More about DE models in pharmacokinetics:

Read this: In class, we talked about the use of linear DEs in modeling the dynamics of a drug in a human body over time (pharmacokinetics). In the drug databases that physicians and nurses utilize, one property that each drug possesses is its half-life. The half-life, usually denoted \( t_{1/2} \), is defined as the amount of time necessary for the human body to reduce (i.e. remove from the bloodstream) the drug concentration to exactly one-half of the starting concentration, under the assumption that no new drug is being input into the blood.

Determining the half-life: To compute the half-life of a drug, we set up a DE model, assuming a non-zero initial concentration, and assuming no new input of drug over time. Thus, the IVP looks like this:

\[
\frac{dy}{dt} = -ky, \\
y(0) = A
\]

where \( t = \text{time} \), \( y = \text{drug concentration at time } t \), \( A = \text{initial concentration} \), and \( k = \text{a proportionality constant, called the clearance rate} \). Then, the half-life \( t_{1/2} \) is the value of \( t \) for which

\[y(t_{1/2}) = \frac{1}{2} A.\]

1. a. Solve the IVP above to get \( y \) as a function of \( t \).
   b. Use part a. to show that \( t_{1/2} = \frac{\ln(2)}{k} \). (Notice that the half-life does not depend on the initial concentration \( A \).)
   c. (How clearance rate is determined in real life.) A patient is given an initial dose of 250mg of a drug. Thirty minutes later, the measured concentration in the blood is 18.2mg/L. Assuming the patient has 5 liters of blood, use parts a. and b. to estimate the clearance rate of this drug.
   d. (How half-life is determined in real life.) A patient is given an initial dose of 80mg of a drug. One hour later, the measured concentration in the blood is 13.4mg/L. Assuming the patient has 5 liters of blood, use parts a., b., and c. to estimate the half-life of this drug.

2. When a drug is used to treat a patient, it is usually necessary to maintain a specific concentration over a sufficiently-long period of time, in order to be effective. To achieve this, the physician must determine the quantity and frequency with which the drug is to be given to the patient. For this reason, long-term behavior of the DE model is very important. Let’s consider the case where the patient is to receive a drug by continuous IV, at a constant rate \( r \), to be determined by the physician (i.e. you!). This constant rate is called the infusion rate. As noted in class, the IVP to use in this case is

\[
\frac{dy}{dt} = r - ky \\
y(0) = 0
\]
a. Calculate the infusion rate (in mg/hour) required to maintain a desired drug concentration of 2 mg/L. Assume the patient has 5.6 liters of blood and the half-life of the drug is 2.7 hours.

b. Using your infusion rate from part a., estimate how long it will take for the concentration in the blood to reach 90% of the desired concentration.

**A DE model of diffusion:**

3. At the cellular-level, transport of individual molecules of a substance across membranes is often driven by diffusion, i.e. the molecules tend to move across the membrane from the higher-concentration (of the substance) side of the membrane, to the lower-concentration side.

   ![Diffusion Diagram](image)

Let $y$ be the concentration of a particular substance inside a cell after $t$ minutes, and let $B$ be the concentration of this substance outside the cell. Assuming $B$ is constant, construct a DE model that is based on the assumption that the IROC of the concentration of the substance inside the cell is proportional to the difference between the outside concentration and the inside concentration.

**Newton and Time-of-death:**

Newton’s law of cooling/heating is the basis for a method used by police to determine time-of-death. The simplest situation is when the death occurs indoors, where the temperature is constant. Then, letting $t$ be the time (usually in hours) since death (so that $t = 0$ represents the moment of death), and letting $y$ be the temperature of the body at time $t$, we can use the Newton’s Law DE to write down a model relating $y$ and $t$:

$$\frac{dy}{dt} = k(B - y)$$

$y(0) = 98.6$

(The initial condition assumes that the victim’s body temperature was 98.6°F at the time of death.) In this model, the temperature of the room plays the role of the environmental temperature $B$.

4. A dead body is found in a 72°F room, 3 hours after death. Assuming the room was the same temperature during the entire 3 hours, solve the IVP model above, then use your solution to compute the temperature of the body at the time it is found (i.e. 3 hours after death).
There are certain situations (e.g. when death occurs outdoors) where it is not realistic to assume that the environmental temperature is constant. In this case, we would replace the constant $B$ with a function $B(t)$, which gives the environmental temperature at time $t$. Then, the IVP model becomes

$$\frac{dy}{dt} = k(B(t) - y)$$
$$y(0) = 98.6$$

The next exercise illustrates another situation that has non-constant environmental temperature.

5. A clever murderer kills a person in a 90°F room, then immediately turns the thermostat down to 72°F. By the time the police arrive, 3 hours later, the room has just reached 72°F.
   a. Verify that the function $B(t) = 90 - 6t$ satisfies $B(0) = 90$ and $B(3) = 72$.
   b. Using the $B(t)$ from part a., solve the IVP to get a formula for the body temperature at time $t$. (Use the same $k$-value as in the previous exercise.)
   c. Use your solution from part b. to compute the body temperature 3 hours after death.
   d. Does the body temperature from part c. differ from the body temperature in Exercise 4? In one or more complete, coherent English sentences, explain how this might make the murder harder to solve.