Math 486/522 - Homework 4 - Pharmacokinetics

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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 = 7 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

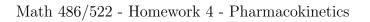
$$I(t) = \left\{ Ae^{-t}, 0 \le t < 2, 0, t \ge 2. \right.$$

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 mg/15.8 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 0.5mg/L < conc. < 10.3mg/L. The value of τ must be an integer to be useful for the patient. Problem 4c answer here.



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Listing 1 Source Code for the Graphs

Source Code Here