# 2

# SYSTEM DYNAMICS PROBLEMS WITH RATE PROPORTIONAL TO AMOUNT

# MODULE 2.1

## System Dynamics Tool—Tutorial 1

### Download

From the textbook's website, download Tutorial 1 in PDF format for your system dynamics tool. We recommend that you work through the tutorial and answer all Quick Review Questions using the corresponding software.

### Introduction

**Dynamic systems**, which change with time, are usually very complex, having many components, with involved relationships. Two examples are systems involving competition among different species for limited resources and the kinetics of enzymatic reactions.

With a system dynamics tool, we can model complex systems using diagrams and equations. Thus, such a tool helps us perform Step 2 of the modeling process—formulate a model—by helping us document our simplifying assumptions, variables, and units; establish relationships among variables and submodels; and record equations and functions. Then, a system dynamics tool can help us solve the model—Step 3 of the modeling process—by performing simulations using the model and generating tables and graphs of the results. We use this output to perform Step 4 of the modeling process—verify and interpret the model's solution. Often such examination leads us to change a model. With its graphical view and built-in functions, a system dynamics tool facilitates cycling back to an earlier step of the modeling process to simplify or refine a model. Once we have verified and validated a model, the tool's diagrams and equations from the design and the results from the simulation should be part of our report, which we do in Step 5 of the modeling process. The tool can even help us as we maintain the model (Step 6) by making corrections, improvements, or enhancements.

This first tutorial is available for download from the textbook's website for several different system dynamics tools. Tutorial 1 in your system of choice prepares you to perform basic modeling with such a tool, including the following:

- Diagramming a model
- Entering equations and values
- Running a simulation
- Constructing graphs
- Producing tables

The module gives examples and Quick Review Questions for you to complete and execute with your desired tool.

# MODULE 2.2

## Unconstrained Growth and Decay

### Introduction

Many situations exist where the rate at which an amount is changing is proportional to the amount present. Such might be the case for a population of people, deer, or bacteria, for example. When money is compounded continuously, the rate of change of the amount is also proportional to the amount present. For a radioactive element, the amount of radioactivity decays at a rate proportional to the amount present. Similarly, the concentration of a chemical pollutant decays at a rate proportional to the concentration of pollutant present.

### Rate of Change

We deal with rate of change every time we drive a car. Suppose our position ($y$) is a function ($s$) of time ($t$), so we write $y = s(t)$. Suppose also that we start driving on a straight road at time $t = 0$ hours (h) at position marker $s(0) = 10$ miles (mi; about 16.1 km), and at time $t = 2$ h we are at position $s(2) = 116$ mi (about 186.7 km). Our **average velocity**, or average rate of change of position with respect to time, is the **change in position** ($\Delta s$) over the **change in time** ($\Delta t$) and incorporates average speed as well as direction by its sign:

$$\textbf{average velocity} = \frac{\Delta s}{\Delta t} = \frac{116 \text{ mi} - 10 \text{ mi}}{2 \text{ h} - 0 \text{ h}} = \frac{106 \text{ mi}}{2 \text{ h}} = 53 \text{ mi/h}$$

or

$$\textbf{average velocity} = \frac{\Delta s}{\Delta t} = \frac{186.7 \text{ km} - 16.1 \text{ km}}{2 \text{ h} - 0 \text{ h}} = \frac{170.6 \text{ km}}{2 \text{ h}} = 85.3 \text{ km/h}$$

We probably are not driving at a constant rate of 53 mi/h (85.3 km/h), but sometimes we are moving faster and other times, slower. To obtain a more accurate measure of

our velocity at time $t = 1$ h, we can use a smaller interval. For instance, at time $t = 1$ h, our position might be at marker $s(1) = 51.2$ mi, while a short time before at $t = 0.98$ h, our position was $s(0.98) = 50.0$ mi. As the following calculation shows, over this interval of 0.02 h (1.2 min), our average velocity is faster, 60 mi/h:

$$\text{average velocity} = \frac{\Delta s}{\Delta t} = \frac{51.2 \text{ mi} - 50 \text{ mi}}{1.00 \text{ h} - 0.98 \text{ h}} = \frac{1.2 \text{ mi}}{0.02 \text{ h}} = 60 \text{ mi/h}$$

or about 96.6 km/h.

**Definition** Suppose $s(t)$ is the position of an object at time $t$, where $a \le t \le b$. Then the **change in time**, $\Delta t$, is $\Delta t = b - a$; and the **change in position**, $\Delta s$, is $\Delta s = s(b) - s(a)$. Moreover, the **average velocity**, or the **average rate of change of $s$ with respect to $t$**, of the object from time $a = b - \Delta t$ to time $b$ is

$$\textbf{average velocity} = \frac{\textbf{change in position}}{\textbf{change in time}} = \frac{\Delta s}{\Delta t}$$

$$= \frac{s(b) - s(a)}{b - a} = \frac{s(b) - s(b - \Delta t)}{\Delta t}$$

## Quick Review Question 1

Suppose on a windless day someone standing on a bridge holds a ball over the side and tosses the ball straight up into the air. After reaching its highest point, the ball falls, eventually landing in the water. The ball's height in meters (m) above the water ($y$) is a function ($s$) of time ($t$) in seconds ($s$), or $y = s(t)$.

**a.** Determine the average velocity with units of the ball from $t = 1$ s to $t = 2$ s if $s(1) = 21.1$ m and $s(2) = 21.4$ m.
**b.** Determine the average velocity with units of the ball from $t = 1$ s to $t = 3$ s if $s(1) = 21.1$ m and $s(3) = 11.9$ m.
**c.** Using the notation of the definition of average velocity, for Part b determine the following, including units: $b$, $s(b)$, $\Delta t$, $b - \Delta t$, $s(b - \Delta t)$, $\Delta s$.

By making the interval smaller and smaller around the time $t = 1$ h, the average velocity calculation approaches our precise velocity at $t = 1$ h, or our **instantaneous rate of change of position with respect to time**, which is our odometer's reading. This instantaneous rate of change of $s$ with respect to $t$ is the **derivative** of $s$ with respect to $t$, written as $\mathbf{s'(t)}$, or $\frac{dy}{dt}$, or $dy/dt$; and $\mathbf{s'(1)}$, or $\left.\frac{ds}{dt}\right|_{t=1}$, indicates the derivative at time $t = 1$ h.

**Definition** The **instantaneous velocity**, or the **instantaneous rate of change of $s$ with respect to $t$**, at $t = b$ is the number the average velocity, $\frac{s(b) - s(b - \Delta t)}{\Delta t}$, approaches as $\Delta t$ comes closer and closer to 0 (provided the ratio approaches a number). In this case, the **derivative of $y = s(t)$ with respect to $t$** at $t = b$, written $s'(b)$ or $\left.\frac{dy}{dt}\right|_{t=b}$, is the instantaneous velocity at $t = b$. In general, the **derivative of $y = s(t)$ with respect to $t$** is written as $s'(t)$, or $\frac{dy}{dt}$, or $dy/dt$.

A function, such as $y = s(t)$, can represent many things other than position. Moreover, we are not restricted to using symbols, such as $s$. For example, $Q(t)$ might represent a quantity (mass) of radioactive carbon-14 at time $t$, and the instantaneous rate of change of $Q$ with respect to $t$, $Q'(t) = dQ/dt$, is the instantaneous rate of decay. As another example, $P(t)$ might symbolize a population at time $t$, so that $P'(t) = dP/dt$, is the rate of change of the population with respect to $t$.

## Differential Equation

Continuing with the population example, suppose we have a population in which no individuals arrive or depart; the only change in the population comes from births and deaths. No constraints, such as competition for food or a predator, exist on growth of the population. When no limiting factor exists, we have the **Malthusian model** for unconstrained population growth, where the rate of change of the population is **directly proportional** ($\propto$) to the number of individuals in the population. If $P$ represents the population and $t$ represents time, then we have the following proportion:

$$\frac{dP}{dt} \propto P$$

For a positive growth rate, the larger the population, the greater the change in the population. With the same positive growth rate in two cities, say New York City and Spartanburg, S.C., the population of the larger New York City increases more in magnitude in a year than that of Spartanburg. In a later section of this module, "Unconstrained Decay," we consider a situation in which the rate is negative.

We write the preceding proportion in equation form as follows:

$$\frac{dP}{dt} = rP$$

The constant $r$ is the **growth rate**, or **instantaneous growth rate**, or **continuous growth rate**, while $dP/dt$ is the **rate of change of the population**.

In "System Dynamics Tool—Tutorial 1" (Module 2.1), we started with a bacterial population of size 100, an instantaneous growth rate of 10% = 0.10, and time measured in hours. Thus, we had

$$\frac{dP}{dt} = 0.10P$$

with $P_0 = 100$. The equation $\frac{dP}{dt} = 0.10P$ with the **initial condition** $P_0 = 100$ is a **differential equation** because it contains a derivative. A **solution** to this differential equation is a function, $P(t)$, whose derivative is $0.10P(t)$, with $P(0) = 100$. We begin by reconsidering this example from Tutorial 1 for reinforcement and a more in-depth examination of the concepts.

**Definitions** A **differential equation** is an equation that contains one or more derivatives. An **initial condition** is the value of the dependent variable when the independent variable is zero. A **solution** to a differential equation is a function that satisfies the equation and initial condition(s).

## Difference Equation

Each diagram in Figure 2.2.1, developed with a choice of modeling tools and with the generic format employed by the text, depicts the situation with *population* indicating $P$, *growth_rate* representing $r$, and *growth* meaning $dP/dt$. A **stock** (**box variable**, or **reservoir**), such as *population*, accumulates with time. By contrast, a **converter** (**variable-auxiliary/constant**, or **formula**), such as *growth_rate*, does not accumulate but stores an equation or a constant. The growth is the additional number of organisms that join the population. Thus, a **flow** (**rate**), such as *growth*, is an activity that changes the magnitude of a stock and represents a derivative. Because both population and growth rate are necessary to determine the growth, we have **arrows** (**connectors**, or **arcs**) from these quantities to the flow indicator.

For a simulation with a system dynamics tool or a program we write, we consider time advancing in small, incremental steps. For time, $t$, and length of a time step, $\Delta t$, the **previous time** is $t - \Delta t$. Thus, if $t$ is 7.75 s and $\Delta t$ is 0.25 s, the previous time is 7.50 s. A system dynamics tool might call the change in time *dt*, *DT*, or something else instead of $\Delta t$. As some tools do to avoid confusion, we replace each blank in a diagram component name with an underscore when using the name in equations and discussions. For example, we employ *growth rate* in the diagrams of Figure 2.2.1 and the corresponding *growth_rate* in the following discussion. Regardless of the notation, with initial *population* = 100, *growth_rate* = 0.1, and *growth* = *growth_rate* * *population*, as in Figure 2.2.1, a system dynamics tool generates an equation similar to the following, where *population*($t$) is the population at time $t$ and *population*($t - \Delta t$) is the population at time $t - \Delta t$:

$$population(t) = population(t - \Delta t) + (growth) * \Delta t$$

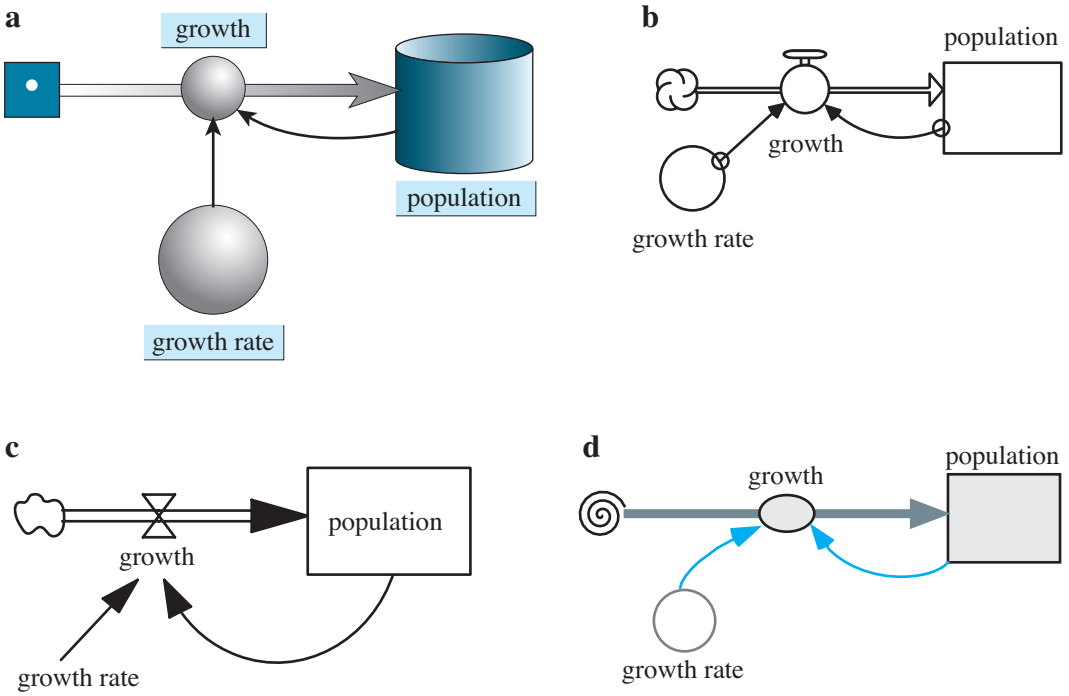


**Figure 2.2.1** Diagrams of population models where growth rate is proportional to population: (a) *Berkeley Madonna*® (b) *STELLA*® (c) *Vensim PLE*® (d) Text's format

This equation, called a **finite difference equation**, indicates that the population at one time step is the population at the previous time step plus the change in population over that time interval:

$$(\text{new population}) = (\text{old population}) + (\text{change in population})$$

or

$$population(t) = population(t - \Delta t) + \Delta population$$

where **Δpopulation** is a notation for the **change in population**. We approximate the change in the population over one time step, $\Delta population$ or $(growth) * \Delta t$, as the finite difference of the populations at one time step and at the previous time step, $population(t) - population(t - \Delta t)$. Thus, solving for *growth*, we have an approximation of the derivative *dP/dt* as follows:

$$growth = \frac{\Delta population}{\Delta t} = \frac{population(t) - population(t - \Delta t)}{\Delta t}$$

Computer programs and system dynamics tools employ such finite difference equations to solve differential equations.

**Definition** A **finite difference equation** is of the following form:

(new value) = (old value) + (change in value)

Such an equation is a discrete approximation to a differential equation.

## Quick Review Question 2

Consider the differential equation $dQ/dt = -0.0004Q$, with $Q_0 = 200$.

**a.** Using delta notation, give a finite difference equation corresponding to the differential equation.
**b.** At time $t = 9.0$ s, give the time at the previous time step, where $\Delta t = 0.5$ s.
**c.** If $Q(t - \Delta t) = 199.32$ and $Q(t) = 199.28$, give $\Delta Q$.

The *growth* is the *growth_rate* (*r* previously) times the current *population* (*P* previously). For example, we can show that the population at time $t = 0.025$ h is approximately *population*(0.025) = 100.250250 bacteria, so that *growth* is about *growth_rate* * *population*(0.025) = 0.1 * 100.250250 = 10.025025 bacteria per hour at that instant. For $\Delta t = 0.005$ h, the change in the population of bacteria to the next time step, 0.025 + 0.005 = 0.030 h, is approximately *growth* * $\Delta t$ = 10.025025 * 0.005 = 0.050125 bacteria[1]. We calculate the population at time 0.030 h as follows:

$$\begin{aligned} \textit{population}(0.030) &= \textit{population}(0.025) + (\textit{growth} \text{ at time } 0.025 \text{ h}) * \Delta t \\ &= 100.250250 + 10.025025 * 0.005 \\ &= 100.250250 + 0.050125 \\ &= 100.300375 \end{aligned}$$

Thus, we compute the value at the line $t = 0.030$ h of Table 2.2.1 using the previous line.

## Quick Review Question 3

Evaluate *population*(0.045), the population at the next time interval after the end of Table 2.2.1, to six decimal places.

**Table 2.2.1**
Table of Estimated Populations, Where the Initial Population is 100, the Continuous Growth Rate is 10% per Hour, and the Time Step is 0.005 h

| $t$ | *population*($t$) | = | *population*($t - \Delta t$) | + | (*growth*) | * | $\Delta t$ |
|---|---|---|---|---|---|---|---|
| 0.000 | 100.000000 | | | | | | |
| 0.005 | 100.050000 | = | 100.000000 | + | 10.000000 | * | 0.005 |
| 0.010 | 100.100025 | = | 100.050000 | + | 10.005000 | * | 0.005 |
| 0.015 | 100.150075 | = | 100.100025 | + | 10.010003 | * | 0.005 |
| 0.020 | 100.200150 | = | 100.150075 | + | 10.015008 | * | 0.005 |
| 0.025 | 100.250250 | = | 100.200150 | + | 10.020015 | * | 0.005 |
| 0.030 | 100.300375 | = | 100.250250 | + | 10.025025 | * | 0.005 |
| 0.035 | 100.350525 | = | 100.300375 | + | 10.030038 | * | 0.005 |
| 0.040 | 100.400701 | = | 100.350525 | + | 10.035053 | * | 0.005 |

[1] Computations in this model use **Euler's Method** for estimating values of a function. In Chapter 6, we examine this and two other techniques for numeric integration.

Because of compounding, the number of bacteria at $t = 1$ h is slightly more than 10% of 100, namely, 110.51. Table 2.2.2 lists the growth and the population on the hour for 20 h, and Figure 2.2.2 graphs the population versus time. The model states and the table and figure illustrate that as the population increases, the growth does, too.

The model gives an estimate of the population at various times. If the model is analytically correct, a simulation estimates the values for *growth* and *population*. Until computer round-off error (discussed in Module 5.2) causes the step size to be zero, it is usually the case that the smaller the step size, the more accurate will be the results. (In Exercise 9, we explore a situation where the smaller step size does not produce better results.) Because the additional computations resulting from a smaller step size cause the simulation to run longer, we often use a larger $\Delta t$ during development and switch to a smaller $\Delta t$ for more accurate results when the project is close to completion.

**Table 2.2.2**
Table of Estimated Growths and Populations, Reported on the Hour, Where the Initial Population is 100, the Growth Rate is 10%, and the Time Step is 0.005 h

| $t$ (h) | *growth* | *population* |
|---|---|---|
| 0.000 | 10.00 | 100.00 |
| 1.000 | 11.05 | 110.51 |
| 2.000 | 12.21 | 122.13 |
| 3.000 | 13.50 | 134.98 |
| 4.000 | 14.92 | 149.17 |
| 5.000 | 16.49 | 164.85 |
| 6.000 | 18.22 | 182.18 |
| 7.000 | 20.13 | 201.34 |
| 8.000 | 22.25 | 222.51 |
| 9.000 | 24.59 | 245.90 |
| 10.000 | 27.18 | 271.76 |
| 11.000 | 30.03 | 300.33 |
| 12.000 | 33.19 | 331.91 |
| 13.000 | 36.68 | 366.81 |
| 14.000 | 40.54 | 405.38 |
| 15.000 | 44.80 | 448.00 |
| 16.000 | 49.51 | 495.11 |
| 17.000 | 54.72 | 547.16 |
| 18.000 | 60.47 | 604.69 |
| 19.000 | 66.83 | 668.27 |
| 20.000 | | 738.54 |

**Rule of Thumb** Although the simulation takes longer because of more computation, it is usually more accurate to use a small step size ($\Delta t$), say, 0.01 or less.

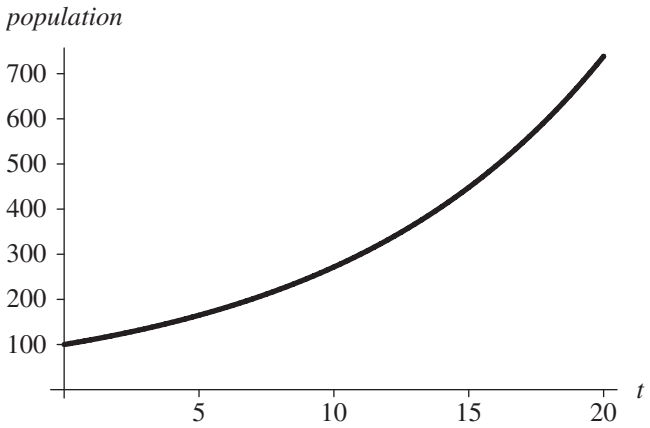


**Figure 2.2.2** Graph of population versus time (hours) for the data in Table 2.2.2

## Simulation Program

In developing a simulation program, we use statements similar to the preceding finite difference equations. We initialize constants, such as *growthRate*, *population*, $\Delta t$, and the length of time the simulation is to run (*simulationLength*), and we update the population repeatedly in a loop. The calculation for the total number of iterations (*numIterations*) of this loop is *simulationLength*/$\Delta t$. For example, if the simulation length is 10 h and $\Delta t$ is 0.25 h, then the number of loop iterations is *numIterations* = 10/0.25 = 40. We have a loop index ($i$) go from 1 through *numIterations*. Inside the loop, we calculate time $t$ as the product of $i$ and $\Delta t$. For example, if $\Delta t$ is 0.25 h, during the first iteration, the index $i$ becomes 1 and the time is 1 * $\Delta t$ = 0.25 h. On loop iteration $i$ = 8, the time gets the value 8 * $\Delta t$ = 8 * 0.25 h = 4.00 h.

Algorithm 1 contains **pseudocode**, or a structured English outline of the design, for generating and displaying the time, growth, and population at each time step. In the algorithm, a **left-facing arrow** (←) indicates assignment of the value of the expression on the right to the variable on the left. For example, *numIterations* ← *simulationLength*/$\Delta t$ represents an assignment statement in which *numIterations* gets the value of *simulationLength*/$\Delta t$.

**Algorithm 1** Algorithm for simulation of unconstrained growth

initialize *simulationLength*
initialize *population*
initialize *growthRate*
initialize length of time step $\Delta t$
*numIterations* ← *simulationLength*/$\Delta t$
for $i$ going from 1 through *numIterations* do the following:
    *growth* ← *growthRate* * *population*
    *population* ← *population* + *growth* * $\Delta t$
    $t \leftarrow i * \Delta t$
    display $t$, *growth*, and *population*

If we do not need to display *growth* (derivative) at each step and the length of a step ($\Delta t$) is constant throughout the simulation, we can calculate the constant growth rate per step (*growthRatePerStep*) before the loop, as follows:

$$growthRatePerStep \leftarrow growthRate * \Delta t$$

Within the loop, we do not compute *growth* but estimate *population* as follows:

$$population \leftarrow population + growthRatePerStep * population$$

Thus, within the loop, we have two assignments instead of three and two multiplications instead of three, saving time in a lengthy simulation. The revised algorithm appears as Algorithm 2.

**Algorithm 2** Alternative algorithm to Algorithm 1 for simulation of unconstrained growth that does not display *growth*

initialize *simulationLength*
initialize *population*
initialize *growthRate*
initialize $\Delta t$
***growthRatePerStep* ← *growthRate* * $\Delta t$***
*numIterations* ← *simulationLength*/$\Delta t$
for *i* going from 1 through *numIterations* do the following:
  ***population* ← *population* + *growthRatePerStep* * *population***
  *t* ← *i* * $\Delta t$
  display *t* and *population*

## Analytical Solution: Introduction

We can solve the preceding model analytically for unconstrained growth, which is the differential equation $\frac{dP}{dt} = 0.10P$ with initial condition $P_0 = 100$, as follows:

$$P = 100\, e^{0.10t}$$

The next three sections develop the analytical solution. The first section starts the explanation using indefinite integrals, while the second section begins the discussion using derivatives without using integrals. Thus, you may select the section that matches your calculus background. The third section completes the development of the analytical solution for both tracks. Those without calculus background may go immediately to the section "Completion of the Analytical Solution."

When it is possible to solve a problem analytically, we should usually do so. We have employed simulation of unconstrained growth with a system dynamic tool as an introduction to fundamental concepts and as a building block to more complex problems for which no analytical solutions exist.

## Analytical Solution: Explanation with Indefinite Integrals (Optional)

We can solve the differential equation $\frac{dP}{dt} = 0.10P$ using a technique called **separation of variables**. First, we move all terms involving $P$ to one side of the equation and all those involving $t$ to the other. Leaving 0.10 on the right, we have the following:

$$\frac{1}{P}dP = 0.10\,dt$$

Then, we integrate both sides of the equation, as follows:

$$\int \frac{1}{P}dP = \int 0.10\,dt$$

$$\ln|P| = 0.10t + C \text{ for an arbitrary constant } C$$

We solve for $|P|$ by taking the exponential function of both sides and using the fact that the exponential and natural logarithmic functions are inverses of each other.

$$e^{\ln|P|} = e^{0.10t+C}$$

$$|P| = e^{0.10t}e^{C} = A\,e^{0.10t}$$

where $A = e^C$. Solving for $P$, we have

$$P = (\pm A)e^{0.10t}$$

or

$$P = ke^{0.10t}$$

where $k = (\pm A)$ is a constant.

## Analytical Solution: Explanation with Derivatives (Optional)

We can solve the differential equation $\frac{dP}{dt} = 0.10P$ for $P$ analytically by finding a function whose derivative is 0.10 times the function itself. The only functions that are their own derivative are exponential functions of the following form:

$$f(t) = ke^t, \text{ where } k \text{ is a constant}$$

For example, the derivative of $5e^t$ is $5e^t$. To obtain a factor of 0.10 through use of the chain rule, we have the general solution

$$P = ke^{0.10t}$$

For example, if $P = 5e^{0.10t}$, we have

$$\frac{dP}{dt} = \frac{d(5e^{0.10t})}{dt} = 5\frac{d(e^{0.10t})}{dt} = 5(0.10e^{0.10t}) = 0.10(5e^{0.10t}) = 0.10P$$

## Completion of the Analytical Solution

Thus, the general solution to $\frac{dP}{dt} = 0.10P$ is $P = ke^{0.10t}$ for a constant $k$. Using the initial condition that $P_0 = 100$, we can determine a particular value of $k$ and, thus, a particular solution of the form $P = ke^{0.10t}$. Substituting 0 for $t$ and 100 for $P$, we have the following:

$$100 = ke^{0.10(0)} = ke^0 = k(1) = k$$

The constant is the initial population. For this example,

$$P = 100e^{0.10t}$$

Figure 2.2.3 displays the dramatic increase in the bacterial population as time advances.

In general, the solution to

$$\frac{dP}{dt} = rP \text{ with initial population } P_0$$

is

$$P = P_0e^{rt}$$

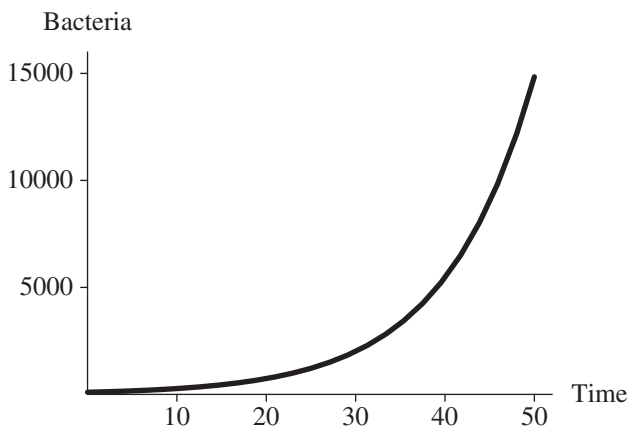


**Figure 2.2.3** Bacterial population with a continuous growth rate of 10% per hour and an initial population of 100 bacteria

### Quick Review Question 4

Give the solution of the differential equation

$$\frac{dP}{dt} = 0.03P \text{, where } P_0 = 57$$

The simulated values for the bacterial population are slightly less than those the model $P = 100e^{0.10t}$ determines. For example, after 20 h, a simulation may display, to two decimal places, a population of 738.54. However, $100e^{0.10(20)}$, expressed to two decimal places, is 738.91. The simulation compounds the population every step, and, in this case, the step size is $\Delta t = 0.005$ h. The analytic model compounds the population continuously; that is, as the step size goes to zero and the number of steps goes to infinity approaches, the simulated values approach the analytic solution.

Both the analytic model and simulation produce valid estimates of the population of bacteria. After 20 h, the number of bacteria will be an integer, not a decimal number, such as 738.54 or 738.91. Moreover, the population probably does not grow in an ideal fashion with a 10%-per-hour growth rate at every instant. Both the analytic model and the simulation produce estimates of the population at various times.

## Further Refinement

We can refine the model further by having separate parameters for birth rate and death rate instead of the combined growth rate. Thus,

$$growth\_rate = birth\_rate - death\_rate$$

## Unconstrained Decay

The rate of change of the mass of a radioactive substance is proportional to the mass of the substance, and the constant of proportionality is negative. Thus, the mass decays with time. For example, the constant of proportionality for radioactive carbon-14 is approximately –0.000120968. The continuous decay rate is about 0.0120968% per year, and the differential equation is as follows, where $Q$ is the quantity (mass) of carbon-14:

$$\frac{dQ}{dt} = -0.000120968Q$$

As indicated in the section "Completion of the Analytical Solution," the analytical solution to this equation is

$$Q = Q_0e^{-0.000120968t}$$

After 10,000 yr, only about 29.8% of the original quantity of carbon-14 remains, as the following shows:

$$Q = Q_0e^{-0.000120968(10,000)} = 0.298292Q_0$$

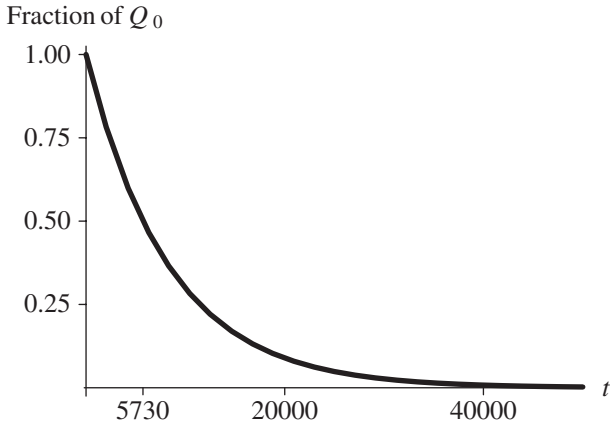


**Figure 2.2.4** Exponential decay of radioactive carbon-14 as a fraction of the initial quantity $Q_0$, with time ($t$) in years

Figure 2.2.4 displays the decay of carbon-14 with time.

**Carbon dating** uses the amount of carbon-14 in an object to estimate the age of an object. All living organisms accumulate small quantities of carbon-14, but accumulation stops when the organism dies. For example, we can compare the proportion of carbon-14 in living bone to that in the bone of a mummy and estimate the age of the mummy using the model.

## Example 1

Suppose the proportion of carbon-14 in a mummy is only about 20% of that in a living human. To estimate the age of the mummy, we use the preceding model with the information that $Q = 0.20Q_0$. Substituting into the analytical model, we have

$$0.20Q_0 = Q_0 e^{-0.000120968t}$$

After canceling $Q_0$, we solve for $t$ by taking the natural logarithm of both sides of the equation. Because the natural logarithm and the exponential functions are inverses of each other, we have the following:

$$\ln(0.20) = \ln(e^{-0.000120968t}) = -0.000120968t$$
$$t = \ln(0.20)/(-0.000120968) \approx 13{,}305 \text{ yr}$$

We often express the rate of decay in terms of the half-life of the radioactive substance. The **half-life** is the period of time that it takes for the substance to decay to half of its original amount. Figure 2.2.5 illustrates that the half-life of radioactive carbon-14 is about 5730 yr. We can determine this value analytically as we did in Example 1 using 50% instead of 20%; $Q = 0.50Q_0$.

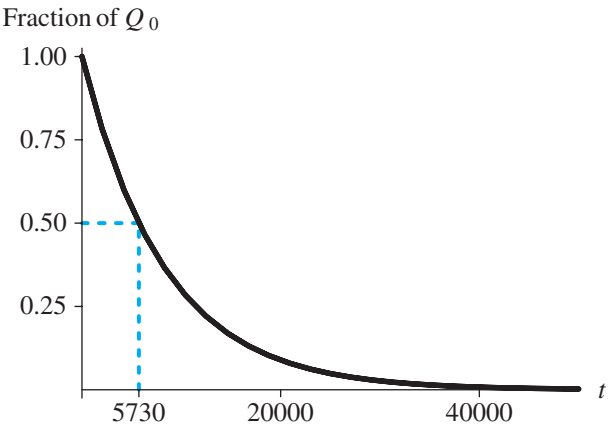


**Figure 2.2.5** The half-life of radioactive carbon-14 indicated as 5730 yr

**Definition** The **half-life** is the period of time that it takes for a radioactive substance to decay to half of its original amount.

### Quick Review Question 5

Radium-226 has a continuous decay rate of about 0.0427869% per year. Determine its half-life in whole years.

## Reports for System Dynamics Models

The fifth step of the modeling process discussed in Module 1.2 is to "Report on the model." The following summarizes the items that would be included in a report for a system dynamics model:

**a. Analysis of the problem:** We begin by describing the problem, such as to model the growth of bacteria in media.

**b. Model design:** In this section, we should list simplifying assumptions, such as those in the section "Differential Equation"; equations, such as $\frac{dP}{dt} = 0.10P$ with $P_0 = 100$; reasoning for choices of constants, such as an instantaneous growth rate of 10%; the basic time step, such as hour; and other units. A diagram of the model, such as in Figure 2.2.1, is also appropriate to include.

**c. Model solution:** This part should contain the analytical solution or an algorithm, such as Algorithm 1.

**d. Results and conclusions:** Part d should include simulation tables, such as Table 2.2.2, and graphs, such as Figure 2.2.2. Moreover, the section should contain an explanation of verification accomplished by comparing the results to real data when available, descriptions of the outcomes of various scenar-

ios, a discussion of our conclusions with support from the results, and suggestions for model refinement.

e. **Appendices:** Usually, a copy of the file created with a system dynamics tool should be submitted with this report. Besides the model, this file should contain appropriate documentation, such as a text box with the authors' names, date, module and problem number, and problem description.

## Exercises

*Answers to marked exercises appear in the appendix "Answers to Selected Exercises."*

**1. a.** For an initial population of 100 bacteria and a continuous growth rate of 10% per hour, determine the number of bacteria at the end of one week.

**b.** How long will it take the population to double?

**2. a.** Suppose the initial population of a certain animal is 15,000 and its continuous growth rate is 2% per year. Determine the population at the end of 20 yr.

**b.** Suppose we are performing a simulation of the population using a step size of 0.083 yr. Determine the growth and the population at the end of the first three time steps.

**3.** Adjust the model in Figure 2.2.1 to accommodate birth rate and death rate instead of just growth rate.

**4. a.** **Newton's Law of Heating and Cooling** states that the rate of change of the temperature ($T$) with respect to time ($t$) of an object is proportional to the difference between the temperatures of the object and of its surroundings. Suppose the temperature of the surroundings is 25 °C. Write the differential equation that models Newton's Law.

**b.** Solve this equation for $T$ as a function of time $t$.

**c.** Suppose cold water at 6 °C is placed in a room that has temperature 25 °C. After 1 h, the temperature of the water is 20 °C. Determine all constants in the equation for $T$.

**d.** What is the temperature of the water after 15 minutes (min)?

**e.** How long will it take for the water to warm to room temperature?

**5. a.** Suppose someone, whose temperature is originally 37 °C, is murdered in a room that has constant temperature 25 °C. The temperature is measured as 28 °C when the body is found and at 27 °C 1 h later. How long ago was the murder committed from discovery of the body? See Exercise 4 for Newton's Law of Heating and Cooling.

**b.** Suppose we are performing a simulation using a step size of 0.004 h. Using the decay rate from Part a, determine the temperature at the end of the first three time steps after discovery of the body.

**6. a.** What proportion of the original quantity of carbon-14 is left after 30,000 yr?

**b.** If 60% is left, how old is the item?

**7. a.** The half-life of radioactive strontium-90 is 29 yr. Give the model for the quantity present as a function of time.

**b.** What proportion of strontium-90 is present after 10 yr?

**c.** After 50 yr?
**d.** How long will it take for the quantity to be 15% of the original amount?

**8.** Suppose an investment has approximately a continuous growth rate of 9.3%. Calculate analytically the value of an initial investment of $500 after
**a.** 10 yr **b.** 20 yr **c.** 30 yr **d.** 40 yr
**d.** How long will it take for the value to double?
**e.** How long to quadruple?

**9.** Suppose the amount of deposited ash, $A$, in millimeters (mm) is a function of time $t$ in days. Suppose the model states that the rate of change of ash with respect to time is 4 mm/day and the initial quantity is 3 mm.
**a.** Using a step size of 0.5 days (da), estimate the amount of ash when $t = 1$ da.
**b.** Repeat Part a using a step size of 0.25 da.
**c.** Does the smaller step size change the result?
**d.** Solve the model for $A$.
**e.** What kind of function do you obtain?

## Projects

*For additional projects, see Module 7.1, "Radioactive Chains—Never the Same Again"; Module 7.2, "Turnover and Turmoil—Blood Cell Populations"; Module 7.3, "Deep Trouble—Ideal Gas Laws and Scuba Diving"; Module 7.4, "What Goes Around Comes Around—The Carbon Cycle"; after completion of "System Dynamics Tool: Tutorial 2," Module 7.9, "Transmission of Nerve Impulses: Learning from the Action Potential Heroes"; Module 7.12 "Mercury Pollution—Getting on Our Nerves."*

**1.** Develop a model for Newton's Law of Heating and Cooling (see Exercise 4). Using this model, answer the questions of Exercises 4 and 5.
**2.** In 1854, Dr. John Snow, the father of epidemiology, identified a particular London water pump as the point source of the Broad Street cholera epidemic, which spread in a radial fashion from the pump. Model such a spread of disease assuming that the rate of change of the number of cases of cholera is proportional to the square root of the number of cases.
**3.** Develop a model for Exercise 8.
**4.** A young professional would like to save enough money to pay cash for a new car. Develop a model to determine when such a purchase will be possible. Take into account the following issues: The price of a new car is rising due to inflation. The buyer plans to trade in a car, which is depreciating. This person already has some savings and plans to make regular monthly payments. Thus, use a $\Delta t$ value of 1 mo. Assume appropriate rates and values.

*Develop a spreadsheet for each of Projects 5–8.*

**5.** Exercise 2
**6.** Exercise 4
**7.** Exercise 5
**8.** Exercise 8

## Answers to Quick Review Questions

**1. a.** Average velocity from 1 to 2 s = $\frac{s(2)-s(1)}{2-1} = \frac{21.4-21.1}{1} = 0.3$ m/s

**b.** Average velocity from 1 to 3 s = $\frac{s(3)-s(1)}{3-1} = \frac{11.9-21.1}{2} = -4.6$ m/s

**c.** $b = 3$ s, $s(b) = 11.9$ m, $\Delta t = 2$ s, $b - \Delta t = 1$ s, $s(b - \Delta t) = 21.1$ m, $\Delta s = 11.9 - 21.1 = -9.2$ m

**2. a.** $Q(t) = Q(t - \Delta t) + \Delta Q$, where $\Delta Q = -0.0004Q(t - \Delta t)\Delta t$ and $Q(0) = 200$

**b.** $t - \Delta t = 9.0 - 0.5 = 8.5$ s

**c.** $\Delta Q = 199.28 - 199.32 = -0.04$

**3.** 100.450901

*growth* = 100.400701 * 0.10 = 10.040070

Thus, *population*(0.045) = 100.400701 + 10.040070 * 0.005 = 100.450901

**4.** $P = 57e^{0.03t}$

**5.** 1620. Reasoning:

$$Q = Q_0 e^{-0.000427869t}$$

For $Q = 0.50Q_0$, $0.50Q_0 = Q_0 e^{-0.000427869t}$ or $0.50 = e^{-0.000427869t}$

$$\ln(0.50) = -0.000427869t$$

$$t = \ln(0.50)/(-0.000427869) = 1620$$

## Reference

Zill, Dennis G. 2013. *A First Course in Differential Equations with Modeling* Applications, 10th ed. Belmont, CA. Brooks-Cole Publishing (Cengage Learning).

tential in their new environments because they are very adaptable to habitat and food sources, they have few or less-fit competitors, and few to no predators.

## Carrying Capacity

In Module 2.2, "Unconstrained Growth and Decay," we considered a population growing without constraints, such as competition for limited resources. For such a population, $P$, with instantaneous growth rate, $r$, the rate of change of the population has the following differential equation model:

$$\frac{dP}{dt} = rP$$

With initial population $P_0$, we saw that the analytical solution is $P = P_0 e^{rt}$. In that module, we also developed the following finite difference equation for the change in $P$ from one time to the next, which we used in simulations:

$$\begin{aligned} \Delta P &= P(t) - P(t - \Delta t) \\ &= (r\, P(t - \Delta t))\, \Delta t \end{aligned}$$

Simulation and analytical solution graphs in Figures 2.2.2 and 2.2.3, respectively, of Module 2.2 display the exponential growth of unconstrained growth.

After developing such a model in Step 2 of the modeling process and solving the model (Step 3) as before, we should verify that the solution (Step 4) agrees with real data. However, as the introduction indicates, no confined population can grow without bound. Competition for food, shelter, and other resources eventually limits the possible growth. For example, suppose a deer refuge can support at most 1000 deer. We say that the carrying capacity ($M$) for the deer in the refuge is 1000.

**Definition** The **carrying capacity** for an organism in an area is the maximum number of organisms that the area can support.

### Quick Review Question 1

Cycling back to Step 2 of the modeling process, this question begins refinement of the population model to accommodate descriptions of population growth from the "Introduction" of this module.

**a.** Determine any additional variable and its units.

**b.** Consider the relationship between the number of individuals ($P$) and carrying capacity ($M$) as time ($t$) increases. List all the statements below that apply to the situation where the population is much smaller than the carrying capacity.

A. $P$ appears to grow almost proportionally to $t$.

B. $P$ appears to grow almost without bound.
C. $P$ appears to grow faster and faster.
D. $P$ appears to grow more and more slowly.
E. $P$ appears to decline faster and faster.
F. $P$ appears to decline more and more slowly.
G. $P$ appears to grow almost linearly with slope $M$.
H. $P$ is appears to be approaching $M$ asymptotically.
I. $P$ appears to grow exponentially.
J. $dP/dt$ appears to be almost proportional to $P$.
K. $dP/dt$ appears to be almost zero.
L. The birth rate is about the same as the death rate.
M. The birth rate is much greater than the death rate.
N. The birth rate is much less than the death rate.

**c.** List all the choices from Part b that apply to the situation where the population is close to but less than the carrying capacity.

**d.** List all the choices from Part b that apply to the situation where the population is close to but greater than the carrying capacity.

## Revised Model

In the revised model, for an initial population much lower than the carrying capacity, we want the population to increase in approximately the same exponential fashion as in the earlier unconstrained model. However, as the population size gets closer and closer to the carrying capacity, we need to dampen the growth more and more. Near the carrying capacity, the number of deaths should be almost equal to the number of births, so that the population remains roughly constant. To accomplish this dampening of growth, we could compute the number of deaths as a changing fraction of the number of births, which we model as $rP$. When the population is very small, we want the fraction to be almost zero, indicating that few individuals are dying. When the population is close to the carrying capacity, the fraction should be almost $1 = 100\%$. For populations larger than the carrying capacity, the fraction should be even larger so that the population decreases in size through deaths. Such a fraction is $P/M$. For example, if the population $P$ is 10 and the carrying capacity $M$ is 1000, then $P/M = 10/1000 = 0.01 = 1\%$. For a population $P = 995$ close to the carrying capacity, $P/M = 995/1000 = 0.995 = 99.5\%$; and for the excessive $P = 1400$, $P/M = 1400/1000 = 1.400 = 140\%$.

Thus, we can model the instantaneous rate of change of the number of deaths ($D$) as the fraction $P/M$ times the instantaneous rate of change of the number of births ($r$), as the following differential equation indicates:

$$\frac{dD}{dt} = \left(r\frac{P}{M}\right)P$$

The differential equation for the instantaneous rate of change of the population subtracts this value from the instantaneous rate of change of the number of births, as follows:

$$\frac{dP}{dt} = \underbrace{(rP)}_{births} - \underbrace{\left(r\frac{P}{M}\right)P}_{deaths}$$

or

$$\frac{dP}{dt} = r\left(1-\frac{P}{M}\right)P \tag{1}$$

For the discrete simulation, where $P(t-1)$ is the population estimate at time $t-1$, the number of deaths from time $t-1$ to time $t$ is

$$\Delta D = \left(r\frac{P(t-1)}{M}\right)P(t-1) \quad \text{for } \Delta t = 1$$

In general, we approximate the number of deaths from time $(t-\Delta t)$ to time $t$ by multiplying the corresponding value by $\Delta t$, as follows:

$$\Delta D = \left(r\frac{P(t-\Delta t)}{M}\right)P(t-\Delta t)\Delta t$$

where $P(t-\Delta t)$ is the population estimate at $(t-\Delta t)$. Thus, the change in population from time $(t-\Delta t)$ to time $t$ is the difference of the number of births and the number of deaths over that period:

$$\Delta P = \text{births} - \text{deaths}$$

$$\Delta P = \underbrace{\left(rP(t-\Delta t)\right)\Delta t}_{\text{births}} - \underbrace{\left(r\frac{P(t-\Delta t)}{M}\right)P(t-\Delta t)\Delta t}_{\text{deaths}}$$

$$= (r\Delta t)\left(1-\frac{P(t-\Delta t)}{M}\right)P(t-\Delta t)$$

or

$$\Delta P = k\left(1-\frac{P(t-\Delta t)}{M}\right)P(t-\Delta t), \text{ where } k=r\Delta t \tag{2}$$

Differential equation (1) and difference equation (2) are called **logistic equations**. Figure 2.3.1 displays the S-shaped curve characteristic of a logistic equation, where the initial population is less than the carrying capacity of 1000. Figure 2.3.2 shows how the population decreases to the carrying capacity when the initial population is 1500. Thus, the model appears to match observations from the "Introduction" qualitatively. To verify a particular model, we should estimate parameters, such as birth rate, and compare the results of the model to real data.

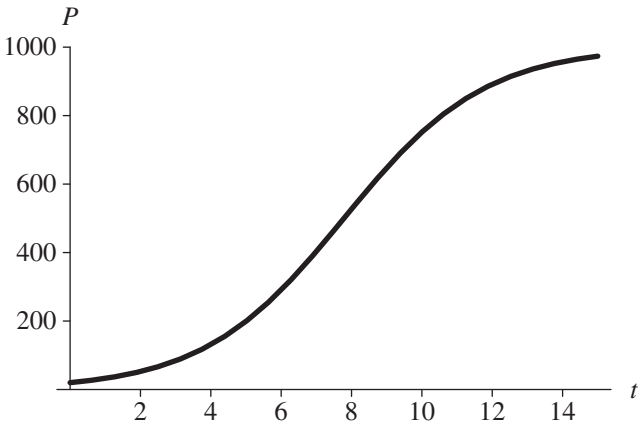


**Figure 2.3.1** Graph of logistic equation, where initial population is 20, carrying capacity is 1000, and instantaneous rate of change of births is 50%, with time ($t$) in years

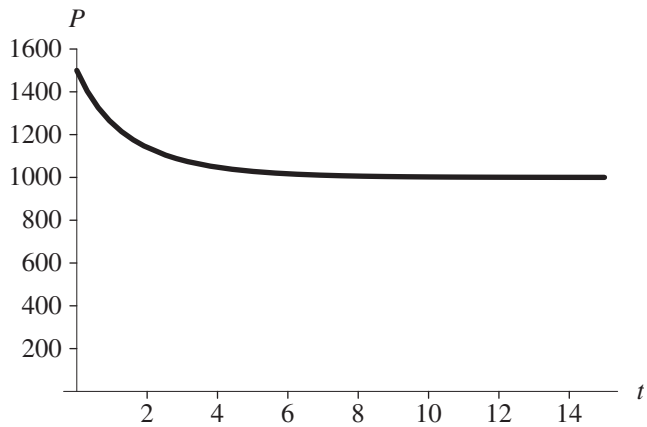


**Figure 2.3.2** Graph of logistic equation, where initial population is 1500, carrying capacity is 1000, and instantaneous rate of change of births is 50%, with time ($t$) in years

## Quick Review Question 2

**a.** Complete the difference equation to model constrained growth of a population $P$ with respect to time $t$ over a time step of 0.1 units, given that the population at time $t - \Delta t$ is $p \leq 1000$, the carrying capacity is 1000, the instantaneous rate of change of births is 105%, and the initial population is 20.
$\Delta P =$ ___(___ ___ _____)($p$)(0.1)

**b.** What is the maximum population?

**c.** Suppose the population at time $t = 5$ yr is 600 individuals. What is the population, rounded to the nearest integer, at time 5.1 yr?

## Equilibrium and Stability

The logistic equation with carrying capacity $M = 1000$ has an interesting property. If the initial population is less than 1000, as in Figure 2.3.1, the population increases to a limit of 1000. If the initial population is greater than 1000, as in Figure 2.3.2, the population decreases to the limit of 1000. Moreover, if the initial population is 1000, we see from Equation (1) that $P/M = 1000/1000 = 1$ and $dP/dt = r(1 - 1)P = 0$. In discrete terms, $\Delta P = 0$. A population starting at the carrying capacity remains there. We say that $M = 1000$ is an **equilibrium** size for the population because the population remains steady at that value or $P(t) = P(t - \Delta t) = 1000$ for all $t > 0$.

**Definitions** An **equilibrium solution** for a differential equation is a solution where the derivative is always zero. An **equilibrium solution** for a difference equation is a solution where the change is always zero.

### Quick Review Question 3

Give another equilibrium size for the logistic differential equation (1) or logistic difference equation (2).

Even if an initial positive population does not equal the carrying capacity $M = 1000$, eventually, the population size tends to that value. We say that the solution $P = 1000$ to the logistic equation (1) or (2) is **stable**. By contrast, for a positive carrying capacity, the solution $P = 0$ is **unstable**. If the initial population is close to but not equal to zero, the population does not tend to that solution over time. For the logistic equation, any displacement of the initial population from the carrying capacity exhibits the limiting behavior of Figure 2.3.1 or 2.3.2. In general, we say that a solution is stable if for a small displacement from the solution, $P$ tends to the solution.

**Definition** Suppose that $q$ is an equilibrium solution for a differential equation $dP/dt$ or a difference equation $\Delta P$. The solution $q$ is **stable** if there is an interval $(a, b)$ containing $q$, such that if the initial population $P(0)$ is in that interval, then

1. $P(t)$ is finite for all $t > 0$;
2. As time, $t$, becomes larger and larger, $P(t)$ approaches $q$.

The solution $q$ is **unstable** if no such interval exists.

## Exercises

**1.** Using calculus, solve the following:

**a.** The differential equation (1),

$$\frac{dP}{dt} = r\left(1 - \frac{P}{M}\right)P$$

where the carrying capacity, $M$, is 1000, $P_0 = 20$, and the instantaneous rate of change of the number of births, $r$, is 50%

**b.** The differential equation (1) in general

**2.** Consider $dy/dt = \cos(t)$.

**a.** Give all the equilibrium solutions.

**b.** Using calculus, find a function $y(t)$ that is a solution.

**c.** Give the most general function $y$ that is a solution.

**3.** It has been reported that a mallard must eat 3.2 ounces (oz) of rice each day to remain healthy. On the average, an acre of rice in a certain area yields 110 bushels (bu) per year; and a bushel of rice weighs 45 lb. Assuming that in the area 100 acres (ac) of rice are available for mallard consumption and mallards eat only rice, determine the carrying capacity for mallards in the area (Reinecke).

**4.** The **Gompertz differential equation**, which follows, is one of the best models for predicting the growth of cancer tumors:

$$\frac{dN}{dt} = kN \ln\left(\frac{M}{N}\right), \quad N(0) = N_0$$

where $N$ is the number of cancer cells and $k$ and $M$ are constants.

**a.** As $N$ approaches $M$, what does $dN/dt$ approach?

**b.** Make the substitution $u = \ln(M/N)$ in the Gompertz equation to eliminate $N$ and convert the equation to be in terms of $u$.

**c.** Using calculus, solve the transformed differential equation for $u$.

**d.** Using the relationship between $u$ and $N$ from Part b, convert your answer from Part c to be in terms of $N$. The result is the solution to the Gompertz differential equation.

**e.** Using calculus, verify that $N(t) = Me^{\ln\left(\frac{N_0}{M}\right)e^{-kt}}$ is the solution to the Gompertz differential equation.

**f.** Using the solution in Part e, what does $N$ approach as $t$ goes to infinity?

**5. a.** Graph $y = e^{-t}$.

Match each of the following scenarios to a differential equation that might model it.

A. $dP/dt = 0.05P$ B. $dP/dt = 0.05P + e^{-t}$

C. $dP/dt = 0.05(1 - e^{-t})P$ D. $dP/dt = 0.05P - 0.0003P^2 - 400$

E. $dP/dt = 0.05e^{-t}P$ F. $dP/dt = 0.05P - 0.0003P^2$

**b.** At first, a bacteria colony appears to grow without bound; but because of limited nutrients and space, the population eventually approaches a limit.

**c.** Because of degradation of nutrients, the growth of a bacterial colony becomes dampened.

**d.** A bacterial colony has unlimited nutrients and space and grows without bound.

**e.** Because of adjustment to its new setting, a bacterial colony grows slowly at first before appearing to grow without bound.

**f.** Each day, a scientist removes a constant amount from the colony.

**6.** Write an algorithm for simulation of constrained growth similar to Algorithm 1 for simulation of unconstrained growth in Module 2.2.

## Projects

*For additional projects, see Module 7.4, "What Goes Around Comes Around—The Carbon Cycle"; Module 7.5, "A Heated Debate—Global Warming"; and Module 7.6, "Plotting the Future: How Will the Garden Grow."*

1. Develop a model for constrained growth.
2. Develop a model for the mallard population in Exercise 3. Have a converter or variable for the number of acres of rice available for mallard consumption, and from this value, have the model compute the carrying capacity. Report on the effect of decreasing the number of acres of rice available (Reinecke).
3. In some situations, the carrying capacity itself is dynamic. For example, the performance of airplanes had one carrying capacity with piston engines and a higher limit with the advent of jet engines. Many think that human population growth over a limited period of time follows such a pattern as technological changes enable more people to live on the available resources. In such cases, we might be able to model the carrying capacity itself as a logistic. Suppose $M_1$ is the first carrying capacity, and $M_1 + M_2$ is the second. The differential equation for the carrying capacity $M(t)$ as a function of time $t$ would be as follows:

$$\frac{dM(t)}{dt} = a(M(t) - M_1)\left(1 - \frac{M(t) - M_1}{M_2}\right) \text{ for some constant } a > 0$$

By using $M(t)$, we have a logistic for the carrying capacity as well as a logistic for the population. Figure 2.3.3 displays population, $P(t)$, in black and $M(t)$ in color with the first carrying capacity $M_1 = 20$; the second, $M_1 + M_2 = 70$; and an inflection point for $M$ at $t = 450$. Notice that we get a "bilogistic," or "doubly logistic," model for $P(t)$.

Develop a model for the following scenario. First, generate an appropriate logistic carrying capacity, $M(t)$. Then, use this dynamic carrying capacity to limit the population.

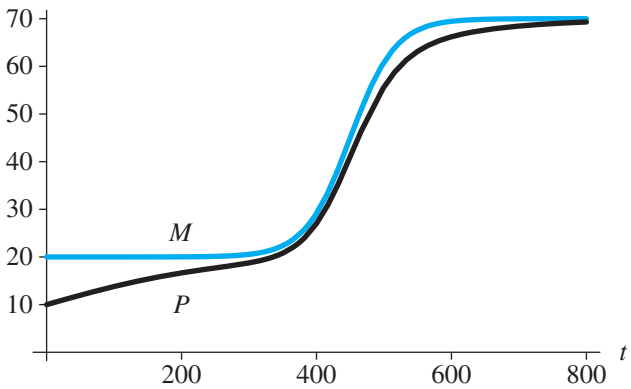


**Figure 2.3.3** Graphs of functions for carrying capacity, $M(t)$, and population, $P(t)$, with time ($t$) in years

In a population study of England from 1541 to 1975, starting with a population of about 1 million, early islanders appear to have a carrying capacity of around 5 million people. However, beginning about 1800 with the advent of the Industrial Revolution, the carrying capacity appears to have increased to about 50 million people. The change in the concavity from concave up to concave down for this new logistic appears to occur in about 1850 (Meyer and Ausubel 1999).

**4.** Refer to Project 3 for a description of a logistic carrying-capacity function. Using that information, develop a model for the Japanese population from the year 1100 to 2000. With an initial population of 5 million, the island population was mainly a feudal society that leveled off to about 35 million. The industrial revolution came to Japan in the latter part of the nineteenth century, and the population rose rapidly over a 77-yr period, with the inflection point occurring about 1908 (Meyer and Ausubel 1999).

**5.** Develop a model for the number of trout in a lake initially stocked with 400 trout. These fish increase at a rate of 15%, and the lake has a carrying capacity of 5000 trout. However, vacationers catch trout at a rate of 8%.

**6.** It has been estimated that for the Antarctic fin whale, $r = 0.08$, $M = 400{,}000$, and $P_0 = 70{,}000$ in 1976. Model this population. Then, revise the model to consider harvesting the whales as a percentage of $rM$. Give various values for this percentage that lead to extinction and other values that lead to increases in the population. Estimate the **maximum sustainable yield**, or the percentage of $rM$ that gives a constant population in the long term (Zill 2013).

**7.** Army ants on a 17-km$^2$ island forage at a rate of 1500 m$^2$/day, clearing the area almost completely of other insects. Once the ants have departed, it takes about 150 days for the number of other insects to recover in the area. Assume an initial number of 1million army ants and a growth rate of 3.6%, where the unit of time is a week. Model the population.

## Answers to Quick Review Questions

**1. a.** carrying capacity, say $M$, in units of the population, such as deer or bacteria

**b.** B. $P$ appears to grow almost without bound.
C. $P$ appears to grow faster and faster.
I. $P$ appears to grow exponentially.
J. $dP/dt$ appears to be almost proportional to $P$.
M. The birth rate is much greater than the death rate.

**c.** D. $P$ appears to grow more and more slowly.
H. $P$ is appears to be approaching $M$ asymptotically.
K. $dP/dt$ appears to be almost zero.
L. The birth rate is about the same as the death rate.

**d.** F. $P$ appears to decline more and more slowly.
H. $P$ is appears to be approaching $M$ asymptotically.
K. $dP/dt$ appears to be almost zero.

L. The birth rate is about the same as the death rate.

**2. a.** $\Delta P = 1.05(1 - p/1000)(p)(0.1)$

**b.** 1000 individuals

**c.** 625 individuals because $P + \Delta P = 600 + 1.05(1 - 600/1000)\ 600(0.1) = 625.2$ individuals

**3.** 0 because $dP/dt = r(1 - P/M)P = r(1 - 0)0 = 0$

## References

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# MODULE 2.4

## System Dynamics Tool: Tutorial 2

*Prerequisite: Module 2.1, "System Dynamics Tool: Tutorial 1"*

### Download

From the textbook's website, download Tutorial 2 in PDF format and the *unconstrained* file for your system dynamics tool. We recommend that you work through the tutorial and answer all Quick Review Questions using the corresponding software.

### Introduction

This tutorial introduces the following functions and concepts, which subsequent modules employ for model formulation and solution using your system dynamics tool:

- Built-in functions and constants, such as the *if-then-else* construct, absolute value, initial value, exponential function, sine, pulse function, time, time step, and $\pi$
- Relational and logical operators
- Comparative graphs
- Graphical input
- Conveyors, an optional topic useful for some of the later projects

# MODULE 2.5

## Drug Dosage

### Downloads

The text's website has *OneCompartAspirin* and *OneCompartDilantin* files, which contain models for examples in this module, available for download in various system dynamics systems.

### Introduction

Errors in the dispensing and administration of medications occur frequently. Although most do not result in great harm, some do. For instance, a Florida pharmacy dispensed 10 times the prescribed dose of a blood thinner to a mother of four, which resulted in her suffering a cerebral hemorrhage (Patel and Ross 2010). In other tragedies, a 10-mo-old infant died after receiving a 10-fold overdose of the chemotherapy agent Cisplatin (Fitzgerald and Wilson 1998), and three nurses were prosecuted for administering a 10-fold (fatal) overdose of penicillin to an infant (Ellis and Hartley 2004).

The National Quality Forum, a nonprofit whose mission involves enabling "private- and public-sector stakeholders to work together to craft and implement cross-cutting solutions to drive continuous quality improvement in the American healthcare system," has estimated that medication errors account for a conservative estimate of $21 billion in costs. This financial expenditure corresponds to serious preventable medication errors for 3.8 million hospital inpatients and 3.3 million outpatients per year (NQF 2010). These cases comprise an extraordinary amount of human suffering and, in some cases, death.

How do these errors occur? According to the Institute of Medicine, medication errors can be classified as errors in

**ordering**—incorrect drug or dosage;
**transcribing**—incorrect frequency of administration or missed dosages;
**dispensing**—incorrect drug, dosage, or timing;

**administering—**wrong dosage, technique;
**monitoring—**not observing effects of medication.

Whether these errors result from poor communication of orders, poor product labeling, or some other cause, the patients and their families suffer the consequences (IOM 2007).

It is not only health-care professionals who make mistakes in drug administration. On June 28, 2003, an Oklahoma teenager died from an overdose of Tylenol (acetaminophen). Suffering from a migraine headache, she took twenty 500-mg capsules, two and one-half times the maximum dosage recommended in 24 h. Apparently, the quantity was enough of the drug to cause liver and kidney failure. Assuming that an over-the-counter analgesic was safe, she apparently did not read the label and made a fatal dosage error (Robert 2004).

There are prescribed dosages for various drugs, but how do we determine what the correct/effective dosage is? There are quite a number of factors that are considered, including drug **absorption**, **distribution**, **metabolism**, and **elimination**. These factors are components of the quantitative science of **pharmacokinetics**.

## One-Compartment Model of Single Dose

Metabolism of a drug in the human body is a complex system to represent in a model. Thus, in Step 2 of the modeling process, particularly for our first attempt, we should make simplifying assumptions about the drug and the body. A **one-compartment model** is a simplified representation of how a body processes a drug. In this model, we consider the body to be one homogeneous compartment, where distribution is instantaneous, the **concentration** of the drug in the system (amount of drug/volume of blood) is proportional to the drug dosage, and the rate of elimination is proportional to the amount of drug in the system. The concentration of a drug instead of the absolute quantity is important because a quantity that might be appropriate for a small child could be ineffective for a large adult. A drug has a **minimum effective concentration** (**MEC**), which is the least amount of drug that is helpful, and a **maximum therapeutic concentration**, or **minimum toxic concentration** (**MTC**), which is the largest amount that is helpful without having dangerous or intolerable side effects. The **therapeutic range** for a drug consists of concentrations between the MEC and MTC. A drug's **half-life**, or the amount of time for half the drug to be eliminated from the system, is useful for modeling as well as patient treatment. Often concentrations and half-life are expressed in relationship to the drug in the plasma or blood serum. The total amount of blood in an adult's body is approximately 5 liters (L), while the amount of **plasma**, or fluid that contains the blood cells, is about 3 L. Blood **serum** is the clear fluid that separates from blood when it clots, and an adult human has about 3 L of blood serum.

We begin by modeling the concentration in the body of aspirin (acetylsalicylic acid). For adults and children over the age of 12, the dosage for a headache is one or two 325-mg tablets every 4 h as necessary, up to 12 tablets/da. Analgesic effectiveness occurs at plasma levels of about 150 to 300 micrograms/milliliter (μg/mL), while toxicity may occur at plasma concentrations of 350 μg/mL. The plasma half-life of a dose from 300 to 650 mg is 3.1 to 3.2 h, with a larger dose having a longer half-life.

For simplicity, we assume a one-compartment model with the aspirin immediately available in the plasma. A stock (box variable), *aspirin_in_plasma*, represents the mass of aspirin in the compartment, which is the person's system, and has an initial value of the mass of two aspirin, (2)(325 mg)(1000 μg/mg), where 1 milligram (mg) is equivalent to 1000 μg.

The flow from *aspirin_in_plasma* (*elimination*) is proportional to the amount present in the system, *aspirin_in_plasma*. Thus, the rate of change of the drug leaving the system is proportional to the quantity of drug in the system (*aspirin_in_plasma*, or $Q$ in the following equation):

$$dQ/dt = -KQ$$

As Module 2.2, "Unconstrained Growth and Decay," shows, the solution to this differential equation is as follows:

$$Q = Q_0 e^{-Kt}$$

Using this solution, as Exercise 1 shows, the constant of proportionality $K$ given earlier and *elimination_constant* in the system dynamics software model have the following relationship to the drug's half-life ($t_{1/2}$):

$$\boldsymbol{K = -\ln(0.5)/t_{1/2}}$$

Pharmaceutical sources widely report a drug's half-life.

## Quick Review Question 1

Determine the elimination constant with units for aspirin, assuming a half-life of 3.2 h.

To compute aspirin's plasma concentration (*plasma_concentration*) in a converter (variable), we have another converter for the volume of the system (*plasma_volume*) with a value of 3000 mL and appropriate connectors and equation. Figure 2.5.1 contains a one-compartment model for one dose of a drug, where the initial value of *plasma_concentration* is the dosage; and Equation Set 2.5.1 gives the corresponding equations and values explicitly entered for the model of aspirin.

## Quick Review Question 2

In terms of the variables in the model of Figure 2.5.1, give the equation for *plasma_concentration*.

## Equation Set 2.5.1

Explicitly entered equations and values for one-compartment model of aspirin:

*half_life* = 3.2 h
*plasma_volume* = 3000 mL
*aspirin_in_plasma*(0) = 2 * 325 * 1000 μg
*elimination_constant* = –ln(0.5)/*half_life*

*elimination = elimination_constant * aspirin_in_plasma*
*plasma_concentration = aspirin_in_plasma/plasma_volume*

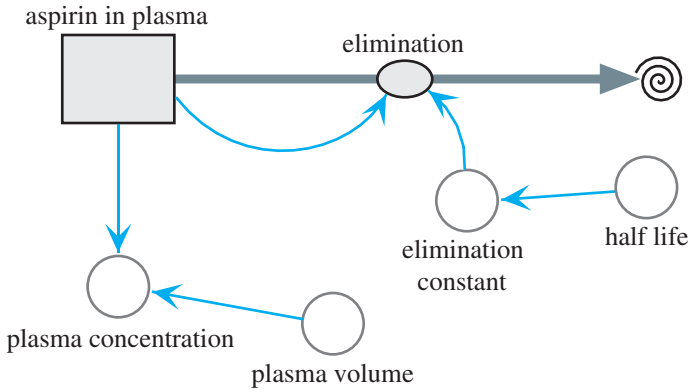


**Figure 2.5.1** One-compartment model of aspirin

Running the simulation for 8 h and plotting *plasma_concentration*, the resulting graph in Figure 2.5.2 indicates that the concentration of the drug in the plasma is initially approximately 217 μg/mL, which is a safe, therapeutic dose. Subsequently, the concentration decreases exponentially.

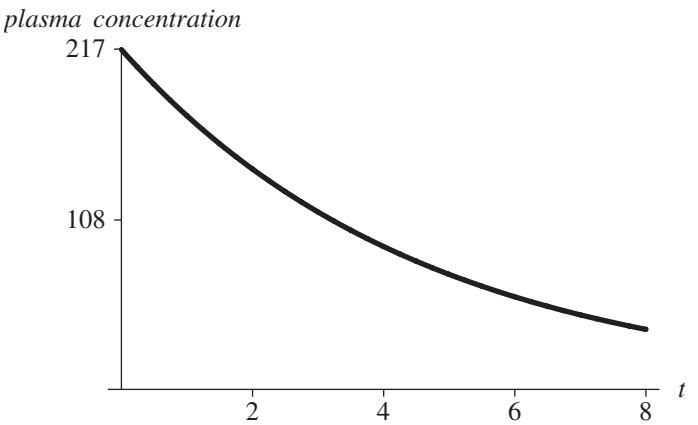


**Figure 2.5.2** Graph of plasma_concentration (μg/mL) for aspirin versus time, t (h)

## One-Compartment Model of Repeated Doses

As another example, we model the concentration in the body of the drug Dilantin, a treatment for epilepsy that the patient takes on a regular basis. Adult dosage is often one 100-mg capsule three times daily. The effective serum blood level is 10 to 20 μg/mL, which may take 7 to 10 da to achieve. Although individual variations occur,

serious side effects can appear at a serum level of 20 μg/mL. The half-life of Dilantin ranges from 7 to 42 h but averages 22 h.

For simplicity, we assume a one-compartment model with instantaneous absorption. A stock (box variable), *drug_in_system*, represents the mass of Dilantin in the compartment, which is the person's blood serum. A flow, *ingested*, into *drug_in_system* is for the drug absorbed into the system. Because of the periodic nature of the dosage, we employ a pulse function with converters/variables for the dose (*dosage*), time of the initial dose (*start*), and time interval between doses (*interval*). Presuming that only a fraction (*absorption_fraction*) actually enters the system, we multiply this constant (say, 0.12, from experimental evidence) and the pulse value together for the equation of *entering*. We can estimate the value of *absorption_fraction* by plotting actual data of drug concentration versus time and employing techniques of curve fitting, which Module 8.3, "Empirical Models," discusses.

## Quick Review Question 3

Give the equation for *entering*.

The flow from *drug_in_system* (*elimination*) is proportional to the amount present in the system, *drug_in_system*. Thus, between doses of a drug, the rate of change of the drug leaving the system is proportional to the quantity of drug in the system. As for the preceding aspirin example, we use a constant of proportionality (*elimination_constant*) of $-\ln(0.5)/t_{1/2}$, where $t_{1/2}$ is Dilantin's half-life.

For comparison purposes, we have converters (variables) for *MEC*, *MTC*, and the concentration of the drug in the system (*concentration*). To compute the latter, we have a converter (variable) for the volume of the blood serum (*volume*) with a possible value of 3000 mL and appropriate connectors and equation. Figure 2.5.3 contains a one-compartment model, and Equation Set 2.5.2 gives the corresponding explicitly entered equations and constants for Dilantin. Note that, except for name

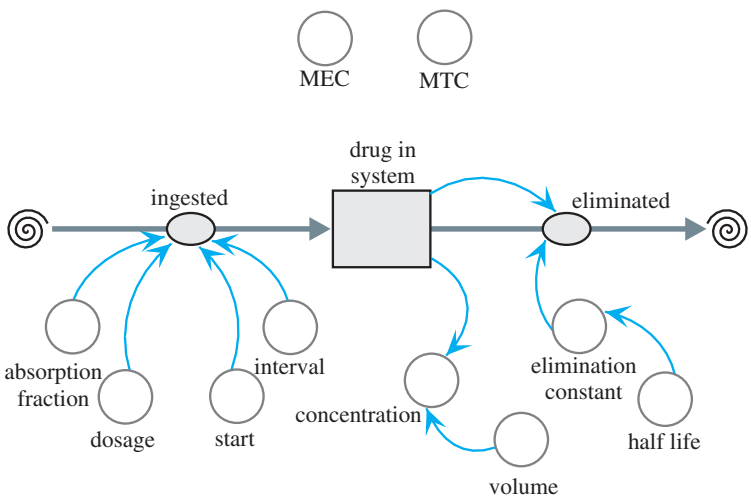


**Figure 2.5.3** One-compartment model of Dilantin

changes, the middle and right side of the diagram agree with those of aspirin in Figure 2.5.1. The inflow for Figure 2.5.3 models the multiple doses of Dilantin, in contrast to no inflow for Figure 2.5.1 because of the assumption that exactly one dose of aspirin is immediately available in the plasma.

### Equation Set 2.5.2

Explicitly entered equations and constants for one-compartment model of Dilantin:

*half_life* = 22 h; *interval* = 8 h; *MEC* = 10 μg/mL; *MTC* = 20 μg/mL; *start* = 0 h; *volume* = 3000 mL; *dosage* = 100 * 1000 μg; *absorption_fraction* = 0.12
*elimination_constant* = –ln(0.5)/*half_life*
*drug_in_system*(0) = 0
*entering* = *absorption_fraction* * (pulse of amount *dosage* beginning at *start* every *interval* hours)
*elimination* = *elimination_constant* * *drug_in_system*
*concentration* = *drug_in_system*/*volume*

Running the simulation and plotting the various concentrations that occur over 168 h (7 da), the resulting Figure 2.5.4 indicates that the concentration of the drug in the system between doses fluctuates. In less than 2 da, the concentration remains within the therapeutic range; and after about 5 da, the drug reaches a steady state.

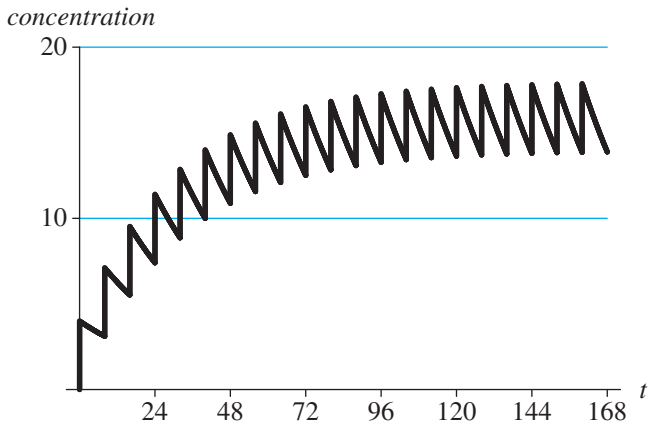


**Figure 2.5.4** Graph of concentrations MEC = 10 μg/mL, MTC = 20 μg/mL, and concentration (μg/mL) versus time (h)

## Mathematics of Repeated Doses

Let us show the mathematics of why the drug concentration in the Dilantin example tends to a fixed value, in this case about 12 μg/mL, immediately after a dose. Suppose that the patient takes a 100-mg tablet every 8 h. In the model, we assumed an absorption level of 0.12, so that the effective dosage is $Q_0 = (0.12)(100) = 12$ mg. With an elimination rate of –ln(0.5)/22, which is about 0.0315, the amount of drug

in the system after 8 h is $Q = Q_0 e^{-0.0315(8)} \approx (12)(0.7772) = 9.3264$ mg = 9326.4 μg. Thus, at the end of 8 h, about 77.72% of the drug remains in the system. The analytical value (9326.4 μg) for the mass of drug in the system is close to the simulated value (9327.91 μg) of *drug_in_system* at time 8.00 h (using a time step of 0.01 h and Runge-Kutta 4 numeric integration, which Module 6.4 discusses).

Suppose $Q_n$ is the quantity (in mg) in the system immediately after the $n$th tablet. Thus, assuming 77.72% of the drug remains in the system at the end of an 8-h interval immediately before a dose, we have the following:

$$Q_1 = 12 \text{ mg}$$

$$Q_2 = \underbrace{(12 \text{ mg})(0.7772)}_{\text{remainder of tablet 1}} + \underbrace{12 \text{ mg}}_{\text{tablet 2}} = 21.3264 \text{ mg}$$

$$Q_3 = \underbrace{Q_2(0.7772)}_{\text{remainder of tablets 1 \& 2}} + \underbrace{12 \text{ mg}}_{\text{tablet 3}}$$

$$= (12(0.7772) + 12)(0.7772) + 12$$

$$= 12(0.7772)^2 + 12(0.7772) + 12 = 28.57488 \text{ mg}$$

$$Q_4 = \underbrace{Q_3(0.7772)}_{\text{remainder of tablets 1-3}} + \underbrace{12 \text{ mg}}_{\text{tablet 4}}$$

$$= (12(0.7772)^2 + 12(0.7772) + 12)(0.7772) + 12$$

$$= 12(0.7772)^3 + 12(0.7772)^2 + 12(0.7772) + 12 = 34.2084 \text{ mg}$$

Continuing in the same pattern, we determine that the general form of the quantity of the drug in the system immediately after the fifth tablet is as follows:

$$\begin{aligned} Q_5 &= 12(0.7772^4) + 12(0.7772^3) + 12(0.7772^2) + 12(0.7772) + 12 \\ &= 12(0.7772^4) + 12(0.7772^3) + 12(0.7772^2) + 12(0.7772^1) + 12(0.7772^0) \\ &= 12(0.7772^4 + 0.7772^3 + 0.7772^2 + 0.7772^1 + 0.7772^0) \end{aligned}$$

Similarly, the quantity of the drug immediately after the $n$th tablet, $Q_n$, follows:

$$Q_n = 12(0.7772^{n-1} + \cdots + 0.7772^2 + 0.7772^1 + 0.7772^0)$$

## Quick Review Question 4

Suppose a patient takes a 200-mg tablet once a day, and within 24 h, 75% of the drug is eliminated from the body. With $Q_n$ being the quantity of the drug in the body after the $n$th dose, determine the following:

**a.** $Q_1$

**b.** $Q_2$ expressed as a sum
**c.** $Q_3$ expressed as a sum
**d.** $Q_4$ expressed as a sum
**e.** $Q_n$ expressed as a sum

We would like to determine what happens to the quantity of the drug in the system over a long period of time. To do so, we need a formula for the sum $0.7772^{n-1} + \cdots + 0.7772^2 + 0.7772^1 + 0.7772^0$ for positive integer $n$. This sum is a **finite geometric series**, and its general form is as follows:

$$a^{n-1} + \cdots + a^2 + a^1 + a^0 \text{ for } a \neq 1 \text{ and positive integer } n$$

As we verify in the next section, this sum is the following ratio:

$$a^{n-1} + \cdots + a^2 + a^1 + a^0 = \frac{(1-a^n)}{(1-a)} \text{ for } a \neq 1$$

Thus, for $a = 0.7772$ and $n = 5$, we can compute the value of $Q_5$:

$$Q_5 = 12(0.7772^4 + 0.7772^3 + 0.7772^2 + 0.7772^1 + 0.7772^0)$$
$$= 12 \cdot \frac{1-0.7772^5}{1-0.7772} = 38.5868 \text{ mg} = 38{,}586.8 \text{ µg}$$

Within simulation error, this value agrees with *drug_in_system* (38,580.92) after the fifth dose, at time 32.01 h. In general, the quantity of the drug immediately after the $n$th tablet, $Q_n$, is as follows:

$$Q_n = 12(0.7772^{n-1} + \cdots + 0.7772^2 + 0.7772^1 + 0.7772^0)$$
$$= 12 \cdot \frac{1-(0.7772)^n}{1-0.7772}$$

**Definition** $a^{n-1} + \cdots + a^2 + a^1 + a^0$ for $a \neq 1$ and positive integer $n$ is a **finite geometric series** with **base** $a$.

## Quick Review Question 5

Using the drug of Quick Review Question 4 and the formula for the sum of a finite geometric series, evaluate the following:

**a.** $Q_{10}$
**b.** $Q_n$

Using the formula for the sum of a finite geometric series, we can compute the quantity of drug after the $n$th tablet. To determine the long-range affect, we let $n$ go to infinity and see that $Q_n$ approaches 53.8599 mg, as follows:

$$Q_n = 12 \cdot \frac{1-(0.7772)^n}{1-0.7772} \to 12 \cdot \frac{1-0}{1-0.7772} \approx 53.8599 \text{ mg}$$

Thus, the serum concentration is about (53.8599 mg)/(3000 mL) = 0.0179533 mg/mL = 17.95 μg/mL, which agrees closely with the peak value of the concentration in Figure 2.5.4.

### Quick Review Question 6

Using the drug of Quick Review Questions 4 and 5, determine the quantity of drug after the *n*th tablet when the patient has been taking the drug for a long time.

## Sum of Finite Geometric Series

To derive the formula for the sum of a finite geometric series, we start by considering a particular example, $Q_5$ as before. Let $s$ be equal to the sum of the powers from 0 through 4 of 0.7772, as follows:

$$s = 0.7772^4 + 0.7772^3 + 0.7772^2 + 0.7772^1 + 0.7772^0 \quad (1)$$

Multiplying both sides by 0.7772, we have the following:

$$0.7772s = (0.7772)\,(0.7772^4 + 0.7772^3 + 0.7772^2 + 0.7772^1 + 0.7772^0)$$
$$0.7772s = 0.7772^5 + 0.7772^4 + 0.7772^3 + 0.7772^2 + 0.7772^1 \quad (2)$$

Subtracting Equation 2 from Equation 1, we subtract off all but two terms on the right:

$$\begin{array}{rrrrrrrrrr} s = & & 0.7772^4 & + & 0.7772^3 & + & 0.7772^2 & + & 0.7772^1 & + 0.7772^0 \\ -0.7772s = & -0.7772^5 & - 0.7772^4 & - & 0.7772^3 & - & 0.7772^2 & - & 0.7772^1 & \\ \hline s - 0.7772s = & -0.7772^5 & & & & & & & & + 0.7772^0 \end{array}$$

With $0.7772^0$ being 1, we factor out $s$ on the left as follows:

$$s(1 - 0.7772) = -0.7772^5 + 1$$

or

$$s(1 - 0.7772) = 1 - 0.7772^5$$

Dividing both sides by the factor (1 – 0.7772), we obtain the following formula:

$$s = \frac{1-0.7772^5}{1-0.7772}$$

By the same reasoning, we have the general formula for the sum of a finite geometric series.

The formula for the sum of a finite geometric series is as follows:

$$a^{n-1} + \cdots + a^2 + a^1 + a^0 = \frac{(1 - a^n)}{(1 - a)} \text{ for } a \neq 1$$

## Two-Compartment Model

The one-compartment model is more appropriate for an injection of a drug into the system than for a pill, which takes time to dissolve, be absorbed, and be distributed within the system. In such cases, a **two-compartment model** might yield better results. The first compartment represents the digestive system (stomach and/or intestines), while the second might indicate the blood, plasma, serum, or a particular organ that the drug targets. A flow pumps the drug from one compartment to the other in the model. One option for modeling the rate of change of absorption from the intestines to blood serum has the rate proportional to the amount of drug in the intestines. Probably a more accurate representation has the rate of change of absorption from the intestines to blood serum be proportional to the volume of the intestines and to the difference of the drug concentrations in the intestines and serum.

Although the one- or two-compartment model is appropriate for most situations, a drug dosage problem could benefit from more compartments in a **multicompartment model**. Various projects employ more than one compartment.

### Quick Review Question 7

This question applies to the rate of change of absorption of a drug from the intestines to blood serum in a two-compartment model. Suppose $k$ is a constant of proportionality; $i$ and $b$ are the masses of the drug in the intestines and blood serum, respectively; $v_i$ and $v_b$ are the volumes of the intestines and blood serum, respectively; $c_i$ and $c_b$ are the drug concentrations in the stomach and blood serum, respectively; and time $t$ is in hours.

**a.** Give the differential equation for this rate if the rate of absorption is proportional to the mass of drug in the intestines.
**b.** In this case, give the units of $k$.
**c.** Give the differential equation for this rate if the rate of absorption is proportional to the volume of the intestines and to the difference of the drug concentrations in the intestines and blood serum.
**d.** In this case, give the units of $k$.

## Exercises

**1.** Assuming that a quantity of a drug ($Q$) is $Q = Q_0e^{Kt}$, show that $K = -\ln(0.5)/t_{1/2}$, where $t_{1/2}$ is the drug's half-life.
**2. a.** In Figure 2.5.4, what are the units for *MEC* and *MTC*?

**b.** What are the units for *dosage*?
**c.** With a dosage of Dilantin being 100 mg, why is the value of *dosage* 100 * 1000?

**3.** Prove the general formula for the sum of a finite geometric series.

**4. a.** In Dilantin example, describe the effect a longer half-life has on *elimination_constant*.
**b.** Evaluate *elimination_constant* for $t_{1/2} = 7$ h.
**c.** Evaluate *elimination_constant* for $t_{1/2} = 22$ h.
**d.** Evaluate *elimination_constant* for $t_{1/2} = 42$ h.

**5. a.** Suppose a patient taking Dilantin decides for convenience to take 300 mg once a day instead of 100 mg every 8 h. Adjusting the model in *OneCompartDilantin*, determine the results of such a decision. Is the decision advisable?
**b.** Mathematically, determine the long-term value of $Q_n$, the quantity of Dilantin in the system immediately after the $n$th dose, assuming absorption of only (0.09)(300 mg).

**6. a.** Determine mathematically the quantity of Dilantin in the system immediately before the fifth dose. Use the same assumptions as in the section "Mathematics of Repeated Doses."
**b.** Determine mathematically the long-term value of the quantity of Dilantin in the system immediately before the $n$th dose.
**c.** Compare your answers to the values in *OneCompartDilantin*.

**7.** How should the one-dose aspirin example be adjusted to incorporate the weight of a male patient? About 65% to 70% of a male's body is liquid. Assume that 1 kilogram (kg) of body liquid has a volume of 1 L. Assume the patient has a mass of 90 kg (comparable to about 198 lb).

## Projects

*For additional projects, see Module 7.7, "Cardiovascular System—A Pressure-Filled Model."*

**1.** Develop a two-compartment model for one dose of aspirin.

**2.** Develop a two-compartment model for aspirin, where someone with a headache takes three aspirin tablets and 2 h later takes two more aspirin tablets.

**3.** In attempt to raise the concentration of a drug in the system to the minimum effective concentration quickly, sometimes doctors give a patient a **loading dose**, which is an initial dosage that is much higher than the maintenance dosage. A loading dose for Dilantin is three doses—400 mg, 300 mg, and 300 mg 2 h apart. Twenty-four hours after the loading dose, normal dosage of 100 mg every 8 h begins. Develop a model for this dosage regime.

**4.** Develop a two-compartment model for Dilantin, where the rate of change of absorption from the stomach to the blood serum is proportional to the amount of drug in the stomach.

**5.** Develop a two-compartment model for Dilantin, where the rate of change of absorption from the stomach to the blood serum is proportional to the

volume of the stomach and to the difference of the drug concentrations in the stomach and serum. Assume the volume of the stomach is 500 mL.

6. Develop a two-compartment model for a pediatric dosage of Dilantin that includes the mass of the patient. The initial dose is 5 mg/kg per day in two or three equally divided doses. The maintenance dosage is usually 4 to 8 mg/kg per day.
7. Develop a model for vancomycin HCI, which is a treatment for serious infections by susceptible strains of methicillin-resistant staphylococci in penicillin-allergic patients. The drug is administered by IV infusion. The intravenous dose is usually 2 g divided either as 500 mg every 6 h or 1 g every 12 h, and the rate is no more than 10 mg/min or over a period of at least 50 min, whichever is longer. When kidney function is normal, multiple intravenous dosing of 1 g results in mean plasma concentrations of about 63 μg/mL immediately after infusion, 23 μg/mL in 2 h, and 8 μg/mL 11 h after infusion. In such patients, the mean elimination half-life from plasma is 4 to 6 h. The mean plasma clearance is approximately 0.058 L/kg/h (liter of drug per kilogram of patient mass each hour), while the mean renal clearance is about 0.048 L/kg/h (Hospira 2010). Thus, include the mass of the patient in the model.
8. Repeat Project 7 for patients with renal dysfunction in which the average half-life of elimination is 7.5 da (Hospira 2010).
9. Develop a model for Vancocin HCI in which the patient initially has normal kidney function (see Project 7). However, at the start of the third day, one of the patient's kidneys stops functioning; and the elimination rate becomes half its previous value. Consider using a step function.
10. Do Project 7 for children, where the dosage is 10 mg/kg every 6 h, and the rate of administration is over a period of at least 60 min (Hospira 2010).
11. Do Project 7 for neonates and young infants. The initial dose is 15 mg/kg. Thereafter, the dosage is 10 mg/kg every 12 h for neonates in their first week of life and afterward, up to age of 1 mo, every 8 h. Administration is more than 60 min (Hospira 2010).
12. Model drug dosage of aspirin for arthritis, where the initial dose is 3 g/da in divided doses. The dosage can be increased. Relief usually occurs at plasma levels of 20 to 30 mg per 100 mL. The plasma half-life of aspirin increases with dosage, so that a dose of 1 g has a half-life of about 5 h and a dose of 2 g has a half-life of about 9 h.
13. Considering the information about mass in Project 7, do any of the previous projects except one involving children or infants, accounting for the mass of a male patient.
14. By consulting a pharmacy reference or website, such as http://www.nlm.nih.gov/medlineplus/druginformation.html, obtain relevant information about some drug. Model the dosage of this drug.

## Answers to Quick Review Questions

1. $K = -\ln(0.5)/3.2$ per hour = 0.22/h
2. *plasma_concentration* = *aspirin_in_plasma* / *plasma_volume*

3. *absorption_fraction* * (pulse of amount *dosage* beginning at *start* every *interval* hours), where the pulse function depends on the particular system dynamics tool
4. **a.** 200 mg
   **b.** (200 mg)(0.25) + 200 mg
   **c.** (200 mg)$(0.25)^2$ + (200 mg)(0.25) + 200 mg
   **d.** (200 mg)$(0.25)^3$ + (200 mg)$(0.25)^2$ + (200 mg)(0.25) + 200 mg
   **e.** (200 mg)$(0.25)^{n-1}$ + · · · + (200 mg)$(0.25)^2$ + (200 mg)(0.25) + 200 mg
5. **a.** (200 mg)$(1 - (0.25)^{10})/(1 - 0.25)$ = 266.67 mg
   **b.** (200 mg)$(1 - (0.25)^n)/(1 - 0.25)$ = (200 mg)$(1 - (0.25)^n)/(0.75)$
6. (200 mg)(1 – 0)/(0.75) = 266.67 mg
7. **a.** $db/dt = ki$
   **b.** 1/h
   **c.** $db/dt = k(v_i)(c_i - c_b)$
   **d.** 1/h

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