Shatalov*[†]

*Department of Mathematics and Statistics

Tshwane University of Technology, Pretoria, South Africa

Email: mathyeph@gmail.com; FedotovI@tut.ac.za; ShatalovM@tut.ac.za

[†]Manufacturing and Materials

Council for Scientific and Industrial Research (CSIR), Pretoria, South Africa

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Abstract—In this paper we apply an inverse method that estimates parameters of deterministic mathematical models to an HIV model. We consider the case where experimental data concerning the values of some variables is incomplete or unknown. The objective is to estimate the parameters and to restore the information concerning the behaviour of the incomplete data. The method is based on integrating both sides of equations of a dynamic system, and applying some minimization methods (for example least square method). Such an approach was first suggested in [7] and [8]. Analysis of the HIV model and a corresponding numerical example is presented.

Keywords—Inverse problem, least square methods, parameter estimation, HIV model, incomplete data.

I. INTRODUCTION

Several HIV vaccine models have been developed over the recent years (e.g., [1] and [4]). These models describe and predict the potential epidemiological impact of vaccination. For the models to give insight into the transmission dynamics of HIV, model parameters are of great significance. The parameters for these model are estimated based on HIV seroprevalence data. Most often the

data on testing and treatment history is incomplete (missing). This barrier can be as a result of the stigma attached to and the discrimination against people living with HIV and AIDS. In studying the dynamics of this world pandemic, the availability of recorded valuable data is thus a challenge.

The proposed method is based on eliminating the unknown (missing) state variables from the original system algebraically. The resultant system is then used to estimate the unknown model parameters. The discussion on the identification of dynamic systems with incomplete data and restoring the missing data is elementary and can be suitable for students in basic courses on dynamic systems identification.

A four dimensional deterministic model for transmission dynamics of HIV in the presence of a preventive vaccine is considered as an example. The model is identified in the cases of incomplete data. It is assumed that the population sizes of individuals infected by the wild type strain and by both the wild and the vaccine strains is unknown.

For this study, the data is artificially generated from the given parameters from Gumel's paper [4]. We then 'forget' about the these parameters and

part of the generated data. Applying the proposed method we estimate the parameters and then restore the 'forgotten' data. The performance of the proposed method with real life data remains to be investigated in the future.

The remainder of the paper is structured as follows. Section II briefly outlines the formulation of the problem. Section III discusses the inverse method used in solving the problem. Section IV gives a description of the mathematical model that is used as an example. Sections V, VI and VII discusses the method of solution, parameter estimations and a numerical simulation respectively. Finally, concluding remarks are made in Section VIII.

II. PROBLEM FORMULATION

Consider a system of ordinary differential equations of the form

$$\frac{dx}{dt} = f(t, x, y, \theta), \tag{1}$$

$$\frac{dy}{dt} = g(t, x, y, \theta), \tag{2}$$

where (x, y) is a vector-function $[0, T] \ni t \rightarrow (x, y) \in \mathbf{R}^m \times \mathbf{R}^n$ subject to experimental information concerning the values of $x(t_j)$ at points $t_j \in [0, T]$, ($t_j = 0, 1, \dots, N$) are known. Now, suppose the information concerning the values $y(t_j)$ is either incomplete or unknown. It may be, for example, some statistical data of the form:

Table 1: Experimental data.

t_0	\dots	t_j	\dots	t_N
$\mathbf{x}_0 = \mathbf{x}(t_0)$	\dots	$\mathbf{x}_j = \mathbf{x}(t_j)$	\dots	$\mathbf{x}_N = \mathbf{x}(t_N)$
$\mathbf{y}_0 = ?$	\dots	$\mathbf{y}_j = ?$	\dots	$\mathbf{y}_N = ?$

The parameter θ is l dimensional, that is $\theta \in \mathbf{A} \subset R^l$ where \mathbf{A} can coincide with R^l (no constrains between the entries of θ) and \mathbf{A} can be subset of \mathbf{R}^n (there are constraints).

The purpose of this study is to identify the model parameters θ and to restore (recover) the information concerning the behaviour of the incomplete or unknown of $y(t)$.

III. INVERSE METHOD

Solve (1) with respect to y to get

$$y = h \left(t, x, \frac{dx}{dt}, \theta \right). \tag{3}$$

Substitute y by $h(t, x, \frac{dx}{dt}, \theta)$ in (2) to obtain

$$\frac{d}{dt} h \left(t, x, \frac{dx}{dt}, \theta \right) = g \left(t, x, h \left(t, x, \frac{dx}{dt}, \theta \right), \theta \right). \tag{4}$$

For this study consider the case where (4) is linear with respect to the coefficients $c_k(\theta)$:

$$\frac{d}{dt} h_0 \left(t, x, \frac{dx}{dt} \right) = \sum_{k=1}^N c_k(\theta) h_k \left(t, x, \frac{dx}{dt}, \frac{d^2x}{dt^2} \right), \tag{5}$$

where $c_k : \mathbf{A} \ni \theta \mapsto c_k(\theta)$ is a scalar function.

The parameter identification for the model is based on the direct integration of the dynamic system with posterior application of a quadrature rule (for example, the adaptive trapezoidal rule). Some minimization methods (for example, least squares method (see for example [5])) is then applied to find the estimates.

Integrating (5) twice with respect to t from t_0 to t_i , ($i = 1, 2, \dots, N$) yields:

$$\mathbb{A}\alpha - \mathbf{h} = 0 \tag{6}$$

where

$$\mathbb{A} = \int_{t_0}^{t_i} (t_i - \tau) h_k \left(\tau, x(\tau), \frac{dx(\tau)}{d\tau}, \frac{d^2x(\tau)}{d\tau^2} \right) d\tau,$$

$$\alpha = c_k(\theta), \text{ and } \mathbf{h} = \int_{t_0}^{t_i} h_0 \left(\tau, x(\tau), \frac{dx(\tau)}{d\tau} \right) d\tau.$$

The values of the unknown parameters α in (6) can be determined using method of least squares.

Suppose there are some constraints to be satisfied amongst the parameters α . The problem is thus to minimize the Lagrangian

$$L(\alpha, \lambda) = (\mathbb{A}\alpha - \mathbf{h})^\top (\mathbb{A}\alpha - \mathbf{h}) + 2\lambda^\top (\mathbf{C}\alpha - \mathbf{b}), \tag{7}$$

where λ is the Lagrange multiplier and

$$\mathbf{C}\alpha = \mathbf{b} \tag{8}$$

the constraints that must be satisfied.

The necessary conditions for a constrained minimum at α^* is the existence of vector λ^* such that

$$\nabla_{\alpha}L(\alpha^*, \lambda^*) = (\alpha^*)^T \mathbb{A}^T \mathbb{A} - \mathbf{h}^T \mathbb{A} + (\lambda^*)^T \mathbf{C} = 0 \tag{9}$$

and

$$\nabla_{\lambda}L(\alpha^*, \lambda^*) = \mathbf{C}\alpha^* - \mathbf{b} = 0. \tag{10}$$

That is, we obtain the system:

$$\begin{pmatrix} \mathbb{A}^T \mathbb{A} & \mathbf{C}^T \\ \mathbf{C} & 0 \end{pmatrix} \begin{pmatrix} \alpha^* \\ \lambda^* \end{pmatrix} = \begin{pmatrix} \mathbb{A} \\ \mathbf{b} \end{pmatrix} \tag{11}$$

where the matrix:

$$\begin{pmatrix} \mathbb{A}^T \mathbb{A} & \mathbf{C}^T \\ \mathbf{C} & 0 \end{pmatrix} \tag{12}$$

is a square matrix with a non-zero determinant. The solution to the linear system (11) is given by

$$\begin{pmatrix} \alpha^* \\ \lambda^* \end{pmatrix} = \begin{pmatrix} \mathbb{A}^T \mathbb{A} & \mathbf{C}^T \\ \mathbf{C} & 0 \end{pmatrix}^{-1} \begin{pmatrix} \mathbb{A} \\ \mathbf{b} \end{pmatrix}. \tag{13}$$

With the the parameters $\alpha = c_k(\theta)$ known, the information concerning the behaviour of the incomplete or unknown state variable $y(t)$ can now be restored from (3).

IV. MATHEMATICAL MODEL

The model monitors four populations namely: HIV susceptible (X), unvaccinated individuals infected by wild type (Y_w), individuals uninfected by the wild type but infected by the vaccine strain (Y_v) and individuals dually-infected with the vaccine and wild strain (Y_{vw}). The total (sexual activity) population size is $N = N(t) = X + Y_v + Y_w + Y_{vw}$. The model is a modified version of those studied by Blower and Gumel in [1] and [4] respectively.

A. HIV susceptible (X)

Individuals are recruited, by birth or immigration, into this population at the rate p_1 . This population is reduced by the natural cessation of sexual activity at a rate μ , infection with the vaccine strain at the rate α_v , the wild strain and

infected by the dual infected individuals at the rate α_w . In this case it is assumed that the dual infected individuals can only transmit the wild strain. Thus,

$$\frac{dX}{dt} = p_1 - \mu_1 X - \alpha_v \frac{XY_v}{N} - \alpha_w \frac{X(Y_w + Y_{vw})}{N} \tag{14}$$

B. Individuals uninfected by the wild type but infected by the vaccine strain (Y_v)

This population increases through the new susceptible being vaccinated at the rate p_2 and by infection by the vaccine strain at the rate α_v . It is decreased by infection with the wild strain and infected by the dual infected individuals at the rate γ . The parameter γ is of the form $(1 - \psi)c\beta_w$ where ψ is the degree of protection that the vaccine provides against infection with the wild-type strain, c the number of sexual partners and β_w the rate of infection by the wild-type strain. The population is further decreased by natural cessation from sexual activity and by death induced by infection with the wild strain at a rate μ_2 .

$$\frac{dY_v}{dt} = p_2 + \alpha_v \frac{XY_v}{N} - \gamma \frac{Y_v(Y_w + Y_{vw})}{N} - \mu_2 Y_v, \tag{15}$$

C. Unvaccinated individuals infected by wild type (Y_w)

This population increases through the susceptible being infected by the wild strain and by the dual infected individuals at the rate α_w . The population is decreased by natural cessation from sexual activity and by death induced by infection with the wild strain at a rate μ_3 .

$$\frac{dY_w}{dt} = \alpha_w \frac{X(Y_w + Y_{vw})}{N} - \mu_3 Y_w, \tag{16}$$

D. Individuals dually-infected with the vaccine and wild strain (Y_{vw})

This population increases through infection with the wild strain and infected by the dual infected individuals at the rate γ . The population is decreased by natural cessation from sexual activity

and by death induced by infection with the wild strain at a rate μ_4 .

$$\frac{dY_{vw}}{dt} = \gamma \frac{Y_v(Y_w + Y_{vw})}{N} - \mu_4 Y_{vw}. \quad (17)$$

The complete model is thus:

$$\left. \begin{aligned} \frac{dX}{dt} &= p_1 - \mu_1 X - \alpha_v \frac{XY_v}{N} - \alpha_w \frac{X(Y_w + Y_{vw})}{N}, \\ \frac{dY_v}{dt} &= p_2 + \alpha_v \frac{XY_v}{N} - \gamma \frac{Y_v(Y_w + Y_{vw})}{N} - \mu_2 Y_v, \\ \frac{dY_w}{dt} &= \alpha_w \frac{X(Y_w + Y_{vw})}{N} - \mu_3 Y_w, \\ \frac{dY_{vw}}{dt} &= \gamma \frac{Y_v(Y_w + Y_{vw})}{N} - \mu_4 Y_{vw}, \end{aligned} \right\} \quad (18)$$

Adding all the equations of the system (18) gives

$$\frac{dN}{dt} = p_1 + p_2 - \mu_1 X - \mu_2 Y_v - \mu_3 Y_w - \mu_4 Y_{vw} \quad (19)$$

All model parameters are nonnegative.

V. METHOD OF SOLUTION

Suppose that $N = N(t)$, $X = X(t)$, $Y_v = Y_v(t)$ are known and that Y_w and Y_{vw} are unknown. From

$$N = X + Y_v + Y_w + Y_{vw}, \quad (20)$$

it is clear that the sum $Y_w + Y_{vw}$ is also known. In fact,

$$Y_w + Y_{vw} = N - X - Y_v, \quad (21)$$

Let

$$Z = Y_w + Y_{vw}. \quad (22)$$

The system with equations (14, 15, 16) and (17) then becomes

$$\frac{dX}{dt} = p_1 - \mu_1 X - \alpha_v \frac{XY_v}{N} - \alpha_w \frac{XZ}{N}, \quad (23)$$

$$\frac{dY_v}{dt} = p_2 + \alpha_v \frac{XY_v}{N} - \gamma \frac{Y_v Z}{N} - \mu_2 Y_v, \quad (24)$$

$$\frac{dY_w}{dt} = \alpha_w \frac{XZ}{N} - \mu_3 Y_w, \quad (25)$$

$$\frac{dY_{vw}}{dt} = \gamma \frac{Y_v Z}{N} - \mu_4 Y_{vw}. \quad (26)$$

By using the inverse method the parameters in Equations (23) and (24) can be determined. That is, parameters $p_1, p_2, \mu_1, \mu_2, \alpha_v, \alpha_w$ and γ can now be considered known. Adding Equations (25) and (26) and rearranging yields

$$\mu_3 Y_w + \mu_4 Y_{vw} = \alpha_w \frac{XZ}{N} + \gamma \frac{Y_v Z}{N} - \frac{dZ}{dt}. \quad (27)$$

Let

$$M = \alpha_w \frac{XZ}{N} + \gamma \frac{Y_v Z}{N} - \frac{dZ}{dt}, \quad (28)$$

Equation (27) then becomes

$$\mu_3 Y_w + \mu_4 Y_{vw} = M. \quad (29)$$

From (22) and (29), form the system

$$Y_w + Y_{vw} = Z, \quad (30)$$

$$\mu_3 Y_w + \mu_4 Y_{vw} = M. \quad (31)$$

Solving this system we obtain

$$Y_w = \frac{\mu_4 Z - M}{\Delta} \quad (32)$$

and

$$Y_{vw} = \frac{M - \mu_3 Z}{\Delta} \quad (33)$$

where

$$\Delta = \mu_4 - \mu_3. \quad (34)$$

Differentiating Equation (32) yields,

$$\frac{dY_w}{dt} = \frac{\mu_4}{\Delta} \frac{dZ}{dt} - \frac{1}{\Delta} \frac{dM}{dt} \quad (35)$$

Equating (25) and (35) yields,

$$\frac{\mu_4}{\Delta} \frac{dZ}{dt} - \frac{1}{\Delta} \frac{dM}{dt} = \alpha_w \frac{XZ}{N} - \mu_3 Y_w \quad (36)$$

Simplifying

$$\frac{\mu_4}{\Delta} \frac{dZ}{dt} - \frac{1}{\Delta} \frac{dM}{dt} = \alpha_w \frac{XZ}{N} - \frac{\mu_3 \mu_4}{\Delta} Z + \frac{\mu_3}{\Delta} M \quad (37)$$

Rearranging gives,

$$\frac{\mu_4}{\Delta} \frac{dZ}{dt} - \frac{1}{\Delta} \frac{dM}{dt} = \alpha_w \frac{XZ}{N} - \frac{\mu_3 \mu_4}{\Delta} Z + \frac{\mu_3}{\Delta} M \quad (38)$$

For convenience,

$$a_1 \frac{dZ}{dt} + a_2 \frac{dM}{dt} + a_3 M + a_4 Z + F = 0 \quad (39)$$

where

$$a_1 = \frac{\mu_4}{\Delta}, a_2 = -\frac{1}{\Delta}, a_3 = -\frac{\mu_3}{\Delta},$$

$$a_4 = \frac{\mu_3\mu_4}{\Delta} \text{ and } F = -\alpha_w \frac{XZ}{N}.$$

The relationship between the parameters a_1, a_2, a_3 and a_4 is given by the following constrains

$$a_1 + a_3 = 1, \tag{40}$$

and

$$a_1a_3 - a_2a_4 = 0. \tag{41}$$

Suppose that the parameters a_1, a_2, a_3 and a_4 are obtained, then

$$\mu_4 = -\frac{a_1}{a_2} \text{ and } \mu_3 = \frac{a_1 - 1}{a_2}.$$

Finally, with Z, M, μ_3 and μ_4 known, the unknown variables Y_w and Y_{vw} can be restored from (32) and (33).

VI. PARAMETER ESTIMATION

Recall (23),

$$\frac{dX}{dt} = p_1 - \mu_1 X - \alpha_v \frac{XY_v}{N} - \alpha_w \frac{XZ}{N}, \tag{42}$$

Integrating both sides with respect to t from t_0 to t_i , gives

$$\Delta X_i = p_1 t_i - \mu_1 J_i - \alpha_v K_i - \alpha_w P_i, \tag{43}$$

where the integrals

$$\Delta X_i = \int_{t_0}^{t_i} \frac{dX(\tau)}{dt} d\tau, K_i = \int_{t_0}^{t_i} \frac{X(\tau)Y_v(\tau)}{N(\tau)} d\tau,$$

$$J_i = \int_{t_0}^{t_i} X(\tau) d\tau \text{ and } P_i = \int_{t_0}^{t_i} \frac{X(\tau)Z(\tau)}{N(\tau)} d\tau,$$

are evaluated using the trapezoidal rules. The system (43) is of the form $\mathbb{A}\mathbf{a} = \mathbf{h}$, where

$$\mathbb{A} = \begin{pmatrix} t_1 & -J_1 & -K & -P_1 \\ \vdots & \vdots & \vdots & \vdots \\ t_N & -J_N & -K & -P_N \end{pmatrix},$$

$$\mathbf{a} = \begin{pmatrix} p_1 \\ \mu_1 \\ \alpha_v \\ \alpha_w \end{pmatrix} \text{ and } \mathbf{h} = \begin{pmatrix} \Delta X_1 \\ \vdots \\ \Delta X_N \end{pmatrix}.$$

Solving the regression problem

$$\text{minimize} \|\mathbb{A}\mathbf{a} - \mathbf{h}\|_2 \tag{44}$$

using least squares method we obtain the estimate $\tilde{\mathbf{a}}$. Thus the parameters p_1, μ_1, α_v and α_w are found.

Now recall (24),

$$\frac{dY_v}{dt} = p_2 + \alpha_v \frac{XY_v}{N} - \gamma \frac{Y_v Z}{N} - \mu_2 Y_v, \tag{45}$$

Similarly, integrating both sides of (45) yields

$$\Delta Y_v = p_2 t_i + \alpha_v K_i - \gamma Q_i - \mu_2 I_i, \tag{46}$$

where

$$\Delta Y_v = \int_{t_0}^{t_i} \frac{dY_v(\tau)}{dt} d\tau, K_i = \int_{t_0}^{t_i} \frac{X(\tau)Y_v(\tau)}{N(\tau)} d\tau,$$

$$Q_i = \int_{t_0}^{t_i} \frac{X(\tau)Z(\tau)}{N(\tau)} d\tau \text{ and } I_i = \int_{t_0}^{t_i} Y(\tau) d\tau.$$

The system (46) is of the form $\mathbb{A}\mathbf{a} = \mathbf{h}$, where

$$\mathbb{A} = \begin{pmatrix} t_1 & -Q & -I_1 \\ \vdots & \vdots & \vdots \\ t_N & -Q & -I_N \end{pmatrix},$$

$$\mathbf{a} = \begin{pmatrix} p_2 \\ \gamma \\ \mu_2 \end{pmatrix} \text{ and } \mathbf{h} = \begin{pmatrix} \Delta Y_1 - \alpha_v K_1 \\ \vdots \\ \Delta Y_N - \alpha_v K_N \end{pmatrix}.$$

Solving the regression problem

$$\text{minimize} \|\mathbb{A}\mathbf{a} - \mathbf{h}\|_2 \tag{47}$$

using least squares method we obtain the estimate $\tilde{\mathbf{a}}$. Thus the parameters γ, μ_2 and p_2 are found.

Lastly recall (39),

$$a_1 \frac{dZ}{dt} + a_2 \frac{dM}{dt} + a_3 M + a_4 Z + F = 0 \tag{48}$$

subject to the constraints

$$a_1 + a_3 - 1 = 0 \text{ and } a_1 a_3 - a_2 a_4 = 0. \tag{49}$$

Integrating both sides of (48) with respect to t from t_0 to t_i , gives

$$a_1 \Delta Z_i + a_2 \Delta M_i + a_3 U_i + a_4 W_i + \Delta F_i = 0 \tag{50}$$

where

$$\Delta Z_i = \int_{t_0}^{t_i} \frac{dZ(\tau)}{dt} \tau, \Delta M_i = \int_{t_0}^{t_i} \frac{dM(\tau)}{dt} \tau,$$

$$U_i = \int_{t_0}^{t_i} M(\tau) d\tau, W_i = \int_{t_0}^{t_i} Z(\tau) d\tau \text{ and}$$

$$\Delta F_i = -\alpha_w \int_{t_0}^{t_i} \frac{X(\tau)Y_v(\tau)}{N(\tau)} d\tau.$$

To find the unknown parameters a_1, a_2, a_3 and a_4 , the Lagrangian L_3 can be written with one constraint as

$$L_3(\mathbf{a}) = \frac{1}{2} \sum_{i=0}^n \left[a_1(Z_i - U_i) + a_2M_i + a_4W_i + (\Delta F_i + U_i) \right]^2 + \lambda(a_1 - a_1^2 - a_2a_4) \tag{51}$$

where λ_1 is the Lagrange multipliers and $\mathbf{a} = (a_1, a_2, a_4)$. To minimize the least-square functional L_3 , set

$$\frac{\partial L_3}{\partial a_1} = \frac{\partial L_3}{\partial a_2} = \frac{\partial L_3}{\partial a_4} = \frac{\partial L_3}{\partial \lambda} = 0. \tag{52}$$

The resultant system of equations is then solved using the method proposed by Fedotov *et al* [3] for finding roots of transcendental algebraic equations. The parameter value a_3 is finally obtained from $a_3 = 1 - a_1$.

VII. NUMERICAL SIMULATION

In order to illustrate the effectiveness of the method a numerical example is presented. The system (18) is solved numerically by Adams method using a mathematical software *Mathcad*. The following parameter values and initial conditions from Gumel [4] are used.

$$p_1 = 400, p_2 = 1.6 \times 10^3, \alpha_v = 2.5, \alpha_w = 2.25,$$

$$\gamma = 0.9\mu_1 = 0.031, \mu_2 = 0.0331, \mu_3 = 0.0281,$$

$$\mu_4 = 0.231, X^0 = 8 \times 10^4, Y_v^0 = 2000,$$

$$Y_w^0 = 8000, Y_{vw}^0 = 8000$$

The solution vectors obtained are taken as experimental data. We then assume that the experimental data concerning the state variables Y_w, Y_{vw} and

the model parameter values to be unknown. The method discussed in the sections above is then applied to estimate the model parameter values and restore the vectors Y_w and Y_{vw} .

The results given in the table below, show a comparison of the actual parameters used, the estimated parameters and the percentage error given by $\|\alpha - \tilde{\alpha}\|/\|\alpha\| \times 100$.

Table 2: The parameter estimates and errors.

Parameter	Actual value	Estimated value	%Error
	α	$\tilde{\alpha}$	
p_1	400	400.142	0.035
p_2	1.6×10^3	1.6×10^3	0.000
μ_1	0.031	0.031	0.000
μ_2	0.331	0.326	1.511
μ_3	0.281	0.282	0.356
μ_4	0.231	0.229	0.866
α_v	2.5	2.495	0.200
α_w	2.25	2.25	0.000
γ	0.9	0.905	0.556

From Table 2 it can be seen that the estimate parameters are close enough to the actual ones. The percentage relative errors for this estimates are mostly low than 1 %.

Let $Y_w := (U^{<3>})_i$ and $(Y_{vw} := U^{<4>})_i$ be the solution vectors obtained from solving the system (18) and YY_{w_i} and YY_{vw_i} the estimated vectors. From Figures 1 and 2, it can be seen that the estimated vectors, YY_{w_i} and YY_{vw_i} are within acceptable limit of error.

VIII. CONCLUSION

In this paper a method to identify dynamic mathematical models with incomplete (missing) data was discussed. The method was applied to a four dimensional HIV vaccination model. The model parameters and the unknown (missing) data were restored.

The proposed method gives a direct hint of what is necessary to measure in practice and what data can be analytically restored (found).

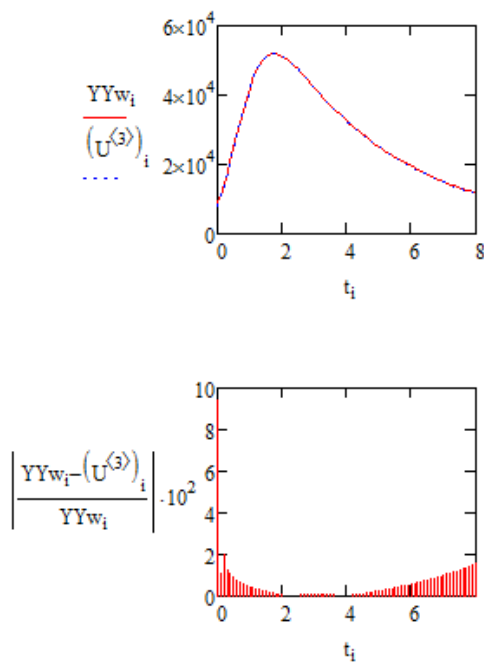


Fig. 1. Comparison of the estimated solutions, YYw_i , with the “experimental data”, $U_i^{<3>}$, and the percentage relative error.

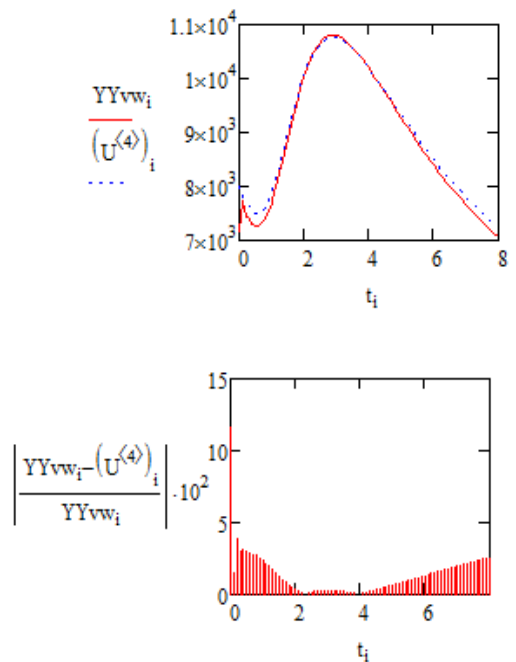


Fig. 2. Comparison of the estimated solutions, $YYvw_i$, with the “experimental data”, $U_i^{<4>}$, and the percentage relative error.

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