Biomedical Control Strategies for Inflammation in SARS-CoV-2-Induced Complement Activation Supplementary File S1

Mathematical Model

$$\frac{d(x_1)}{dt} = -k_{on1}x_1x_2 + k_{off1}x_3 \tag{1}$$

$$\frac{d(x_2)}{dt} = -k_{on1}x_1x_2 + k_{off1}x_3 \tag{2}$$

$$\frac{d(x_3)}{dt} = k_{on1}x_1x_2 - k_{off1}x_3 - k_{on2}x_3x_4 \tag{3}$$

$$\frac{d(x_4)}{dt} = k_{on2}x_3x_4 - k_{on5}x_4x_9 + k_{off5}x_{10} \tag{4}$$

$$\frac{d(x_5)}{dt} = -k_{on3}x_5x_7 - k_{on7}x_5x_{11} + k_{on16}x_{30}x_5 \tag{5}$$

$$\frac{d(x_6)}{dt} = k_{on3}x_5x_7 \tag{6}$$

$$\frac{d(x_7)}{dt} = -k_{on3}x_5x_7 - k_{on4}x_8x_7 + k_{off4}x_9 \tag{7}$$

$$\frac{d(x_8)}{dt} = -k_{on4}x_8x_7 + k_{off4}x_9 \tag{8}$$

$$\frac{d(x_9)}{dt} = k_{on4}x_8x_7 - k_{off4}x_9 - k_{on5}x_4x_9 + k_{off5}x_{10} \tag{9}$$

$$\frac{d(x_{10})}{dt} = k_{on5}x_4x_9 - k_{off5}x_{10} - k_{7cat}x_{10} \tag{10}$$

$$\begin{aligned}\frac{d(x_{11})}{dt} = -k_{on7}x_5x_{11} - k_{on15}x_{11}x_{30} + k_{off15}x_{35}\\ +k_{7cat}x_{10}\end{aligned} \tag{11}$$

$$\frac{d(x_{12})}{dt} = -\frac{k_{1cat}x_{12}x_{11}}{(k_{1m}+x_{12})} - k_{on13}x_{30}x_{12} + k_{off13}x_{33} \tag{12}$$

$$\frac{d(x_{13})}{dt} = \frac{k_{1cat}x_{12}x_{11}}{(k_{1m}+x_{12})} \tag{13}$$

$$\begin{aligned}\frac{d(x_{14})}{dt} = \frac{k_{1cat}x_{12}x_{11}}{(k_{1m}+x_{12})} - k_{on6}x_{16}x_{14} + k_{off6}x_{18}\\ -k_{on9}x_{14}x_{20} + k_{off9}x_{21} - \frac{k_{6cat}x_{14}x_{30}}{(k_{6m}+x_{14})}\end{aligned} \tag{14}$$

$$\frac{d(x_{15})}{dt} = -\frac{k_{4cat}x_{15}x_{11}}{(k_{4m}+x_{15})} - k_{on14}x_{30}x_{15} + k_{off14}x_{34} \tag{15}$$

$$\frac{d(x_{16})}{dt} = \frac{k_{4cat}x_{15}x_{11}}{(k_{4m}+x_{15})} - k_{on6}x_{16}x_{14} + k_{off6}x_{18} \tag{16}$$

$$\frac{d(x_{17})}{dt} = \frac{k_{4cat}x_{15}x_{11}}{(k_{4m}+x_{15})} \tag{17}$$

$$\begin{aligned}\frac{d(x_{18})}{dt} = k_{on6}x_{16}x_{14} - k_{off6}x_{18} - k_{on8}x_{20}x_{18}\\ +k_{off8}x_{22} - k_{on10}x_{25}x_{18} + k_{off10}x_{26}\end{aligned} \tag{18}$$

$$\frac{d(x_{19})}{dt} = k_{on7}x_5x_{11} \tag{19}$$

$$\begin{aligned}\frac{d(x_{20})}{dt} = -k_{on8}x_{20}x_{18} + k_{off8}x_{22} - k_{on9}x_{14}x_{20}\\ +k_{off9}x_{21}\end{aligned} \tag{20}$$

$$\frac{d(x_{21})}{dt} = k_{on9}x_{14}x_{20} - k_{off9}x_{21} \tag{21}$$

$$\frac{d(x_{22})}{dt} = k_{on8}x_{20}x_{18} - k_{off8}x_{22} \tag{22}$$

$$\frac{d(x_{23})}{dt} = -\frac{k_{2cat}x_{23}x_{18}}{(k_{2m}+x_{23})} - k_{on12}x_{30}x_{23} + k_{off12}x_{32} \tag{23}$$

$$\frac{d(x_{24})}{dt} = \frac{k_{2cat}x_{23}x_{18}}{(k_{2m}+x_{23})} - k_{on17}x_{24}x_{36} + k_{off17}x_{37} \tag{24}$$

$$\begin{aligned}\frac{d(x_{25})}{dt} = \frac{k_{2cat}x_{23}x_{18}}{(k_{2m}+x_{23})} - k_{on10}x_{25}x_{18} + k_{off10}x_{26}\\ -\frac{k_{5cat}x_{25}x_{30}}{(k_{5m}+x_{25})}\end{aligned} \tag{25}$$

$$\frac{d(x_{26})}{dt} = k_{on10}x_{25}x_{18} - k_{off10}x_{26} \tag{26}$$

$$\frac{d(x_{27})}{dt} = -\frac{k_{3cat}x_{27}x_{26}}{(k_{3m}+x_{27})} - k_{on11}x_{27}x_{30} + k_{off11}x_{31} \tag{27}$$

$$\frac{d(x_{28})}{dt} = \frac{k_{3cat}x_{27}x_{26}}{(k_{3m}+x_{27})} - k_{on18}x_{28}x_{38} + k_{off18}x_{39} \tag{28}$$

$$\frac{d(x_{29})}{dt} = \frac{k_{3cat}x_{27}x_{26}}{(k_{3m}+x_{27})} \tag{29}$$

$$\begin{aligned}\frac{d(x_{30})}{dt} = -k_{on11}x_{27}x_{30} + k_{off11}x_{31}\\ -k_{on12}x_{30}x_{23} + k_{off12}x_{32}\\ -k_{on13}x_{30}x_{12} + k_{off13}x_{33}\\ -k_{on14}x_{30}x_{15} + k_{off14}x_{34}\\ -k_{on15}x_{11}x_{30} + k_{off15}x_{35}\\ -k_{on16}x_{30}x_5 + U(t)\end{aligned} \tag{30}$$

$$\frac{d(x_{31})}{dt} = k_{on11}x_{27}x_{30} - k_{off11}x_{31} \tag{31}$$

$$\frac{d(x_{32})}{dt} = k_{on12}x_{30}x_{23} - k_{off12}x_{32} \tag{32}$$

$$\frac{d(x_{33})}{dt} = k_{on13}x_{30}x_{12} - k_{off13}x_{33} \tag{33}$$

$$\frac{d(x_{34})}{dt} = k_{on14}x_{30}x_{15} - k_{off14}x_{34} \tag{34}$$

$$\frac{d(x_{35})}{dt} = k_{on15}x_{11}x_{30} - k_{off15}x_{35} \tag{35}$$

$$\frac{d(x_{36})}{dt} = -k_{on17}x_{24}x_{36} + k_{off17}x_{37} \tag{36}$$

$$\frac{d(x_{37})}{dt} = k_{on17}x_{24}x_{36} - k_{off17}x_{37} \tag{37}$$

$$\frac{d(x_{38})}{dt} = -k_{on18}x_{28}x_{38} + k_{off18} * x_{39} \tag{38}$$

$$\frac{d(x_{39})}{dt} = k_{on18}x_{28}x_{38} - k_{off18}x_{39} \tag{39}$$

Controller design

Sliding mode control (SMC) is a nonlinear strategy for controlling system behavior by establishing a sliding surface, which represents the distinction between desired and actual system states. Through this surface, the controller applies input to guide the system towards alignment with it. SMC boasts robustness within this mode, making it adept at managing uncertainties, time-varying parameters, and disturbances. It delivers swift, precise responses to alterations in system conditions, all while offering design simplicity and enhanced control performance over traditional linear methods in certain scenarios. Notably, SMC can ensure finite-time convergence with high precision, eliminating steady-state error. Nevertheless, its drawbacks include intricate design, susceptibility to measurement noise and modeling inaccuracies, potential for higher-order sliding surfaces, and a phenomenon known as chattering. This chattering effect illustrates fluctuations before the system stabilizes near the sliding surface. To implement SMC, one must first select a sliding surface and then derive a control law to guide the system towards it.

Double integral Sliding Mode Controller

Consider the model of classical pathway of the complement system as given in Eqs (1)–(39). Choose the equations in which the drug Heparin (x_{30}) binds to the targets. Therefore, consider state equations of variables $x_5, x_{11}, x_{12}, x_{14}, x_{15}, x_{23}, x_{25}, x_{27}, x_{31}, x_{32}, x_{33}, x_{34}, x_{35}$ and x_{30}. To ensure the states reach the reference or settle point, the errors are defined as follows:

$$\begin{gathered}
e_{\phi 1} = x_5 - x_{5r}, e_{\phi 2} = x_{11} - x_{11r},\\
e_{\phi 3} = x_{12} - x_{12r}, e_{\phi 4} = x_{14} - x_{14r},\\
e_{\phi 5} = x_{15} - x_{15r}, e_{\phi 6} = x_{23} - x_{23r},\\
e_{\phi 7} = x_{25} - x_{25r}, e_{\phi 8} = x_{27} - x_{27r},\\
e_{\phi 9} = x_{31} - x_{31r}, e_{\phi 10} = x_{32} - x_{32r},\\
e_{\phi 11} = x_{33} - x_{33r}, e_{\phi 12} = x_{34} - x_{34r},\\
e_{\phi 13} = x_{35} - x_{35r}, e_{\phi 14} = x_{30} - x_{30r}.
\end{gathered} \tag{40}$$

In the design process, an integral of the error term is utilized to eliminate the steady-state error in the control response, which can be described as follows:

$$\begin{gathered}
e_{\theta 1} = \int (x_5 - x_{5r})dt, e_{\theta 2} = \int (x_{11} - x_{11r})dt,\\
e_{\theta 3} = \int (x_{12} - x_{12r})dt, e_{\theta 4} = \int (x_{14} - x_{14r})dt,\\
e_{\theta 5} = \int (x_{15} - x_{15r})dt, e_{\theta 6} = \int (x_{23} - x_{23r})dt,\\
e_{\theta 7} = \int (x_{25} - x_{25r})dt, e_{\theta 8} = \int (x_{27} - x_{27r})dt,\\
e_{\theta 9} = \int (x_{31} - x_{31r})dt, e_{\theta 10} = \int (x_{32} - x_{32r})dt,\\
e_{\theta 11} = \int (x_{33} - x_{33r})dt, e_{\theta 12} = \int (x_{34} - x_{34r})dt,\\
e_{\theta 13} = \int (x_{35} - x_{35r})dt, e_{\theta 14} = \int (x_{30} - x_{30r})dt.
\end{gathered} \tag{41}$$

Taking integration of Eq. (41) we have:

$$\begin{gathered}
e_{\eta 1} = \int(\int (x_5 - x_{5r})dt)dt,\\
e_{\eta 2} = \int(\int (x_{11} - x_{11r})dt)dt,\\
e_{\eta 3} = \int(\int (x_{12} - x_{12r})dt)dt,\\
e_{\eta 4} = \int(\int (x_{14} - x_{14r})dt)dt,\\
e_{\eta 5} = \int(\int (x_{15} - x_{15r})dt)dt,\\
e_{\eta 6} = \int(\int (x_{23} - x_{23r})dt)dt,\\
e_{\eta 7} = \int(\int (x_{25} - x_{25r})dt)dt,\\
e_{\eta 8} = \int(\int (x_{27} - x_{27r})dt)dt,\\
e_{\eta 9} = \int(\int (x_{31} - x_{31r})dt)dt,\\
e_{\eta 10} = \int(\int (x_{32} - x_{32r})dt)dt,\\
e_{\eta 11} = \int(\int (x_{33} - x_{33r})dt)dt,\\
e_{\eta 12} = \int(\int (x_{34} - x_{34r})dt)dt,\\
e_{\eta 13} = \int(\int (x_{35} - x_{35r})dt)dt,\\
e_{\eta 14} = \int(\int (x_{30} - x_{30r})dt)dt.
\end{gathered} \tag{42}$$

The time derivative of these errors can be defined as follows:

$$\begin{gathered}
\dot{e}_{\eta 1} = \int (x_5 - x_{5r})dt = e_{\theta 1}\\
\dot{e}_{\eta 2} = \int (x_{11} - x_{11r})dt = e_{\theta 2}\\
\dot{e}_{\eta 3} = \int (x_{12} - x_{12r})dt = e_{\theta 3}\\
\dot{e}_{\eta 4} = \int (x_{14} - x_{14r})dt = e_{\theta 4}\\
\dot{e}_{\eta 5} = \int (x_{15} - x_{15r})dt = e_{\theta 5}\\
\dot{e}_{\eta 6} = \int (x_{23} - x_{23r})dt = e_{\theta 6}\\
\dot{e}_{\eta 7} = \int (x_{25} - x_{25r})dt = e_{\theta 7}\\
\dot{e}_{\eta 8} = \int (x_{27} - x_{27r})dt = e_{\theta 8}\\
\dot{e}_{\eta 9} = \int (x_{31} - x_{31r})dt = e_{\theta 9}\\
\dot{e}_{\eta 10} = \int (x_{32} - x_{32r})dt = e_{\theta 10}\\
\dot{e}_{\eta 11} = \int (x_{33} - x_{33r})dt = e_{\theta 11}\\
\dot{e}_{\eta 12} = \int (x_{34} - x_{34r})dt = e_{\theta 12}\\
\dot{e}_{\eta 13} = \int (x_{35} - x_{35r})dt = e_{\theta 13}\\
\dot{e}_{\eta 14} = \int (x_{30} - x_{30r})dt = e_{\theta 14}
\end{gathered} \tag{43}$$

Consider a first-order sliding surface (S) defined as

$$\begin{gathered}
S = d_1 e_{\phi 1} + d_2 e_{\phi 2} + d_3 e_{\phi 3} + d_4 e_{\phi 4} + d_5 e_{\phi 5}\\
+ d_6 e_{\phi 6} + d_7 e_{\phi 7} + d_8 e_{\phi 8} + d_9 e_{\phi 9} + d_{10} e_{\phi 10}\\
+ d_{11} e_{\phi 1} + d_{12} e_{\phi 12} + d_{13} e_{\phi 13} + d_{14} e_{\phi 14} + d_{15} e_{\theta 1}\\
+ d_{16} e_{\theta 2} + d_{17} e_{\theta 3} + d_{18} e_{\theta 4} + d_{19} e_{\theta 5} + d_{20} e_{\theta 6}\\
+ d_{21} e_{\theta 7} + d_{22} e_{\theta 8} + d_{23} e_{\theta 9} + d_{24} e_{\theta 10} + d_{25} e_{\theta 11}\\
+ d_{26} e_{\theta 12} + d_{27} e_{\theta 13} + d_{28} e_{\theta 14} + d_{29} e_{\eta 1} + d_{30} e_{\eta 2}\\
+ d_{31} e_{\eta 3} + d_{32} e_{\eta 4} + d_{33} e_{\eta 5} + d_{34} e_{\eta 6} + d_{35} e_{\eta 7}\\
+ d_{36} e_{\eta 8} + d_{37} e_{\eta 9} + d_{38} e_{\eta 10} + d_{39} e_{\eta 11} + d_{40} e_{\eta 12}\\
+ d_{41} e_{\eta 13} + d_{42} e_{\eta 14}
\end{gathered} \tag{44}$$

By taking the time derivative of Eq. (44), we obtain:

$$\begin{gathered}
\dot{S} = d_1 \dot{e}_{\phi 1} + d_2 \dot{e}_{\phi 2} + d_3 \dot{e}_{\phi 3} + d_4 \dot{e}_{\phi 4} + d_5 \dot{e}_{\phi 5}\\
+ d_6 \dot{e}_{\phi 6} + d_7 \dot{e}_{\phi 7} + d_8 \dot{e}_{\phi 8} + d_9 \dot{e}_{\phi 9} + d_{10} \dot{e}_{\phi 10}\\
+ d_{11} \dot{e}_{\phi 1} + d_{12} \dot{e}_{\phi 12} + d_{13} \dot{e}_{\phi 13} + d_{14} \dot{e}_{\phi 14} + d_{15} \dot{e}_{\theta 1}\\
+ d_{16} \dot{e}_{\theta 2} + d_{17} \dot{e}_{\theta 3} + d_{18} \dot{e}_{\theta 4} + d_{19} \dot{e}_{\theta 5} + d_{20} \dot{e}_{\theta 6}\\
+ d_{21} \dot{e}_{\theta 7} + d_{22} \dot{e}_{\theta 8} + d_{23} \dot{e}_{\theta 9} + d_{24} \dot{e}_{\theta 10} + d_{25} \dot{e}_{\theta 11}\\
+ d_{26} \dot{e}_{\theta 12} + d_{27} \dot{e}_{\theta 13} + d_{28} \dot{e}_{\theta 14} d_{29} \dot{e}_{\eta 1} + d_{30} \dot{e}_{\eta 2}\\
+ d_{31} \dot{e}_{\eta 3} + d_{32} \dot{e}_{\eta 4} + d_{33} \dot{e}_{\eta 5} + d_{34} \dot{e}_{\eta 6} + d_{35} \dot{e}_{\eta 7}\\
+ d_{36} \dot{e}_{\eta 8} + d_{37} \dot{e}_{\eta 9} + d_{38} \dot{e}_{\eta 10} + d_{39} \dot{e}_{\eta 11} + d_{40} \dot{e}_{\eta 12}\\
+ d_{41} \dot{e}_{\eta 13} + d_{42} \dot{e}_{\eta 14}
\end{gathered} \tag{45}$$

Substituting the derivatives of the error terms into Eq.(45).

$$\begin{aligned}\dot{S} &= d_1(\dot{x}_5 - \dot{x}_{5r}) + d_2(\dot{x}_{11} - \dot{x}_{11r}) \\ &+d_3(\dot{x}_{12} - \dot{x}_{12r}) + d_4(\dot{x}_{14} - \dot{x}_{14r}) \\ &+d_5(\dot{x}_{15} - \dot{x}_{15r}) + d_6(\dot{x}_{23} - \dot{x}_{23r}) \\ &+d_7(\dot{x}_{25} - \dot{x}_{25r}) + d_8(\dot{x}_{27} - \dot{x}_{27r}) \\ &+d_9(\dot{x}_{31} - \dot{x}_{31r}) + d_{10}(\dot{x}_{32} - \dot{x}_{32r}) \\ &+d_{11}(\dot{x}_{33} - \dot{x}_{33r}) + d_{12}(\dot{x}_{34} - \dot{x}_{34r}) \\ &+d_{13}(\dot{x}_{35} - \dot{x}_{35r}) + d_{14}(\dot{x}_{30} - \dot{x}_{30r}) \\ &d_{15}e_{\phi 1} + d_{16}e_{\phi 2} + d_{17}e_{\phi 3} + d_{18}e_{\phi 4} \\ &+d_{19}e_{\phi 5} + d_{20}e_{\phi 6} + d_{21}e_{\phi 7} + d_{22}e_{\phi 8} \\ &+d_{23}e_{\phi 9} + d_{24}e_{\phi 10} + d_{25}e_{\phi 11} + d_{26}e_{\phi 12} \\ &+d_{27}e_{\phi 13} + d_{28}e_{\phi 14}d_{29}e_{\theta 1} + d_{30}e_{\theta 2} \\ &+d_{31}e_{\theta 3} + d_{32}e_{\theta 4} + d_{33}e_{\theta 5} + d_{34}e_{\theta 6} \\ &+d_{35}e_{\theta 7} + d_{36}e_{\theta 8} + d_{37}e_{\theta 9} + d_{38}e_{\theta 10} \\ &+d_{39}e_{\theta 11} + d_{40}e_{\theta 12} + d_{41}e_{\theta 13} + d_{42}e_{\theta 14}\end{aligned} \tag{46}$$

To reduce the chattering in DISMC, a strong reachability condition is used to design the control law [1] by considering Eq. (47):

$$\dot{S} = -\tau|S|^{\delta} sign(\frac{S}{\rho}) \tag{47}$$

Here, τ represents a design coefficient, chosen as a positive number, while δ can be any value within the range of 0 to 1. ρ is employed to mitigate chattering and typically takes a very small value. $|S|^{\delta}$ guarantees enhanced convergence of the error or increases the speed of trajectory toward the sliding surface, effectively expediting the reaching phase. The Signum function, denoted by sign, is defined as follows:

$$Sign(S) = \begin{cases} 1, & if\ S > 0 \\ 0, & if\ S = 0 \\ -1, & if\ S < 0 \end{cases}$$

Eq. (46) and Eq. (47) implies that

$$\begin{aligned}-\tau|S|^{\delta} sign(\tfrac{S}{\rho}) &= d_1(\dot{x}_5 - \dot{x}_{5r}) \\ &+d_2(\dot{x}_{11} - \dot{x}_{11r}) + d_3(\dot{x}_{12} - \dot{x}_{12r}) \\ &+d_4(\dot{x}_{14} - \dot{x}_{14r}) + d_5(\dot{x}_{15} - \dot{x}_{15r}) \\ &+d_6(\dot{x}_{23} - \dot{x}_{23r}) + d_7(\dot{x}_{25} - \dot{x}_{25r}) \\ &+d_8(\dot{x}_{27} - \dot{x}_{27r}) + d_9(\dot{x}_{31} - \dot{x}_{31r}) \\ &+d_{10}(\dot{x}_{32} - \dot{x}_{32r}) + d_{11}(\dot{x}_{33} - \dot{x}_{33r}) \\ &+d_{12}(\dot{x}_{34} - \dot{x}_{34r}) + d_{13}(\dot{x}_{35} - \dot{x}_{35r}) \\ &+d_{14}(-k_{on11} * x_{27} * x_{30} + k_{off11} * x_{31} \\ &-k_{on12} * x_{30} * x_{23} + k_{off12} * x_{32} \\ &-k_{on13} * x_{30} * x_{12} + k_{off13} * x_{33} \\ &-k_{on14} * x_{30} * x_{15} + k_{off14} * x_{34} \\ &-k_{on15} * x_{11} * x_{30} + k_{off15} * x_{35} \\ &-k_{on16} * x_{30} * x_5 + U - \dot{x}_{30r}) \\ &d_{15}e_{\phi 1} + d_{16}e_{\phi 2} + d_{17}e_{\phi 3} \\ &+d_{18}e_{\phi 4} + d_{19}e_{\phi 5} + d_{20}e_{\phi 6} \\ &+d_{21}e_{\phi 7} + d_{22}e_{\phi 8} + d_{23}e_{\phi 9} \\ &+d_{24}e_{\phi 10} + d_{25}e_{\phi 11} + d_{26}e_{\phi 12} \\ &+d_{27}e_{\phi 13} + d_{28}e_{\phi 14}d_{29}e_{\theta 1} \\ &+d_{30}e_{\theta 2} + d_{31}e_{\theta 3} + d_{32}e_{\theta 4} \\ &+d_{33}e_{\theta 5} + d_{34}e_{\theta 6} + d_{35}e_{\theta 7} \\ &+d_{36}e_{\theta 8} + d_{37}e_{\theta 9} + d_{38}e_{\theta 10} \\ &+d_{39}e_{\theta 11} + d_{40}e_{\theta 12} \\ &+d_{41}e_{\theta 13} + d_{42}e_{\theta 14}\end{aligned} \tag{48}$$

$$\begin{aligned}U &= -\tfrac{1}{d_{14}}\tau|S|^{\delta} sign(\tfrac{S}{\rho}) - \tfrac{1}{d_{14}}\Big(d_1(\dot{x}_5 - \dot{x}_{5r}) \\ &+d_2(\dot{x}_{11} - \dot{x}_{11r}) + d_3(\dot{x}_{12} - \dot{x}_{12r}) \\ &+d_4(\dot{x}_{14} - \dot{x}_{14r}) + d_5(\dot{x}_{15} - \dot{x}_{15r}) \\ &+d_6(\dot{x}_{23} - \dot{x}_{23r}) + d_7(\dot{x}_{25} - \dot{x}_{25r}) \\ &+d_8(\dot{x}_{27} - \dot{x}_{27r}) + d_9(\dot{x}_{31} - \dot{x}_{31r}) \\ &+d_{10}(\dot{x}_{32} - \dot{x}_{32r}) + d_{11}(\dot{x}_{33} - \dot{x}_{33r}) \\ &+d_{12}(\dot{x}_{34} - \dot{x}_{34r}) + d_{13}(\dot{x}_{35} - \dot{x}_{35r})\Big) \\ &-\tfrac{1}{d_{14}}\Big(d_{15}e_{\phi 1} + d_{16}e_{\phi 2} + d_{17}e_{\phi 3} + d_{18}e_{\phi 4} \\ &+d_{19}e_{\phi 5} + d_{20}e_{\phi 6} + d_{21}e_{\phi 7} + d_{22}e_{\phi 8} \\ &+d_{23}e_{\phi 9} + d_{24}e_{\phi 10} + d_{25}e_{\phi 11} + d_{26}e_{\phi 12} \\ &+d_{27}e_{\phi 13} + d_{28}e_{\phi 14} + d_{29}e_{\theta 1} + d_{30}e_{\theta 2} \\ &+d_{31}e_{\theta 3} + d_{32}e_{\theta 4} + d_{33}e_{\theta 5} + d_{34}e_{\theta 6} \\ &+d_{35}e_{\theta 7} + d_{36}e_{\theta 8} + d_{37}e_{\theta 9} + d_{38}e_{\theta 10} \\ &+d_{39}e_{\theta 11} + d_{40}e_{\theta 12} + d_{41}e_{\theta 13} + d_{42}e_{\theta 14}\Big) \\ &-\Big(- k_{on11} * x_{27} * x_{30} + k_{off11} * x_{31} \\ &-k_{on12} * x_{30} * x_{23} + k_{off12} * x_{32} \\ &-k_{on13} * x_{30} * x_{12} + k_{off13} * x_{33} \\ &-k_{on14} * x_{30} * x_{15} + k_{off14} * x_{34} \\ &-k_{on15} * x_{11} * x_{30} + k_{off15} * x_{35} \\ &-k_{on16} * x_{30} * x_5 - \dot{x}_{30r}\Big)\end{aligned} \tag{49}$$

The mathematical formulation in Eq. (49) provides the necessary control law for administering heparin using DISMC.

REFERENCES

[1] Ali Hamza, Muhammad Uneeb, Iftikhar Ahmad, Komal Saleem, and Zunaib Ali. Variable structure based control strategy for treatment of hcv infection. *Biomedical Signal Processing and Control*, 89:105803, 2024.