HBV Epidemic Control Using Time-Varying Sliding Mode Control Method

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Abstract

Hepatitis B virus (HBV) infection is one of the life-threatening diseases due to causing cirrhosis and liver cancer in the infected person. Setting the policy to control the HBV epidemic is an important issue that can be achieved by using feedback controller design procedure through the compartment model. In this article, the sliding mode controller with a time-varying sliding surface was utilized to set the multiple measures control policy for controlling the HBV epidemic. The stability of the control HBV epidemic system was examined. The simulation of the control system was conducted to confirm the feasibility of applying the time-varying sliding mode controller for setting the HBV control policy. The simulation results showed that the designed control policy could drive the target subpopulation to the desired levels. The convergence rate of the control HBV system could be improved. Thus, the time-varying sliding mode controller is a feasible approach to set the measures for controlling the HBV epidemic.

Keywords: Hepatitis B, Epidemic system, Compartment model, Time-varying sliding mode control.

1. Introduction

Hepatitis B is a viral infection causing high morbidity and mortality rate from both chronic and acute liver infection[1-3]. This virus is hepatotropic DNA virus in the family of Hepadnaviridae[1, 3, 4]. The spread of hepatitis B is caused by both vertical (perinatal) and horizontal transmission routes through infected body fluids. After

being exposed to the HBV, the disease can develop either acute or chronic hepatitis B[2,7,8]. Acute hepatitis B patients typically have the symptoms such as fever, fatigue, dark urine, and jaundice. Chronic infection refers to the long-term inflammation leading to liver damage. This damage causes cirrhosis and liver cancer which are deadly diseases[3, 6]. According to WHO[2], in 2019 almost three million people were chronic hepatitis B, and more than 800,000 people were dead. A feasible treatment for acute HBV patients is required to provide the comfort and to balance nutrient and fluids of the patients[2,6]. For the chronic HBV patients, the purpose of treatment is to reduce the viral load to prevent cirrhosis and liver cancer. This can be achieved by using the immunomodulatory and antiviral drugs[2,3,8]. The vaccine is an important preventive measure of the hepatitis B in susceptible individuals since it can provide high effective protection and safe[2,5]. For epidemic control, other measures such as treatment for HBV patients, screening and diagnosis of high-risk population can also be included in the control policy isolation[3,9,10].

Many mathematical models representing the dynamic of HBV epidemic have been developed based on different compartment models[10-17]. With these compartment models, control policies including measures such as vaccination, and treatment and isolation controls can be drawn by using dynamic optimization approach according to Pontryagin's maximum principle[10-17]. Another potential approach is to use feedback control approach to set the policy[18-30]. Feedback control could deal with the uncertainties and disturbances which occur in the system. Moreover, it is an efficient approach to set the policy in an analytical form[31]. Applying feedback control to define the measures of the control policy showed the feasibility and the efficiency in the previous studies of this approach[18-30]. Sliding mode control (SMC) is a robust feedback control which has been employed to control various nonlinear dynamical systems[32-34]. Moreover, the SMC method has been applied to synthesize the control policy for the biological systems such as ecosystems and epidemic models[18,24,27-30, 35-36]. For the epidemic systems, the sliding mode control was applied to set the control policy of the epidemic systems in the form of a compartment model[18,24,27-30]. The SMC with an integral sliding surface can eliminate the steady state errors of the control systems as applied to control various engineering systems[37,40,41]. Specifically, this SMC has been used for controlling epidemic systems[18, 27]. Ibeas et al. [18,27] used the integral sliding mode control to set the vaccination control policy with robustness for handling the uncertainties of the model parameters. The improvement in terms of the convergence rate of the sliding mode control systems can be achieved by using the time-varying sliding mode control (TVSMC) where the constant sliding surface is replaced by the time-varying sliding surface. As shown in Refs. 37-40, 42-44, the time varying sliding surface is defined such that the initial condition is located on or crossed by the sliding surface. The development and applications of the TVSMC method can be found in the literature[37-40, 42-44].

Even though the feasibility of applying feedback control for controlling the HBV system was presented in Ref. 21, the robustness of the control policy was not presented. As integral sliding mode control can provide the robustness and the concept of time-varying sliding surface can improve the convergence rate of a control system, this study focuses on studying of applying time-varying sliding mode control (TVSMC) with the integral sliding surface to set the HBV control policy with multiple measures based on the compartment model. To the best of authors' knowledge, setting the HBV control policy with multiple measures using the time-varying sliding mode controller design procedure has not been presented.

The rest of this paper consists of four following sections. The mathematical model of the HBV system is presented in Section 2. Section 3 provides the details of the time varying sliding mode controller design for setting the control policy. The simulation of the control system including a simulation example and simulation results is presented in Section 4. The conclusion is stated in Section 5.

2. Model of HBV Epidemic System

The mathematical model presented by Ullah et al. [17] was used for setting the control policy based on the time-varying sliding mode controller design procedure. This model consists of six subpopulations which are susceptible (S), exposed (E), acute infected (A), carrier (C), hospitalized (H), and recovered (R) individuals. The mathematical model from Ref. 17 is presented in (1):

$$\left.\begin{aligned}
\dot{S}(t) &= b-\psi bC-dS-(A+\mu C)\beta S(1-u_1)\\
\dot{E}(t) &= (A+\mu C)\beta S(1-u_1)+\psi bC-dE-\delta E\\
\dot{A}(t) &= \delta E-h_1A-dA-d_AA-\gamma A-Au_2\\
\dot{C}(t) &= \gamma A-dC-d_CC-h_2C-Cu_2\\
\dot{H}(t) &= h_2C+h_1A-(d+\xi)H+Au_2+Cu_2-Hu_3\\
\dot{R}(t) &= \xi H-dR+Hu_3
\end{aligned}\right\}. \quad (1)$$

The parameters of this HBV system are presented as follows [17]: the rate b and the rate d represent the birth and natural death rates of the population in the HBV system, respectively. The rate h_1 and the rate h_2 refer to the rates of acute and carrier individuals who were hospitalized, respectively. The coefficient β is the transmission coefficient. The parameter δ defines the flow rate of changing from the exposed subpopulation to the carrier subpopulation. The mortality rate caused by acute infection is denoted by d_A. The carrier individual death rate is defined by d_C. The rate γ defines the rate of changing from the acute subpopulation to the carrier subpopulation. The recovery rate is defined by ξ. The rate of the unimmunized children who were born to the carrier mothers is denoted by ψ. The parameter μ is the carriers' infectiousness caused by acute infection. The first control measure, $u_1(t)$, is the isolation measure for preventing transmission between infected and uninfected individuals. The second measure, $u_2(t)$, refers the human intervention which consists of public education and awareness of sending the infected persons to the hospital. The third measure, $u_3(t)$, represents the treatment for the hospitalized individuals. All of these measures are constrained as $0 \le u_1, u_2, u_3 \le 1$ [17]. The total population of the HBV epidemic system is defined by $N(t) = S(t) + E(t) + A(t) + C(t) + H(t) + R(t)$.

After defining subpopulations of the HBV system in (1) as $S = x_1$, $E = x_2$ $A = x_3$, $C = x_4$, $H = x_5$, and $R = x_6$, the input-output model of the system in (1) can then be expressed as (2):

$$\dot{x} = f(x) + g(x)u, \quad (2)$$

where $x = [x_1\ x_2\ x_3\ x_4\ x_5\ x_6]^T$, $u = [u_1\ u_2\ u_3]^T$,

$$f(x) = \begin{bmatrix} f_1\\ f_2\\ f_3\\ f_4\\ f_5\\ f_6 \end{bmatrix} = \begin{bmatrix} b-\psi bx_4-dx_1-(x_3+\mu x_4)\beta x_1\\ (x_3+\mu x_4)\beta x_1+\psi bx_4-dx_2-\delta x_2\\ \delta x_2-h_1x_3-dx_3-d_Ax_3-\gamma x_3\\ \gamma x_3-dx_4-d_Cx_4-h_2x_4\\ h_2x_4+h_1x_3-(d+\xi)x_5\\ \xi x_5-dx_6 \end{bmatrix}, \text{ and}$$

$$g(x) = \begin{bmatrix} g_{11} & 0 & 0\\ g_{21} & 0 & 0\\ 0 & g_{32} & 0\\ 0 & g_{42} & 0\\ 0 & g_{52} & g_{53}\\ 0 & 0 & g_{63} \end{bmatrix} = \begin{bmatrix} (x_3+\mu x_4)\beta x_1 & 0 & 0\\ -(x_3+\mu x_4)\beta x_1 & 0 & 0\\ 0 & -x_3 & 0\\ 0 & -x_4 & 0\\ 0 & (x_3+x_4) & -x_5\\ 0 & 0 & x_5 \end{bmatrix}.$$

3. Controller Design

3.1. *Time-varying Sliding Mode Controller Design*

Based on the control objective in Ref. 17, the control objective of TVSMC controller design procedure is defined to manipulate the exposed, acute, hospitalized subpopulations to the desired values. The error corresponding to the control objective is defined as (3):

$$\{e_2 = x_2 - x_{2r},\ e_3 = x_3 - x_{3r}\ e_5 = x_5 - x_{5r}\}. \quad (3)$$

where x_{2r}, x_{3r}, and x_{5r} are the desired values and set as $x_{2r} = x_{3r} = x_{5r} = 0$ [17].

Based on Refs. 32-34, 37, 39-41, and 45, the design procedure of synergetic control is presented as follows.

It is referred to Refs. 37, 39, and 40, the time-varying integral sliding surface are defined as

$$\left.\begin{aligned}
s_2 &= e_2 + k_{I2}\int_0^t e_2(\tau)d\tau + \phi_2\\
s_3 &= e_3 + k_{I3}\int_0^t e_3(\tau)d\tau + \phi_3\\
s_5 &= e_5 + k_{I5}\int_0^t e_5(\tau)d\tau + \phi_5
\end{aligned}\right\}, \quad (4)$$

where $\phi_2 = m_{c2}e^{-t/n_{c2}}$, $\phi_3 = m_{c3}e^{-t/n_{c3}}$, and $\phi_5 = m_{c5}e^{-t/n_{c5}}$. The controller parameters $k_{I2}, k_{I3}, k_{I5}, n_{c2}, n_{c3} n_{c5}$ are real positive numbers. The coefficients, m_{c2}, m_{c3}, and m_{c5} are defined based on the sliding surfaces at the initial time, $s_2(0) = s_3(0) = s_5(0) = 0$. This yields that $m_{c2} = -e_2(0)$, $m_{c3} = -e_3(0)$, and $m_{c5} = -e_5(0)$ [37, 39, 40].

The classical constant plus proportional reaching law[45] or exponential reaching law[34] was utilized in this study as (5):

$$\left.\begin{aligned}\dot{s}_2 &= -k_{sw2}sign(s_2) - k_{p2}s_2 \triangleq \theta_2\\ \dot{s}_3 &= -k_{sw3}sign(s_3) - k_{p3}s_3 \triangleq \theta_3\\ \dot{s}_5 &= -k_{sw5}sign(s_5) - k_{p5}s_5 \triangleq \theta_5\end{aligned}\right\}. \quad (5)$$

Substituting sliding surfaces (4) into the set of reaching laws (5) yields

$$\left.\begin{aligned}\dot{e}_2 + k_{I2}e_2 + \dot{\phi}_2 &= \theta_2\\ \dot{e}_3 + k_{I3}e_3 + \dot{\phi}_3 &= \theta_3\\ \dot{e}_5 + k_{I5}e_5 + \dot{\phi}_5 &= \theta_5\end{aligned}\right\}.. \quad (6)$$

From the HBV dynamic system, (6) can be obtained as

$$\begin{aligned}&f_2(x) - (x_3 + \mu x_4)\beta x_1 u_1 - \dot{x}_{2r} + k_{I2}e_2 + \dot{\phi}_2 = \theta_2\\ &f_3(x) - x_3 u_2 - \dot{x}_{3r} + k_{I3}e_3 + \dot{\phi}_3 = \theta_3\\ &f_5(x) + (x_3 + x_4)u_2 - x_5 u_3 - \dot{x}_{5r} + k_{I3}e_3 + \dot{\phi}_3 = \theta_3.\end{aligned} \quad (7)$$

The control measures can be obtained as (8):

$$\begin{bmatrix}u_1\\ u_2\\ u_3\end{bmatrix} = \begin{bmatrix}-(x_3+\mu x_4)\beta x_1 & 0 & 0\\ 0 & -x_3 & 0\\ 0 & (x_3+x_4) & -x_5\end{bmatrix}^{-1}\begin{bmatrix}-\varphi_2 + \theta_2\\ -\varphi_3 + \theta_3\\ -\varphi_5 + \theta_5\end{bmatrix}, \quad (8)$$

where $\varphi_2 = f_2(x) - \dot{x}_{2r} + k_{I2}e_2 + \dot{\phi}_2$,

$\varphi_3 = f_3(x) - \dot{x}_{3r} + k_{I3}e_3 + \dot{\phi}_3$,

and $\varphi_5 = f_5(x) - \dot{x}_{5r} + k_{I5}e_5 + \dot{\phi}_5$.

3.2. *Proof of Stability*

According to Liu and Wang[34], the stability of the control HBV system can be investigated based on the Lyapunov stability. The Lyapunov function of the control HBV system is defined as (9):

$$V = 0.5s_2^2 + 0.5s_3^2 + 0.5s_5^2. \quad (9)$$

The derivative of the Lyapunov function is obtained as (10):

$$\begin{aligned}\dot{V} &= s_2\dot{s}_2 + s_3\dot{s}_3 + s_5\dot{s}_5\\ \dot{V} &= s_2[\dot{e}_2 + k_{I2}e_2 + \dot{\phi}_2] + s_3[\dot{e}_3 + k_{I3}e_3 + \dot{\phi}_3]\\ &\quad + s_5[\dot{e}_5 + k_{I5}e_5 + \dot{\phi}_5]\end{aligned} \quad (10)$$

Assuming that there are external bounded disturbances in the $\dot{x}_2$, $\dot{x}_3$, and $\dot{x}_5$ of (2), $\dot{V}$ in (10) is obtained as (11):

$$\begin{aligned}\dot{V} &= s_2[f_2(x) - (x_3 + \mu x_4)\beta x_1 u_1 + d_2(t) - \dot{x}_{2r} + k_{I2}e_2 + \dot{\phi}_2]\\ &\quad + s_3[f_3(x) - x_3 u_2 + d_3(t) - \dot{x}_{3r} + k_{I3}e_3 + \dot{\phi}_3]\\ &\quad + s_5[f_5(x) + (x_3 + x_4)u_2 - x_5 u_3 + d_5(t) - \dot{x}_{5r} + k_{I5}e_5 + \dot{\phi}_5]\\ \dot{V} &= \begin{bmatrix}s_2 & s_3 & s_5\end{bmatrix}\left(\begin{bmatrix}\varphi_2\\ \varphi_3\\ \varphi_5\end{bmatrix} + \begin{bmatrix}d_2(t)\\ d_3(t)\\ d_5(t)\end{bmatrix}\right.\\ &\quad \left. + \begin{bmatrix}-(x_3+\mu x_4)\beta x_1 & 0 & 0\\ 0 & -x_3 & 0\\ 0 & (x_3+x_4) & -x_5\end{bmatrix}\begin{bmatrix}u_1\\ u_2\\ u_3\end{bmatrix}\right)\end{aligned} \quad (11)$$

where $|d_2(t)| \le D_2$, $|d_3(t)| \le D_3$, and $|d_5(t)| \le D_5$ for $D_2, D_3, D_5 \ge 0$

Substituting (8) into (11) yields

$$\begin{aligned}\dot{V} &= \begin{bmatrix}s_2 & s_3 & s_5\end{bmatrix}\left(\begin{bmatrix}\varphi_2\\ \varphi_3\\ \varphi_5\end{bmatrix} + \begin{bmatrix}d_2(t)\\ d_3(t)\\ d_5(t)\end{bmatrix} + \begin{bmatrix}-\varphi_2 + \theta_2\\ -\varphi_3 + \theta_3\\ -\varphi_5 + \theta_5\end{bmatrix}\right)\\ &= \begin{bmatrix}s_2 & s_3 & s_5\end{bmatrix}\begin{bmatrix}-k_{sw2}sign(s_2) - k_{p2}s_2 + d_2(t)\\ -k_{sw3}sign(s_3) - k_{p3}s_3 + d_3(t)\\ -k_{sw5}sign(s_5) - k_{p5}s_5 + d_5(t)\end{bmatrix}.\\ \dot{V} &= -k_{p2}s_2^2 - k_{p3}s_3^2 - k_{p5}s_5^2 + s_2d_2(t) + s_3d_3(t) + s_5d_5(t)\\ &\quad - k_{sw2}|s_2| - k_{sw3}|s_3| - k_{sw5}|s_5|.\\ \dot{V} &\le -k_{p2}s_2^2 - k_{p3}s_3^2 - k_{p5}s_5^2 + |s_2|D_2 + |s_3|D_3 + |s_5|D_5\\ &\quad - k_{sw2}|s_2| - k_{sw3}|s_3| - k_{sw5}|s_5|\end{aligned} \quad (12)$$

If k_{sw2}, k_{sw3}, and k_{sw5} are chosen as $k_{sw2} = D_2 + \kappa_2$, $k_{sw3} = D_3 + \kappa_3$, and $k_{sw5} = D_5 + \kappa_5$, where κ_2, κ_3, $\kappa_5 > 0$, it can be obtained that

$$\begin{aligned}\dot{V} &\le -k_{p2}s_2^2 - k_{p3}s_3^2 - k_{p5}s_5^2\\ &\quad - \kappa_2|s_2| - \kappa_3|s_3| - \kappa_5|s_5| < 0.\end{aligned} \quad (13)$$

The inequality (13) implies that control measures $u_1(t)$, $u_2(t)$, and $u_3(t)$, can stabilize the control HBV system under the bounded disturbances. Based on (4), at $s_2 = s_3 = s_5 = 0$, the error e_2, e_3, and e_5, approach to zero as time increases. Thus, the target subpopulations of the control system can track the reference signals[37,38].

4. Simulation

The control measures synthesized in (8) were applied to the simulation example of the HBV system in Section 4.1. The simulation results are presented in Section 4.2.

4.1. *Simulation Example*

The HBV epidemic system in (2) with system parameters from Ref. 17 was used as a simulation example to show the feasibility of applying TVSMC controller design procedure to set the HBV epidemic control policy. The parameters of the system and the initial conditions presented in Ref. 17 are as follows: $b = 0.5$, $d = 0.008$, $h_1 = 0.2$, $\beta = 0.5$ ($0 \le \beta \le 1$), $\delta = 6$, $\gamma = 0.5$ ($0 \le \gamma \le 1$), $\mu = 0.5$ ($0 \le \mu \le 1$), $d_C = 0.005$, $d_A = 0.005$, $\delta = 6$, $\xi = 0.1$, and $\psi = 0.2$. The initial condition was assumed based on information provided in Ref. 17 and denoted as $x(0) = [180, 40, 18, 10, 20, 0]^T$. The incremental time step is 0.01 year. The initial time and final time were t=0 day and t=10 years respectively[17]. The Runge-Kutta method was used for numerical integration.

The robustness of the control policy was demonstrated by adding the bounded disturbance into the rate of change of the hospitalized subpopulation as (14):

$$d(t) = [0 \; d_3(t) \; 0]^T, \tag{14}$$

where $d_3(t)$ is defined as (15):

$$d_3(t) = \begin{cases} 0, t < 2 \\ d_m \sin(\omega_d t) + \varphi_d, \; 2 \le t \le 4, \\ 0, t > 4 \end{cases} \tag{15}$$

where $d_m = 0.5$, $\omega_d = 20\pi$, and $\varphi_d = 2.5$.

The controller parameters for this simulation example are set as follows: $k_{I2} = 0.01$, $k_{I3} = 0.01$, $k_{I5} = 0.01$. $k_{p2} = 2$, $k_{p3} = 2$, $k_{p5} = 2$, $k_{sw2} = 4$, $k_{sw3} = 4$, $k_{sw5} = 4$ $n_{c2} = n_{c3} = n_{c5} = 0.2$.

In order to show the capability of the TVSMC policy in terms of convergence, the simulation results of the designed control policy were compared with those of the SMC policy using the sliding surface in (4) with $\phi_2 = \phi_3 = \phi_5 = 0$.

4.2. *Simulation Results*

The time responses of interested subpopulations which are the exposed, acute, hospitalized under TVSMC and SMC policies are shown in Fig. 1. The control measures of both TVSMC and SMC polices are presented in Fig. 2. The exposed, acute, and hospitalized subpopulations of the TVSMC policy converge to the zero faster than those the SMC policy as shown in Fig. 1. The isolation measures of both TVSMC and SMC start from certain levels slightly below their maximum levels. Then, they increase rapidly to their maximum levels and stay on these levels for rest of time as shown Fig 2. In Fig. 2, the human intervention and the treatment measure of both policies are at the maximum level from the beginning until the end of time. It is clear that the policy synthesized by TVSMC design procedure can suppress the HBV epidemic. Also, improvement of the convergence rate of the control system can be achieved.

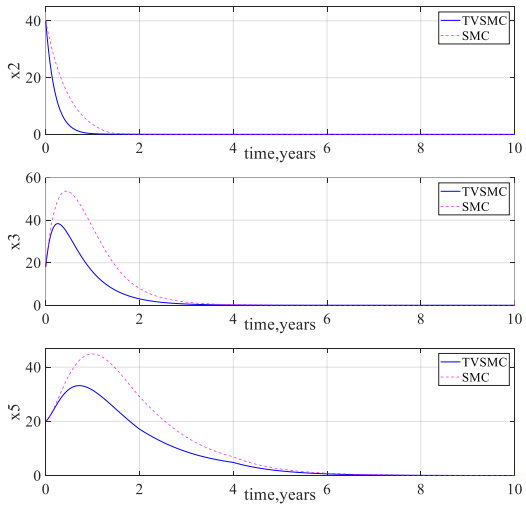

Fig. 1. Time response of interested subpopulations including exposed (x_2), acute (x_3), and hospitalized (x_5) subpopulations.

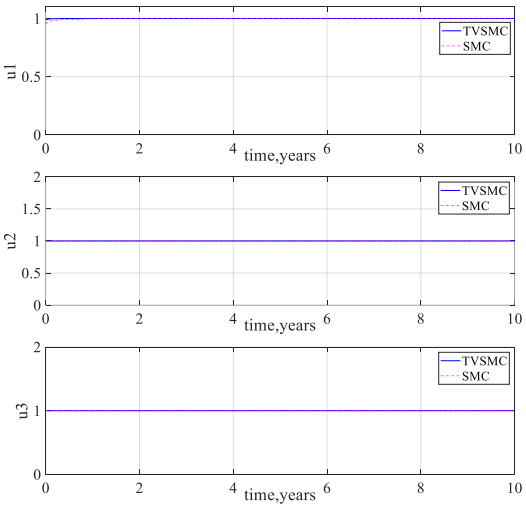

Fig. 2. Control measures including isolation (u_1), human intervention (u_2), and treatment for hospitalized individuals (u_3).

5. Conclusion

In this study, the time-varying sliding mode control was applied to set the HBV control policy with multiple measures. The HBV system can be stabilized by the synthesized control policy under the bounded disturbances. Thus, the epidemic of HBV was eradicated. The simulation results confirmed that the subpopulations according to the control objective were driven to the desired levels. According to the simulation results, the improvement of the convergence rate of the HBV control system could be achieved by using the time-varying sliding mode control policy. Therefore, it is appropriate to utilize the time-varying sliding mode controller design procedure for setting the HBV control policy.

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