1 Mathematical model

$$\text{target cells} \quad \frac{dT}{dt} = -\beta TV \tag{1}$$

$$\text{infected cells} \quad \frac{dI}{dt} = \beta TV - k_R T_R I - \delta I \tag{2}$$

$$\text{viral titer} \quad \frac{dV}{dt} = pI - cV - f(A_O, V) * k_A V A_O - f(A_V, V) * k_A V A_V \tag{3}$$

$$\text{B-cells for old strain} \quad \frac{dB_O}{dt} = g(A_O, V) * \frac{\sigma V}{\phi_A + V} \tag{4}$$

$$\text{antibodies for old strain} \quad \frac{dA_0}{dt} = \kappa B_0 - d_A A_O \tag{5}$$

$$\text{B-cells for vaccine strain} \quad \frac{dB_V}{dt} = g(A_V, V) * \frac{\sigma V}{\phi_A + V} \tag{6}$$

$$\text{antibodies for vaccine strain} \quad \frac{dA_V}{dt} = \kappa B_V - d_A A_V \tag{7}$$

$$\text{expanding} \quad \frac{dT_E}{dt} = \rho T_E\Big(\frac{I}{\phi + I}\Big) - (\alpha + r) T_E\Big(1 - \frac{I}{\phi + I}\Big) - \mu T_E \tag{8}$$

$$\text{memory} \quad \frac{dT_M}{dt} = r T_E\Big(1 - \frac{I}{\phi + I}\Big) \tag{9}$$

$$\text{resident} \quad \frac{dT_R}{dt} = \mu T_E - d_R T_R \tag{10}$$

where the parameter $f(Ab, V)$ is a multiplier modifying the antibody response as a function of antigenic-antibody distance. This function is a Hill-type function, given by:

$$f(x) = \frac{-Mx^n}{K^n + x^n} + 1$$

M, K, and n are parameters to be determined. The variable x measures the percentage of antigenic distance between antibodies A and virus V. The antigenic distance can be given by any of the available distances (there are many antigenic distances out there, starting with the one proposed by Smith et al in 1999). I like to think about this as the fraction of amino acid differences in the dominant epitope between the antibody and the virus (taken from Gupta et al, 2006). With this set of parameters, the function $f(x)$ looks like this:

If $x = 0$, it is a perfect match. The parameters were chosen so that once the distance reaches 25% (left panel) or 75% (right panel) , the antibody stops being reactive to the antigen.

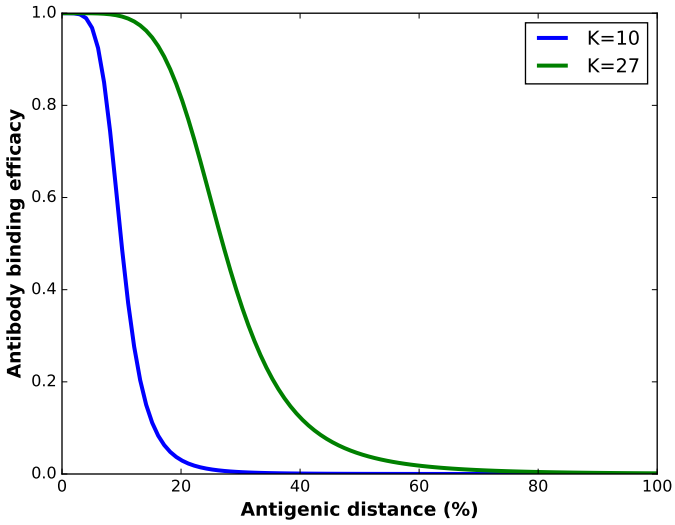

Figure 1: Antibody efficacy as a function of antigenic distance for two different values of K.

Table 1: Model parameters defintions and values.

Model parameter	Symbol	Units	Value	Reference
Rate of apoptosis for T_E	α			
Virus infectivity	β			
Rate of viral clearance	c			
Infected-cell lifespan	$1/\delta$			
Rate of antibody decay	d_A			
Death rate of T_R	d_R			
Rate of antibody production	κ			
Rate of killing of virus by antigen	k_A			
Rate of killing of infected cells by T_R	k_R			
Rate of conversion from T_E to T_R	μ			
Virus production per cell	p			
Number of infected cells for half-max. proliferation	ϕ			
Number of virus for half-max. B-cell activation	ϕ_A			
Rate of conversion from T_E to T_M	r			
T-cell proliferation rate	ρ			
Max. activation rate of B-cells	σ			