SUPPLEMENTARY MATERIAL No.1



Global dynamics of humoral and cellular immune responses to virus infection

Appendix

I. To compute the basic reproductive number of the model (1) with immunity, we follow [14], [15] to form the next generation matrix, then

$$F = \begin{bmatrix} 0 & \beta_I \frac{k_s}{\mu_s} \\ N_1(\mu_I + \mu_s) & -N_2 \beta_I \frac{k_s}{\mu_s} \end{bmatrix}, \quad V = \begin{bmatrix} \alpha_I \frac{k_T}{\mu_T} + (\mu_I + \mu_s) & 0 \\ 0 & \alpha_v \frac{k_B}{\mu_B} + \mu_v \end{bmatrix},$$
$$FV^{-1} = \begin{bmatrix} 0 & \beta_I \frac{k_s}{(\alpha_v \frac{k_B}{\mu_B} + \mu_v)\mu_s} \\ N_1 \frac{(\mu_I + \mu_s)}{\alpha_I \frac{k_T}{\mu_T} + (\mu_I + \mu_s)} & N_2 \beta_I \frac{k_s}{(\alpha_v \frac{k_B}{\mu_B} + \mu_v)\mu_s} \end{bmatrix}.$$

From the last matrix the corresponding characteristic polynomial is

$$\lambda^{2} - \left(-N_{2}\beta_{I}\frac{k_{s}}{(\alpha_{v}\frac{k_{B}}{\mu_{B}} + \mu_{v})\mu_{s}}\right)\lambda - N_{1}\frac{(\mu_{I} + \mu_{s})}{\alpha_{I}\frac{k_{T}}{\mu_{T}} + (\mu_{I} + \mu_{s})}\beta_{I}\frac{k_{s}}{(\alpha_{v}\frac{k_{B}}{\mu_{B}} + \mu_{v})\mu_{s}}.$$

We cannot use [15], but we can use an extended result, which appears in Part II of this Appendix. Then we have

$$R_{0} = \frac{\beta_{I} \left[\frac{(\mu_{s} + \mu_{I})}{\left(\alpha_{I} \frac{k_{T}}{\mu_{T}} + \mu_{s} + \mu_{I} \right)} N_{1} - N_{2} \right] k_{s}}{\left(\alpha_{v} \frac{k_{B}}{\mu_{B}} + \mu_{v} \right) \mu_{s}}.$$
(35)

Similarly, if the humoral and cellular immune response is not present, the basic reproductive number of the model (3) is

$$R_{0w} = \frac{\beta_I [N_1 - N_2] k_s}{\mu_v \mu_s}.$$
(36)

The only difference with the previous number R_0 is that the immune activity is not present in the control of free viral particles and infected cells.

II.

Conjecture 12.1. Let the characteristic polynomial of order *n* corresponding to the next generation matrix FV^{-1} be written as

$$\Lambda(\lambda) = \lambda^n - a_{n-1}\lambda^{n-1} - \dots - a_1\lambda - a_0$$

with $a_i \ge 0$, i = 0, ..., k and $a_j \le 0$, j = k + 1, ..., n - 1. Let R_0 denote the spectral radius of the next generation matrix, that is, $R_0 = \rho(FV^{-1})$ and

 $R_0^* = a_0 + \dots + a_{n-1}.$

Then R_0^* is a threshold value for the disease to take off or to die out in the sense that:

- 1. $R_0^* < 1$ if and only if $R_0 < 1$.
- 2. $R_0^* = 1$ if and only if $R_0 = 1$.
- 3. $R_0^* > 1$ if and only if $R_0 > 1$.

Proof. It is the same proof as the one of Conjecture 1 in [15, p. 103]. \Box