Math 486/522 - Homework 4 - Pharmacokinetics

Fall 2024 **Len Washington III**

Please review Dawkin's ODE notes, particularly Laplace Transforms, if needed. You **must** include your computer code for any computations and graphs.

1. Consider the system of ODEs

$$x' = -2y + \delta(t-1),\ x(0) = 0$$
$$y' = -3x = y,\ y(0) = 0$$

(a) Solve the system using **Laplace Transforms**. Clearly show **all** steps. Problem 1a answer here.

(b) Graph the solutions $x(t)$ and $y(t)$ from $t = 0$ to $t = 2$ on the same axes and label each curve. Problem 1b answer here.

2. A pharmacokinetics model with one compartment (plasma) is used to model a drug that is administered with dose D at $t = 0$. A booster of dose $D/3$ is given at $t = 5$. The clearance rate from the compartment is $k = 1/4$. Define $x(t)$ be the amount of drug in the plasma at time t.

(a) Derive a differential equation models for $x(t)$ with the proper initial condition. You must use Dirac delta functions in your model. Problem 2a answer here.

(b) Use Laplace transforms to solve the ODE. Problem 2b answer here.

(c) Plot $x(t)$ from $t = 0$ to $t = 10$ with $D = 4$. Problem 2c answer here.

3. Consider a one compartment model for the amount $x(t)$, a drug in the plasma with $x(0) = 0$. Assume the elimination rate is $k > 0$. The drug is administered using intravenous infusion (IV) for 2 hours but the amount of drug in the IV (drip rate) is reduced in time by a factor of e^{-t}. The drug input $I(t)$ is given by

$$I(t) = \{\ Ae^{-t}, 0 \leq t < 2, 0, t \geq 2.$$

Here time is in hours.

(a) Set up a differential equation for $x(t)$ by converting $I(t)$ to a single line function using the Heaviside step function. Problem 3a answer here.

(b) Use Laplace transform to solve the ODE assuming $x(0) = 0$. Show all details. Problem 3b answer here.

(c) The total amount of drug that is removed or eliminated is equal to $k\int_0^\infty x(t)dt$. Verify that all the drug is removed. Problem 3c answer here.

(d) Plot $x(t)$ for $0 < t < 8$ is the half-life of the drug in the blood is 5 hours, and $A = 3$. Problem 3d answer here.

4. A maintenance drug such as Lipitor is taken daily for a long period of time. It reduces cholesterol levels and lowers the risk of a heart attack. A single compartment pharmacokinetics model is used to track the concentration of the drug in the plasma. Suppose each dose has concentration C and it taken at fixed time intervals τ. The elimination rate for the compartment is k.

(a) Derive difference equations for the sequence of local maxima, u_n, and local minima, v_n, assuming the concentration in the blood is 0 just before the first dose. Problem 4a answer here.

(b) Solve the equations in **(a)**. Compute the limits of the sequences as $n \to \infty$. These need to be inside the therapeutic window for the maintenance drug. Problem 4b answer here.

(c) The data for the drug is:

- half-life is plasma in 2 hours.
- $C = 150\text{mg}/15.8\text{L}$. Here the volume of distribution is 15.8L, which is not realistic.

Find the smallest does interval τ such that the drug remains in the therapeutic window $0.5\text{mg/L} < conc. < 10.3\text{mg/L}$. The value of τ must be an integer to be useful for the patient. Problem 4c answer here.