

1                    **Supporting information for the article**  
2                    **“Superinfection and cell regeneration can lead to**  
3                    **chronic viral coinfections”**

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10                   **1 Detailed steady states of model 1**

11                   Here we show all the possible chronic coinfection equilibria of the model where super-  
12                   infection with cell regeneration and death are considered (model 1, according to main  
13                   text).

14                   **1.1 Steady states of model 1**

In model 1 or the most general case of superinfection model that includes target cell  
regeneration along with natural cell death, we found five different equilibria. Among  
them one is the infection free equilibrium ( $Q_1^*$ )

$$Q_1^* = (T^*, 0, 0, 0, 0, 0, 0, 0, 0), \text{ where } T^* \in \mathbb{R}_{\geq} \text{ or } \{T^* \in \mathbb{R} \mid T^* \geq 0\}.$$

The rest four are the chronic coinfection equilibria ( $Q_2^*$ ,  $Q_2^{*'}$ ,  $Q_2^{*''}$ ,  $Q_2^{*'''}$ ). Follow-  
ing are the four possible chronic coinfection equilibria with their respective parameter

constraints.

### Chronic coinfection equilibrium, $Q_2^*$

$$\begin{aligned}
T^{*'} &= \frac{r}{\beta_1 V_1^{*'} + \beta_2 V_2^{*'} + a}, \quad E_1^{*'} = \frac{\beta_1 T^{*'} V_1^{*'}}{k_1 + \beta_{21} V_2^{*'}}, \quad E_2^{*'} = \frac{\beta_2 T^{*'} V_2^{*'}}{k_2 + \beta_{12} V_1^{*'}}, \\
E_3^{*'} &= \frac{1}{k_3} (\beta_{12} E_2^{*'} V_1^{*'} + \beta_{21} E_1^{*'} V_2^{*'}), \quad I_1^{*'} = \frac{k_1}{\delta_1} E_1^{*'}, \quad I_2^{*'} = \frac{k_2}{\delta_2} E_2^{*'}, \quad I_3^{*'} = \frac{k_3}{\delta_3} E_3^{*'}, \\
V_1^{*'} &= \frac{1}{2\beta_1 \beta_{12} c_1 \delta_1 \delta_3 (k_1 + \beta_{21} V_2^{*'})} \left[ \left\{ r\beta_1 \beta_{12} (p_1 k_1 \delta_3 + p_{12} \delta_1 V_2^{*'}) - c_1 \delta_1 \delta_3 (k_1 + \beta_{21} V_2^{*'}) \right. \right. \\
&\quad \left. \left. (\beta_1 k_2 + \beta_2 \beta_{12} V_2^{*'} + a\beta_{12}) \right\} + \sqrt{\left[ \left\{ c_1 \delta_1 \delta_3 (k_1 + \beta_{21} V_2^{*'}) (\beta_1 k_2 + \beta_2 \beta_{12} V_2^{*'} + a\beta_{12}) \right\}^2 \right. \right. \\
&\quad \left. \left. + \left\{ r\beta_1 \beta_{12} (p_1 k_1 \delta_3 + p_{12} \delta_1 V_2^{*'}) \right\}^2 + 4r\beta_2 V_2^{*'} p_{12} \beta_1 \beta_{12}^2 c_1 \delta_1^2 \delta_3 (k_1 + \beta_{21} V_2^{*'})^2 \right. \right. \\
&\quad \left. \left. + 4r\beta_1^2 k_2 \beta_{12} c_1 \delta_1 \delta_3 (k_1 + \beta_{21} V_2^{*'}) (p_1 k_1 \delta_3 + p_{12} \beta_{21} \delta_1 V_2^{*'}) \right. \right. \\
&\quad \left. \left. - \left( 4\beta_1 \beta_{12} c_1^2 \delta_1^2 \delta_3^2 (k_1 + \beta_{21} V_2^{*'})^2 (\beta_2 k_2 V_2^{*'} + a k_2) \right. \right. \right. \\
&\quad \left. \left. \left. + 2r c_1 \delta_1 \delta_3 \beta_1 \beta_{12} (k_1 + \beta_{21} V_2^{*'}) (\beta_1 k_2 + \beta_2 \beta_{12} V_2^{*'} + a\beta_{12}) (p_1 k_1 \delta_3 + p_{12} \delta_1 V_2^{*'}) \right) \right] \right], \\
V_2^{*'} &= \frac{1}{2\beta_2 \beta_{21} c_2 \delta_2 \delta_3 (k_2 + \beta_{12} V_1^{*'})} \left[ \left\{ r\beta_2 \beta_{21} (p_2 k_2 \delta_3 + p_{21} \delta_2 V_1^{*'}) - c_2 \delta_2 \delta_3 (k_2 + \beta_{12} V_1^{*'}) \right. \right. \\
&\quad \left. \left. (\beta_2 k_1 + \beta_1 \beta_{21} V_1^{*'} + a\beta_{21}) \right\} + \sqrt{\left[ \left\{ c_2 \delta_2 \delta_3 (k_2 + \beta_{12} V_1^{*'}) (\beta_2 k_1 + \beta_1 \beta_{21} V_1^{*'} + a\beta_{21}) \right\}^2 \right. \right. \\
&\quad \left. \left. + \left\{ r\beta_2 \beta_{21} (p_2 k_2 \delta_3 + p_{21} \delta_2 V_1^{*'}) \right\}^2 + 4r\beta_1 V_1^{*'} p_{21} \beta_2 \beta_{21}^2 c_2 \delta_2^2 \delta_3 (k_2 + \beta_{12} V_1^{*'})^2 \right. \right. \\
&\quad \left. \left. + 4r\beta_2^2 k_1 \beta_{21} c_2 \delta_2 \delta_3 (k_2 + \beta_{12} V_1^{*'}) (p_2 k_2 \delta_3 + p_{21} \beta_{12} \delta_2 V_1^{*'}) \right. \right. \\
&\quad \left. \left. - \left( 4\beta_2 \beta_{21} c_2^2 \delta_2^2 \delta_3^2 (k_2 + \beta_{12} V_1^{*'})^2 (\beta_1 k_1 V_1^{*'} + a k_1) \right. \right. \right. \\
&\quad \left. \left. \left. + 2r c_2 \delta_2 \delta_3 \beta_2 \beta_{21} (k_2 + \beta_{12} V_1^{*'}) (\beta_2 k_1 + \beta_1 \beta_{21} V_1^{*'} + a\beta_{21}) (p_2 k_2 \delta_3 + p_{21} \delta_2 V_1^{*'}) \right) \right] \right].
\end{aligned}$$

Given the term inside the square root generates real positive number with the parameters, this chronic coinfection equilibrium exists if the following conditions are satisfied.

The conditions for  $V_1$  and  $V_2$  are respectively

$$r\beta_1\beta_{12}\frac{(p_1k_1\delta_3 + p_{12}\delta_1V_2^{*'})}{(k_1 + \beta_{21}V_2^{*'})} \geq c_1\delta_1\delta_3(\beta_1k_2 + \beta_2\beta_{12}V_2^{*'} + a\beta_{12}), \text{ and}$$

$$r\beta_2\beta_{21}\frac{(p_2k_2\delta_3 + p_{21}\delta_2V_1^{*'})}{(k_2 + \beta_{12}V_1^{*'})} \geq c_2\delta_2\delta_3(\beta_2k_1 + \beta_1\beta_{21}V_1^{*'} + a\beta_{21}).$$

### Chronic coinfection equilibrium, $Q_2^{**}$

$$T^{**} = \frac{r}{\beta_1V_1^{**} + \beta_2V_2^{**} + a}, \quad E_1^{**} = \frac{\beta_1T^{**}V_1^{**}}{k_1 + \beta_{21}V_2^{**}}, \quad E_2^{**} = \frac{\beta_2T^{**}V_2^{**}}{k_2 + \beta_{12}V_1^{**}},$$

$$E_3^{**} = \frac{1}{k_3}(\beta_{12}E_2^{**}V_1^{**} + \beta_{21}E_1^{**}V_2^{**}), \quad I_1^{**} = \frac{k_1}{\delta_1}E_1^{**}, \quad I_2^{**} = \frac{k_2}{\delta_2}E_2^{**}, \quad I_3^{**} = \frac{k_3}{\delta_3}E_3^{**},$$

$$V_1^{**} = \frac{1}{2\beta_1\beta_{12}c_1\delta_1\delta_3(k_1 + \beta_{21}V_2^{**})} \left[ \left\{ r\beta_1\beta_{12}(p_1k_1\delta_3 + p_{12}\delta_1V_2^{**}) - c_1\delta_1\delta_3(k_1 + \beta_{21}V_2^{**}) \right. \right.$$

$$(\beta_1k_2 + \beta_2\beta_{12}V_2^{**} + a\beta_{12}) \left. \right\} - \sqrt{\left[ \left\{ c_1\delta_1\delta_3(k_1 + \beta_{21}V_2^{**})(\beta_1k_2 + \beta_2\beta_{12}V_2^{**} + a\beta_{12}) \right\}^2 \right.$$

$$+ \left\{ r\beta_1\beta_{12}(p_1k_1\delta_3 + p_{12}\delta_1V_2^{**}) \right\}^2 + 4r\beta_2V_2^{**}p_{12}\beta_1\beta_{12}^2c_1\delta_1^2\delta_3(k_1 + \beta_{21}V_2^{**})^2$$

$$+ 4r\beta_1^2k_2\beta_{12}c_1\delta_1\delta_3(k_1 + \beta_{21}V_2^{**})(p_1k_1\delta_3 + p_{12}\beta_{21}\delta_1V_2^{**})$$

$$- \left( 4\beta_1\beta_{12}c_1^2\delta_1^2\delta_3^2(k_1 + \beta_{21}V_2^{**})^2(\beta_2k_2V_2^{**} + ak_2) \right.$$

$$\left. \left. + 2rc_1\delta_1\delta_3\beta_1\beta_{12}(k_1 + \beta_{21}V_2^{**})(\beta_1k_2 + \beta_2\beta_{12}V_2^{**} + a\beta_{12})(p_1k_1\delta_3 + p_{12}\delta_1V_2^{**}) \right] \right]},$$

$$V_2^{**} = \frac{1}{2\beta_2\beta_{21}c_2\delta_2\delta_3(k_2 + \beta_{12}V_1^{**})} \left[ \left\{ r\beta_2\beta_{21}(p_2k_2\delta_3 + p_{21}\delta_2V_1^{**}) - c_2\delta_2\delta_3(k_2 + \beta_{12}V_1^{**}) \right. \right.$$

$$(\beta_2k_1 + \beta_1\beta_{21}V_1^{**} + a\beta_{21}) \left. \right\} - \sqrt{\left[ \left\{ c_2\delta_2\delta_3(k_2 + \beta_{12}V_1^{**})(\beta_2k_1 + \beta_1\beta_{21}V_1^{**} + a\beta_{21}) \right\}^2 \right.$$

$$+ \left\{ r\beta_2\beta_{21}(p_2k_2\delta_3 + p_{21}\delta_2V_1^{**}) \right\}^2 + 4r\beta_1V_1^{**}p_{21}\beta_2\beta_{21}^2c_2\delta_2^2\delta_3(k_2 + \beta_{12}V_1^{**})^2$$

$$+ 4r\beta_2^2k_1\beta_{21}c_2\delta_2\delta_3(k_2 + \beta_{12}V_1^{**})(p_2k_2\delta_3 + p_{21}\beta_{12}\delta_2V_1^{**})$$

$$\begin{aligned}
& - \left( 4\beta_2\beta_{21}c_2^2\delta_2^2\delta_3^2(k_2 + \beta_{12}V_1^{*''})^2(\beta_1k_1V_1^* + ak_1) \right. \\
& \left. + 2rc_2\delta_2\delta_3\beta_2\beta_{21}(k_2 + \beta_{12}V_1^{*''})(\beta_2k_1 + \beta_1\beta_{21}V_1^{*''} + a\beta_{21})(p_2k_2\delta_3 + p_{21}\delta_2V_1^{*''}) \right) \Bigg].
\end{aligned}$$

Similarly, this chronic coinfection equilibrium exists if the following conditions are satisfied. The conditions for  $V_1$  and  $V_2$  are respectively

$$\begin{aligned}
r\beta_1\beta_{12} \frac{(p_1k_1\delta_3 + p_{12}\delta_1V_2^{*''})}{(k_1 + \beta_{21}V_2^{*''})} &\geq c_1\delta_1\delta_3(\beta_1k_2 + \beta_2\beta_{12}V_2^{*''} + a\beta_{12}), \text{ and} \\
r\beta_2\beta_{21} \frac{(p_2k_2\delta_3 + p_{21}\delta_2V_1^{*''})}{(k_2 + \beta_{12}V_1^{*''})} &\geq c_2\delta_2\delta_3(\beta_2k_1 + \beta_1\beta_{21}V_1^{*''} + a\beta_{21}).
\end{aligned}$$

### Chronic coinfection equilibrium, $Q_2^{*'''}$

$$\begin{aligned}
T^{*'''} &= \frac{r}{\beta_1V_1^{*'''} + \beta_2V_2^{*'''} + a}, \quad E_1^{*'''} = \frac{\beta_1T^*V_1^{*'''} }{k_1 + \beta_{21}V_2^{*'''}}, \quad E_2^{*'''} = \frac{\beta_2T^*V_2^{*'''} }{k_2 + \beta_{12}V_1^{*'''}}, \\
E_3^{*'''} &= \frac{1}{k_3}(\beta_{12}E_2^{*'''}V_1^{*'''} + \beta_{21}E_1^{*'''}V_2^{*'''}), \quad I_1^{*'''} = \frac{k_1}{\delta_1}E_1^{*'''}, \quad I_2^{*'''} = \frac{k_2}{\delta_2}E_2^{*'''}, \quad I_3^{*'''} = \frac{k_3}{\delta_3}E_3^{*'''}, \\
V_1^{*'''} &= \frac{1}{2\beta_1\beta_{12}c_1\delta_1\delta_3(k_1 + \beta_{21}V_2^{*'''})} \left[ \left\{ -r\beta_1\beta_{12}(p_1k_1\delta_3 + p_{12}\delta_1V_2^{*'''}) + c_1\delta_1\delta_3(k_1 + \beta_{21}V_2^{*'''}) \right. \right. \\
& \left. \left. (\beta_1k_2 + \beta_2\beta_{12}V_2^{*'''} + a\beta_{12}) \right\} + \sqrt{\left[ \left\{ c_1\delta_1\delta_3(k_1 + \beta_{21}V_2^{*'''}) (\beta_1k_2 + \beta_2\beta_{12}V_2^{*'''} + a\beta_{12}) \right\}^2 \right. \right. \\
& \left. \left. + \left\{ r\beta_1\beta_{12}(p_1k_1\delta_3 + p_{12}\delta_1V_2^{*'''}) \right\}^2 + 4r\beta_2V_2^{*'''} p_{12}\beta_1\beta_{12}^2c_1\delta_1^2\delta_3(k_1 + \beta_{21}V_2^{*'''})^2 \right. \right. \\
& \left. \left. + 4r\beta_1^2k_2\beta_{12}c_1\delta_1\delta_3(k_1 + \beta_{21}V_2^{*'''}) (p_1k_1\delta_3 + p_{12}\beta_{21}\delta_1V_2^{*'''}) \right. \right. \\
& \left. \left. - \left( 4\beta_1\beta_{12}c_1^2\delta_1^2\delta_3^2(k_1 + \beta_{21}V_2^{*'''})^2(\beta_2k_2V_2^{*'''} + ak_2) \right. \right. \right. \\
& \left. \left. \left. + 2rc_1\delta_1\delta_3\beta_1\beta_{12}(k_1 + \beta_{21}V_2^{*'''}) (\beta_1k_2 + \beta_2\beta_{12}V_2^{*'''} + a\beta_{12})(p_1k_1\delta_3 + p_{12}\delta_1V_2^{*'''}) \right) \right] \right],
\end{aligned}$$

$$\begin{aligned}
V_2^{*''''} = & \frac{1}{2\beta_2\beta_{21}c_2\delta_2\delta_3(k_2 + \beta_{12}V_1^{*''''})} \left[ \left\{ -r\beta_2\beta_{21}(p_2k_2\delta_3 + p_{21}\delta_2V_1^{*''''}) + c_2\delta_2\delta_3(k_2 + \beta_{12}V_1^{*''''}) \right. \right. \\
& \left. \left. (\beta_2k_1 + \beta_1\beta_{21}V_1^{*''''} + a\beta_{21}) \right\} + \sqrt{\left[ \left\{ c_2\delta_2\delta_3(k_2 + \beta_{12}V_1^{*''''})(\beta_2k_1 + \beta_1\beta_{21}V_1^{*''''} + a\beta_{21}) \right\}^2 \right. \right. \\
& \left. \left. + \left\{ r\beta_2\beta_{21}(p_2k_2\delta_3 + p_{21}\delta_2V_1^{*''''}) \right\}^2 + 4r\beta_1V_1^{*''''} p_{21}\beta_2\beta_{21}^2 c_2\delta_2^2\delta_3(k_2 + \beta_{12}V_1^{*''''})^2 \right. \right. \\
& \left. \left. + 4r\beta_2^2k_1\beta_{21}c_2\delta_2\delta_3(k_2 + \beta_{12}V_1^{*''''})(p_2k_2\delta_3 + p_{21}\beta_{12}\delta_2V_1^{*''''}) \right. \right. \\
& \left. \left. - \left( 4\beta_2\beta_{21}c_2^2\delta_2^2\delta_3^2(k_2 + \beta_{12}V_1^{*''''})^2(\beta_1k_1V_1^{*''''} + ak_1) \right. \right. \right. \\
& \left. \left. \left. + 2rc_2\delta_2\delta_3\beta_2\beta_{21}(k_2 + \beta_{12}V_1^{*''''})(\beta_2k_1 + \beta_1\beta_{21}V_1^{*''''} + a\beta_{21})(p_2k_2\delta_3 + p_{21}\delta_2V_1^{*''''}) \right) \right] \right].
\end{aligned}$$

Similarly, this chronic coinfection equilibrium exists if the following conditions are satisfied. The conditions for  $V_1$  and  $V_2$  are respectively

$$\begin{aligned}
r\beta_1\beta_{12} \frac{(p_1k_1\delta_3 + p_{12}\delta_1V_2^{*''''})}{(k_1 + \beta_{21}V_2^{*''''})} & \leq c_1\delta_1\delta_3(\beta_1k_2 + \beta_2\beta_{12}V_2^{*''''} + a\beta_{12}), \text{ and} \\
r\beta_2\beta_{21} \frac{(p_2k_2\delta_3 + p_{21}\delta_2V_1^{*''''})}{(k_2 + \beta_{12}V_1^{*''''})} & \leq c_2\delta_2\delta_3(\beta_2k_1 + \beta_1\beta_{21}V_1^{*''''} + a\beta_{21}).
\end{aligned}$$

### Chronic coinfection equilibrium, $Q_2^{*''''}$

$$\begin{aligned}
T^{*''''} &= \frac{r}{\beta_1V_1^{*''''} + \beta_2V_2^{*''''} + a}, \quad E_1^{*''''} = \frac{\beta_1T^{*''''}V_1^{*''''}}{k_1 + \beta_{21}V_2^{*''''}}, \quad E_2^{*''''} = \frac{\beta_2T^{*''''}V_2^{*''''}}{k_2 + \beta_{12}V_1^{*''''}}, \\
E_3^{*''''} &= \frac{1}{k_3}(\beta_{12}E_2^{*''''}V_1^{*''''} + \beta_{21}E_1^{*''''}V_2^{*''''}), \quad I_1^{*''''} = \frac{k_1}{\delta_1}E_1^{*''''}, \quad I_2^{*''''} = \frac{k_2}{\delta_2}E_2^{*''''}, \quad I_3^{*''''} = \frac{k_3}{\delta_3}E_3^{*''''},
\end{aligned}$$

$$\begin{aligned}
V_1^{*''''} &= \frac{1}{2\beta_1\beta_{12}c_1\delta_1\delta_3(k_1 + \beta_{21}V_2^{*''''})} \left[ \left\{ -r\beta_1\beta_{12}(p_1k_1\delta_3 + p_{12}\delta_1V_2^{*''''}) + c_1\delta_1\delta_3(k_1 + \beta_{21}V_2^{*''''}) \right. \right. \\
&\quad \left. \left. (\beta_1k_2 + \beta_2\beta_{12}V_2^{*''''} + a\beta_{12}) \right\} - \sqrt{\left[ \left\{ c_1\delta_1\delta_3(k_1 + \beta_{21}V_2^{*''''}) (\beta_1k_2 + \beta_2\beta_{12}V_2^{*''''} + a\beta_{12}) \right\}^2 \right. \right. \\
&\quad \left. \left. + \left\{ r\beta_1\beta_{12}(p_1k_1\delta_3 + p_{12}\delta_1V_2^{*''''}) \right\}^2 + 4r\beta_2V_2^{*''''} p_{12}\beta_1\beta_{12}^2c_1\delta_1^2\delta_3(k_1 + \beta_{21}V_2^{*''''})^2 \right. \right. \\
&\quad \left. \left. + 4r\beta_1^2k_2\beta_{12}c_1\delta_1\delta_3(k_1 + \beta_{21}V_2^{*''''}) (p_1k_1\delta_3 + p_{12}\beta_{21}\delta_1V_2^{*''''}) \right. \right. \\
&\quad \left. \left. - \left( 4\beta_1\beta_{12}c_1^2\delta_1^2\delta_3^2(k_1 + \beta_{21}V_2^{*''''})^2 (\beta_2k_2V_2^{*''''} + ak_2) \right. \right. \right. \\
&\quad \left. \left. \left. + 2rc_1\delta_1\delta_3\beta_1\beta_{12}(k_1 + \beta_{21}V_2^{*''''}) (\beta_1k_2 + \beta_2\beta_{12}V_2^{*''''} + a\beta_{12}) (p_1k_1\delta_3 + p_{12}\delta_1V_2^{*''''}) \right) \right] \right], \\
V_2^{*''''} &= \frac{1}{2\beta_2\beta_{21}c_2\delta_2\delta_3(k_2 + \beta_{12}V_1^{*''''})} \left[ \left\{ -r\beta_2\beta_{21}(p_2k_2\delta_3 + p_{21}\delta_2V_1^{*''''}) + c_2\delta_2\delta_3(k_2 + \beta_{12}V_1^{*''''}) \right. \right. \\
&\quad \left. \left. (\beta_2k_1 + \beta_1\beta_{21}V_1^{*''''} + a\beta_{21}) \right\} - \sqrt{\left[ \left\{ c_2\delta_2\delta_3(k_2 + \beta_{12}V_1^{*''''}) (\beta_2k_1 + \beta_1\beta_{21}V_1^{*''''} + a\beta_{21}) \right\}^2 \right. \right. \\
&\quad \left. \left. + \left\{ r\beta_2\beta_{21}(p_2k_2\delta_3 + p_{21}\delta_2V_1^{*''''}) \right\}^2 + 4r\beta_1V_1^{*''''} p_{21}\beta_2\beta_{21}^2c_2\delta_2^2\delta_3(k_2 + \beta_{12}V_1^{*''''})^2 \right. \right. \\
&\quad \left. \left. + 4r\beta_2^2k_1\beta_{21}c_2\delta_2\delta_3(k_2 + \beta_{12}V_1^{*''''}) (p_2k_2\delta_3 + p_{21}\beta_{12}\delta_2V_1^{*''''}) \right. \right. \\
&\quad \left. \left. - \left( 4\beta_2\beta_{21}c_2^2\delta_2^2\delta_3^2(k_2 + \beta_{12}V_1^{*''''})^2 (\beta_1k_1V_1^{*''''} + ak_1) \right. \right. \right. \\
&\quad \left. \left. \left. + 2rc_2\delta_2\delta_3\beta_2\beta_{21}(k_2 + \beta_{12}V_1^{*''''}) (\beta_2k_1 + \beta_1\beta_{21}V_1^{*''''} + a\beta_{21}) (p_2k_2\delta_3 + p_{21}\delta_2V_1^{*''''}) \right) \right] \right].
\end{aligned}$$

Similarly, this chronic coinfection equilibrium exists if the following conditions are satisfied. The conditions for  $V_1$  and  $V_2$  are respectively

$$\begin{aligned}
r\beta_1\beta_{12} \frac{(p_1k_1\delta_3 + p_{12}\delta_1V_2^{*''''})}{(k_1 + \beta_{21}V_2^{*''''})} &\leq c_1\delta_1\delta_3(\beta_1k_2 + \beta_2\beta_{12}V_2^{*''''} + a\beta_{12}), \text{ and} \\
r\beta_2\beta_{21} \frac{(p_2k_2\delta_3 + p_{21}\delta_2V_1^{*''''})}{(k_2 + \beta_{12}V_1^{*''''})} &\leq c_2\delta_2\delta_3(\beta_2k_1 + \beta_1\beta_{21}V_1^{*''''} + a\beta_{21}).
\end{aligned}$$

15 **1.2 Simulation results**

16 Numerical simulations of infected cell populations from model 1 and 2 (according to  
 17 main text) are compared in figure 1. Figure 1 shows that chronic infection with both  
 18 virus is maintained by the superinfected cells in the presence of cell regeneration (green  
 19 solid lines in the plots).

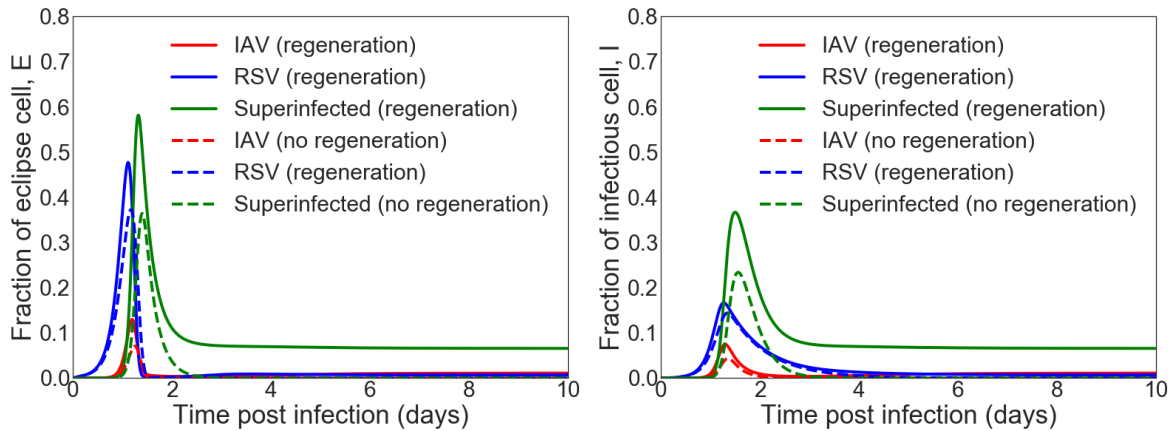


Figure 1: Comparison of infected cell dynamics during superinfection with (model 1) and without (model 2) target cell regeneration.

20 **2 Sensitivity analysis**

21 For sensitivity simulations, we calculated percentage change in model dynamics, i.e.  
 22 viral peaks and infection durations for each superinfection scenario for models 1 (sub-  
 23 section 2.2) and 2 (subsection 2.1) by varying model parameters individually 10% higher  
 24 and lower than their baseline values given in table 1 and used in figures 2, 3 and 6 in  
 25 the main text. The effects that each parameter has on the viral dynamics are shown in  
 26 figures 2, 3, 4, 5, 6 and 7. These analysis show that small changes in the production  
 27 rates,  $p_1, p_{12}, p_2$  and  $p_{21}$ , result in intermediate to small level changes in viral peak loads,  
 28 while infection durations are mostly influenced by the viral clearance rates,  $c_1$  and  $c_2$ ,

29 for each scenario.

## 30 **2.1 Superinfection with no cell regeneration and death (model** 31 **2)**

32 **Viral peak load** Model 2 solutions in figures 2 and 3 show percentage increase and  
33 decrease in viral peaks for 10% increase and decrease in model parameters, respectively.  
34 With 10% increase in the baseline value of IAV production rate,  $p_1$ , the model produces  
35 0.9% higher peak load for influenza virus (figure 2, top row) while 10% decrease in the  
36 production rate leads to decline in the peak level (figure 3, top row). IAV peak increases  
37 and decreases by almost 0.6% higher than the normal value due to 10% increase and  
38 decrease in the ability of superinfected cells to produce IAV ( $p_{12}$ ). Increases in IAV  
39 eclipse transition rate ( $k_1$ ) leads to higher IAV peak level while increases in the rate  
40 of IAV clearance ( $c_1$ ) and superinfected infectious cell death ( $\delta_3$ ) lower the IAV peak  
41 level. This model has no effect in response to change in superinfection rate,  $\beta_{21}$  and  
42 production rate,  $p_{21}$ , of RSV. Other parameters of IAV such as the infection rates ( $\beta_1$   
43 and  $\beta_{12}$ ), infectious cell death rate ( $\delta_1$ ) and superinfected eclipse transition rate ( $k_3$ )  
44 slightly influence the IAV peak level. All RSV infection parameters such as  $\beta_2$ ,  $k_2$ ,  $p_2$ ,  
45  $c_2$ ,  $\delta_2$  have negligible impacts on IAV peak load. Perturbation in the RSV production  
46 rate ( $p_2$ ) elevates the RSV peak load by 2% higher than the normal level. However, the  
47 RSV peak load also increases for increase in the other RSV parameters such as  $\beta_2$ ,  $k_2$ ,  
48  $p_{21}$ , it declines in response to increase in the RSV clearance rate ( $c_2$ ). In addition, if  
49 the infection rate of IAV is increased, the peak level of RSV decreases by 1%. All other  
50 parameters cause slight change in the model dynamics.

51 **Coinfection duration** Model 2 solutions in figures 4 and 5 show percentage change  
52 in infection durations for 10% increase and decrease in model parameters, respectively.



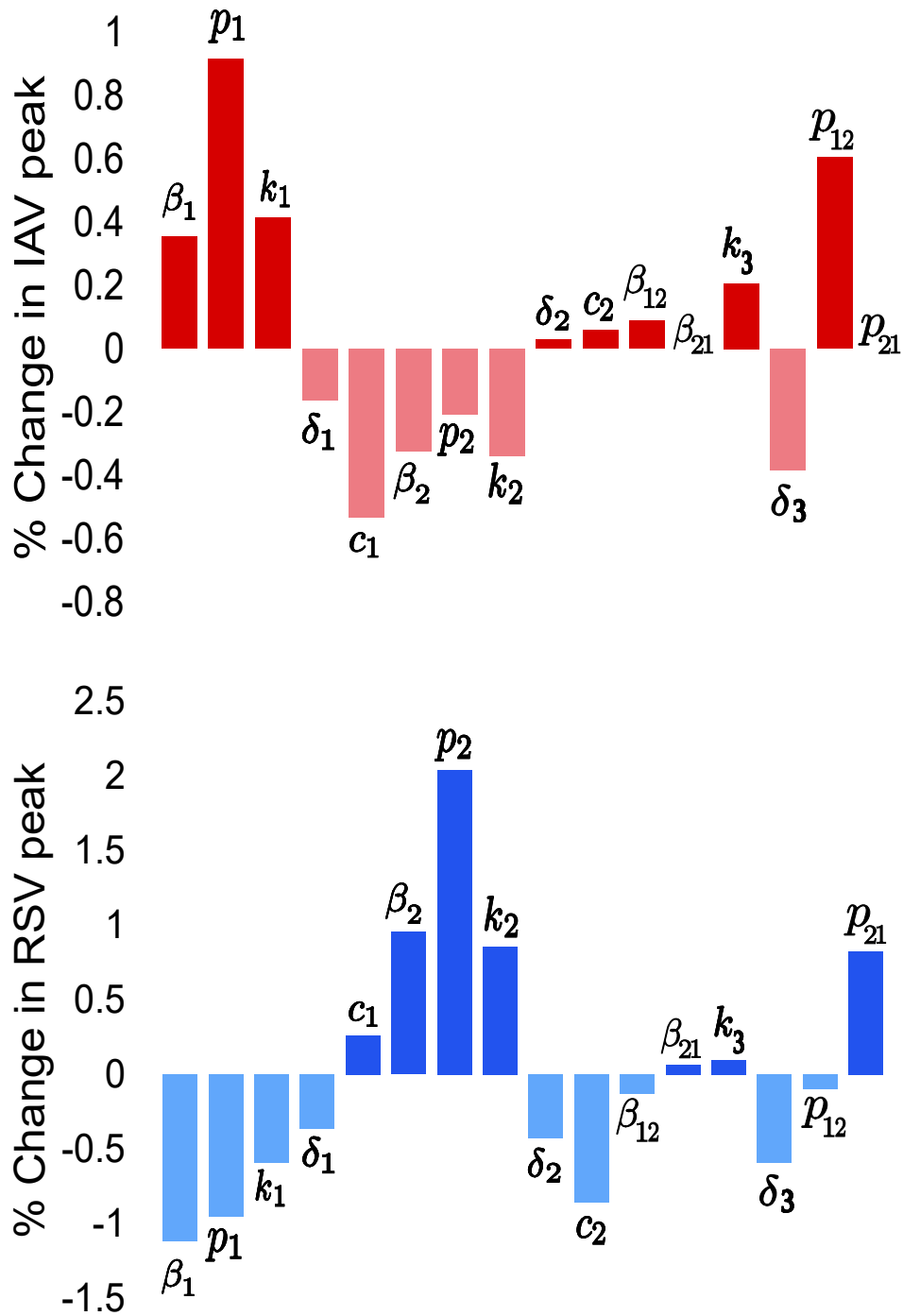


Figure 2: Sensitivity analysis of superinfection model with no cell regeneration and death for viral peak load; model 2, main text. Percentage increase in IAV and RSV peak load is calculated for 10% increased parameter values from the baseline values.

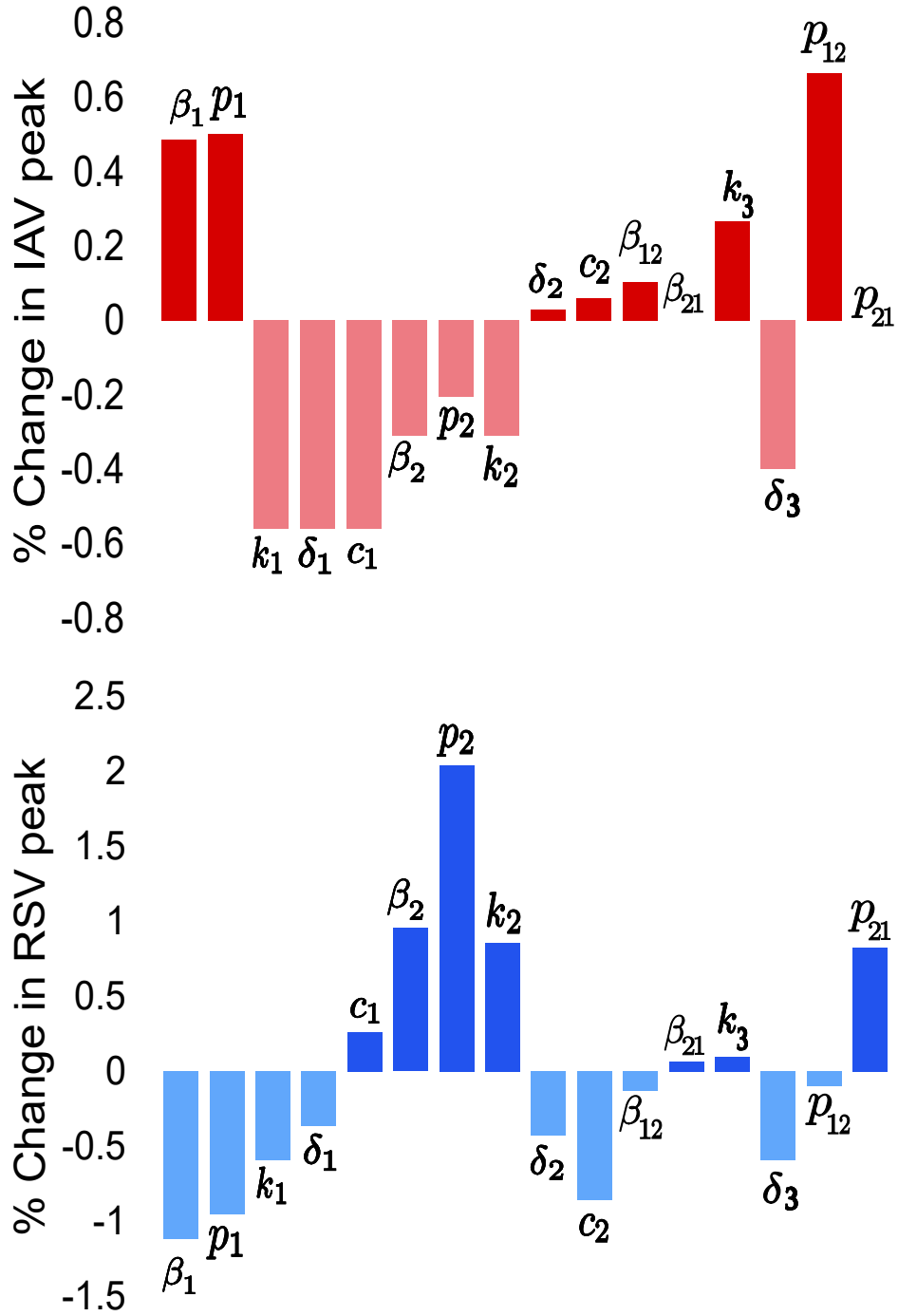


Figure 3: Sensitivity analysis of superinfection model with no cell regeneration and death for viral peak load; model 2, main text. Percentage decrease in IAV and RSV peak load is calculated for 10% decreased parameter values from the baseline values.

53 Decreases in the viral clearances rates ( $c_1$  and  $c_2$ ) lead to prolong the single and coin-  
54 fection durations (figures 5) while increasing the clearance rates decrease the durations  
55 with less amount (figure 4). Only increase in the superinfection production rate,  $p_{12}$ ,  
56 results in longer coinfection duration. Among the parameters that characterize super-  
57 infection, the slower eclipse transition rate ( $k_3$ ) and superinfection infectious cell death  
58 ( $\delta_3$ ) change the infection durations. In this model the coinfection duration is mostly  
59 dominated by the IAV dynamics.

## 60 **2.2 Superinfection with cell regeneration and cell death (model** 61 **1)**

62 Model 1 solutions in figures 6 and 7 show percentage change in viral peaks for 10%  
63 increase and decrease in model parameters, respectively. The viral peaks are similarly  
64 influenced by the model parameters as were found in the previous model analysis (model  
65 2, main text). In this model (model 1, main text) changes in the model parameters  
66 have no effect on the infection durations.

## 67 **3 Octave code for generating solutions to Figure 2,** 68 **3 and 6**

```
69 #!/usr/bin/octave
70 global par;
71
72 function xdot = superinfection(x,t)
73
74 global par;
```

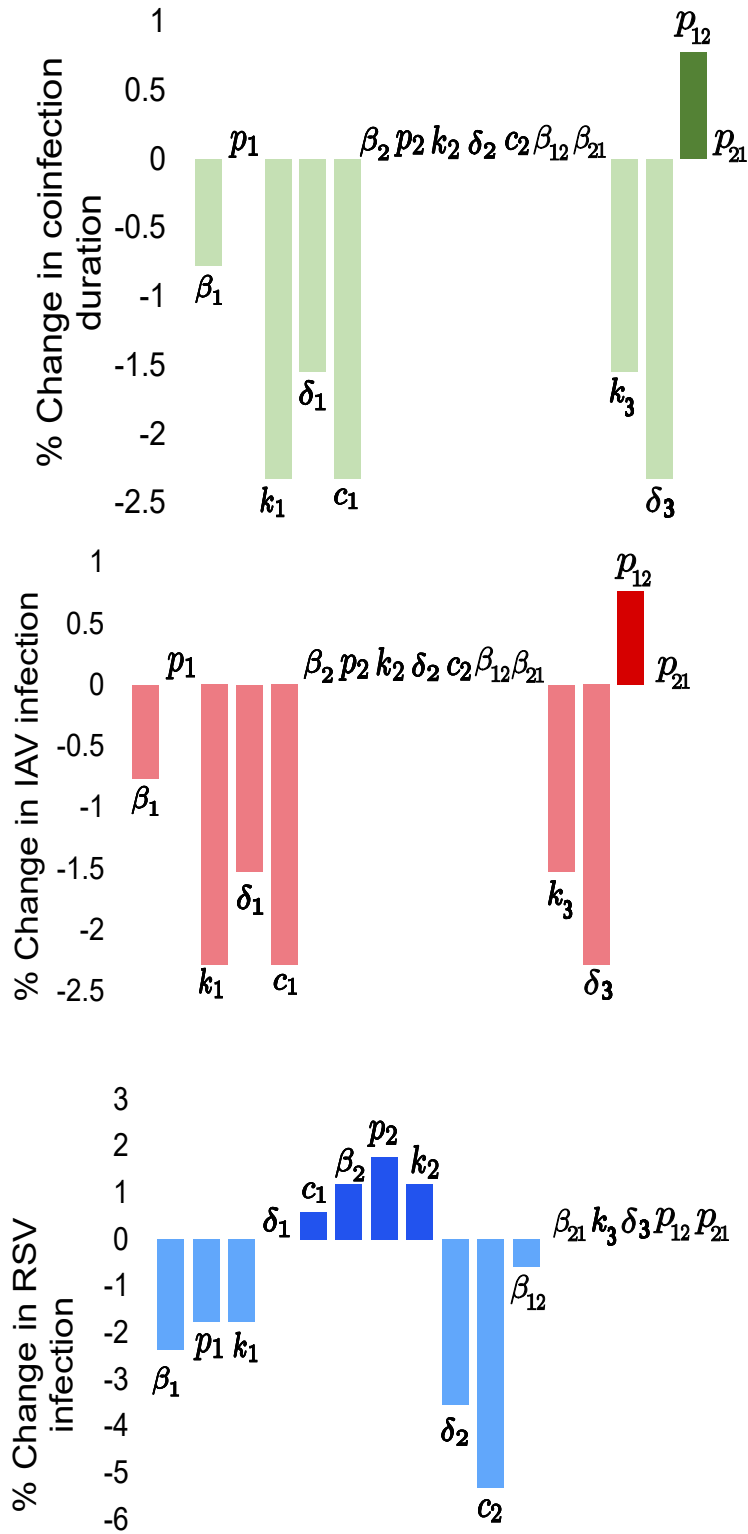


Figure 4: Sensitivity analysis of superinfection model with no cell regeneration and death for coinfection and single infection durations; model 2, main text. Percentage increase in IAV and RSV single viral infection duration and coinfection are calculated for 10% increased parameter values from the baseline values.

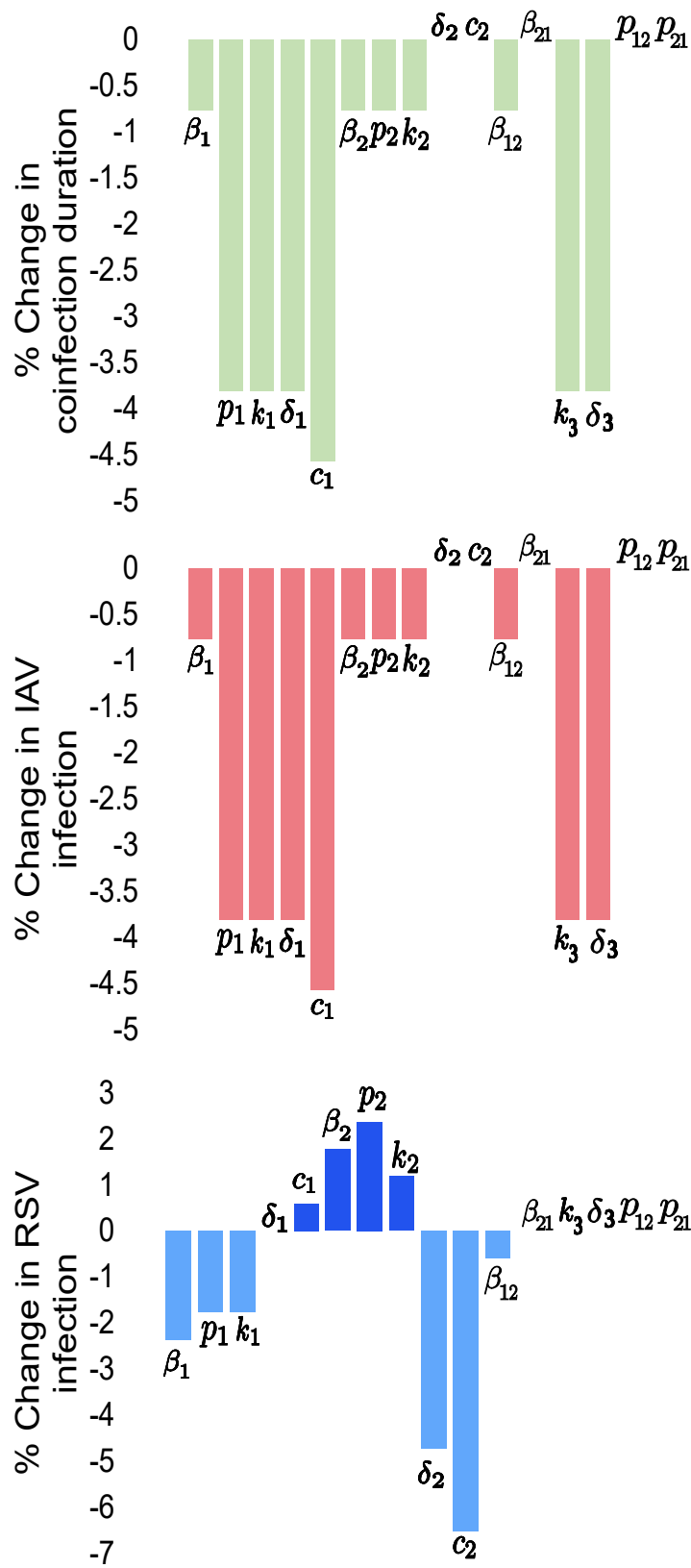


Figure 5: **Sensitivity analysis of superinfection model with no cell regeneration and death for coinfection and single infection duration; model 2, main text.** Percentage decrease in IAV and RSV single viral infection duration and coinfection are calculated for 10% decreased parameter values from the baseline values.

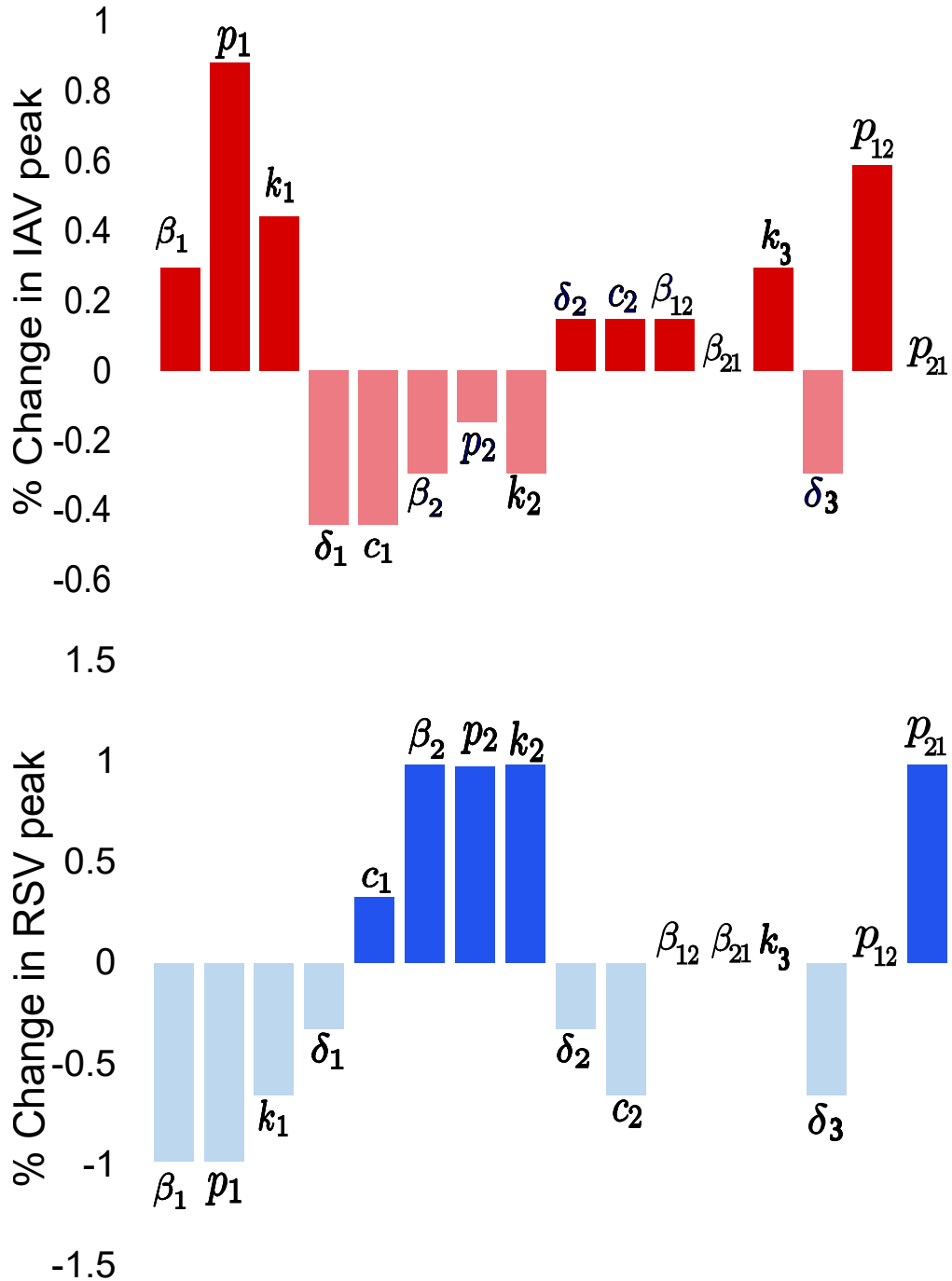


Figure 6: Sensitivity analysis of superinfection model with cell regeneration and cell death for peak viral load; model 1, main text. Percentage increase in IAV and RSV peak load is calculated for 10% increased parameter values from the baseline values.

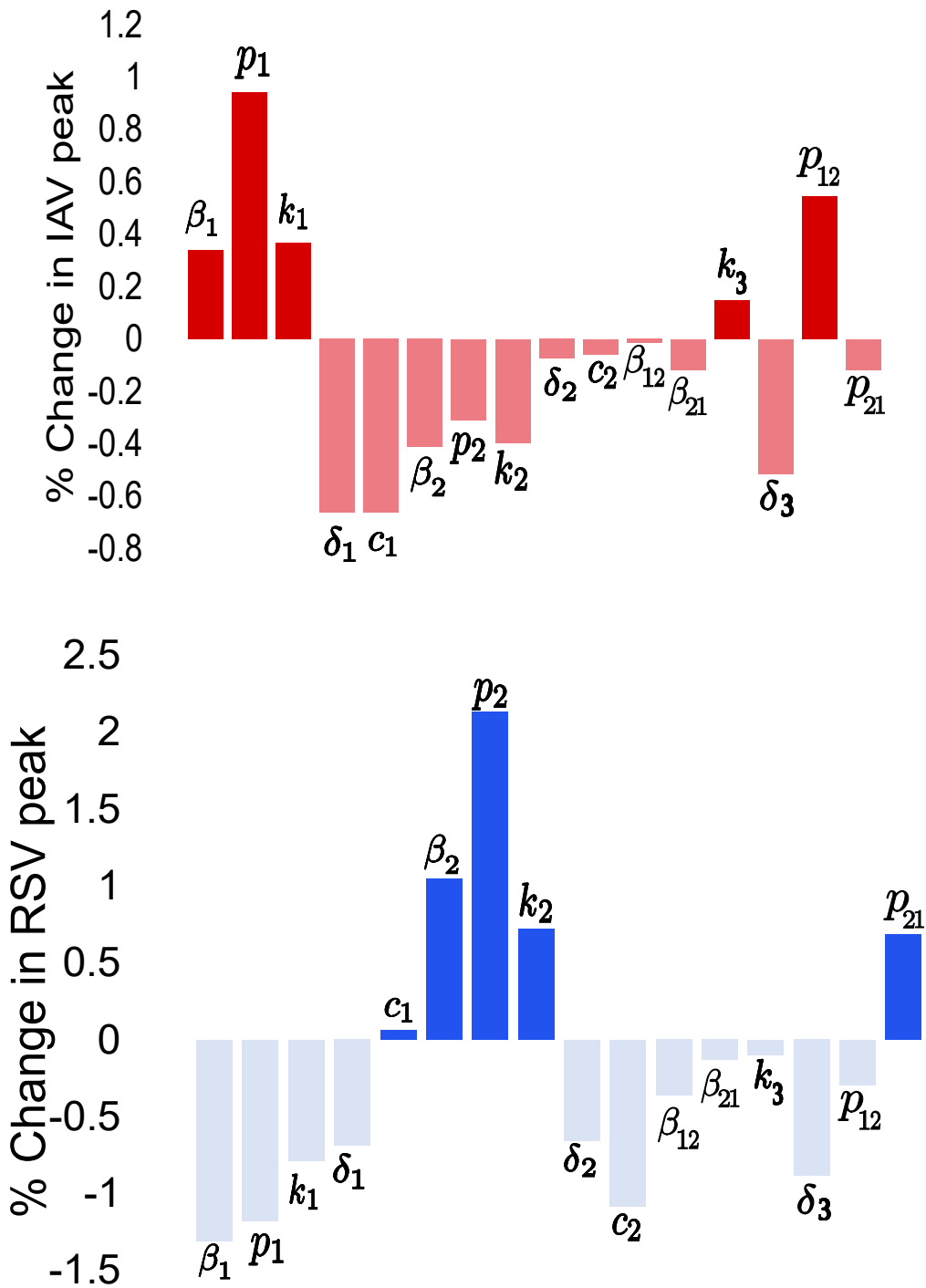


Figure 7: Sensitivity analysis of superinfection model with cell regeneration and cell death for viral peak load; model 1, main text. Percentage decrease in IAV and RSV peak load is calculated for 10% decreased parameter values from the baseline values.

```

75 b_1=par(1); k_1=par(2); d_1=par(3); p_1=par(4); c_1=par(5);
76 b_2=par(6); k_2=par(7); d_2=par(8); p_2=par(9); c_2=par(10);
77 k_3=par(11); d_3 =par(12); p_12=par(13); p_21=par(14); r=par(15);
78
79     T = 1; E_1 = 2; E_2 = 3; E_3 = 4; I_1 = 5; I_2 = 6; I_3 = 7;
80     D_1 = 8; D_2 = 9; D_3 = 10; V_1 = 11; V_2 = 12;
81
82     xdot = zeros(12,1);
83     xdot(T) = -(b_1)*x(V_1)*x(T)-(b_2)*x(V_2)*x(T)+r;
84     xdot(E_1) = (b_1)*x(V_1)*x(T)-(k_1)*x(E_1)-(b_2)*x(E_1)*x(V_2);
85     xdot(E_2) = (b_2)*x(V_2)*x(T)-(k_2)*x(E_2)-(b_1)*x(E_2)*x(V_1);
86     xdot(E_3) = (b_2)*x(E_1)*x(V_2)+(b_1)*x(E_2)*x(V_1)-(k_3)*x(E_3);
87     xdot(I_1) = (k_1)*x(E_1) - (d_1)*x(I_1);
88     xdot(I_2) = (k_2)*x(E_2) - (d_2)*x(I_2);
89     xdot(I_3) = (k_3)*x(E_3) - (d_3)*x(I_3);
90     xdot(D_1) = (d_1)*x(I_1);
91     xdot(D_2) = (d_2)*x(I_2);
92     xdot(D_3) = (d_3)*x(I_3);
93     xdot(V_1) = (p_1)*x(I_1)+(p_12)*x(I_3)- (c_1)*x(V_1);
94     xdot(V_2) = (p_2)*x(I_2)+(p_21)*x(I_3)- (c_2)*x(V_2);
95
96 endfunction
97
98 # Open a file for superinfection model solution
99 fd = fopen("Vtiter_IAVRSV.dat","w");
100 # Open a file for superinfection with cell regeneration model solution

```



```

101 #fdr = fopen("Vtiter_IAVRSV_r.dat","w");
102
103 # Model parameters
104 #b1 k1 d1 p1 c1
105 #Flu :82.73e-7 4.2 4.2 0.12e9 4.03
106 #b2 k2 d2 p2 c2
107 #rsv : 0.0308 1.272 1.272 7645.649 1.272
108
109 # Model parameters for superinfection model
110 #b1 k1 d1 p1 c1 b2 k2 d2 p2 c2 k3=k1 d3=d1 p12=p1 p21=p2
111 par= [82.73e-7 4.2 4.2 0.12e9 4.03 0.0308 1.272 1.272
112 7645.649 1.272 4.2 4.2 0.12e9 7645.649];
113
114 # Model parameters for superinfection model with cell regeneration model
115 #par= [82.73e-7 4.2 4.2 0.12e9 4.03 0.0308 1.272 1.272
116 7645.649 1.272 4.2 4.2 0.12e9 7645.649 0.033];
117
118 # Initial conditions
119 x0 = [1 zeros(1,9) 1.0 1.0];
120
121 # Solve model for untreated case
122 t = [0:0.01:100]';
123 y= lsode("superinfection",x0',t);
124
125 fprintf(fd,"%g %g %g %g\n",[t y(:,1) y(:,2) y(:,3) y(:,4) y(:,5)
126 y(:,6) y(:,7) y(:,11) y(:,12)]');

```

```

127 #fprintf(fdr,"%g %g %g %g\n",[t y(:,1) y(:,2) y(:,3) y(:,4) y(:,5)
128         y(:,6) y(:,7) y(:,11) y(:,12)]');
129
130 fclose(fd);
131 #fclose(fdr);

```

## 132 4 Octave code for generating solutions to Figure 4 133 and 7

```

134 #!/usr/bin/octave
135 global par;
136 # Set of differential equations
137 function xdot = superinfection(x,t)
138
139 global par;
140 b_1=par(1); k_1=par(2); d_1=par(3); p_1=par(4); c_1=par(5);
141 b_2=par(6); k_2=par(7); d_2=par(8); p_2=par(9); c_2=par(10);
142 k_3=par(11); d_3 =par(12); p_12=par(13); p_21=par(14);#r=par(15);
143
144 T = 1; E_1 = 2; E_2 = 3; E_3 = 4; I_1 = 5; I_2 = 6; I_3 = 7;
145 D_1 = 8; D_2 = 9; D_3 = 10; V_1 = 11; V_2 = 12;
146
147 xdot = zeros(12,1);
148 xdot(T) = -(b_1)*x(V_1)*x(T)-(b_2)*x(V_2)*x(T);#+r;
149 xdot(E_1) = (b_1)*x(V_1)*x(T)-(k_1)*x(E_1)-(b_2)*x(E_1)*x(V_2);
150 xdot(E_2) = (b_2)*x(V_2)*x(T)-(k_2)*x(E_2)-(b_1)*x(E_2)*x(V_1);

```

```

151     xdot(E_3) = (b_2)*x(E_1)*x(V_2)+(b_1)*x(E_2)*x(V_1)-(k_3)*x(E_3);
152     xdot(I_1) = (k_1)*x(E_1) - (d_1)*x(I_1);
153     xdot(I_2) = (k_2)*x(E_2) - (d_2)*x(I_2);
154     xdot(I_3) = (k_3)*x(E_3) - (d_3)*x(I_3);
155     xdot(D_1) = (d_1)*x(I_1);
156     xdot(D_2) = (d_2)*x(I_2);
157     xdot(D_3) = (d_3)*x(I_3);
158     xdot(V_1) = (p_1)*x(I_1)+(p_12)*x(I_3)- (c_1)*x(V_1);
159     xdot(V_2) = (p_2)*x(I_2)+(p_21)*x(I_3)- (c_2)*x(V_2);
160
161     endfunction
162
163     # Open a file
164     fd = fopen("tcoin_rp_IAVRSV.dat","w");
165
166     # Model parameters
167     #Flu :82.73e-7 4.2 4.2 0.12e9 4.03
168     #rsv : 0.0308 1.272 1.272 7645.649 1.272
169
170     rP12=logspace(0,10,100);
171     rP21=logspace(0,10,100);
172
173     for i=1:length(rP12)
174     for j=1:length(rP21)
175
176     #b1    k1    d1    p1    c1    b2    k2    d2    p2    c2    k3    d3    p12    p21

```

```

177 par= [82.73e-7 4.2 4.2 0.12e9 4.03 0.0308 1.272 1.272
178 7645.649 1.272 4.2 4.2 rP12(i) rP21(j)];#0.033];
179
180 # Initial conditions
181 x0 = [1.0 zeros(1,9) 1.0 1.0];
182
183 # Solve model for untreated case
184 t = [0:0.01:100]';
185 y= lsode("superinfection",x0',t);
186
187 #Find coinfection time for both viruses
188 V1=find(y(:,11)>1.0);
189 V2=find(y(:,12)>1.0);
190
191 if isempty(V1) | isempty(V2)
192     tcoin(i,j) = 0;
193 else
194     tcoin(i,j) = (min([V1(end),V2(end)])- max([V1(1),V2(1)]))/100;
195 end
196 fprintf(fd,"%g %g %g\n",[rP12(i) rP21(j) tcoin(i,j)]');
197 endfor;
198 endfor;
199
200 #Draw Contour plot of the coinfection duration
201 pcolor(tcoin)
202 colorbar(tcoin)

```

```

203 drawnow
204 pause(10)
205 fclose(fd);

```

## 206 5 Octave code for generating solutions to Figure 5

```

207 #!/usr/bin/octave
208 global par;
209 function xdot = superinfection(x,t)
210 global par;
211 b_1=par(1); k_1=par(2); d_1=par(3); p_1=par(4); c_1=par(5);
212 b_2=par(6); k_2=par(7); d_2=par(8); p_2=par(9); c_2=par(10);
213 k_3=par(11); d_3 =par(12); p_12=par(13); p_21=par(14);
214
215 T = 1; E_1 = 2; E_2 = 3; E_3 = 4; I_1 = 5; I_2 = 6; I_3 = 7;
216 D_1 = 8; D_2 = 9; D_3 = 10; V_1 = 11; V_2 = 12;
217
218 xdot = zeros(12,1);
219 xdot(T) = -(b_1)*x(V_1)*x(T)-(b_2)*x(V_2)*x(T);
220 xdot(E_1) = (b_1)*x(V_1)*x(T)-(k_1)*x(E_1)-(b_2)*x(E_1)*x(V_2);
221 xdot(E_2) = (b_2)*x(V_2)*x(T)-(k_2)*x(E_2)-(b_1)*x(E_2)*x(V_1);
222 xdot(E_3) = (b_2)*x(E_1)*x(V_2)+(b_1)*x(E_2)*x(V_1)-(k_3)*x(E_3);
223 xdot(I_1) = (k_1)*x(E_1) - (d_1)*x(I_1);
224 xdot(I_2) = (k_2)*x(E_2) - (d_2)*x(I_2);
225 xdot(I_3) = (k_3)*x(E_3) - (d_3)*x(I_3);
226 xdot(D_1) = (d_1)*x(I_1);

```

```

227     xdot(D_2) = (d_2)*x(I_2);
228     xdot(D_3) = (d_3)*x(I_3);
229     xdot(V_1) = (p_1)*x(I_1)+(p_1)*x(I_3)- (c_1)*x(V_1);
230     xdot(V_2) = (p_2)*x(I_2)+(p_2)*x(I_3)- (c_2)*x(V_2);
231
232 endfunction
233
234 # Open a file
235 fd1 = fopen("V1max_rkd_IAVRSV.dat","w");
236 fd2 = fopen("V2max_rkd_IAVRSV.dat","w");
237 #fd3 = fopen("VmaxRatio_rkd_IAVRSV.dat","w");
238
239 rk=linspace(0,10,100);
240 rd=linspace(0,10,100);
241
242 for i=1:length(rk)
243 for j=1:length(rd)
244
245 # Model parameters
246 # b1 k1 d1 p1 c1 b2 k2 d2   p2c2 k3 d3 #p12 p21
247
248 par= [82.73e-7 4.2 4.2 0.12e9 4.03 0.0308 1.272 1.272
249 7645.649 1.272 rk(i) rd(j) 0.12e9 7645.649];
250
251 # Initial conditions
252 # T E I D V

```

```

253 x0 = [1.0 zeros(1,9) 1.0 1.0];
254
255 # Solve model for untreated case
256 t = [0:0.01:100]';
257 y= lsode("superinfection",x0',t);
258
259 V1max(i,j)=max(y(:,11));
260 V2max(i,j)=max(y(:,12));
261 #VmaxRatio(i,j)=max(y(:,12))/max(y(:,11));
262
263 fprintf(fd1,"%g %g %g\n",[rk(i) rd(j) V1max(i,j)]');
264 fprintf(fd2,"%g %g %g\n",[rk(i) rd(j) V2max(i,j)]');
265 #fprintf(fd3,"%g %g %g\n",[rk(i) rd(j) VmaxRatio(i,j)]');
266
267 endfor;
268 endfor;
269
270 fclose(fd1);
271 fclose(fd2);
272 #fclose(fd3);

```

## 273 **6 Octave code for generating solutions to Figure 8**

```

274 #!/usr/bin/octave
275 global par;
276 # Set of differential equations

```

```

277 function xdot = superinfection_r(x,t)
278
279 global par;
280 b_1=par(1); k_1=par(2); d_1=par(3); p_1=par(4); c_1=par(5);
281 b_2=par(6); k_2=par(7); d_2=par(8); p_2=par(9); c_2=par(10);
282 k_3=par(11); d_3 =par(12); p_12=par(13); p_21=par(14); r=par(15);
283
284
285 T = 1; E_1 = 2; E_2 = 3; E_3 = 4; I_1 = 5; I_2 = 6; I_3 = 7;
286 D_1 = 8; D_2 = 9; D_3 = 10; V_1 = 11; V_2 = 12;
287
288     xdot = zeros(12,1);
289     xdot(T) = -(b_1)*x(V_1)*x(T)-(b_2)*x(V_2)*x(T)+r;
290     xdot(E_1) = (b_1)*x(V_1)*x(T)-(k_1)*x(E_1)-(b_2)*x(E_1)*x(V_2);
291     xdot(E_2) = (b_2)*x(V_2)*x(T)-(k_2)*x(E_2)-(b_1)*x(E_2)*x(V_1);
292     xdot(E_3) = (b_2)*x(E_1)*x(V_2)+(b_1)*x(E_2)*x(V_1)-(k_3)*x(E_3);
293     xdot(I_1) = (k_1)*x(E_1) - (d_1)*x(I_1);
294     xdot(I_2) = (k_2)*x(E_2) - (d_2)*x(I_2);
295     xdot(I_3) = (k_3)*x(E_3) - (d_3)*x(I_3);
296     xdot(D_1) = (d_1)*x(I_1);
297     xdot(D_2) = (d_2)*x(I_2);
298     xdot(D_3) = (d_3)*x(I_3);
299     xdot(V_1) = (p_1)*x(I_1)+(p_12)*x(I_3)- (c_1)*x(V_1);
300     xdot(V_2) = (p_2)*x(I_2)+(p_21)*x(I_3)- (c_2)*x(V_2);
301
302 endfunction

```



```

303
304 # Open a file
305 fd = fopen("r_IAVRSV.dat","w");
306
307 # Model parameters
308 #Flu :82.73e-7 4.2 4.2 0.12e9 4.03
309 #rsv : 0.0308 1.272 1.272 7645.649 1.272
310
311 rpoints=linspace(0,0.1,1000);
312 for i=1:length(rpoints)
313
314 #b1 k1 d1 p1 c1 b2 k2 d2 p2 c2 k3 d3 p12 p21
315 par= [82.73e-7 4.2 4.2 0.12e9 4.03 0.0308 1.272 1.272 7645.649
316 1.272 4.2 4.2 0.12e9 7645.649 rpoints(i)];
317
318 # Initial conditions
319 # T E I D V
320 x0 = [1.0 zeros(1,9) 1.0 1.0];
321
322 # Solve model for untreated case
323 t = [20:21:1000]';
324 y= lsode("superinfection_r",x0',t);
325 endfor;
326
327 #Find viral load as a fuction of cell regeneration
328 fprintf(fd,"%g %g %g\n",[rpoints(i) y(:,11) y(:,12)]');

```

```
329 fclose(fd);
```

## 330 7 Octave code for generating solutions to Figure 9

```
331 #!/usr/bin/octave
```

```
332 global par;
```

```
333 # Set of differential equations
```

```
334 function xdot = superinfection(x,t)
```

```
335
```

```
336 global par;
```

```
337
```

```
338 b_1=par(1); k_1=par(2); d_1=par(3); p_1=par(4); c_1=par(5);
```

```
339 b_2=par(6); k_2=par(7); d_2=par(8); p_2=par(9); c_2=par(10);
```

```
340 k_3=par(11); d_3 =par(12); p_12=par(13); p_21=par(14); r=par(15);
```

```
341
```

```
342 T = 1; E_1 = 2; E_2 = 3; E_3 = 4; I_1 = 5; I_2 = 6; I_3 = 7;
```

```
343 D_1 = 8; D_2 = 9; D_3 = 10; V_1 = 11; V_2 = 12;
```

```
344
```

```
345 xdot = zeros(12,1);
```

```
346 xdot(T) = -(b_1)*x(V_1)*x(T)-(b_2)*x(V_2)*x(T)+r;
```

```
347 xdot(E_1) = (b_1)*x(V_1)*x(T)-(k_1)*x(E_1)-(b_2)*x(E_1)*x(V_2);
```

```
348 xdot(E_2) = (b_2)*x(V_2)*x(T)-(k_2)*x(E_2)-(b_1)*x(E_2)*x(V_1);
```

```
349 xdot(E_3) = (b_2)*x(E_1)*x(V_2)+(b_1)*x(E_2)*x(V_1)-(k_3)*x(E_3);
```

```
350 xdot(I_1) = (k_1)*x(E_1) - (d_1)*x(I_1);
```

```
351 xdot(I_2) = (k_2)*x(E_2) - (d_2)*x(I_2);
```

```
352 xdot(I_3) = (k_3)*x(E_3) - (d_3)*x(I_3);
```

```

353     xdot(D_1) = (d_1)*x(I_1);
354     xdot(D_2) = (d_2)*x(I_2);
355     xdot(D_3) = (d_3)*x(I_3);
356     xdot(V_1) = (p_1)*x(I_1)+(p_12)*x(I_3)- (c_1)*x(V_1);
357     xdot(V_2) = (p_2)*x(I_2)+(p_21)*x(I_3)- (c_2)*x(V_2);
358
359 endfunction
360
361
362 # Open a file
363 fd = fopen("data/FluFirstRSV24hoursDelay.dat","w");
364
365 # Model parameters
366 #b1  k1  d1  p1  c1  b2  k2  d2  p2  c2 k3 d3 p12 p21
367 par= [82.73e-7 4.2 4.2 0.12e9 4.03 0.0308 1.272 1.272 7645.649
368 1.272 4.2 4.2 0.12e9 7645.649 0.033];
369
370 # Initial conditions
371 x0 = [1.0 zeros(1,9) 1.0 0];
372
373 # Solve model for untreated case
374 t = [ 0:0.01:1.0 ]';
375 y1 = lsode("Superinfection",x0',t);
376
377 x0 = y1(end,:);
378 x0(12) = 1.0;

```

```
379 t = [ 1.0:0.01:100 ]';
380 y2= lsode("Superinfection",x0',t);
381 t = [0:0.01:100]';
382 y=[y1(1:end-1,:);y2];
383
384 fprintf(fd,"%g %g %g\n",[t y(:,11) y(:,12)]');
385 fclose(fd);
```