Abstract

Effect of Virus Evolution on an HIV Positive Patient
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We consider the following ODE model for AID's development:

$$x_1'[t] = A_1 x_1 - A_2 x_1^2 - A_3 u_1 x_1 + B_1 x_4 \quad \ldots\ (1a)$$
$$x_2'[t] = A_4 u_1 x_1 - A_5 x_2 + A_6 x_3 - A_{11} u_2 x_2 \quad \ldots\ (1b)$$
$$x_3'[t] = A_7 u_1 x_1 - A_8 x_3 \quad \ldots\ (1c)$$
$$x_4'[t] = A_{12} x1 - A_{13} x4 \quad \ldots\ (1d)$$
$$u_1'[t] = A_9 x_2 - c_1 u_1 \quad \ldots\ (1e)$$
$$u_2'[t] = A_{10} u_1 - c_3 u_2 \quad \ldots\ (1f)$$

where x_1, x_2, x_3, and x_4 are the susceptible, infected, latent and inhibited cells respectively, u_1 is the virus count and u_2 is the number of antibodies in the body. All the parameters A's B's and c's are considered to be positive. We calculate the reproduction number R_0, and the points of equilibrium. We show that there are three points of equilibrium. The first one, the origin, is always unstable, while the second one, the disease free equilibrium point P_2, is stable for $R_0<1$ and unstable for $R_0>1$. The third point of equilibrium, P_3, which denotes endemic disease and is stable for $R_0>1$, exhibits a number of bifurcations (sudden changes of behaviour) as this point is approached. For $A_{12} = 0$, in the beginning for $0 < e_0 < A_3 > e_1$, where e_0 and e_1 are appropriate constants, all the five eigenvalues of the characteristic matrix are negative, and P_3 is a node. As the infection coefficient A_3 is increased, two of the real (negative) eigenvalues come very close to each other and then change to two complex conjugate eigenvalues with negative real parts. Further increase of A_3 results in the same thing happening to the two remaining (real) eigenvalues. P_3 is stable all this time. Still further increase of A_3 results in two of the complex conjugate eigenvalues becoming real negative. This is similar to what would happen in a 2D case where the discriminant of the quadratic goes from negative to zero to positive. As A_3 is increased still further, the real parts of the two remaining complex eigenvalues become positive and P_3 loses stability. As three of the eigenvalues are negative, motion takes place in what is essentially a plane and the solution exhibits what appear to be limit cycles in this plane. These limit cycles give rise to what appear to be HIV blips. Such blips have been observed in patients.

We show that the equilibrium value of u_1 , the virus count, goes steadily down as the infection coefficient A_3 is increased. However, u_1 cannot stay down for long because the infection coefficient is high and this results in what are observed as HIV blips.

We also show that for given values of other parameters, increase in the value of A_{12} ($A_{12}x_1$ is the rate at which the inhibited cells are being produced and is an indicator of the amount of drug in the body) will decrease the equilibrium value of u_1 and high enough values of A_{12} will suppress the hiv blips. It has been observed in clinical cases that hiv blips appear in a patient after the patient has experienced low levels of viremia even for a long time if and when the treatment is interrupted. This is in accordance with our results.