Math 486/522 - Homework 5

Fall 2024 **Len Washington III**

1. Strep throat, sinus infections, etc. usually require an antibiotic to help bring the infection under control. Zithromax (azithromycin) is often prescribed for these infections as a Z Pak containing 6 pills. Suppose we design a two compartment model for Zithromax with the first compartment being the GI tract $x(t)$ and the second compartment being the blood stream, $y(t)$ with the following system of ODE's:

$$\begin{aligned} x' &= -k_1 x + I(t) \\ y' &= k_1 x - k_2 y \end{aligned}$$

where $I(t)$ is the input of the pills. The initial amount in each compartment equal to 0. The dosing regimen for a Z Pak is 2 pills the first day and then 1 pill for the following 4 days (5 day regimen). The time between the doses is 1 day and each pill delivers D units of the drug.

   (a) Find the amount of the drug in each compartment from days 1 to 8. Model each pill dose by a Dirac delta function spiked at the appropriate time. Problem 1a answer here.

   (b) If each pill is 400mg, $k_1 = 0.9$, and half-life of the drug in the blood is 2.3 days, graph $x(t)$ and $y(t)$ on the same axes from day 1 to day 8. Problem 1b answer here.

2. Consider a system of ODE's with initial conditions.

$$\frac{d\vec{x}}{dt} = A\vec{x} + \vec{b} = \begin{bmatrix} -2 & 1 \\ 1 & -2 \end{bmatrix} \vec{x} + \begin{bmatrix} 3 \\ -1 \end{bmatrix}, \vec{x}(0) = \begin{bmatrix} 2 \\ 2 \end{bmatrix} \tag{1}$$

Answer **(a)**-**(d)** on paper using matrix methods.

   (a) Find a fundamental set of solutions to the associated homogenous equation. Problem 2a answer here.

   (b) Find a particular solution $x_p(t)$ using undetermined coefficients, i.e. just guess a constant solution. Problem 2b answer here.

   (c) Form the general solution and then find the specific solution of the initial value problem. Problem 2c answer here.

   (d) Describe the behavior at $t \to \infty$. Problem 2d answer here.

   (e) Use the *Mathematica* notebook attached for the following questions:

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In[◦]:= A = {{-2, 1}, {1, -2}}

In[◦]:= A // MatrixForm

In[◦]:= b = {3, -1}

In[◦]:= b // MatrixForm

In[◦]:= Eigenvalues[A]

In[◦]:= Eigenvectors[A]

In[◦]:= X[t_] = {x1[t], x2[t]}

In[◦]:= prob = X'[t] == A.X[t] + b

In[◦]:= sol = DSolve[{prob, x1[0] == 2, x2[0] == 2}, {x1, x2}, t]

In[◦]:= solns = {x1[t], x2[t]} /. sol[[1]]

In[◦]:= Plot[Evaluate[solns], {t, 0, 3}]

In[◦]:= x[t_] = solns[[1]]

In[◦]:= x[2.0]

In[◦]:= Plot[x[t], {t, 0, 3}]

In[1]:= SetDirectory[NotebookDirectory[]]

Out[1]= /mnt/d/Academic/math486/src/homework/homework5

In[2]:= Export["homework5-mathematica.pdf", SelectedNotebook[]]

Out[◦]= homework5-mathematica.pdf
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Figure 1: Mathematica notebook

(i) Find the eigenvalues and eigenvectors of the coefficient matrix A. Do they agree with your hand calculation? Problem 2e(i) answer here.

(ii) Use DSolve to construct the solution (1). Problem 2e(ii) answer here.

(iii) Graph $x_1(t)$ and $x_2(t)$ for $0 \le t \le 3$ on the same axes. Problem 2e(iii) answer here.

3. In the lecture, a lead uptake model discussed as is a 3 compartment model with compartments - plasma, soft tissue and bones. The amount of lead in the compartments is measured in micrograms and time is measured in days. Let $x_1(t)$ be the amount in the blood, $x_2(t)$ is the amount in the soft tissues, and $x_3(t)$ is the amount in the bones. The following data was given in Rabinowitz, Wetherill, and Kopple, *Science*, **182**, 1973, pp. 725-727:

$$\begin{array}{lll} k_{01} = 0.0211 & k_{21} = 0.0111 & k_{31} = 0.0039 \\ k_{02} = 0.0162 & k_{12} = 0.0124 & k_{13} = 0.000035 \end{array} \tag{2}$$

Note: You cannot do this problem by hand (easily) so use Mathematica or equivalent. The Mathematica notebook from problem 1 should help.

(a) Re-derive the system of ODE's $\frac{d\vec{x}}{dt} = A\vec{x} + \vec{I}$ for the amount in each compartment based on the figure in the notes, i.e. check to make sure the equations in the lecture notes are correct. Problem 3a answer here.

(b) Again assume $I = 0$ but now $x_1(0) = 0$, $x_2(0) = 0$, and $x_3(0) = 6$:

(i) Construct the solution of the system of ODE's. Problem 3b(i) answer here.

(ii) Graph the three amounts in the different compartments on the different axes for 1000 days. Problem 3b(ii) answer here.

(iii) By using the graph of $x_3(t)$, estimate the initial half-life $\tau_{1/2}$ in days for the amount of leads in the bones, i.e. how long to go from $x_3(0) = 6$ to $x_3(\tau_{1/2}) = 3$. You may need to increase the time range. Can you obtain an analytic estimate for the half-life? Problem 3b(iii) answer here.

(c) Suppose there is a drug that speeds the removal of lead from the bones such that the removal rate k_{13} is tripled. Re-do steps **(i)**-**(iii)** in part **(b)**. Compare the results in **(b)** and **(c)**. Problem 3c answer here.