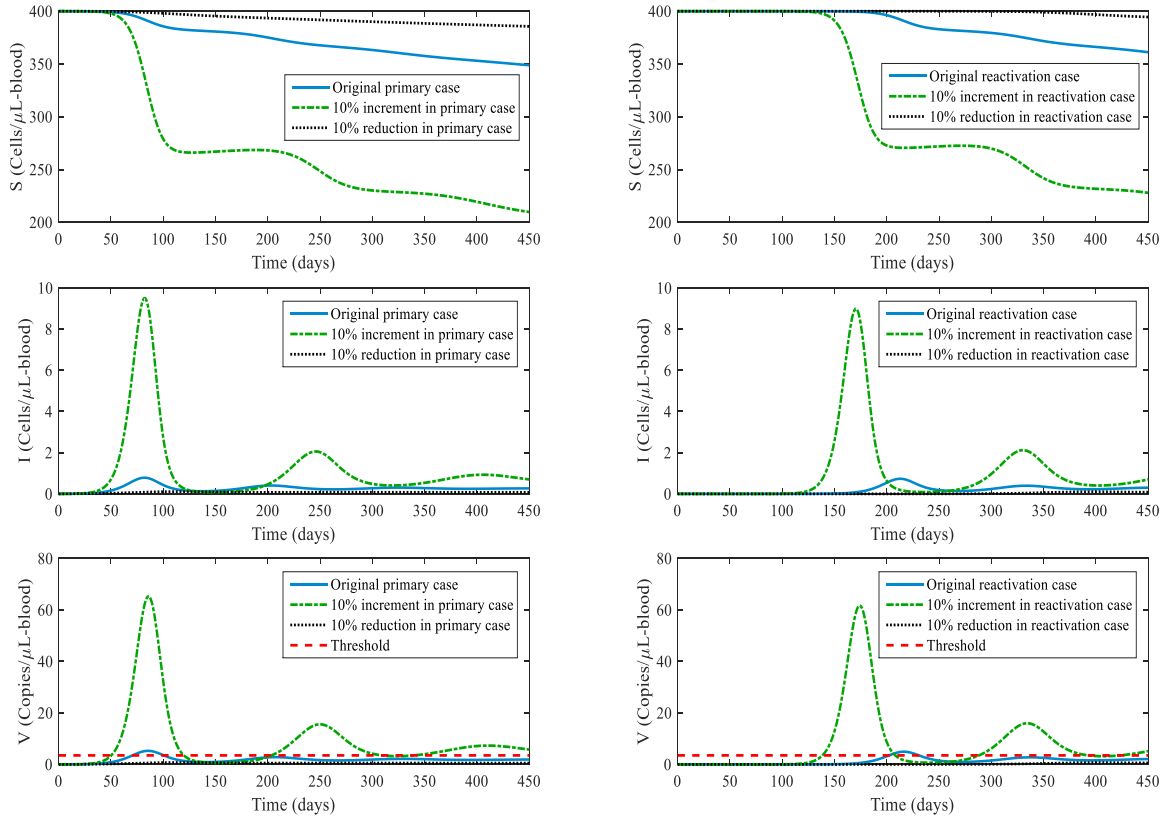

FIG. 7 *S*, *I* and *V* in the presence of a 10% change in λ_C. Susceptible cells *(top graphs)*, infected cells *(middle graphs)* and viral loads *(bottom graphs)* all are representing a significant change in both the primary *(left)* and reactivation *(right)* cases.

5. CONCLUSION REMARKS

In this chapter, a sliding mode control strategy was developed based on a nonlinear mathematical model of the immune response in renal transplant recipients, with the goal of maintaining a balance between under-suppression case (with the possibility of kidney rejection) and over-suppression case (with a viral load threatening the body). The desired trajectories were defined for allospecific $CD8^+$ T cells that target the kidney. Investigating the sliding mode control law, appropriate dosages of the immunosuppressive drug were determined to track the desired trajectories in both primary and reactivation infection cases. The Lyapunov stability method was employed to prove the tracking convergence to the designed goals. The results showed that for both primary and reactivation infection cases, the controller maintained the serum creatinine below its admissible limit; however, the viral load violated its normal range in some periods of the treatment. As a result, considering an antiviral drug as the second control input to hold the viral load below its limit can be studied in future work. Furthermore, the control signals reached their final constant values without any chattering in less than 50 days after initiation of treatment. Finally, a comprehensive sensitivity analysis was conducted to evaluate the effects of five main parameters of the model on the system's response. It is obtained that the system is highly sensitive to parameters in the dynamics of the blood's serum creatinine, in which the desired final value for the concentration of allospecific $CD8^+$ T cells was calculated. Two other parameters in the dynamics of allospecific $CD8^+$ T cells were also investigated as the next most effective ones in the system's response based on the presented sensitivity analysis in this work. In future studies, some hybrid and adaptive control strategies can be developed for this nonlinear HCMV infection to take both the immunosuppressive and antiviral drugs into account, in addition to considering the possible modeling uncertainties.