NAME:_____

MATH 5110
The Final

Do all problems. Feel free to use or hand in additional paper if necessary. Make sure I can find both the answer and how you got it. Two pages of notes, no calculators, cell phones etc. Do all five problems, with all equally weighted. The theme of this test is the battle between the immune system and cancer, where T typically represents the number of T cells that fight the cancer, and C the number of cancer cells.

1. Suppose cancer cells and T cells are measured weekly in an experimental mouse, and obey the dynamics

$$\begin{aligned} C_{t+1} &= \lambda C_t(1 - e^{-aT_t}) \\ T_{t+1} &= \rho C_t(1 - e^{-aT_t}) \end{aligned}$$

a. Explain the terms in these equations. How do they differ from the Nicholson-Bailey equations?

b. Find the equilibrium.

c. Find the stability of the equilibrium. If you get stuck, explain clearly how far you got and what you'd need to compute to demonstrate stability.

2. Suppose there are two lineages of T cells, described by the variables T_1 and T_2, that are competing for the opportunity to kill the cancer. They obey the following system of differential equations

$$\begin{aligned} \frac{dC}{dt} &= rC - \mu G(T_1, T_2)C \\ \frac{dT_1}{dt} &= \sigma_1 + \rho_1 C - \delta_1 T_1 \\ \frac{dT_2}{dt} &= \sigma_2 + \rho_2 C - \delta_2 T_2 \end{aligned}$$

where $G(T_1, T_2)$ is a function that is increasing in T_1 and T_2.

a. How do these differ from the competition equations?

b. Suppose first that $T_2 = 0$. What are the conditions for eliminating the cancer with just T_1?

c. Show that both T cells lineages can coexist. Is this possible when $C > 0$?

d. Suppose σ_1, ρ_1, and δ_1 are all small. Which equation or equations could you put into quasi-steady state? What is the remaining system of equations? When might this occur?

3. T cells are regulated by regulatory T cells, or Tregs, with a population we denote by R. Suppose that the population of cancer cells C is constant, and that the numbers of T cells and Tregs obey

$$\begin{aligned} \frac{dT}{dt} &= \sigma + \rho CT - \delta_T T - \theta RT \\ \frac{dR}{dt} &= \epsilon(\alpha T - \delta_R R) \end{aligned}$$

where ϵ is small.

a. What does that small ϵ mean?

b. Show that this system has just one equilibrium. What is different in the cases where $\rho C < \delta_T$ and $\rho C > \delta_T$?

c. Use the phase plane to describe the dynamics. What happens when the system is perturbed from equilibrium by an increase in the number of T cells?

d. Sketch how the phase plane would have to change in order for this to be an excitable system, where an increase in the number of T cells is amplified but eventually repressed by the Tregs.

4. The immune system does not respond immediately to a cancer. Suppose that

$$\begin{aligned} \frac{dC}{dt} &= rC - \mu TC \\ \frac{dT}{dt} &= \rho C(t-\tau) - \delta T. \end{aligned}$$

for some positive value of τ.

a. Find the equilibria and their stability if $\tau = 0$.

b. Linearize the system around the positive equilibrium (for any τ).

c. Substitute the exponential "ansatz" (assume solutions behave like exponentials near the equilibrium) and find an equation for the eigenvalues.

d. Explain how you would check whether the equilibrium can change stability due to the delay.

5. Suppose that each cancer cell divides at probabilistic rate β, and dies at rate μI where I is a constant that describes the state of the immune system.

a. What are the conditions for the cancer to grow on average?

b. What is the probability that a single cancer cell will grow to become a large tumor? How does this depend on I?

c. Suppose that the immune system doesn't kill cancer cells one at a time. Instead, if there are n cancer cells, death events occur at rate μI and kill 1, 2, 3, $\ldots n$ cells with equal probability. Draw a diagram showing this.

d. Write differential equations for the probabilities that there are k cancer cells in this case.

e. **Extra credit** In the situation in **d**, show that the only equilibrium is where $p_0 = 1$.