in which k is a positive constant. The continuous function $\tanh(s)$ is used instead of $\text{sgn}(s)$ to avoid or reduce chattering phenomenon as an undesirable phenomenon. Employing the controller (13), $\dot{V}$ is obtained as

$$\dot{V} = s\dot{s} = -ks\tanh(s) \tag{14}$$

It is chosen $k \geq \eta$ to satisfy the sliding mode condition for $\dot{V}$:

$$\dot{V} \leq -\eta s\tanh(s) \tag{15}$$

As mentioned before, η is positive. Moreover, $s\tanh(s)$ is a positive function. Consequently, $\dot{V}$ is negative definite and the system is asymptotically stable.

4. SIMULATION RESULTS

4.1. Primary Infection Case

In healthy individuals without a history of HCMV infection, primary infection can occur due to the immunosuppression drug. Initial values for the primary infection case are as follows [40]:

$$[S_0, I_0, V_0, E_{V0}, E_{K0}, C_0] = [400, 10^{-12}, 10^{-2}, 10^{-12}, 10^{-12}, 1] \tag{16}$$

Fig. 1 shows the simulation results of the primary infection case for six variables with the immunosuppression drug using the proposed controller. It can be seen that the controller satisfies the constraints for viral load ($V \leq 3.5$) and the serum creatinine ($C \leq 1.2$). The viral load constraint is satisfied and only violated one time due to the over-suppression case; however, the desired value of E_K is followed appropriately. A high correlation can be seen between the desired and actual trajectories, which indicates that the control performance is suitable.

4.2. Reactivation Case

Latent infection is the next stage after primary infection, in which the virus remains in cells and the HCMV disease can occur [41]. The initial conditions are obtained from [39] that obtained as the equilibrium point of the untreated system. Fig. 2 demonstrates the results for the reactivation case with the following initial conditions:

$$[S_0, I_0, V_0, E_{V0}, E_{K0}, C_0] = [399.999, 8.56\times10^{-7}, 7.34\times10^{-6}, 10, 5, 1.625] \tag{17}$$

Simulation results show that in reactivation case, the serum creatinine will also eventually come below its limit (after 40 days), the viral load is less than its threshold except for a period that needs an antiviral drug ($197th$ day to $225th$ day), and the desired concentration of allospecific $CD8^+$ T cells targeted kidney (E_K) is followed appropriately. In comparison with the primary case (Fig. 1), there is a little more concentration of the susceptible cells, infected cells, viral loads, HCMV-specific $CD8^+$ T cells and serum creatinine of the blood in reactivation case (Fig. 2). However, in both cases, the desired trajectory for E_K is tracked appropriately as illustrated in Fig. 3. Fig. 3 depicts the error signals in primary infection and the reactivation cases. In both cases, a small error (with the order of 10^{-3}) is seen in the first days that tends to zero eventually.

4.3. Control Signals

Fig. 4 shows the normalized immunosuppressive drug dosage as the control input, for the primary and reactivation cases. It is observed that 70% of the immunosuppressive drug dosage is enough to satisfy the constraints below their threshold for both cases in Figs. 1 and 2.

4.4. Sensitivity Analysis

Sensitivity analysis is a significant tool in the evaluation of systems and their controllers and making decisions. It determines the effect of magnitude change of any parameters and inputs on the system response. Its results can be used to get a broad understanding of parameters effect, validating the model and predicting future results [42].

In this section, a sensitivity analysis is developed for the HCMV infection. For this purpose, five immune system parameters λ_{EK}, δ_{EK}, λ_C, δ_C and k_{EK} in Eqs. (5), (6) are changed and their influences are investigated in detail. These equations are the only ones that can affect the control input design. The effect of each parameter change is studied and demonstrated separately in Fig. 5 to Fig. 10. Note that only variables or outputs that will be influenced considerably in this sensitivity analysis for each case are shown here. The percentage of changes after parameter variations is calculated in comparison with the original case results. We considered 30% change for less sensitive parameters (λ_{EK} and δ_{EK}) and 10% change for parameters with high sensitivity (λ_C, δ_C and k_{EK}). It should be taken into account that each change in λ_C, δ_C and k_{EK} will affect the final steady-state value of E_{Kf} obtained based on Eq. (9).

Regarding Fig. 5, four main variables that change significantly with respect to 30% variation in λ_{EK}, are the susceptible cells (S), infected cells (I), viral loads (V) and control signal (ε). The susceptible cells' final population increased 7% due to a 30% reduction in λ_{EK}, while a 30% increment of this parameter results in 8% less susceptible cells for both primary and reactivation cases in