BM5063 Systems Medicine

Problem Set 5

Instructions

1. You are not expected to submit answers to these problems

Questions

1. Consider a simple model: The immune system attacks healthy tissue. This releases auto-antigens, making the immune killing stronger, in a cooperative way, with Hill coefficient $n = 2$. The variable is the amount of autoantigen $a(t)$. The autoantigen is removed at rate β and we have
$$\dot{a} = \alpha \frac{a^n}{k^n + a^n} - \beta a.$$
   (a) Draw a rate plot showing the fixed points. Consider (graphically) different scenarios (different parameters) with different numbers of fixed points. When is there bistability?
   (b) Which scenario corresponds to an autoimmune disease? Which corresponds to no autoimmune disease?
   (c) Suppose that individuals vary in their genetics in a way that affects the parameters of the equation. Does an increase in the parameter α increase the risk for autoimmune disease? Repeat for the parameters k and β.

2. Consider an antigen $u(t)$ presented by antigen-presenting cells to T cells. This activates effector T cells $T(t)$ that perform the response functions, and also regulatory T cells denoted $R(t)$ that inhibit the effector T cells. The dynamics is given by
$$\begin{aligned}\dot{R} &= \alpha_1 u - \beta_1 R \\ \dot{T} &= \alpha_2 \frac{u}{R_0 + R} - \beta_2 T.\end{aligned}$$
   (a) For a given fixed value of u, draw the phase diagram and identify the fixed points and their stability.
   (b) Consider a step-function change in u from level u_1 to level u_2. Sketch the change in the levels of T and R due to this as a function of time.
   (c) Consider another scenario where antigen rises exponentially, $u(t) = u_0 e^{t/T}$. What happens to the T cell levels over time?
   (d) Solve the system numerically.

3. Consider a model for the concentrations of virus, $u(t)$, effector T cells $T(t)$, and regulatory T cell $R(t)$. The system follows the following dynamical equations
$$\begin{aligned}\dot{u} &= (\alpha_v - \beta_v T)u \\ \dot{R} &= u - R \\ \dot{T} &= \frac{u}{k + R} - T.\end{aligned}$$
   (a) Explain the equations and draw the interaction diagram between cells and the virus.
   (b) Calculate the steady-state solution.
   (c) Numerically solve the equations for various values of α_v. Use $\beta_v = 1$, $k = 1$, $R(0) = T(0) = 0$, and $u(0) = 1$. Explain the meaning of these initial conditions.
   (d) Assume that when the virus concentration goes below a minimal dose, $u_c = 0.01$, it is killed by the innate immune system. What is the maximal viral growth rate α_v for which the virus is killed by the immune system? What happens if α_v is larger than this value?

4. Read this paper.