

Parameter identification in mathematical model of HIV infection with drug therapy

Master Project

Abstract The goal of this Master project is development of the method for the solution of a parameter identification problem for ODE system which describes dynamics of primary HIV infection with drug therapy. Algorithm for the solution of the problem should be formulated and numerically tested.

1 Statements of the forward model and parameter identification problem

Let us denote by $\Omega_T = [0, T]$ the time domain for $T > 0$, where T is the final observation time in some mathematical model. We will consider a first order system of ordinary differential equations (ODE) in the general form

$$\frac{du}{dt} = f(u(t), \eta(t)), \quad t \in [0, T] \quad (1)$$

$$u(0) = u^0. \quad (2)$$

Here, $u(t) \in C^2(\Omega_T)$, $u(t) = (u_1(t), \dots, u_n(t))^T$ are functions depending of time $t \in \Omega_T$. The right hand side of equation (1) depends also on the parameter $\eta(t) \in C(\Omega_T)$. Further we assume that $f \in C^1(\Omega_T)$ is Lipschitz continuous and such that

$$f(u(t), \eta(t)) = (f_1(u_1, \dots, u_n, \eta(t)), \dots, f_n(u_1, \dots, u_n, \eta(t)))^T.$$

In our mathematical model the function $\eta(t) \in C(\Omega_T)$ represents the drug efficiency and belongs to the set of admissible functions M_η :

$$M_\eta = \{\eta(t) : \eta(t) \in (0, 1) \text{ in } \Omega_T, \eta(t) = 0 \text{ outside of } \Omega_T\}. \quad (3)$$

In this paper we consider the mathematical model for the effect of Reverse Transcriptase Inhibitor (RTI) on the dynamics of HIV infection proposed in [1]:

$$\begin{aligned}
\dot{u}_1 &= s - ku_1u_4 - \mu u_1 + (\eta\alpha + b)u_2, \\
\dot{u}_2 &= ku_1u_4 - (\mu_1 + \alpha + b)u_2, \\
\dot{u}_3 &= (1 - \eta)\alpha u_2 - \delta u_3, \\
\dot{u}_4 &= N\delta u_3 - cu_4,
\end{aligned} \tag{4}$$

which also can be presented in the form (1) with $u = u(t) = (u_1(t), u_2(t), u_3(t), u_4(t))^T$, $\dot{u} = \frac{\partial u}{\partial t}$ and $f = (f_1, f_2, f_3, f_4)^T = (f_1(u_1, \dots, u_4, \eta(t)), \dots, f_4(u_1, \dots, u_4, \eta(t)))^T$, where

$$\begin{aligned}
f_1 &= s - ku_1u_4 - \mu u_1 + (\eta\alpha + b)u_2, \\
f_2 &= ku_1u_4 - (\mu_1 + \alpha + b)u_2, \\
f_3 &= (1 - \eta)\alpha u_2 - \delta u_3, \\
f_4 &= N\delta u_3 - cu_4.
\end{aligned} \tag{5}$$

In system (4) function u_1 represents uninfected target cells population, u_2 – infected target cells before Reverse Transcription (pre-RT class), u_3 – infected target cells in which Reverse Transcription is completed and they are capable of producing virus (post-RT class), u_4 is virus population function. The initial data for system (4) are chosen as one of the having two steady states accordingly to [1]:

$$\begin{aligned}
u_1(0) = u_1^0 &= 300 \text{ mm}^{-3}, \quad u_2(0) = u_2^0 = 10 \text{ mm}^{-3}, \\
u_3(0) = u_3^0 &= 10 \text{ mm}^{-3}, \quad u_4(0) = u_4^0 = 10 \text{ mm}^{-3}.
\end{aligned} \tag{6}$$

We assume that all parameters in system (4) are known from the literature: see [1] and references therein, except the parameter η which describes efficiency of the drug and should be determined. The typical values of the vector of parameters $\{s, \mu, k, \mu_1, \alpha, b, \delta, c, N\}$ are given in Table 1.

Table 1

Parameter	Value	Units	Description
s	10	$\text{mm}^{-3}\text{day}^{-1}$	inflow rate of T cells
μ	0.01	day^{-1}	natural death rate of T cells
k	2.4E-5	$\text{mm}^3\text{day}^{-1}$	interaction-infection rate of T cells
μ_1	0.015	day^{-1}	death rate of infected cells
α	0.4	day^{-1}	transition rate from pre-RT infected T cells class to post-RT class
b	0.05	day^{-1}	reverting rate of infected cells return to uninfected class
δ	0.26	day^{-1}	death rate of actively infected cells
c	2.4	day^{-1}	clearance rate of virus
N	1000	vir/cell	total number of viral particles produced by an infected cell

We solve the above problem on the time interval $[0, T]$, but assume that observations are known on the more narrow interval $[T_1, T_2] \subset [0, T]$.

Parameter Identification Problem (PIP). Let conditions (3) hold and set of parameters $\{s, \mu, k, \mu_1, \alpha, b, \delta, c, N\}$ in system (4) are known. Assume that the function $\eta(t)$ is unknown inside the domain Ω_T . Determine this function for $t \in \Omega_T$, assuming that the following function $g(t)$ is known

$$u(t) = g(t), \quad t \in [T_1, T_2], 0 < T_1 < T_2 < T. \quad (7)$$

The function $g(t)$ represents observations of the function $u(t)$ inside the observation interval $[T_1, T_2]$.

References

1. P.K. Srivastava, M. Banerjee, and P. Chandra, Modeling the drug therapy for HIV infection, *Journal of Biological Systems*, 17(2), 213-223, 2009.