Chapter 10 Application Project: A Spoonful of Sugar

In this project, you will build a model that sheds light on the mathematics behind medicine dosage. Your knowledge of sequences and exponential decay will be essential for this work. It is important to note, however, that pharmacology is a complicated science, and numerous factors are taken into consideration when actual drug dosage for the treatment of a particular condition is determined. The model in this project, while it illustrates the basic ideas behind drug dosage, should not be used in real-life situations.

1. Clinical experiments have shown that the concentration $C(t)$ of a drug in the bloodstream decays at a rate proportional to the instantaneous level of concentration.

- **a.** Using k for the constant of proportionality and assuming an initial level of concentration $C(0) = D,$ set up an initial value problem to find $C(t)$. Assume t is measured in hours.
- **b.** Solve your initial value problem to find a formula for $C(t)$.

2.
- **a.** Starting with a concentration level of $C(0) = D,$ another dose is administered after a *dosage period* of p hours that raises the concentration level by D. Construct a formula for the level of concentration just before the new dose is administered, and denote it by C_1. The reason for this naming convention is that this is the concentration level just before the first so-called *maintenance dose* is administered. Note, however, that in practice the initial, so-called *loading dose*, and the maintenance dose are usually different. (**Hint:** Note that $C_1 = C(p)$.)
- **b.** After yet another period of p hours, the same dosage D is administered again. Find the level of concentration just before this second maintenance dose and denote it by C_2.

3. Iterating the process in Question 2, find a formula for $C_n,\ n \geq 2$. (**Hint:** Use the formula for the sum of a finite sequence.)

4. Find $C = \lim\limits_{n\to\infty} C_n$ to determine the long-term concentration after many repeated doses.

The minimum concentration at which a drug is effective is often abbreviated as MEC (for minimum effective concentration). In this project, we will denote that concentration by m_e. On the other extreme, above a certain concentration level, a drug will typically cause unwanted side effects and is said to be toxic. This concentration level is often referred to as the MTC (for minimum toxic concentration), and we will denote it by m_t. The interval $[m_e, m_t]$ is called the *therapeutic window*. In order for a given drug to work, that is, to achieve the desired therapeutic effects without causing harm, we need to keep its concentration level in this interval.

Now suppose we want to prescribe a dosage amount with an optimal dosage period that keeps the drug concentration within the therapeutic window for the duration of treatment. One possible approach is to try to maximize the time between subsequent doses for the patient's convenience. In order to achieve that, we administer a loading dose that raises the concentration level to just below m_t, the top of the therapeutic window. Then we wait until the concentration drops down to m_e and administer a maintenance dose that raises the concentration by $D_m = m_t - m_e$ to bring the concentration level back to (near) m_t. In other words, the goal is to achieve a long-term concentration $C = m_e$ with repeated maintenance doses D_m. In Question 5, we will determine the dosage interval to achieve this.

5. Substitute $C = m_e$ and $D = m_t - m_e$ into the formula you obtained for C in your answer to Question 4, and then solve for p to obtain a formula for the optimal dosage interval.

6. Suppose that a certain medication's therapeutic window ranges from a concentration of 150 nanograms per milliliter $(\mathrm{ng/mL})$ to $600\ \mathrm{ng/mL}$ and that its half-life is 12 hours. Suppose one tablet raises the concentration by $150\ \mathrm{ng/mL}$. (A nanogram is one-billionth of a gram.)
   - **a.** What loading dose of this drug would your model recommend?
   - **b.** Based on your work on Question 5, what would be the optimal dosage and dosage interval for this drug? (**Hint:** Recall the definition of half-life from Exercises 66–67 in Section 1.2.)