Differential Equations - Project 3

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8, April 2022

1 Introduction

In this project we will be modeling the flow of medication through the body. Specifically between the gastrointestinal tract and the blood stream. By modeling the gastrointestinal tract and blood stream as compartments we can observe how the medication enters and leaves each compartment. We will be looking at the case where a pill dissolves and release medication into the gastrointestinal tract. From the gastrointestinal tract it enters the blood stream at a rate proportional to the amount present in gastrointestinal tract. We can write the relationship between the gastrointestinal tract and the medication, as well as the relationship between blood stream, gastrointestinal tract, and the medication as a pair of linear equations. By writing the relationships as a pair of linear equations we can put them into matrix form and solve for eigenvectors and eigenvalues. Eigenvectors and values are useful because eigenvalues tell us the distortion that is caused by the matrix transformation. The eigenvector tells us the direction of the distortion. Using these principles of linear algebra we can model a system of linear equations to map the relationship between compartments.

2 Methodology

Problem 1

After looking at how the medicine enters the GI tract and blood stream we created a differential equation to model the amount of medicine in each bodily function with respect to time.

$$\boldsymbol{x} = \begin{bmatrix} x \\ y \end{bmatrix}$$

$$\frac{d\boldsymbol{x}}{dt} = \begin{bmatrix} -k_1 & 0 \\ k_1 & -k_2 \end{bmatrix} \begin{bmatrix} x \\ y \end{bmatrix}$$

Figure 1: System of Differential Equations in Matrix Form

Problem 2 Using the eigenvalue method for systems of ODEs, we will solve for the initial value problem.

$$\begin{vmatrix} -k_1 - \lambda & 0 \\ k_1 & -k_2 - \lambda \end{vmatrix} = 0$$

$$k_1 k_2 + \lambda k_1 + \lambda k_2 + \lambda^2 = 0$$

$$\lambda_1 = -k_1, \; \lambda_2 = -k_2$$

$$\boldsymbol{v_1} = \begin{bmatrix} a \\ b \end{bmatrix}$$

$$\begin{bmatrix} -k_1 + k_1 & 0 \\ k_1 & -k_2 + k_1 \end{bmatrix} \begin{bmatrix} a \\ b \end{bmatrix} = 0$$

$$\boldsymbol{v_1} = \begin{bmatrix} \dfrac{k_2 - k_1}{k_1} \\ 1 \end{bmatrix}$$

$$\boldsymbol{v_2} = \begin{bmatrix} c \\ d \end{bmatrix}$$

$$\begin{bmatrix} -k_1 + k_2 & 0 \\ k_1 & -k_2 + k_2 \end{bmatrix} \begin{bmatrix} c \\ d \end{bmatrix} = 0$$

$$\boldsymbol{v_2} = \begin{bmatrix} 0 \\ 1 \end{bmatrix}$$

Figure 2: Here we found the lambda's of our characteristic equation, and solve each compnonent of our model.

$$\begin{bmatrix} x \\ y \end{bmatrix} = c_1 \begin{bmatrix} \frac{k_2 - k_1}{k_1} \\ 1 \end{bmatrix} e^{-k_1 t} + c_2 \begin{bmatrix} 0 \\ 1 \end{bmatrix} e^{-k_2 t}$$

x(0) = A

y(0) = 0

$$A = c_1 \frac{k_2 - k_1}{k_1}$$

$$0 = c_1 + c_2$$

$$c_1 = \frac{Ak_1}{k_2 - k_1}, c_2 = -\frac{Ak_1}{k_2 - k_1}$$

Figure 3: Now we plug in our initial value of A medicine entering the blood stream initially and no medicine in the blood initially.

$$\begin{bmatrix} x \\ y \end{bmatrix} = \frac{Ak_1}{k_2 - k_1} \begin{bmatrix} \frac{k_2 - k_1}{k_1} \\ 1 \end{bmatrix} e^{-k_1 t} + \frac{-Ak_1}{k_2 - k_1} \begin{bmatrix} 0 \\ 1 \end{bmatrix} e^{-k_2 t}$$

Figure 4: This is our final model

Problem 5

Alternatively, lets suppose we had a model that instead of an initial dose of medicine A, we instead had a constant dosage of I medicine every hour with no initial medicine in the blood stream. We will solve this equation by using the method of undetermined coefficients.

$$\boldsymbol{x} = \begin{bmatrix} x \\ y \end{bmatrix}$$

$$\frac{d\boldsymbol{x}}{dt} = \begin{bmatrix} -k_1 & 0 \\ k_1 & -k_2 \end{bmatrix} \begin{bmatrix} x \\ y \end{bmatrix} + \begin{bmatrix} I \\ 0 \end{bmatrix}$$

$$\boldsymbol{x_h} = c_1 \begin{bmatrix} \dfrac{k_2 - k_1}{k_1} \\ 1 \end{bmatrix} e^{-k_1 t} + c_2 \begin{bmatrix} 0 \\ 1 \end{bmatrix} e^{-k_2 t}$$

Figure 5: This is our new Differential equation

$$\boldsymbol{f} = \begin{bmatrix} I \\ 0 \end{bmatrix}$$

First Guess: $\boldsymbol{x_p} = \begin{bmatrix} At \\ Bt \end{bmatrix}$

Plug back into original differential Equation

$$\begin{bmatrix} 0 \\ 0 \end{bmatrix} = \begin{bmatrix} -k_1 & 0 \\ k_1 & -k_2 \end{bmatrix} \begin{bmatrix} A \\ B \end{bmatrix} + \begin{bmatrix} I \\ 0 \end{bmatrix}$$

$$A = \frac{I}{k_1}$$

$$B = \frac{I}{k_2}$$

$$\boldsymbol{x_p} = \begin{bmatrix} \dfrac{I}{k_1} \\ \dfrac{I}{k_2} \end{bmatrix}$$

Figure 6: We use the method of undetermined coefficients.

$$\boldsymbol{x} = c_1 \begin{bmatrix} \frac{k_2 - k_1}{k_1} \\ 1 \end{bmatrix} e^{-k_1 t} + c_2 \begin{bmatrix} 0 \\ 1 \end{bmatrix} e^{-k_2 t} + \begin{bmatrix} \frac{I}{k_1} \\ \frac{I}{k_2} \end{bmatrix}$$

x(0) = 0

y(0) = 0

$$c_1 = \frac{I}{k_1 - k_2}$$

$$c_2 = \frac{I(k_1 - 2k_2)}{k_2(k_1 - k_2)}$$

Figure 7: Now we plug in our initial value of no medicine entering the blood stream initially and no medicine in the blood initially.

$$\boldsymbol{x} = \frac{I}{k_1 - k_2} \begin{bmatrix} \frac{k_2 - k_1}{k_1} \\ -1 \end{bmatrix} e^{-k_1 t} + \frac{I(k_1 - 2k_2)}{k_2(k_1 - k_2)} \begin{bmatrix} 0 \\ -1 \end{bmatrix} e^{-k_2 t} + \begin{bmatrix} \frac{I}{k_1} \\ \frac{I}{k_2} \end{bmatrix}$$

Figure 8: This is our final model.

With these two models we can project the amount medicine if we only give an initial dose or if we constantly injecting the medicine every hour.

3 Results

Problem 3

Suppose scientists at Merck estimate that the values of the rate constants for the antihistamine in the cold pills it makes are

$$k_1 = .6931\ (hour)^{-1} \tag{1}$$

$$k_2 = 0.1386\ (hour)^{-1} \tag{2}$$

Suppose that we Start with $A = 1$ units of medication. We can model when the medication in the blood is at its maximum level by using Figure 4. We can visualize the system of linear equations as two linear equations.

$$x(t) = (\frac{Ak_1}{k_2 - k_1})(\frac{k_2 - k_1}{k_1})e^{-k_1 t} \tag{3}$$

$$y(t) = \frac{Ak_1}{k_2 - k_1}e^{-k_1 t} + \frac{-Ak_1}{k_2 - k_1}e^{-k_2 t} \tag{4}$$

Substituting in initial conditions into our model we can graph.

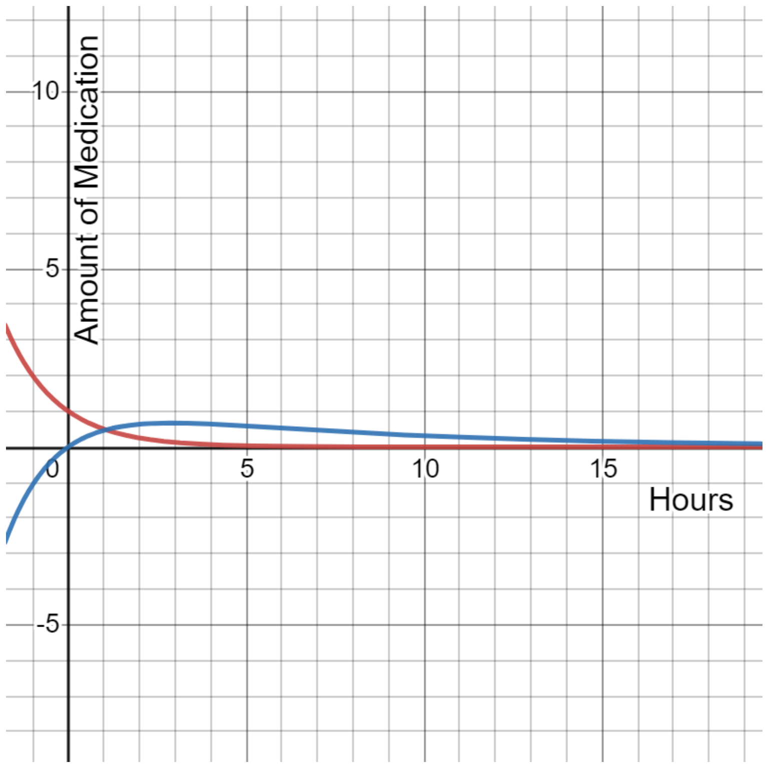

Figure 9: The red line is $x(t)$. The Blue line is $y(t)$.

In figure above we see the red graph as the amount of medicine in the GI Tract and the blue graph is the amount of medicine in the blood stream.

Based on our graph the medication is at it's maximum in the blood stream after 2.9 hours, which at that .669 of medicine A is in the blood stream.

Problem 4

Let k_2 take on the values

$$k_2 = 0.00231\ (hour)^{-1} \tag{5}$$

$$k_2 = 0.1386\ (hour)^{-1} \tag{6}$$

or

$$k_2 = 0.231\ (hour)^{-1} \tag{7}$$

The constant k_2 is the clearance coefficient of medication from the blood. By plotting $y(t)$ we can see how levels of medication in the bloodstream changes when the value of k_2 changes

$$y(t) = \frac{Ak_1}{k_2 - k_1}e^{-k_1 t} + \frac{-Ak_1}{k_2 - k_1}e^{-k_2 t} \tag{8}$$

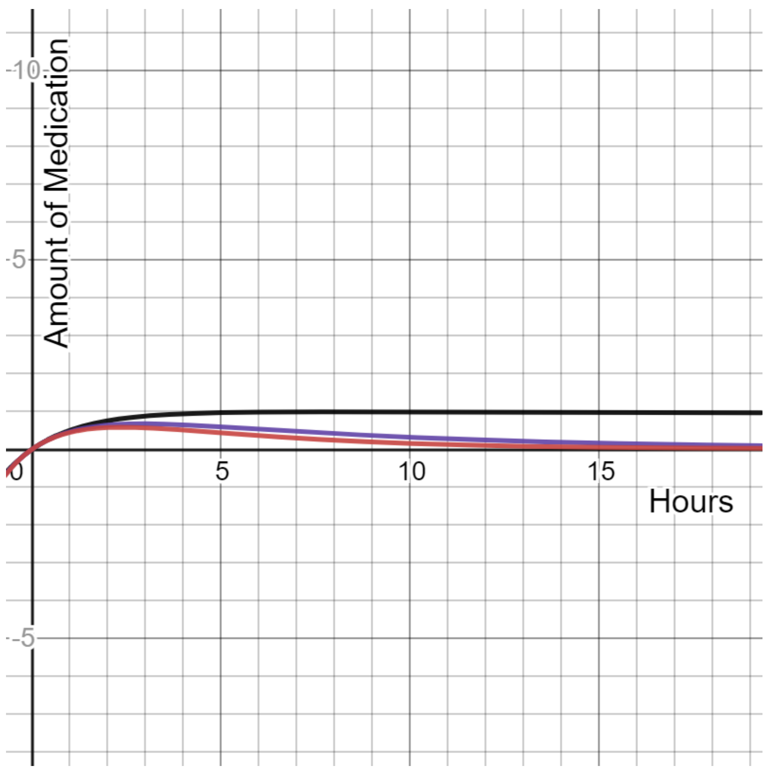

Figure 10: Black represents $k_2 = 0.00231$. Purple represents $k_2 = 0.1386$. Red represents $k_2 = 0.231$

We can see that Purple and Red both reach the same equilibrium point, while the black line has a different equilibrium point. Purple and Red are closer in value while black has a value of 10^{-2} more.

Problem 5

The final model establishes that our final model has cold pills dissolve continuously in the GI tract. We are also given a few parameters to graph the new models, these being $k_1 = 0.6931$ (hour)$^{-1}$, $k_2 = 0.1386$ (hour)$^{-1}$, and $I = 0.5$

units of drug per hour. The graph of the new model comes out to be:

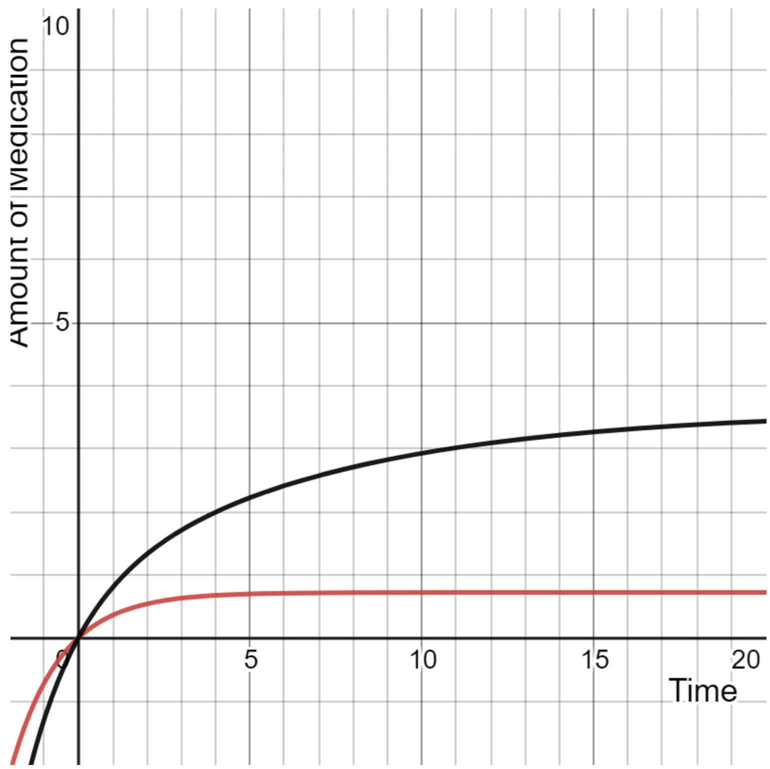

Figure 11: Red represents x(t) and black represents y(t)

This shows that the medication is absorbed into the bloodstream significantly quicker when the medication dissolves continuously in the GI tract. We take the limit as $t \to \infty$ to determine how much of the medication stays within the GI tract compared to the bloodstream.

$$\lim_{t \to \infty} x(t) = 0.721 \tag{9}$$

$$\lim_{t \to \infty} y(t) = 3.608 \tag{10}$$

As time goes on, the amount of the medication within the GI tract eventually stabilizes at 0.721 units, while the amount of the medication in the bloodstream stabilizes at 3.608 units.

4 Discussion

Understanding how oral medication dissolves within the body is important to the medical field. In this model, we looked at how much of the medication is concentrated in the Gastrointestinal tract compared to the bloodstream. It was found that a basic model where an instantaneous dose of medication is introduced had significantly less effect than a model where the medication constantly dissolves within the GI tract. This model, while useful, assumes a great deal about the nature of the medication and can be expanded upon by looking at other forms of medication that may not dissolve instantly or may dissolve at a variable rate. Ultimately, we hope that this does contribute to the understanding of the dissolution of oral medication.