HIV Evolution

The HIV virus is so difficult for the body to control because it evolves very rapidly: typically, there are about 10^{10} new virus strains generated *each day*. The immune system targets a virus by using T cells which can identify cells infected by the virus by protein markers on the outside of the cell. However, the HIV virus is particularly challenging to control because, roughly speaking, it affects the ability of the T cells to fight infection. In this problem, we will explore a simple model for the HIV virus.

Let v_i be the number of viral cells with mutated strain i. The label i can run from 1 to ∞. Let x_i be the number of specific T cells which can target virus strain i, and let z correspond to a "master" T cell which can attack all strains.[1] The key with HIV is that as the number of viral cells increases, the ability of the T cells to fight back decreases. We model this with the ODEs

$$\begin{aligned}\dot{v}_i &= \epsilon v_i\,(r - cx_i - qz)\\ \dot{x}_i &= cv_i - (b+uv)x_i\\ \dot{z} &= kv - (b+uv)z\end{aligned}$$

where

$$v = \sum_i v_i$$

with $b, c, p, u, k, r, q > 0$ and all O(1), and $0 < \epsilon \ll 1$.

(a) Because ϵ is small, we have a separation of time scales in this problem. Using this fact, reduce the dynamics to the dynamics of v_i.

(b) Now, let us begin analyzing what the possible behaviors of the virus are. Show that if $ur > cp + qk$, then only one strain of HIV needs to be present to be uncontained (i.e., $v \to \infty$ at large t).

(c) Now, suppose that $ur < qk$. Find a solution where $v_i = \overline{v}$ for $i \leq n$, and $v_i = 0$ for $i > n$, which is a fixed point of the effective dynamics for v_i. Comment on what happens for large n.

(d) Now, let us ask the question of whether or not a new viral strain can be introduced to the body. Consider starting from the fixed point of the previous part, and now let $v_{n+1} = \delta$ at time $t = 0$. Show that when $ur < qk$, there is a critical n_1^* such that if $n > n_1^*$, the new strain will be introduced into the system, whereas for $n < n_1^*$, the new strain will be suppressed.

(e) Finally, let us consider the regime where $cp + qk > ur > qk$. Show that there is a critical value n_2^* such that if $n > n_2^*$, $v \to \infty$ at large t. Show that typically, for $n \lesssim n_2^*$, new viral strains will be suppressed, but for small n new viral strains may be promoted as well upon introduction.

What we have just derived in this model is a so called "diversity threshold" – when the HIV virus mutates into enough unique strains, the body will become unable to control it and the virus will grow out of control. This effect is actually observed in patients with the HIV virus, suggesting strongly that the evolutionary dynamics of HIV is primarily responsible for its danger as an infectious disease.

[1] What actually happens is that there is an immune response which is somewhat effective against all strains. It is this response which we model as z. Since it has the same appearance as the other T cell terms in the dynamics, we will just call it the "master T cell".