(1) Dynamics of CD4$^+$ T cells, $\boldsymbol{X(t)}$

- Generated from the thymus at a rate r_1;
- τ is the fraction of cells inhibition by AZT;
- Loss due to finite lifespan at a rate μ_1;
- Generated by Antigen(A)-induced proliferation at a rate β_1.

These can be summarized in the differential equation:

$$\frac{dX}{dt} = r_1(1-\tau) - \mu_1 X + \beta_1(1-\tau)XA. \tag{1}$$

(2) Dynamics of CD8$^+$ T cells, $\boldsymbol{Y(t)}$

- Generated from the thymus at a rate r_2;
- Loss due to finite lifespan at a rate μ_2;
- Generated by Antigen-induced proliferation with the help of CD4$^+$ T cells at rate β_2.

Thus:

$$\frac{dY}{dt} = r_2(1-\tau) - \mu_2 Y + \beta_2(1-\tau)XYA. \tag{2}$$

(3) Dynamics of antigen(A)-specific CTLs, $C(t)$

- Generated from antigen-specific $CD8^+$ T cells with the help of $CD4^+$ T cells at a rate of θ;
- Loss due to natural death at a rate μ_3.

This gives:

$$\frac{dC}{dt} = \theta XYA - \mu_3 C. \tag{3}$$

(4) Dynamics of antibody-producing B cells, $Z(t)$

- Generated from bone marrow at a rate r_3;
- Loss due to natural death at a rate μ_4;
- Generated by Antigen-induced proliferation with the help of $CD4^+$ T cells at a rate β_3.

Then:

$$\frac{dZ}{dt} = r_3(1-\tau) - \mu_4 Z + \beta_3(1-\tau)XZA. \tag{4}$$

(5) Dynamics of Antigen, $A(t)$

- Produced due to vaccination or infection at a rate α;
- Loss due to B cells at a rate γ.

$$\frac{dA}{dt} = \alpha A - \gamma Z A. \tag{5}$$

In summary, the model consists of the equations:

$$\begin{aligned}
\frac{dX}{dt} &= r_1(1-\tau) - \mu_1 X + \beta_1(1-\tau)XA, && (1)\\
\frac{dY}{dt} &= r_2(1-\tau) - \mu_2 Y + \beta_2(1-\tau)XYA, && (2)\\
\frac{dC}{dt} &= \theta Y X A - \mu_3 C, && (3)\\
\frac{dZ}{dt} &= r_3(1-\tau) - \mu_4 Z + \beta_3(1-\tau)XZA, && (4)\\
\frac{dA}{dt} &= \alpha A - \gamma Z A. && (5)
\end{aligned}$$

Critical points

The model has two critical points:

$$E_1 = \left(\frac{r_1(1-\tau)}{\mu_1}, \frac{r_2(1-\tau)}{\mu_2}, 0, \frac{r_2(1-\tau)}{\mu_4}, 0 \right).$$

and

$$E_2 = (X^*, Y^*, C^*, Z^*, A^*),$$

where

$$\begin{aligned}
X^* &= \frac{r_1\alpha\beta_3(1-\tau) + \beta_1[\alpha\mu_4 - r_3\gamma(1-\tau)]}{\alpha\beta_3\mu_1}, \\
Y^* &= \frac{r_2\alpha\beta_3(1-\tau)}{\alpha\beta_3\mu_2 - \beta_2[\alpha\mu_4 - r_3\gamma(1-\tau)]}, \\
C^* &= \frac{r_2\theta[\alpha\mu_4 - r_3\gamma(1-\tau)]}{\alpha\beta_3\mu_2 - \beta_2[\alpha\mu_4 - r_3\gamma(1-\tau)]}, \\
Z^* &= \frac{\alpha}{\gamma}, \\
A^* &= \frac{\mu_1[\alpha\mu_4 - r_3\gamma(1-\tau)]}{(1-\tau)\{r_1\alpha\beta_3(1-\tau) + \beta_1[\alpha\mu_4 - r_3\gamma(1-\tau)]\}}.
\end{aligned}$$

Stability of the critical points

To establish the local stability of E_1 we apply the standard linearization method. To achieve this, the Jacobian of the model is computed and evaluated at E_1. Stability of this equilibrium is then determined based on the eigenvalues of the Jacobian, which are functions of the model parameters. After some calculations, it can be seen that the eigenvalues of the Jacobian are:

$$\lambda_1 = -\mu_1, \quad \lambda_2 = -\mu_2, \quad \lambda_3 = -\mu_3,$$

$$\lambda_4 = -\mu_4, \quad \lambda_5 = \alpha - \frac{r_3\gamma(1-\tau)}{\mu_4}.$$

Since $\lambda_1,\ \lambda_2,\ \lambda_3,\ \lambda_4$ are all negative, the critical point E_1 is stable if and only if $\lambda_5 < 0$. Thus E_1 is locally asymptotically stable if

$$\boxed{\mathcal{R} = \frac{\alpha\mu_4}{r_3\gamma(1-\tau)} < 1.}$$

Now suppose $\mathcal{R} < 1$. In this case, $C^* < 0$ which implies that E_2 does not exist in the biologically meaning region. Therefore, to ensure that all components of E_2 are positive, we require $\mathcal{R} > 1$. For positivity of E_2, we also need

$$\alpha\beta_3\mu_2 - \beta_2[\alpha\mu_4 - r_3\gamma(1-\tau)] > 0.$$

Let

$$\mathcal{R}_1 = \frac{\beta_2\mu_4(\mathcal{R}-1)}{\beta_3\mu_2\mathcal{R}}.$$

Then the conditions for the existence of positive critical point E_2 can be summarized as follows:

$$\boxed{\mathcal{R} > 1, \quad \text{and} \quad \mathcal{R}_1 < 1.}$$

In general, if $\mathcal{R} < 1$, then E_1 is the only positive critical point of the model and it is locally asymptotically stable. If $\mathcal{R} > 1$, then E_1 is unstable and another positive critical point of the model (E_2) exists provided $\mathcal{R}_1 < 1$.

By a similar method (using the Jacobian of the model at E_2), we can see that if E_2 exists (which means that $\mathcal{R} > 1$ and $\mathcal{R}_1 < 1$), then E_2 is locally asymptotically stable.

Result: *If $\mathcal{R} < 1$, then E_1 is globally asymptotically stable.*

Conjecture: *If $\mathcal{R} > 1$ and $\mathcal{R}_1 < 1$, then E_2 is globally asymptotically stable.*

Analysis of the Mathematical model

The analysis of the model consists of identifying the two "critical points" which is obtained by setting the right hand sides of the equations (1)-(5) to zero. This will enable us to discuss the nature of the populations in the neighborhood of these critical points.

Local stability

The local stability of a critical point defined as a local property of the critical point. This means that there is a neighborhood around the critical point such that every solution with an initiating point (initial sizes of the populations) in this neighborhood will approach to the critical point.

Global stability

The global stability of a critical point does not depend on the initiating points of the solutions which means that every solution will approach to the critical point (regardless of the initial conditions).

These situations are discussed based on the parameter values available in published clinical studies.