

# Geometric series and effective medicine dosage

## Introduction

This lab concerns a model for a drug being given to a patient at regular intervals. As the drug is broken down by the body, its concentration in the bloodstream decreases. However, it doesn't disappear completely before the next dose is given. This means that there is a tendency for the average drug concentration to increase over time. It turns out that a geometric series is the key to understanding how high the concentration can go.

## Getting Started

To assist you, there is a worksheet associated with this lab that contains examples and even solutions to some of the exercises. You can open this worksheet after you start up Maple by choosing `Open...` from the `File` menu and then typing the following file name.

```
\\storage\academics\math\calclab\MA1023\Drug_start_2018.mw
```

You should read through the lab before you load this worksheet into Maple. Once you have read to the exercises, start up Maple, load the worksheet `Drug_start.mw`, and go through it carefully by reading the text and running the commands. Then you can start working on the exercises.

## Background

### Exponential decay and effective medicine dosage

In this section, we describe an exponential decay model for the concentration of a drug in a patient's bloodstream. We assume that the drug is administered intravenously, so that the concentration of the drug in the bloodstream jumps almost immediately to its highest level. The concentration of the drug then decays exponentially. If we use  $C(t)$  to represent the concentration at time  $t$ , and  $C_0$  to represent the concentration just after the first dose is administered then our exponential decay model would be given by

$$C(t) = C_0 e^{-kt}$$

where  $k$  is the decay constant, and is a property of the particular drug being used. It is usually obtained experimentally. The worksheet `Drug_start.mws` has examples of how to compute  $k$  from experimental data.

Now suppose that an additional dose of the drug is given to the patient. Since we are assuming that when the drug is administered it is diffused so rapidly throughout the bloodstream that, for all practical purposes, it reaches its highest concentration instantaneously, we would see a jump in the concentration of the drug when the new dose is given, as shown in the graph below.

After the additional dose is given, the concentration again decays over time.

A problem facing physicians is the fact that for most drugs, there is a concentration,  $m$ , below which the drug is ineffective and a concentration,  $M$ , above which the drug is dangerous. Thus the physician would like the have the concentration  $C(t)$  satisfy

$$m \leq C(t) \leq M$$

This requirement helps determine the initial dose of a drug and when the next dose should be administered. For example, the first dose should never raise the concentration above  $M$ . That is, we must have  $C_0 \leq M$ . To get a handle on the time between doses, we can calculate the maximum possible time between doses. That is, suppose an initial dose is given such that the concentration immediately after the dose is  $M$ , the maximum safe dose. If we calculate the time at which the concentration has decayed to  $m$ , then this gives the maximum time interval between doses. This gives us an upper bound on the time between doses. The worksheet contains examples of this kind of calculation. Note that many factors could be important in determining the time between doses that is actually used, including practical considerations like hospital schedules and shift changes.

### Equal, regularly-spaced doses

We next consider what happens if equal doses of the drug are given at regular time intervals. Recall that a drug has a maximum safe concentration,  $M$ , and a minimum effective concentration,  $m$ . We say that a treatment program of equal, regularly-spaced doses is safe and effective if the concentration  $C(t)$  of the drug satisfies

$$m \leq C(t) \leq M$$

during the treatment.

In the first part of this lab, we presented the expression

$$C(t) = C_0 e^{-kt}$$

for the concentration of the drug after the first dose. This expression is valid as long as only a single dose is given. However, suppose that at  $t = L$  a second dose is given and that the amount of the drug administered is the same as the first dose. According to our model, the concentration will jump immediately by an amount equal to  $C_0$  when the second dose is given. However, when the second dose is given, there is still some of the drug in the bloodstream remaining from the first dose. This means that to compute the concentration just after the second dose, we have to add the value  $C_0$  to the concentration remaining from the first dose. During the time between the second and third doses, the concentration decays exponentially from this value. To find the concentration after the third dose, we would have to repeat this process, but now we have contributions from the first and second doses to include.

We can calculate the concentration just before the second dose is administered by setting  $t = L$  in our equation

$$C(t) = C_0 e^{-kt}$$

to get

$$C(L^-) = C_0 e^{-kL}$$

where by  $C(L^-)$  we mean the

$$\lim_{t \rightarrow L^-} C(t)$$

Now, when the second dose is administered the concentration jumps by an increment  $C_0$  so that the concentration just after the second dose is given is

$$C_0 + C(L^-) = C_0 + C_0 e^{-kL} = C_0(1 + e^{-kL})$$

The concentration then decays from this value according to our exponential decay rule, but with a slight twist. The twist is that the “initial” concentration is at  $t = L$ , instead of the more familiar case of  $t = 0$ . One way to handle this is to write the exponential term as

$$e^{-k(t-L)}$$

so that at  $t = L$ , the exponent is 0. If we do this, then we can write the concentration as a function of time as

$$C(t) = C_0(1 + e^{-kL})e^{-k(t-L)}$$

This function is only valid after the second dose is administered and before the third dose is given. That is, for  $L \leq t < 2L$ .

Now, suppose that a third dose of the drug is given at  $t = 2L$ . The concentration just before the third dose is given is  $C(2L^-)$ , which is

$$C(2L^-) = C_0(1 + e^{-kL})e^{-kL}$$

which we can also write as

$$C(2L^-) = C_0(e^{-kL} + e^{-2kL})$$

When the third dose is given, the concentration would jump again by  $C_0$  and the concentration just after the third dose would be

$$C(2L) = C_0(1 + e^{-kL} + e^{-2kL})$$

This process can be continued and leads to the following two formulas. The first is the concentration just before the  $N$ th dose of the drug. This is

$$C((N-1)L^-) = C_0 \sum_{i=1}^{N-1} e^{-ikL}$$

The second result we need is the concentration just after the  $N$ th dose, which is

$$C((N-1)L) = C_0 \sum_{i=0}^{N-1} e^{-ikL}$$

## Geometric series

At this point, you are probably wondering how geometric series fit into this lab. The answer should be a lot clearer if we define a parameter  $r$  by

$$r = e^{-kL}$$

Note that  $0 < r < 1$ , since  $k$  and  $L$  are both positive constants. The properties of the exponential function can be used to show that

$$r^i = e^{-ikL}$$

where  $i$  is a non-negative integer. We can write our two formulas for the concentration just before and after the  $N$ th dose in terms of  $r$  as

$$C((N-1)L^-) = C_0 \sum_{i=1}^{N-1} r^i = C_0 \frac{r - r^N}{1 - r}$$

and

$$C((N-1)L) = C_0 \sum_{i=0}^{N-1} r^i = C_0 \frac{1 - r^N}{1 - r}$$

where the formula for the partial sum of a geometric series has been used to obtain the last equality in each of the equations above.

Now, suppose a treatment program is to be continued indefinitely. The formulas above show that  $C((N-1)L^-)$  and  $C((N-1)L)$  both increase with  $N$ . This means that the minimum concentration is the concentration just before the second dose or

$$C_{\min} = C_0 r$$

and that the maximum concentration occurs just after the last dose. Thus we have that

$$C_{\max} \leq \lim_{N \rightarrow \infty} C_0 \frac{1 - r^N}{1 - r} = \frac{C_0}{1 - r}$$

## Exercises

1. Suppose that for a certain drug, which we'll refer to as drug B, the following results were obtained. Immediately after the drug was administered, the concentration was 3.3 mg/ml. Six hours later, the concentration had dropped to 3.55 mg/ml. Determine the value of  $k$  for this drug.
2. Suppose that for drug B, the maximum safe level is  $M = 8$  mg/ml and the minimum effective level is  $m = 1.8$  mg/ml. What is the maximum possible time between doses for this drug?
3. Consider drug B, assuming that doses are given every six hours, or  $L = 6$ . Compute the minimum initial dose  $C_0$  that will keep the concentration above the minimum effective level for the first six hours, i.e before the second dose is given.

4. Consider drug B again, with doses to be given every six hours. Can you find a dose  $C_0$  such that the concentration stays below  $M = 8$  and above  $m = 1.8$  for at least 48 hours?
5. Trials of another drug, which we'll call drug D, produced the following data. The concentration just after the drug was administered was 6 mg/ml and 5 hours later the concentration was 1.2 mg/ml. Find the value of  $k$  for this drug and label it  $k_2$  in your worksheet.
6. Suppose that for drug D, the maximum safe concentration is 10 mg/ml and the minimum effective concentration is 2 mg/ml. Assuming that doses are to be given every 4 hours, find a value of  $C_0$  that will keep the concentration above the minimum effective level for the first four hours, i.e before the second dose is given.
7. Consider drug D again. Using the value  $L = 4$ , find one value of  $C_0$  that provides a safe and effective treatment program for at least 48 hours.
8. For drug A, find the constant  $k$  (call it  $k_3$ ) where the initial concentration is 6.5 mg/ml which drops to 1.5 mg/ml after 8 hours. Then use this value to create two safe drug protocols. Drug A is safe only in the concentration between 1.4 mg/ml and 7mg/ml.
  - (a) In the first protocol, the doses will be given every four hours, find a safe initial concentration.
  - (b) In the second protocol, the initial dose is 4.9mg/ml. find the safe time between doses.