Passivity-based Design of Controller and Observer for a Class of Nonlinear Systems with Application to Hepatitis B Disease

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Abstract: In this paper, a strictly passive formulation has been developed to design a passive state-observer for both time-invariant and time-varying Lipschitz nonlinear systems. During this formulation, a convergence and strictly passive state-observer is provided to have passive closed-loop system. Some definitions and charts are defined here for time-invariant and time-varying systems in different scenarios. A new interconnection between passivity of subsystems and passivity/stability of the closed-loop system has been introduced from a different point of view. All definitions are organized based on the systematic method called "virtually Euler-Lagrange" form of passivation. Utilizing this form and theses definitions, make the design process simpler and straightforward, while, some conditions of design will be released due to using these definitions. The designed controller/observer has been applied to control the hepatitis B virus infection disease. The reliability of the proposed definitions are examined by using MATLAB/SIMULINK, while, the results demonstrate the ability and power of this novel approach.

Keywords: passivity-based design, state-observer, adaptive control, Lipschitz nonlinear systems, virtually Euler-Lagrange, hepatitis B virus.

1. Introduction

Passivity-based method is a powerful and well-known nonlinear tool to design and analysis of systems. Passive systems are a class of dynamical systems where the exchanging energy with the environment plays a major role in them. Besides, the feature of "passivity" is preserved in feedback connection [1]. The concept of passivity-based control (PBC) has been established for the first time in [2]. A systematic method for passivation of non-Euler-Lagrange systems is proposed in [3]. Passivity-based observer and controller have been designed in some PHD dissertations [4,5]. This well-established technique has been used to control/observe in a wide range of systems, including biologic [3,6], robot manipulators [7,8], real-time systems [9] induction motors [10,11], swash-mass helicopter and pendulum [12,13], and so on.

The field of observer design has been activated for many years. Typically, observers are designed to estimate the system states based on the available measurements, which are called state-observer (SO). Passivity concepts for state-observer design is pursued in [4,14]. For the set-valued Lur'e systems, a convergence and passive SO is designed in [15]. Observer-based robust control has been used for multi-agent systems in [16]. For a class of Lipschitz nonlinear systems, some important issues are stated for observer design in papers [17-18].Also, for one-sided Lipschitz systems some nonlinear observer is designed [19]. Some authors study on the interval observer design [20-22].

The hepatitis B virus (HBV) viral disease has always been a serious infectious disease all around the world. This dangerous virus is almost classified into two phases, acute and chronic. The chronic phase of HBV causes the liver cirrhosis and liver cancer to progress [23]. In this phase, most of the sick people must carry on drug consumption up to the end of life [24]. Authors in [3], [25] and [26], respectively apply adaptive passivity-based control (APBC), Kalman-filter and Lyapunov-based methods in order to treat infected body. Some adaptive approaches are employed in [27,28], while in [29], a robust method is applied to handle the parametric and non-parametric uncertainties in HBV model. In this paper, the Lyapunov direct method (based on [30]) has been exerted as the compared method. Besides, due to the importance of controlling human diseases, many authors have worked in various biological fields, such as Ebola [31] and Corona virus[32].

According to availability of variable states and system parameters, four scenarios will be appeared. Some definitions are presented based on papers [3] for time-invariant and time-varying nonlinear Lipschitz systems. These definitions have been provided to analyze and design

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control systems in the sense of passivity. Using these definitions, link the passivity of several subsystems to the stability of total closed-loop system in a new point of view. In this regard, some charts are structured here to pursue the issue in the best way. All of the definitions are shaped based on virtually Euler-Lagrange form (VEL-form) of passivation in order to possess the advantages of this form. During using these definitions, one will face into less complexity and more speed in passivity-based analysis and control. The capability of proposed definitions is confirmed by applying them on the HBV viral disease model.

This paper is structured as follows. Some definitions are presented in Section 2 for both time-varying and time-invariant systems. Moreover, two charts are provided to better follow up the design process. The under-study time-invariant HBV model has been investigated in Section 3. While, in Section 4, the controller/observer is designed for HBV model in different scenarios for the passivity-based method and compared method. The simulation results have been depicted for 1000-days drug therapy in Section 5, and finally, Section 6 has been dedicated to the conclusion of the paper.

2. Definitions

Nonlinear Time-Varying Systems:

Consider the nonlinear time-varying system

$$\begin{cases} \dot{X} = f(t, X, \varpi); \ t \in \mathbb{R}, & X \in \mathbb{R}^n, & \varpi \in \\ Y = CX; & Y \in \mathbb{R}^p \end{cases} \quad (1)$$

where f is piecewise continuous in t and Lipchitz (at least locally)in (X, ϖ) and $f(t,0,0) = 0;\ \forall t \geq 0$. Rewrite (1)into the following form

$$\begin{cases} \dot{X} = AX + \Psi(t, X, \varpi) \\ Y = CX \end{cases}, \quad (2)$$

where A is a constant matrix and Ψ is a Lipschitz nonlinear term (at least locally).

Definition 1: If system(2)with the mapping $\varpi(X) \rightarrow Y$,is strictly passive (SP)in the sense of VEL-form, by choosing a suitable function $\varpi = -\phi(Y)$, s.t. ϕ is any locally Lipchitz function and $\phi(0) = 0, Y^T\phi(Y) > 0;\ \forall Y \neq 0$, the origin of system (2)will be globally uniformly asymptotically stable [3].

For adaptive case, rewrite (2) in the following form

$$\begin{cases} \dot{X} = A_1 X + \Psi(t, X, \varpi)\ ; \ t \in \mathbb{R}, \varpi \in \mathbb{R}^m, X \in \mathbb{R}^n \\ Y = CX \end{cases}, \quad (3)$$

with

$$\Psi(t, X, \varpi) = \Psi'(t, X, \varpi) + A_2 X. \quad (4)$$

Let Ψ' be a nonlinear Lipschitz term which is piecewise continuous in$t$, and $\Psi'(t,0,0) = 0$.Suppose that$A_1$and A_2 contain the fix and unknown system parameters, respectively.

Definition2: If system(2)with the mapping $\varpi(X) \rightarrow Y$,is strictly passive (SP)in the sense of VEL-form, and there exists an estimation mechanism as

$$\dot{\hat{\theta}} = \Gamma\left(\hat{\Phi}^T \mathrm{Y} + \hat{K}\right), \quad (5)$$

with a radially unbounded (RU) and positive definite (PD)storage function; therefore, the closed-loop system (3)will be output strictly passive(OSP),and the sufficient condition to asymptotically stabilizing the origin $X = 0$ is that $\dot{X} \in L_\infty$. So, the origin of system (3) with the mapping $\varpi(X, \hat{\theta}) \rightarrow Y$, will be globally uniformly asymptotically stabilized by $\varpi = -\phi(Y)$, s.t. ϕ is any locally Lipchitz function, where $\phi(0) = 0$ and $Y^T\phi(Y) > 0;\ \forall Y \neq 0$. While, it is guaranteed that $\hat{\theta}$and $\tilde{\theta}$remain bounded($\hat{\theta}, \tilde{\theta} \in L_\infty$).

Definition3: Consider system (2)with Lipschitz constant$\varrho \geq 0$, i.e.,

$$\left\|\Psi(t, X, \varpi) - \Psi\left(t, \hat{X}, \varpi\right)\right\| \leq \varrho\left\|X - \hat{X}\right\|, \quad (6)$$

and, with the following state-observer

$$\dot{\hat{X}} = A\hat{X} + \Psi\left(t, \hat{X}, \varpi\right) + L\left[Y - C\hat{X}\right]. \quad (7)$$

This SO is asymptotically convergence and strictly passive, if for the LMI

$$\begin{bmatrix} (A - LC)^T P + P(A - LC) + I + \frac{1}{2}C^T C & P \\ P & -\varrho^{-2} I \end{bmatrix} \prec 0, \quad (8)$$

there exists a PD symmetric solution P [6].

Definition4: If system (2) with the mapping $\varpi(X) \rightarrow Y$,is strictly passive (SP)in the sense of VEL-form, and there exists a strictly passive SO as (7) with a RU and PD storage function, therefore, the closed-loop system given by

$$\begin{cases} \dot{X} = AX + \Psi\left(t, X, \varpi(\hat{X})\right);\ t \in \mathbb{R}, \varpi \in \mathbb{R}^m, X \in \mathbb{R}^n \\ \dot{\hat{X}} = A\hat{X} + \Psi\left(t, \hat{X}, \varpi(\hat{X})\right) + L[Y - \mathbb{Y}];\ Y \in \mathbb{R}^m, \hat{X} \in \\ \mathbb{Y} = C\hat{X}; \quad \mathbb{Y} \in \mathbb{R}^m \end{cases} \quad (9)$$

with the mapping $\varpi(\hat{X}) \rightarrow \mathbb{Y}$, is strictly passive. By defining$\chi = [X \quad \hat{X}]^T$,the origin $(\chi = 0)$ can be globally uniformly asymptotically stabilized by $\varpi = -\phi(\mathbb{Y})$, s.t. ϕ is any locally Lipchitz function, where $\phi(0) = 0$ and $\mathbb{Y}^T\phi(\mathbb{Y}) > 0;\ \forall \mathbb{Y} \neq 0$ [**Error! Bookmark not defined.**].

Definition5: If system (2)with the mapping $\varpi(X) \rightarrow Y$, is strictly passive (SP)in the sense of VEL-form, and there exists a strictly passive SO as

$$\dot{\hat{X}} = A_1\hat{X} + \Psi\left(t, \hat{X}, \varpi\right) + L[Y - \mathbb{Y}], \quad (10)$$

with a RU and PD storage function; and an estimation machine as

$$\dot{\hat{\theta}} = \Gamma\left(\hat{\Phi}^T \mathbb{Y} + \hat{K}\right), \tag{11}$$

with a RU and PD storage function; therefore, the closed-loop system $\varpi(\hat{X}, \hat{\theta}) \to \mathbb{Y}$given by

$$\begin{cases} \dot{X} = A_1 X + \Psi\big(t, X, \varpi(\hat{X}, \hat{\theta})\big);\ t \in \mathbb{R}, \varpi \in \mathbb{R}^m, \\ \dot{\hat{X}} = A_1 \hat{X} + \Psi\big(t, \hat{X}, \varpi(\hat{X}, \hat{\theta})\big) + L[Y - \mathbb{Y}];\ Y \in \mathbb{R}^m, \\ \mathbb{Y} = C\hat{X};\quad \mathbb{Y} \in \mathbb{R}^m \end{cases} \tag{12}$$

will be output strictly passive (OSP). By defining$\chi = [X \quad \hat{X}]^T$, the sufficient condition to asymptotically stabilizing the origin $\chi = 0$ is that $\dot{X} \in L_\infty$. So, the origin will be globally uniformly asymptotically stabilized by $\varpi = -\phi(\mathbb{Y})$, s.t. ϕ is any locally Lipchitz function, where $\phi(0) = 0$ and $\mathbb{Y}^T\phi(\mathbb{Y}) > 0;\ \forall\, \mathbb{Y} \neq 0$. While, it is guaranteed that$\hat{\theta}$and $\tilde{\theta}$ will be bounded$(\hat{\theta}, \tilde{\theta} \in L_\infty)$ [6].

Nonlinear Time-Invariant Systems:

Consider the nonlinear time-invariant system

$$\begin{cases} \dot{X} = f(X, \varpi);\ X \in \mathbb{R}^n, \quad \varpi \in \mathbb{R}^p \\ Y = CX;\ \ Y \in \mathbb{R}^p \end{cases}, \tag{13}$$

where f is Lipchitz (at least locally) in (X, ϖ) and $f(0,0) = 0$. Rewrite (13) into the form

$$\begin{cases} \dot{X} = AX + \Psi(X, \varpi) \\ Y = CX \end{cases}, \tag{14}$$

where A is a constant matrix and Ψ is a Lipschitz nonlinear term (at least locally).

Definition6: If system(14)with the mapping $\varpi(X) \to Y$,is strictly passive (SP)in the sense of VEL-form, by choosing a suitable function $\varpi = -\phi(Y)$, s.t. ϕ is any locally Lipchitz function and $\phi(0) = 0, Y^T\phi(Y) > 0;\ \forall\, Y \neq 0$, the origin of the system (14)will be globally asymptotically stable.

For adaptive case, rewrite (14) in the form of

$$\begin{cases} \dot{X} = A_1 X + \Psi(X, \varpi)\ ;\ \varpi \in \mathbb{R}^m, X \in \mathbb{R}^n \\ Y = CX \end{cases}, \tag{15}$$

with

$$\Psi(X, \varpi) = \Psi'(X, \varpi) + A_2 X. \tag{16}$$

where Ψ' is nonlinear Lipschitz term and $\Psi'(0,0) = 0$. Suppose A_1 and A_2 as the known and unknown system parameters, respectively.

Definition 7: If system(14)with the mapping $\varpi(X) \to Y$,is strictly passive (SP)in the sense of VEL-form, and there exists an estimation mechanism as

$$\dot{\hat{\theta}} = \Gamma\left(\hat{\Phi}^T \mathrm{Y} + \hat{K}\right), \tag{17}$$

with a RU and PD storage function; therefore, the closed-loop system with the mapping $\varpi(X, \hat{\theta}) \to Y$will be output strictly passive(OSP).The sufficient condition to asymptotically stabilizing the origin $X = 0$ is that $\dot{X} \in L_\infty$. So, the origin will be globally uniformly asymptotically stabilized by $\varpi = -\phi(Y)$, s.t. ϕ is any locally Lipchitz function, where $\phi(0) = 0$ and $Y^T\phi(Y) > 0;\ \forall\, Y \neq 0$. While, it is guaranteed that $\hat{\theta}$and $\tilde{\theta}$remain bounded.

Definition 8: Consider system (14)with Lipschitz constant$\varrho \geq 0$, i.e.,

$$\big\|\Psi(X, \varpi) - \Psi\big(\hat{X}, \varpi\big)\big\| \leq \varrho\big\|X - \hat{X}\big\|, \tag{18}$$

and, with the following state-observer

$$\dot{\hat{X}} = A\hat{X} + \Psi\big(\hat{X}, \varpi\big) + L\big[Y - C\hat{X}\big]. \tag{19}$$

This SO is asymptotically convergence and strictly passive, if for the LMI

$$\begin{bmatrix} (A - LC)^T P + P(A - LC) + I + \frac{1}{2}C^T C & P \\ P & -\varrho^{-2} I \end{bmatrix} \prec 0, \tag{20}$$

there exists a PD symmetric solution P.

Definition 9: If system (14) with the mapping $\varpi(X) \to Y$,is strictly passive (SP)in the sense of VEL-form, and there exists a strictly passive SO as (19) with a RU and PD storage function, therefore, the closed-loop system given by

$$\begin{cases} \dot{X} = AX + \Psi\big(X, \varpi(\hat{X})\big);\ \varpi \in \mathbb{R}^m, X \in \mathbb{R}^n \\ \dot{\hat{X}} = A\hat{X} + \Psi\big(\hat{X}, \varpi(\hat{X})\big) + L[Y - \mathbb{Y}];\ \hat{X} \in \mathbb{R}^n, \\ \mathbb{Y} = C\hat{X};\quad \mathbb{Y} \in \mathbb{R}^m, \quad Y \in \mathbb{R}^m \end{cases} \tag{21}$$

with the mapping $\varpi(\hat{X}) \to \mathbb{Y}$, is strictly passive. By defining$\chi = [X \quad \hat{X}]^T$,the origin $(\chi = 0)$ can be globally asymptotically stabilized by $\varpi = -\phi(\mathbb{Y})$, s.t. ϕ is any locally Lipchitz function, where $\phi(0) = 0$and $\mathbb{Y}^T\phi(\mathbb{Y}) > 0;\ \forall\, \mathbb{Y} \neq 0$.

Definition 10: If system (14)with the mapping $\varpi(X) \to Y$, is strictly passive (SP)in the sense of VEL-form, and there exists a strictly passive SO as

$$\dot{\hat{X}} = A_1\hat{X} + \Psi\big(\hat{X}, \varpi\big) + L[Y - \mathbb{Y}], \tag{22}$$

with a RU and PD storage function; and an estimation machine as

$$\dot{\hat{\theta}} = \Gamma\left(\hat{\Phi}^T \mathbb{Y} + \hat{K}\right), \tag{23}$$

with a RU and PD storage function; therefore, the closed-loop system

$$\begin{cases} \dot{X} = A_1 X + \Psi\big(X, \varpi(\hat{X}, \hat{\theta})\big);\ \varpi \in \mathbb{R}^m, X \in \mathbb{R}^n \\ \dot{\hat{X}} = A_1\hat{X} + \Psi\big(\hat{X}, \varpi(\hat{X}, \hat{\theta})\big) + L[Y - \mathbb{Y}];\ \hat{X} \in \mathbb{R}^n, \\ \mathbb{Y} = C\hat{X};\quad \mathbb{Y} \in \mathbb{R}^m, Y \in \mathbb{R}^m \end{cases} \tag{24}$$

with the mapping $\varpi(\hat{X},\hat{\theta}) \rightarrow \mathbb{Y}$,will be output strictly passive (OSP). By defining $\chi = [X \quad \hat{X}]^T$, the sufficient condition to asymptotically stabilizing the origin $(\chi = 0)$ is that $\dot{\chi}$ is bounded. So, the origin can be globally asymptotically stabilized by $\varpi = -\phi(\mathbb{Y})$, s.t. ϕ is any locally Lipchitz function, where $\phi(0) = 0$and $\mathbb{Y}^T\phi(\mathbb{Y}) > 0;\ \forall\, \mathbb{Y} \neq 0$. While, it is guaranteed that $\hat{\theta}$ and $\tilde{\theta}$ will be bounded.

Remark 1: The VEL-form is a systematic formulation for system passivation which has been proposed in details in paper [3].In this formulation,ϖ is called virtual input,and thereis a relationship between $\varpi$and actual input$u$ in all definitions here. Foraffine-in-control systems one will have$u = a + b\varpi$,where,

- $a$is continuously differentiable in X(and piecewise continuous in t for TV systems), in the state space or work space.
- $b$is nonsingular in X(and piecewise continuous in t for TV systems), in the state space or work space.

Remark 2: These definitions are presented according to the VEL-form and theorems in [3] and [6].All the related proofs are omitted here due to limits on the paper volume.

For better follow-up of the issue, one can pursue the charts below. Different categories of nonlinear systems have been illustrated in Fig. **1**. After finding a suitable u, i.e. the input which forces the system to be passive, refer to Fig. **2** and track the process related to your current scenario.

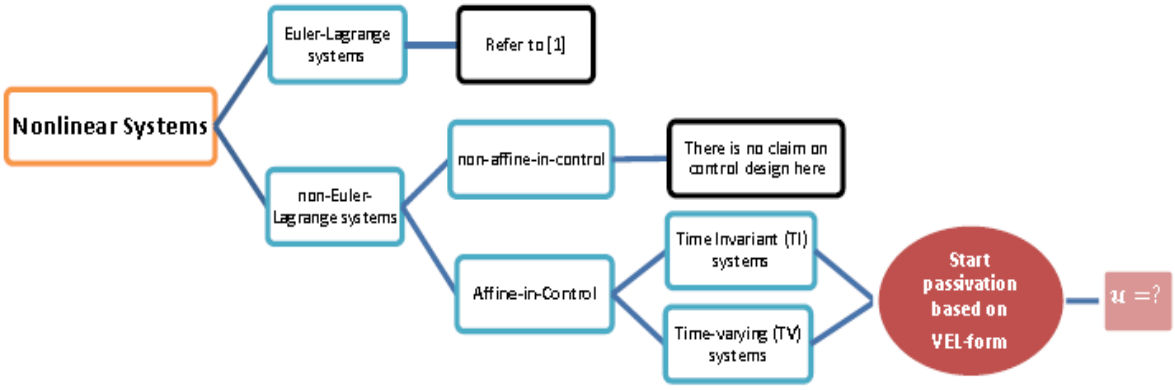

Fig. 1: A classification for nonlinear systems to use VEL-form of passivation

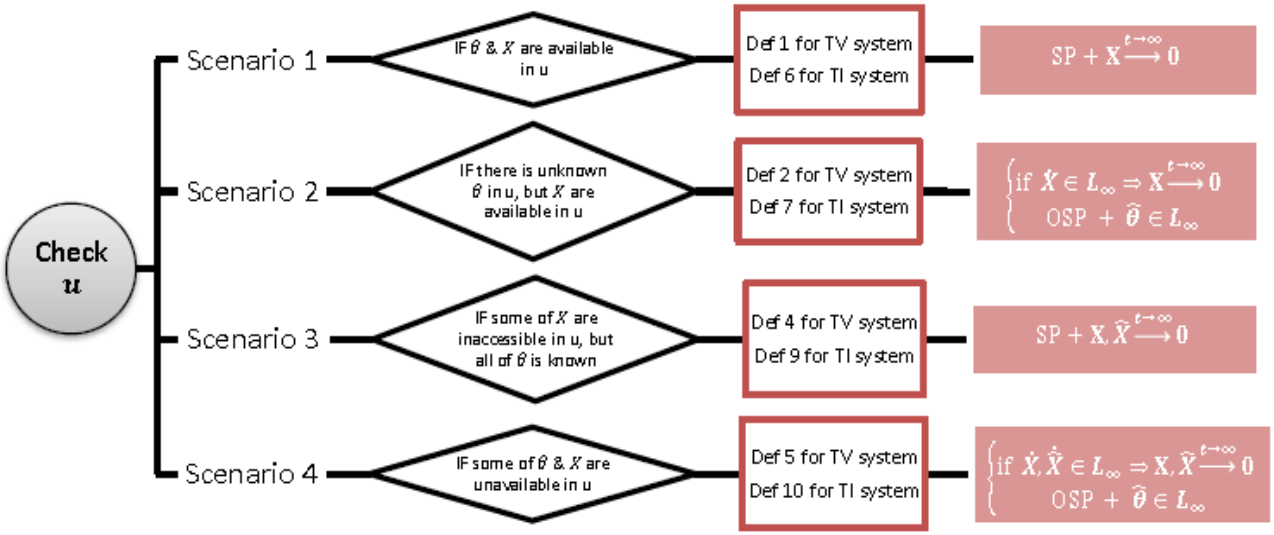

Fig. 2: Different scenarios in passivity-based control/ observe in the sense of VEL-form; SP: strictly passive, OSP: output strictly passive, TV: time-varying, TI: time-invariant

3. HBV disease model

The time-invariant HBV infection model is considered as [33-34].

$$\begin{cases} \dot{x} = \lambda - dx - \beta xv \\ \dot{y} = \beta xv - \delta y \\ \dot{v} = (1-\mu u)py - cv \end{cases}, \quad (25)$$

where x, y and v are respectively uninfected hepatocytes (healthy cells), infected hepatocytes (sick cells) and free viruses in blood. The system parameters and initial conditions are listed in Table 1.Control input$u$has been exerted to infection treatment in the infected body, whereis bounded in [0, 1].The untreated HBV model (without drug usage) is given by

$$\begin{cases} \dot{x} = \lambda - dx - \beta xv \\ \dot{y} = \beta xv - \delta y \\ \dot{v} = py - cv \end{cases}, \quad (26)$$

which has two equilibrium points, infection-free point (unstable) and endemic point (stable) as

$$X^*_{inf-free} = \begin{bmatrix} \frac{\lambda}{d} \\ 0 \\ 0 \end{bmatrix}, \quad X^*_{endemic} = \begin{bmatrix} \frac{c\delta}{p\beta} \\ \frac{\lambda}{\delta} - \frac{dc}{p\beta} \\ \frac{\lambda p}{c\delta} - \frac{d}{\beta} \end{bmatrix}. \quad (27)$$

In this study, all investigations will be done based on the infection-free point. The shifted model around the infection-free equilibrium point will be presented as

$$\begin{cases} \dot{\bar{x}} = -d\bar{x} - \beta v(\bar{x} + x^*) \\ \dot{y} = \beta v(\bar{x} + x^*) - \delta y \\ \dot{v} = (1-\mu u)py - cv \end{cases}, \quad Y = v, \quad (28)$$

where, $\bar{x} = x - x^*$ and $x^* = \frac{\lambda}{d}$, and Y states system output vector.The most significant criterion in observing the infection status is HBV DNA serum level which is related directly to the free virus quantity (v). HBV DNA is distinguished by some serological tests such as RT-PCR, therefore, the signal v can be selected as measurable system output.

4. Controller/ observer design

In this section, all scenarios are investigated for passivity-based approach and compared method (Lyapunov direct method).

Scenario 1: Here, the controller is designed for nominal model in the absence of state-observer.

-Passivity based design: For the system (28) one can find the following matrices by using the VEL method [**Error! Bookmark not defined.**]as

$$M = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}, N = \begin{bmatrix} d & 0 & \beta(\bar{x} + x^*) \\ 0 & \delta & -\beta(\bar{x} + x^*) \\ 0 & -p & c \end{bmatrix},$$
$$D = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}, K'_d = \begin{bmatrix} d & 0 & 0 \\ 0 & \delta & 0 \\ 0 & 0 & c \end{bmatrix}.$$

According to [**Error! Bookmark not defined.**], the storage function and its time-derivative will be

$$V = \frac{1}{2} X^T D X, \qquad \dot{V} \le -X^T K'_d X + \varpi^T Y, \quad (29)$$

with the virtual input

$$\varpi = \beta(\bar{x} + x^*)(y - \bar{x}) + py(1 - \mu u). \quad (30)$$

Thus, the mapping $\varpi(X) \to Y$ is SP and according to Definition 6, a suitable choose for ϖ can be $\varpi = -\alpha v$.Finally, it concludes

$$u = \frac{1}{p\mu y}[\beta(\bar{x} + x^*)(y - \bar{x}) + py + \alpha v]. \quad (31)$$

With the control input (31), the origin of (28)will be globally asymptotically stable. In order to avoid making the paper longer, it is neglected to show $\Psi$is Lipschitzand $\Psi(0,0) = 0$in the HBV model based on general form of (14).The process of this proof could be similar to [3].

-Lyapunov based design: For compared method, the Lyapunov function can be selected as

$$H = \frac{1}{2} X^T X, \quad (32)$$

and, taking time derivative of H yields

$$\dot{H} \le -d\bar{x}^2 - \delta y^2 - cv^2 + \beta(y - \bar{x})(\bar{x} + x^*)v + pvy - \mu pyvu.$$

By selecting the control input as

$$u = \frac{1}{p\mu y}[\beta(\bar{x} + x^*)(y - \bar{x}) + py], \quad (33)$$

one has

$$\dot{H} \le -X^T \begin{bmatrix} d & 0 & 0 \\ 0 & \delta & 0 \\ 0 & 0 & c \end{bmatrix} X,$$

whered, δ and c are PD constants, so,$\dot{H}$ is ND. Since the Lyapunov function (32)is RU, the origin of (28)will be globally asymptotically stable.

Scenario 2: The controller is designed for adaptive model in the absence of state-observer, while, the unknown system parameters are considered as$\theta = [\beta \quad \mu]$. Thus, the estimation error of unknown parameters is $\tilde{\theta} = [\tilde{\beta} \quad \tilde{\mu}]$, where $\tilde{\theta} = \theta - \hat{\theta}$ and $\hat{\theta}$ states the estimation vector of parameters.

-Passivity based design: Based on (15), (16) and (28),

$$\Psi' = \begin{bmatrix} -\beta\bar{x}v \\ \beta\bar{x}v \\ -\mu puy \end{bmatrix}, \quad A_1 = \begin{bmatrix} -d & 0 & 0 \\ 0 & -\delta & 0 \\ 0 & p & -c \end{bmatrix},$$
$$A_2 = \begin{bmatrix} 0 & 0 & -\beta x^* \\ 0 & 0 & \beta x^* \\ 0 & 0 & 0 \end{bmatrix}.$$

For HBV model, the adaptation mechanism is given as

$$\dot{\hat{\theta}} = \Gamma \begin{bmatrix} (\bar{x} + x^*)(y - \bar{x}) \\ -upy \end{bmatrix} v, \tag{34}$$

with a RU and PD storage function as $V_\theta = \frac{1}{2}\tilde{\theta}^T\Gamma^{-1}\tilde{\theta}$, where Γ is a free PD gain matrix. According to (23), one has

$$\widehat{\Phi} = [(\bar{x} + x^*)(y - \bar{x}) \quad 0], \ \widehat{K} = [0 \quad -upyv]^T.$$

On the other hand, Scenario 1 reveals that the nominal system $(\varpi(X) \to Y)$ is SP with (30).Therefore, based on Definition 7, if $\dot{X} \in L_\infty$, the origin of adaptive model will be stabilized. Since all states and control input in (28)are considered finite, thus, $\dot{X}$ is bounded. Thereupon, by choosing $\varpi = \alpha v$, the origin $X = 0$ is globally asymptotically stable by using the adaptive control input as

$$u_{(X,\hat{\theta})} = \frac{1}{p\hat{\mu}y}[\hat{\beta}(\bar{x} + x^*)(y - \bar{x}) + py + \alpha v]. \tag{35}$$

-Lyapunov based design: For compared method, one can choose the Lyapunov function for adaptive closed-loop system as

$$H_{Acl(X,\tilde{\theta})} = \frac{1}{2}X^TX + \frac{1}{2}\tilde{\theta}^T\Gamma^{-1}\tilde{\theta}. \tag{36}$$

By select the following control input

$$u_{(X,\hat{\theta})} = \frac{1}{p\hat{\mu}y}[\hat{\beta}(\bar{x} + x^*)(y - \bar{x}) + py], \tag{37}$$

and the adaptation law similar to (34), $\dot{H}_{Acl}$ will benegative semi-definite (NSD). Based on previous section, $\dot{X} \in L_\infty$. Accordingly, $X \to 0$asymptotically, while, $\tilde{\theta}$only can remain bounded.

Scenario 3: The nominal system in the presence of SO has been studied here. Suppose that all using parameters in control inputs are available, while, some of using states are unavailable.

-Passivity based design: Consider the SO (19) with a RU and PD storage function $V_{ob} = \tilde{X}^TP\tilde{X}$, where $\tilde{X}$ is defined as estimation error of states and $\tilde{X} = X - \hat{X}$. Let define $L = L_0\text{ones}(3,1)$; $L_0 > 0$. By setting $L_0 = 200$ a solution $P = P^T > 0$ is found for LMI (20), while, $A - LC$ is Hurwitz. Thus,based on Definition 8, one will have a strictly passive SO for HBV model. According to Definition 9, since the mapping $\varpi(X) \to Y$ is SP,the closed-loop HBV model will be SP with

$$\varpi_{(\hat{X})} = \beta(\hat{\bar{x}} + x^*)(\hat{y} - \hat{\bar{x}}) + p\hat{y}(1 - \mu u).$$

With suitable choice of $\varpi = \alpha\tan^{-1}(\hat{v})$, the origin will be globally asymptotically stabilized by the following control input

$$u_{(\hat{X})} = \frac{1}{p\mu\hat{y}}[\beta(\hat{\bar{x}} + x^*)(\hat{y} - \hat{\bar{x}}) + p\hat{y} + \alpha\tan^{-1}(\hat{v})]. \tag{38}$$

-Lyapunov based design: Consider the Lyapunov function as

$$H_{cl(\hat{X},\tilde{X})} = \frac{1}{2}\hat{X}^T\hat{X} + \tilde{X}^TP\tilde{X}, \tag{39}$$

and the following LMI instead of (20)

$$\begin{bmatrix} (A - LC)^TP + P(A - LC) + I & P \\ P & -\varrho_0{}^{-2}I \end{bmatrix} < 0.$$

Choosing $L_0 = 200$ leads to have a suitable solution $P$for this LMI.Now, by selecting the following control input

$$u_{(\hat{X})} = \frac{1}{p\mu\hat{y}}[\beta(\hat{\bar{x}} + x^*)(\hat{y} - \hat{\bar{x}}) + p\hat{y}], \tag{40}$$

$\dot{H}_{cl}$will beND and the origin of the system is globally asymptotically stable.

Scenario 4: In this case, the adaptive model in the presence of SO has been investigated. In other words, there are some inaccessible parameters and variable states in the control inputs which need to be estimated.

-Passivity based design: By setting $L_0 = 300$,a strictly passive SO is achieved for adaptive HBV model. On the other hand, the mapping $\varpi(X) \to Y$ is SP, and the passive adaptive law is as

$$\dot{\hat{\theta}} = \Gamma \begin{bmatrix} (\hat{\bar{x}} + x^*)(\hat{y} - \hat{\bar{x}}) \\ -up\hat{y} \end{bmatrix} \hat{v}, \tag{41}$$

where Γ is a free PD gain matrix.According to Definition 10, the closed-loop HBV model will be SP with

$$\varpi_{(\hat{X},\hat{\theta})} = \hat{\beta}(\hat{\bar{x}} + x^*)(\hat{y} - \hat{\bar{x}}) + p\hat{y}(1 - \hat{\mu}u).$$

Now, if $\dot{X}$ and $\dot{\hat{X}}$ are bounded, the origin can be stabilized. Since all states and estimation signals and control input are considered finite, therefore, $\dot{X}, \dot{\hat{X}} \in L_\infty$and with suitable choice of $\varpi = \alpha\tan^{-1}(\hat{v})$, the origin will be globally asymptotically stabilized by the following control input

$$u_{(\hat{X},\hat{\theta})} = \frac{1}{p\hat{\mu}\hat{y}}[\hat{\beta}(\hat{\bar{x}} + x^*)(\hat{y} - \hat{\bar{x}}) + p\hat{y} + \alpha\tan^{-1}(\hat{v})]. \tag{42}$$

-Lyapunov based design: Consider the Lyapunov function as

$$H_{Acl(\hat{X},\tilde{X},\tilde{\theta})} = \frac{1}{2}\hat{X}^T\hat{X} + \tilde{X}^TP\tilde{X} + \frac{1}{2}\tilde{\theta}^T\Gamma^{-1}\tilde{\theta}, \tag{43}$$

Choosing $L_0 = 300$ leads to have a convergence SO. Now, by selecting the following control input

$$u_{(\hat{X},\hat{\theta})} = \frac{1}{p\hat{\mu}\hat{y}}[\hat{\beta}(\hat{\bar{x}} + x^*)(\hat{y} - \hat{\bar{x}}) + p\hat{y}], \tag{44}$$

$\dot{H}_{Acl}$ will beNSD. Since $\dot{X}, \dot{\hat{X}} \in L_\infty$, thus, $\dot{X}$ and $\dot{\hat{X}}$ are

uniformly continuous. Finally, it leads to have $X \xrightarrow{t\to\infty} 0and\tilde{\theta} \in L_\infty$.

5. Simulation results

In the first step, according to the open-loop system (26), Fig. **3**illustrates the behavior of the HBV dynamics in the absence of drug therapy in 5000 days.

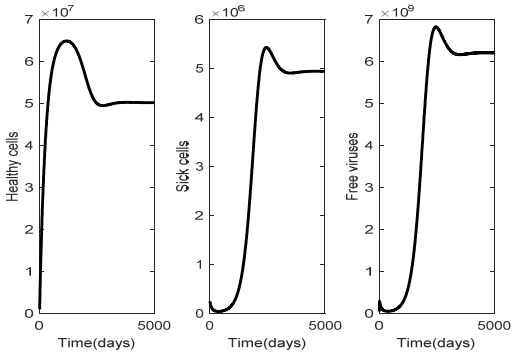

Fig. 3: Open-loop states in untreated infected body during 5000 days (without drug consumption)

In the following, the closed-loop HBV model has been simulated for both control approaches in four different scenarios during 1000-days drug therapy. To have a better comprehension of preference of the proposed method, Table 2 is provided to show the comparison criteria (norm 2) for some signals in both methods.

Scenario 1: Themost important signals are the number of free viruses and drug dosage which are depicted in Fig. **4**. For PBC approach set $\alpha = 50$ in (31).

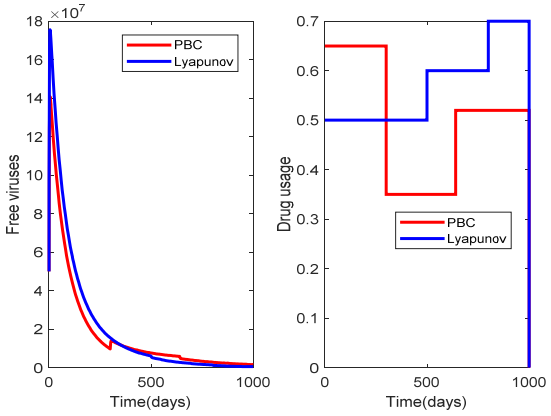

Fig. 4: Number of free viruses (v) and drug dosage (u) for PBC and Lyapunovdirect method during 1000-day drug therapy

Scenario 2: Here, the signals v and u have been simulated in Fig. **5** for APBC and adaptive Lyapunov direct method based on (35) and (37).Besides, the parametric estimation errors, i.e.$\tilde{\beta}$and $\tilde{\mu}$, are demonstrated in Fig. **6** by setting

$$\Gamma = \mathrm{diag}([10^{-20}, 10^{-15}]),$$

in(34)for both methods, and $\alpha = 1000$ in (35).

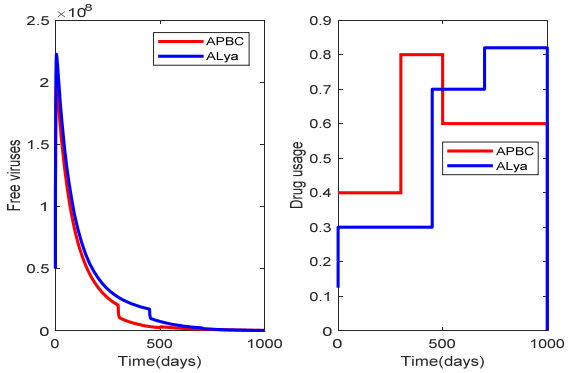

Fig. 5:Number of free viruses (v) and drug dosage (u) for APBC and adaptive Lyapunov direct method during 1000-day drug therapy

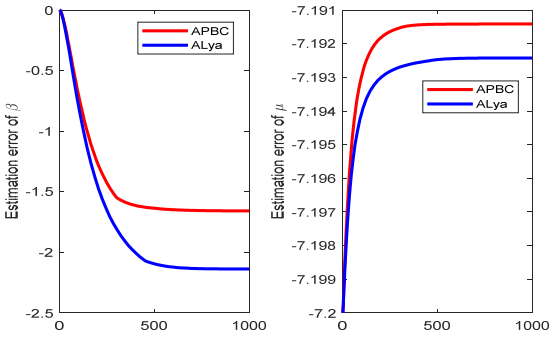

Fig. 6: Estimation error of unknown system parameters for APBC and adaptive Lyapunov direct method during 1000-day drug therapy

Scenario 3: In this case, set$\alpha = 500$ in (38). According to the control inputs in (38) and (40) free viruses and its estimation error are displayed in Figure 7 for PBC and Lyapunov method in the presence of SO. Fig. **8** depicts the drug usage in 1000 days. For more information, one can refer to Table 2.

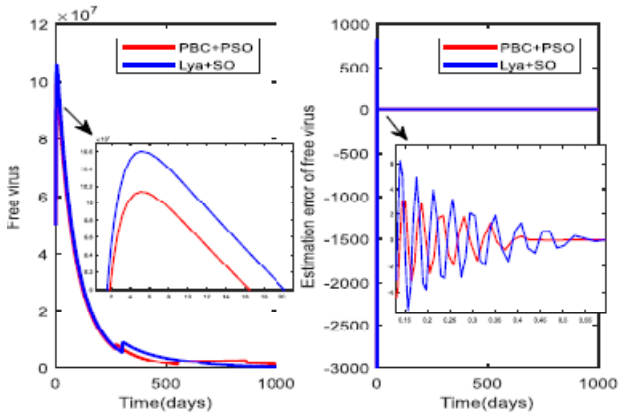

Fig. 7:Number of free viruses (v) and estimation error of free viruses $(\tilde{v})$ for PBC/PSO and Lyapunov direct method/SOduring 1000-day drug therapy

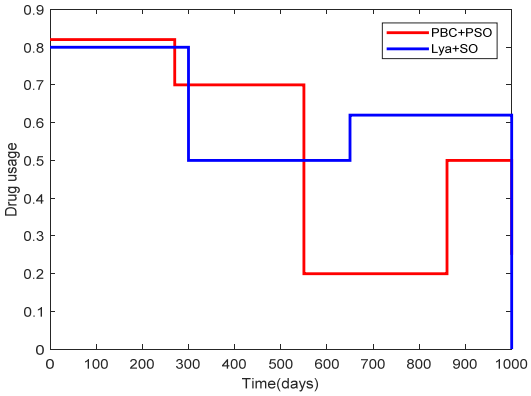

Fig. 8: Drug dosage in PBC/PSO and Lyapunov direct method/SO during 1000-daydrug therapy

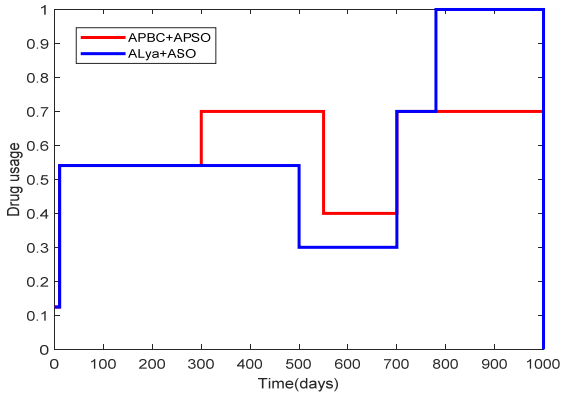

Fig.10: Drug dosage in APBC/APSO and adaptive Lyapunov direct method/ASO during 1000-day drug therapy

Scenario 4: For the last scenario, the status of free viruses and its error of estimation have been indicated in Fig. 9. In addition, one can follow the drug consumption for treated body in Fig.10 based on (42) and (44). The estimation errors of unknown parameters are depicted inFig. 11for both control methods as well. Set $\alpha = 100$ in (42) and

$$\Gamma = \mathrm{diag}([10^{-23}, 10^{-18}]),$$

in(41) for both control approaches.

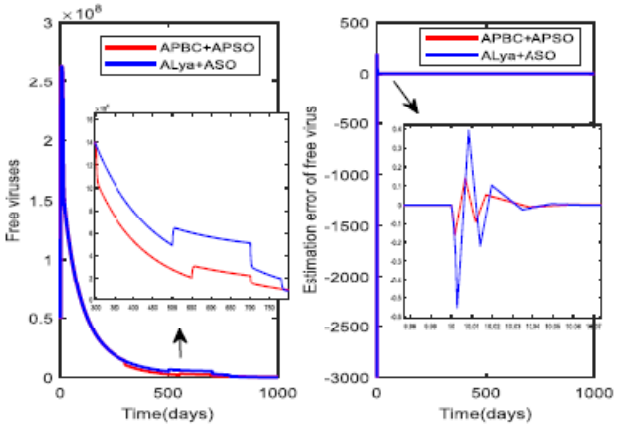

Fig. 9: Number of free viruses $(\tilde{v})$ and estimation error of free viruses $(\tilde{v})$ for APBC/APSO and adaptive Lyapunov direct method/ASOduring 1000-day drug therapy

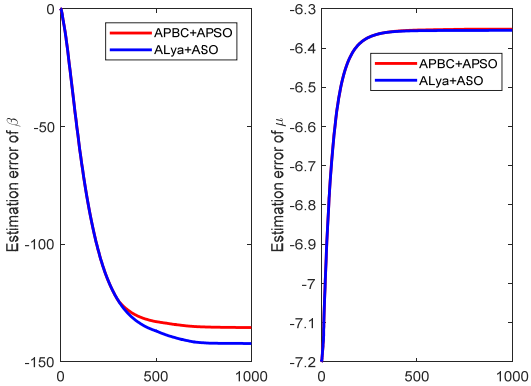

Fig. 11: Estimation error of unknown system parameters for APBC/APSO and adaptive Lyapunov direct method/ASO during 1000-day drug therapy

6.Conclusion

In this paper, a formulation based on LMI is provided to have a passive SO for time-varying and time-invariant Lipschitz nonlinear systems. According to the definitions, passivity and stability of the closed-loop can be connected to passivity of subsystems in a different way for both time-varying and time-invariant systems. A passivity-based controller/ observer is designed based on VEL-form and some definitions, which offer significant advantages, e.g. decreasing design complexities and accelerating the analysis and design process. Different scenarios are categorized in a char to guide the designer. These contributions have been validated on the HBV disease model, while, the capability of the proposed approach is confirmed based on the simulation results. As stated in the definitions, the parametric estimation errors will only be guaranteed to remain bounded in all adaptive cases, and as is clear from the results, the main goal of control has been achieved during this situation. From simulations and Table 2, it is revealed that the proposed method has more acceptable performance rather than the compared method. Norm 2 of drug input in the proposed approach is less in all scenarios. Moreover, it is obvious that the status of free viruses in passivity-based method is in a better condition.

Table 1: Parameters and initial conditions for HBV model [33]

Parameters	*Definitions*	*Numeric values*
λ	Constant production rate of new target cells (healthy hepatocytes)	2.5251×10^5
d	Death rate of healthy hepatocytes	0.0038
β	Infection rate of healthy hepatocytes	1.981×10^{-13}
δ	Death rate of Infected cells(sick hepatocytes)	0.0125
μ	Efficacy of drug usage	0.8
p	Production rate of free viruses by sick hepatocytes	842.0948
c	Death rate of free viruses	0.67
$x(0)$	Initial number of uninfected hepatocytes	10^6
$y(0)$	Initial number of infected hepatocytes	2.5×10^5
$v(0)$	Initial number of free viruses	0.5×10^8

Table 2: Comparison of the control approaches in four different scenarios during 1000-day drug therapy

Scenario	*Control Method*	*Explanations*	*Norm 2*		
			$\sqrt{\int_{t=0}^{1000} v^2}$	$\sqrt{\int_{t=0}^{1000} \tilde{v}^2}$	$\sqrt{\int_{t=0}^{1000} u^2}$
1	PBC	Nominal case without state-observer	10^9	-	16.3
	Lyapunov		1.28×10^9	-	18.2
2	APBC	Adaptive case without state-observer	1.47×10^9	-	18.8
	Adaptive Lyapunov		1.69×10^9	-	19.1
3	PBC/ PSO	Nominal case with state-observer	7.1×10^8	150	19.1
	Lyapunov/ SO		7.5×10^8	163	20.3
4	APBC/ APSO	Adaptive case with state-observer	1.36×10^9	210	19.5
	ALyapunov/ ASO		1.37×10^9	220	20.6

References

[[1] R. Ortega, et al, *Passivity-based Control of Euler-Lagrange Systems*, London: Springer-Verlag, 1998.

[2] R. Ortega and M.Spong, "Adaptive motion control of rigid robots: a tutorial", *Automatica*,vol. 25, pp. 877-888, 1989.

[3] S. Gorji, A. Fakharian and R.Abbasi,"Virtually Euler-Lagrange form for feedback passivation of a wide range of non-Euler-Lagrange systems: Adaptive Passivity-Based Control of Hepatitis B Disease", *Proceedings of the Institution of Mechanical Engineers, Part I: Journal of Systems and Control Engineering,* vol. 237, pp. 1313-1330, 2023.

[4] H.Shim,"*A Passivity-based Nonlinear Observer and a Semi-global Separation Principle"*, PhD Thesis, Seoul National University, 2000.

[5] TE.Pare ,"*Passivity-based analysis and control of nonlinear systems"*, PhD Thesis, Stanford University, 2000.

[6] S. Gorji, A. Fakharian and R.Abbasi ,"Passive observer-based controller design for a class of Lipschitz nonlinear time-varying systems with application to Hepatitis B disease", *Proceedings of the Institution of Mechanical Engineers, Part I: Journal of Systems and Control Engineering,*2024,doi:10.1177/09596518241236925.

[7] M. Ali and CK.Alexander,"Robust tracking control of a robot manipulator using a passivity-based extended-state observer approach",*IET Cyber-syst Robot*, vol. 1, pp. 63-71, 2019.

[8]F. Bouakrif, D. Boukhetala and F.Boudjema,"Passivity-based controller-observer for robot manipulators",*3rd International Conference on Information and Communication Technologies: From Theory to Applications*, Damascus, Syria, 7-11 April, 2008.

[9] LDH. Peiris, JL. Du Bois and AR. Plummer, "Passivity-based adaptive delay compensation for real-time hybrid tests",*Proceedings of the Institution of Mechanical Engineers, Part I: Journal of Systems and Control Engineering*, vol. 235, pp.427-432, 2020.

[10] R. Salim, et al,"Sensorless passivity based control for

induction motor via an adaptive Observer",*ISA Transactions,* vol. 84, pp. 118-127, 2019.

[11] Y. Liu, et al, "Passivity Control of Induction Motors based on Adaptive Observer Design",*3rd IFAC International Conference on Intelligent Control and Automation Science*, Chengdu, China, 2-4 Sep. 2013, pp. 176-181.

[12] B. Salamat and AM.Tonello,"Energy Based Control of a Swash Mass Helicopter through Decoupling Change of Coordinates",*IEEE Access,* vol. 8, pp. 77449-77458, 2020.

[13] B. Salamat and AM.Tonello,"A Swash Mass Pendulum with Passivity-Based Control",*IEEE Robotics and Automation Letters,* vol. 6, pp. 199-206, 2021.

[14] L. Tiitinen, M. Hinkkanen and L.Harnefors,"Stable and Passive Observer-Based V/Hz Control for Induction Motors",*IEEE Energy Conversion Congress and Exposition*, Detroit, MI, USA, 9-13 Oct. 2022, pp. 1-8.

[15] B. Brogliato, R. Lozano, et al,*Dissipative systems analysis and control*, 3rd ed. Switzerland AG: Springer Nature, 2020.

[16] M. Salimifard and HA.Talebi,"Robust output feedback fault-tolerant control of non-linear multi-agent systems based on wavelet neural networks",*IET Control Theory & Applications*, vol. 11, pp. 3004-3015, 2017.

[17] R. Rajamani and YM.Cho,"Existence and design of observers for nonlinear systems: relation to distance to unobservability"*, International Journal of Control*, vol. 69, pp. 717-731, 1998.

[18] R.Rajamani,"Observers for Lipschitz Nonlinear Systems",*IEEE Transaction on Automatic Control,* vol. 43, pp. 397-401, 1998.

[19] Y. Dong, W. Liu and S.Liang,"Nonlinear observer design for one-sided Lipschitz systems with time-varying delay and uncertainties",*International Journal of Robust and Nonlinear Control,* vol. 27, pp.1974-1998, 2017.

[20] T. Raïssi, D. Efimov and A.Zolghadri,"Interval state estimation for a class of nonlinear systems",*IEEE Trans. Automatic Control,* vol. 57, pp. 260-265, 2012.

[21] T. Raïssi, G. Videau and A.Zolghadri,"Interval observers design for consistency checks of nonlinear continuous-time systems",*Automatica,* vol. 46, pp. 518-527, 2010.

[22] D. Efimov, et al,"Interval State Observer for Nonlinear Time Varying Systems",*Automatica*, vol. 49, pp. 200-205, 2013.

[23] S. Manzoor, et al,"Hepatitis B virus therapy: What's the future holding for us?",*World J. Gastroenterol,*vol. 21, pp. 12558-12575, 2015.

[24] World Health Organization.*Online Referencing*, http://www.who.int.

[25] J.Jang,"Feedback control of an HBV model based on ensemble kalman filter and differential evolution", *Mathematical Biosciences and Engineering,* vol. 15, pp. 667-691, 2018.

[26] Y. Ding and WJ.Wang,"Control strategy design for the anti-HBV mathematical model", *IET Syst. Biol,*vol. 13, pp. 186-193, 2019.

[27] O. Aghajanzadeh, et al,"Robust adaptive Lyapunov-based control of hepatitis B infection", *IET Syst. Biol,* vol.12, pp. 62-67, 2018.

[28] O. Aghajanzadeh, et al,"Nonlinear Adaptive Control Method for Treatment of Uncertain Hepatitis B Virus Infection",*Biomedical Signal Processing and Control,*vol. 38, pp. 174-181, 2017.

[29] O. Aghajanzadeh, M. Sharifi andA.Falsafi,"Robust control strategy for HBV treatment: Considering parametric and nonparametric uncertainties",*Control Applications for Biomedical Engineering Systems,*vol. 5, pp. 127-147, 2020.

[30] JJE. Slotin and W.Li,*Applied nonlinear control,* Englewood Cliffs, NJ: Prentice Hall, 1991.

[31] R. Shadi, F. Bouzari Liavoli and A.Fakharian,"Nonlinear Sub-Optimal Controller for Ebola Virus Disease: State-Dependent Riccati Equation Approach",*7th International Conference on Control, Instrumentation and Automation*, Tabriz, Iran, 23-24 Feb. 2021, pp. 1-6.

[32] R. Shadi, A. Fakharian and H. Khaloozadeh,"Transmission Dynamics and Optimal Control Strategy to Mitigate the Spread of Novel Coronavirus: The Case of Iran",*The 30th Iranian Conference on Electrical Engineering (ICEE*), Tehran, Iran, 17-19 May. 2022, pp. 356-361.

[33] M. Sheikhan and SA. Ghoreishi, "Antiviral therapy using a fuzzy controller optimized by modified evolutionary algorithms: a comparative study", *Neural Computing and Applications*, vol. 23, pp. 1801-1813, 2013.

[34] MA. Nowak, et al, "Viral dynamics in hepatitis B virus infection", *Proceedings of the National Academy of* Sciences, vol. 93, pp. 4398-4402, 1996.