3.6 Modeling other phenomena

In this section, we consider various other systems that can be modeled using initial value problems.

Throughout, our emphasis will be on how assumptions about the behavior of a system can be translated into equations describing rates of change. And we will take an analytic, "term-by-term" approach. In other words we will endeavor, where possible, to demonstrate how each assumption corresponds to one or more terms in one or more of the rate equations involved.

We will certainly also give some justification for, or explanation of, each of the assumptions. Still, our focus will be less on debating the validity of the assumptions themselves than it will be on accepting a given set of assumptions and deriving a mathematical model from it. (This is not to say that careful analysis of the assumptions is not important. It *is* important – it's essential – in science. But it's not our focus.)

Circadian rhythms

"Circadian" means "occurring naturally on a 24-hour cycle."

In 2017, US scientists Jeffrey Hall, Michael Rosbash, and Michael Young received the Nobel Prize in Physiology or Medicine, for their discoveries concerning circadian rhythms. Central to their work was analysis of two genes – a "period" gene and a "timeless" gene – and of the proteins expressed by these genes. (The work of Michael Young also concerned a third gene, which he named the "doubletime" gene. For simplicity, though, we will study only the first two genes.)

Here we consider some earlier studies that laid some of the groundwork for the Nobel-Prize-winning research. In particular, we reference the article "A Simple Model of Circadian Rhythms Based on Dimerization and Proteolysis of PER and TIM," by John J. Tyson, Christian I. Hong, C. Dennis Thron, and Bela Novak, in *Biophysical Journal*, Volume 77, November 1999, pages 241–2417. We focus especially on the differential equations developed in this article to model circadian rhythms.

According to this article, "body clocks" (in fruit flies) are regulated by the *feedback* of two proteins, PER – short for "periodic" – and TIM– short for "timeless" – on the "per" and "tim" mRNA (messenger RNA) that express these proteins.

This feedback loop may be expressed in terms of three basic variables:

- the concentration of per and tim mRNA (taken together), denoted by M;
- the concentration P_1 of PER and TIM *monomers*. A monomer is a basic building block of proteins.
- the concentration P_2 of PER and TIM *dimers*. A dimer is two monomers joined together.

Remark 3.6.1. Here we have followed the authors' practice in grouping together the per and tim mRNA, as well as the PER and TIM monomers and the PER and TIM dimers. As the authors note, one could alternatively separate per from tim, and PER from TIM, resulting in a system of six separate variables and a corresponding system of six differential equations. But the authors

argue that "Such a complicated set of equations would not effectively illustrate the importance of positive feedback in the reaction mechanism." In other words, many salient results can be obtained by considering only the variables M, P_1, and P_2 described above.

The authors' model results in a system of differential equations that we will present first, and then explain, in terms of the assumptions behind the model. The system, which we denote by (CR) (for "Circadian Rhythms"), is:

$$\begin{aligned}
\frac{dM}{dt} &= -cM + \frac{a}{1+bP_2^2} \\
&\qquad \text{(i)} \qquad \text{(ii)} \\
\frac{dP_1}{dt} &= dM - \frac{eP_1}{f+P_1+gP_2} - hP_1 - 2kP_1^2 + 2\ell P_2 \\
&\qquad \text{(iii)} \quad \text{(iv)} \qquad \text{(v)} \quad \text{(vi)} \quad \text{(vii)} \\
\frac{dP_2}{dt} &= - \frac{mP_2}{f+P_1+gP_2} - nP_2 + kP_1^2 - \ell P_2 \\
&\qquad \text{(viii)} \qquad \text{(ix)} \quad \text{(x)} \quad \text{(xi)}
\end{aligned} \tag{CR}$$

The Circadian Rhythm (CR) system of differential equations

Here, the letters a,b,c,d,e,f,g,h,k,ℓ all indicate positive parameters.

Notice that we have marked each term, in the above system of equations, with a lower-case roman numeral. We now explain the implications of each of these terms.

(i) This term indicates that mRNA is degraded, or used up, at a rate proportional to the amount of mRNA present.

(ii) This term indicates the fact that P_2 *inhibits* growth of M. Indeed, as P_2 increases, the denominator $1+bP_2^2$ increases, so that the term $a/(1+bP_2^2)$ decreases. And since this term contributes to dM/dt, the ultimate effect of an increase in P_2 is a decrease in dM/dt, and therefore a slowing down, or inhibition, of the growth of M.

Note that the term (ii) involves the square of P_2, rather than P_2 to the first power. The exponent 2 here is called the "Hill coefficient," and measures certain biochemical binding properties of the molecules involved.

A larger Hill coefficient indicates a greater rate of inhibition. This is because, the larger the exponent h, the faster P_2^h grows as a function of P_2. So a larger h means a smaller $a/(1+bP_2^h)$, and therefore a smaller contribution of this term to dM/dt.

We also note that the "1" in the denominator of term (ii) prevents the possibility of division by zero: if the denominator of (i) were simply bP_2^2, or P_2^2, then this denominator would be zero whenever P_2 is zero. But as long as P_2 is nonnegative (and a negative concentration does not make sense), then $1+bP_2^2 > 0$.

(iii) This term indicates that PER/TIM monomers are expressed by per/tim mRNA at a rate proportional to the amount of mRNA present.

(iv) and (viii) These are the most complicated terms. They represent a phenomenon known as *phosphorylation*. This is a process whereby both monomers and dimers combine with phosphates and, through this combination, are deactivated.

To understand what these terms are indicating, let's consider their numerators and denominators separately. Were the denominator in term (iv) not present – that is, were term (iv) simply to equal $-eP_1$ – then this term would be telling us that monomers are deactivated at a rate proportional to the amount of monomers present. Similarly, without the denominator, term (viii) would imply that the rate of dimer deactivation is proportional to the amount of dimers present. Such behavior on its own would make sense much in the way that radioactive decay makes sense: if a substance decays, or "goes away," at a certain rate per unit of that substance, then the more of that substance is present, the more of that substance will "go away" in a given amount of time.

However, the situation here is more complicated than that of radioactive decay: it turns out that, at the same time, protein monomers and dimers inhibit their own decay. This inhibitive effect is captured by the denominators $f + P_1 + gP_2$ in terms (iv) and (viii). (Again, these denominators get larger as P_1 or P_2 does.)

(v) and (ix) These terms represent a process known as *proteolysis*, which is a simpler type of degradation of proteins.

(vi) and (x) These terms represent "dimerization," or the combination of two monomers to form a dimer.

Observe that term (vi) has coefficient $-2k$, whereas (x) has coefficient $+k$. This can be explained as follows:

(a) The coefficient of (vi) is negative, while that of (x) is positive, because dimerization means we are *losing* monomers and *gaining* dimers.

(b) Term (vi) involves a "$2k$," while term (x) involves only a single "k," because for every dimer gained, two monomers are lost.

Also observe that, in (vi) and (x), the variable P_1 occurs to the *second* power. This is because a dimer results from the combination of a monomer with another monomer, so the rate at which dimerization occurs is proportional to the number of *possible* monomer-to-monomer interactions. But the number of such interactions is itself proportional to M^2. (Think of it this way: If there are M people in a room, then there are roughly M^2 possible handshakes that can happen, since every one of the M people can shake hands with any of one M others. Actually there are $M(M-1)$ possible handshakes, if one excludes handshakes with oneself. But M^2 and $M(M-1)$ are "commensurate:" they differ by M, which is small compared to M^2 if M is large.)

(vii) and (xi) represent the process where a dimer splits into monomers. Through this process, each dimer lost results in two dimers gained, and this explains the "$+2\ell$" in term (vii) versus the "$-\ell$" in term (xi).

Note that, in (vii) and (xi), the variable P_2 appears only to the *first* power: a dimer does not have to interact with another to split into monomers, so the number of *possible* dimer splits is only proportional to P_2, not to P_2^2. Contrast this with the analysis of terms (vi) and (x) above.

One nice feature of the above model is that it allows us to see quite clearly how certain natural aberrations can affect circadian rhythms.

To illustrate this most simply, it will be helpful first to combine monomers and dimers into a single variable P (for "proteins"). As the authors of the paper show, we can, under certain "equilibrium" conditions, then also combine the above differential equations defining dP_1/dt and dP_2/dt into a single equation for dP/dt. We skip the mathematical details here – they are not completely beyond the scope of this book, but are a bit messy. (These details may be found in the original article.)

The result of this combination is a system of *two* differential equations, one for mRNA M and one for proteins P. Specifying known "normal" values for the parameters in question, we may then create plots of P and M together, using a variant of our program SIR.sws. The resulting graph looks like this.

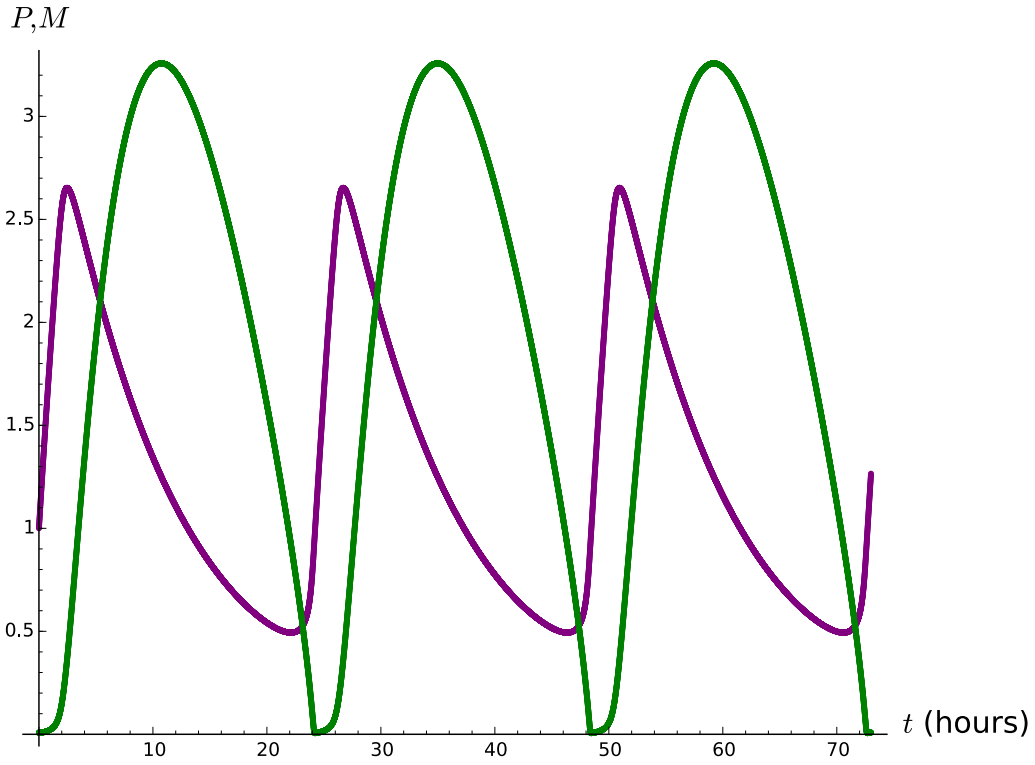

Figure 3.8. Circadian rhythms under "normal" conditions: mRNA (in purple) and protein (in green)

Note that the phenomena represented by above graph are circadian: the graphs of both M and P repeat themselves every 24 hours. (Actually, the period of these graphs turns out to be closer to 24.2 hours, reflective of the fact that, in nature, circadian rhythms are often not precisely circadian, even under "normal" conditions.)

But now we consider an anomalous situation. It's known that a certain *mutation*, denoted per^L, of per mRNA causes a change in the "dimerization rate." By the latter, we mean the parameter k that appears in terms (vi) and (x) above, and that governs the rate at which monomers combine to form dimers. Graphing M and P with a value of k that corresponds to this mutation then yields a result like the following.

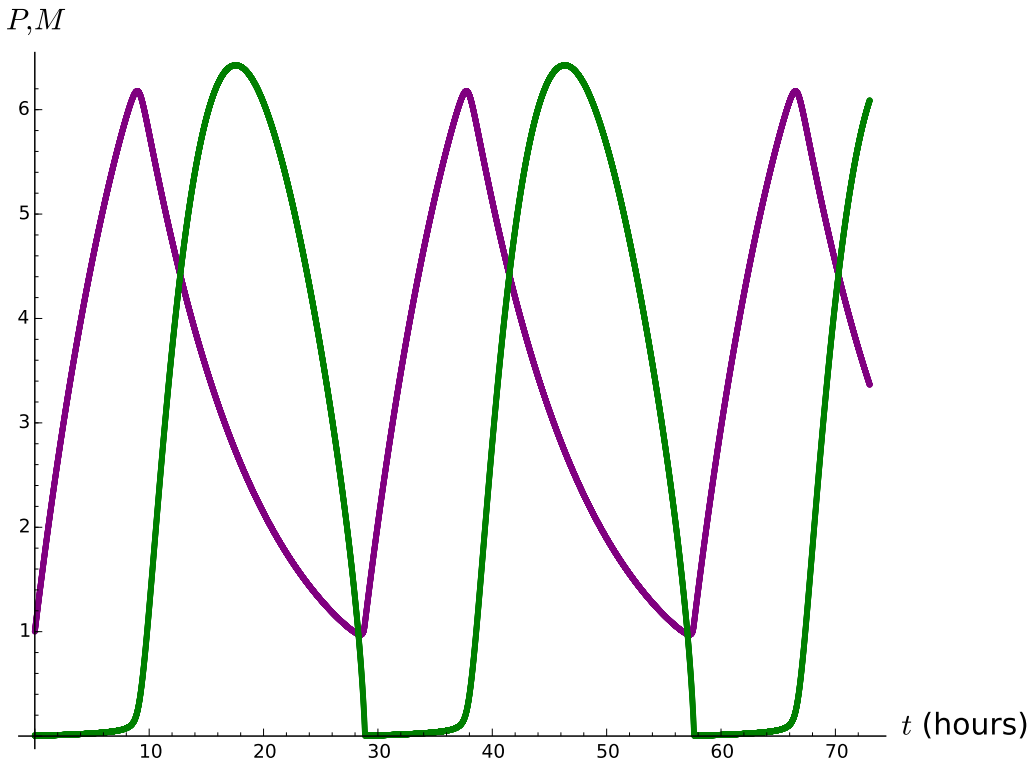

Figure 3.9. Circadian rhythms under "mutant" conditions: mRNA (in purple) and protein (in green)

The phenomena represented by this graph are quite far from circadian!

We have endeavored to understand the system (CR) by studying each term in the right-hand sides of the differential equations there. In our analysis of these terms, we have encountered a variety of important notions, some of these notions we've seen previously:

- Notions of growth and decay, generally indicated by "plus" and "minus" signs, respectively.

  The convention that all parameters be positive, as imposed above, helps us insure that plus and minus signs do, in fact, indicate growth and decay, respectively. For example: since M must

always be nonnegative, requiring that c be positive means that we immediately recognize the term $-cM$ (cf. term (i) above) as representative of decay, rather than growth.

We have seen this convention previously, in our discussions of exponential growth and decay in Section 3.1. There, we stipulated that the parameter k, which represented a growth rate or a decay rate depending on the situation, always be positive. Such a requirement allows us to immediately recognize the equation $P' = kP$ as representative of a growth situation, and the equation $P' = -kP$ as representative of a decay situation (since the quantity P in question generally does not assume negative values).

- The notion of proportionality, where a term in the differential equation for one quantity equals a constant times that quantity, or times some other quantity;

- The notion of inhibition of one quantity on the growth of another, generally reflected by the former quantity appearing in the *denominator* of a term in the differential equation for the latter;

- The notion of exchange, where the transformation of certain quantities into others is reflected by "matching" terms in the differential equations for the quantities involved. (Those terms don't necessarily cancel *per se*. For example: again, since one dimer can become two monomers, the above term (vii) cancels against *twice* the term (xi).)

- The notion of *combinatorics*, where we *count* the number of interactions of a certain type, and this count determines the exponents of the variables in the corresponding terms of the differential equations. (See, again, the analysis of terms (vi) and (x), and terms (vi) and (x), above.)

Many of these notions arise frequently in the modeling of phenomena by differential equations.

Neural impulses

There are many mathematical models for *action potential*, meaning a rapid rise and fall – a "spike" – in voltage across a cell membrane. Here we consider the seminal model developed by Sir Alan Hodgkin and Sir Andrew Huxley in the 1940's. This model was the first to exhibit truly predictive power, and laid the groundwork for a vast amount of subsequent research on neural impulses. For their work, Hodgkin and Huxley received the 1963 Nobel Prize in Physiology and Medicine (shared with Sir John Eccles, for his work on transmission across a synapse). Throughout this subsection, we will use lowercase letters to represent parameters (always assumed positive), as well as the independent variable t; dependent variables will be denoted by upper-case letters.

We begin our analysis by considering several fundamental quantities: charge Q, capacitance c, which is a measure of charge *storage capacity* across a cell membrane, and voltage V, which measures the amount of *work* required to move a charge against an electric field. These three quantities are related by the basic equation

$$Q = cV. \tag{3.6.1}$$

Next, *current* I is defined as the rate of change of charge, with respect to time: $I = \dfrac{dQ}{dt}$ or, by equation (3.6.1),

$$I = \frac{d}{dt}[cV] = c\frac{dV}{dt}. \tag{3.6.2}$$

In the Hodgkin-Huxley model, I comprises four components:

$$I = I_E - I_{Na} - I_K - I_L, \tag{3.6.3}$$

where:

- I_E represents an externally applied current;
- I_{Na} represents sodium ion current flowing through sodium channels in the cell membrane;
- I_K represents potassium ion current flowing through potassium channels in the cell membrane;
- I_L represents "leakage" current (coming mostly from chloride ions), due to natural permeability of the cell membrane.

So we can rewrite equation (3.6.2):

$$c\frac{dV}{dt} = I_E - I_{Na} - I_K - I_L. \tag{3.6.4}$$

Let's now look more closely at each of the four terms on the right-hand side of equation (3.6.4).

(A): I_E. The externally applied current is assumed to be known (and is often constant or zero).

(B): I_{Na}. By *Ohm's Law*, we know that

$$I_{Na} = G_{Na}(V - e_{Na}). \tag{3.6.5}$$

Here, G_{Na} is *conductance* of the sodium channels (a measure of "compliance" of these channels to current flow), and e_{Na} is the "equilibrium potential" for these channels. (By equation (3.6.5), e_{Na} is the voltage that makes I_{Na} equal to zero.)

To better understand equation (3.6.5), let's study G_{Na} more closely.

Each particular sodium channel comprises four so-called "gates," which are possible avenues for the passage of sodium ions. These gates are of two types. Three of these gates are known as "activation gates," and all three activation gates have the same probability, call it M, of being open, and allowing sodium ions through. The fourth gate is an "inactivation gate," and this fourth gate has a different probability, call it H, of letting sodium ions through. An important point to make here is that *M and H are variables; they change with time.*

Because of the way probabilities work, this means that the probability of sodium ions following through all four gates of any given sodium channel is M^3H. But there are many sodium channels. Let g_{Na} denote the *maximum possible conductance*, meaning conductance when all

gates in all sodium channels are open. We can conclude that the actual conductuance G_{Na} then satisfies the equation

$$G_{Na} = g_{Na}M^3H. \tag{3.6.6}$$

Combining equations (3.6.5) and (3.6.6) yields the equation

$$I_{Na} = g_{Na}M^3H(V - e_{Na}). \tag{3.6.7}$$

(C): I_K. The analysis of I_K is similar to that of I_{Na}. But it's simpler, because all four potassium ion gates are of the same type. Let's denote each gate's "permissivity probability," or probability of being open, by N – which, like M and H above, is a function of time. Then by arguments like those in part (B) above,

$$I_K = g_K N^4(V - e_K), \tag{3.6.8}$$

where e_K is the equilibrium potential for the potassium channels, and g_K is the maximum possible conductance of these channels, meaning the conductance that would result were all gates in all potassium channels open.

(D): I_L. The analysis here is even simpler, because the maximum possible conductance due to leakage turns out to be a constant, call it g_L. So

$$I_L = g_L(V - e_L), \tag{3.6.9}$$

where e_L is the equilibrium potential for leakage current.

We now put equations (3.6.7), (3.6.8), and (3.6.9) into equation (3.6.4), to get

$$c\frac{dV}{dt} = I_E - g_{Na}M^3H(V - e_{Na}) - g_K N^4(V - e_K) - g_L(V - e_L). \tag{3.6.10}$$

The quantities M, H, V, and N are the dependent variables here. And (3.6.10) is, of course, an equation for dV/dt. To complete our model, then, we'd like to develop equations for dM/dt, dH/dt, and dN/dt.

We first consider H, the probability of a sodium ion gate being permissive (allowing the flow of sodium ions). Such a gate has probability $1 - H$ of being impermissive. Now suppose we know that such a gate transitions from the permissive state to the impermissive state at the rate A_H, and transitions in the reverse direction (from impermissivity to permissivity) at the rate B_H. We can conclude that

$$\frac{dH}{dt} = A_H H + B_H(1 - H). \tag{3.6.11}$$

Similarly,

$$\frac{dM}{dt} = A_M M + B_M(1 - M) \tag{3.6.12}$$

and

$$\frac{dN}{dt} = A_N H + B_H(1 - H). \tag{3.6.13}$$

Equations (3.6.10), (3.6.11), (3.6.12), and (3.6.13) *are* the differential equations of the Hodgkin-Huxley model. For clarity, we present them all together, here:

$$\begin{aligned} c\frac{dV}{dt} &= I_E - g_{Na}M^3H(V-e_{Na}) - g_K N^4(V-e_K) - g_L(V-e_L) \\ \frac{dH}{dt} &= A_H H + B_H(1-H) \\ \frac{dM}{dt} &= A_M M + B_M(1-M) \\ \frac{dN}{dt} &= A_N N + B_N(1-N) \end{aligned} \tag{HH}$$

The Hodgkin-Huxley (HH) system of differential equations

The above system entails a number of parameters: $g_{Na}, e_{Na}, g_K, e_K, g_L$, and e_L. But note also that there are a number of *dependent variables* appearing on the right-hand sides of these equations, beyond the ones appearing on the left-hand sides. Specifically, there are the variables I_E,A_H, B_H, A_M,B_M,A_N, and B_N. To make equations (HH) into a viable system – one that we could, for example, solve using Euler's method (together with a set of given initial conditions), we would need to know more about these variables. It's already been noted that I_E will, generally (at least in our present model), be known or specified. Further, relatively simple formulas for the functions A_H, B_H, A_M,B_M,A_N, and B_N, *in terms of the voltage* V, can also be given, based on experimentation and various assumptions. See, for example, the chapter "Electrophysiological Models," by M. E. Nelson, in the text *Databasing the Brain: From Data to Knowledge* (S. Koslow and S. Subramaniam, eds.), Wiley, New York (2004).

Exercises

Part 1: Fermentation

Wine is made by yeast; yeast digests the sugars in grape juice and produces alcohol as a waste product. This process is called fermentation. The alcohol is toxic to the yeast, though, and the yeast is eventually killed by the alcohol. This stops fermentation, and the liquid has become wine, with about 8–12% alcohol.

The following exercises develop a sequence of models to take into account the interactions between sugar, yeast, and alcohol.

1. (a) In the first model assume that the sugar supply is not depleted, that no alcohol appears, and that the yeast simply grows *logistically*. Begin by adding 0.5 lb of yeast to a large vat of grape juice whose carrying capacity is 10 lbs of yeast. Assume that the natural growth rate of the yeast is 0.2 lbs of yeast per hour, per pound of yeast. Let $Y(t)$ be the number of pounds of live yeast present after t hours; what differential equation describes the growth of Y?

(b) Graph the solution $Y(t)$, for example by using a suitable modification of the program SIR.sws. Indicate on your graph approximately when the yeast reaches one-half the carrying capacity of the vat, and when it gets to within 1% of the carrying capacity.

(c) Suppose you use a second strain of yeast whose natural growth rate is only half that of the first strain of yeast. If you put 0.5 lb of *this* yeast into the vat of grape juice, when will it reach one-half the carrying capacity of the vat, and when will it get to within 1% of the carrying capacity? Compare these values to the values produced by the first strain of yeast: are they larger, or smaller? Sketch, on the same graph as in part (b), the way this yeast grows over time.

2. (a) Now consider how the yeast produces alcohol. Suppose that waste products are generated at a rate proportional to the amount of yeast present; specifically, suppose each pound of yeast produces 0.05 lbs of alcohol per hour. (The other major waste product is carbon dioxide gas, which bubbles out of the liquid.) Let $A(t)$ denote the amount of alcohol generated after t hours. Write a differential equation that describes the growth of A.

(b) Consider the toxic effect of the alcohol on the yeast. Assume that yeast cells die at a rate proportional to the amount of alcohol present, and also to the amount of yeast present. Specifically, assume that, in each pound of yeast, a pound of alcohol will kill 0.1 lb of yeast per hour. Then, if there are Y lbs of yeast and A lbs of alcohol, how many pounds of yeast will die in one hour? Modify the original logistic equation for Y (strain 1) to take this effect into account. The modification involves subtracting off a new term that describes the rate at which alcohol kills yeast. What is the new differential equation?

(c) You should now have two differential equations describing the rates of growth of yeast and alcohol. The equations are **coupled**, in the sense that the yeast equation involves alcohol, and the alcohol equation involves yeast. Assuming that the vat contains, initially, 0.5 lb of yeast and no alcohol, describe by means of a graph what happens to the yeast. How close does the yeast get to carrying capacity, and when does this happen? Does the fermentation end? If so, when; and how much alcohol has been produced by that time? (Note that since Y will never get all the way to 0, you will need to adopt some convention like $Y \leq .01$ to specify the end of fermentation.)

3. What happens if the rates of toxicity and alcohol production are different? Specifically, increase the rate of alcohol production by a factor of five – from 0.05 to 0.25 lbs of alcohol per hour, per pound of yeast – and at the same time reduce the toxicity rate by the same factor – from 0.10 to 0.02 lb of yeast per hour, per pound of alcohol and pound of yeast. How do these changes affect the time it takes for fermentation to end? How do they affect the amount of alcohol produced? What happens if only the rate of alcohol production is changed? What happens if only the toxicity rate is reduced?

4. (a) The third model will take into account that the sugar in the grape juice is consumed. Suppose the yeast consumes 0.15 lb of sugar per hour, per lb of yeast. Let $S(t)$ be the amount of sugar in the vat after t hours. Write a differential equation that describes what happens to S over time.

(b) Since the carrying capacity of the vat depends on the amount of sugar in it, the carrying

capacity must now vary. Assume that the carrying capacity of S lbs of sugar is $.4\,S$ lbs of yeast. How much sugar is needed to maintain a carrying capacity of 10 lbs of yeast? How much is needed to maintain a carrying capacity of 1 lb of yeast? Rewrite the logistic equation for yeast so that the carrying capacity is $.4\,S$ lbs, instead of 10 lbs, of yeast. Retain the term you developed in 9.b to reflect the toxic impact of alcohol on the yeast.

(c) There are now three differential equations. Using them, describe what happens to .5 lbs of yeast that is put into a vat of grape juice that contains 25 lbs of sugar at the start. Does all the sugar disappear? Does all the yeast disappear? How long does it take before there is only .01 lb of yeast? How much sugar is left then? How much alcohol has been produced by that time?

Part 2: Newton's law of cooling

Suppose that we start off with a freshly brewed cup of coffee at 90°C and set it down in a room where the temperature is 20°C. What will the temperature of the coffee be in 20 minutes? How long will it take the coffee to cool to 30°C?

If we let the temperature of the coffee be Q (in °C), then Q is a function of the time t, measured in minutes. We have $Q(0) = 90$°C, and we would like to find the value t_1 for which $Q(t_1) = 30$°C.

It is not immediately apparent how to give Q as a function of t. However, we can describe the *rate* at which a liquid cools off, using **Newton's law of cooling**: the rate at which an object cools (or warms up, if it's cooler than its surroundings) is proportional to the *difference* between its temperature and that of its surroundings.

5. In our example, the temperature of the room is 20°C, so Newton's law of cooling states that $Q'(t)$ is proportional to $Q-20$, the difference between the temperature of the liquid and the room. In symbols, we have

$$Q' = -k\,(Q - 20)$$

where k is some positive constant.

(a) Why is there a minus sign in the equation?

The particular value of k would need to be determined experimentally. It will depend on things like the size and shape of the cup, how much sugar and cream you use, and whether you stir the liquid. Suppose that k has the value of 0.1° per minute per °C of temperature difference. Then the differential equation becomes:

$$Q' = -0.1(Q - 20) \quad \text{°C per minute.}$$

(b) Use Euler's method to determine the temperature Q after 20 minutes. Write a table of successive approximations with smaller and smaller step sizes. The values in your table should stabilize to the second decimal place.

(c) How long does it take for the temperature Q to drop to 30°C? Use a DO-WHILE loop to construct a table of successive approximations that stabilize to the second decimal place.

6. On a hot day, a cold drink warms up at a rate approximately proportional to the difference in temperature between the drink and its surroundings. Suppose the air temperature is 90°F and the drink is initially at 36°F. If Q is the temperature of the drink at any time, we shall suppose that it warms up at the rate

$$Q' = -0.2(Q - 90) \quad \text{°F per minute.}$$

According to this model, what will the temperature of the drink be after 5 minutes, and after 10 minutes. In both cases, produce values that are accurate to two decimal places.

7. In our discussion of cooling coffee, we assumed that the coffee did not heat up the room. This is reasonable because the room is large, compared to the cup of coffee. Suppose, in an effort to keep it warmer, we put the coffee into a small insulated container – such as a microwave oven (which is turned off). We must assume that the coffee *does* heat up the air inside the container. Let A be the air temperature in the container and Q the temperature of the coffee. Then both A and Q change over time, and Newton's law of cooling tells us the *rates* at which they change. In fact, the law says that both Q' and A' are proportional to $Q - A$. Thus,

$$\begin{aligned} Q' &= -k_1(Q - A) \\ A' &= k_2(Q - A), \end{aligned}$$

where k_1 and k_2 are positive constants.

(a) Explain the signs that appear in these differential equations.

(b) Suppose $k_1 = .3$ and $k_2 = 0.1$. If $Q(0) = 90$°C and $A(0) = 20$°C, when will the temperature of the coffee be 40°C? What is the temperature of the air at this time? Your answers should be accurate to one decimal place.

(c) What does the temperature of the coffee become eventually? How long does it take to reach that temperature?

Part 3: SIR revisited

Consider the spread of an infectious disease that is modelled by the SIR differential equations

$$\begin{aligned} S' &= -.00001\,SI, \\ I' &= .00001\,SI - .08\,I, \\ R' &= \ .08\,I. \end{aligned}$$

Take the initial condition of the three populations to be

$$\begin{aligned} S(0) &= 35{,}400 \text{ persons}, \\ I(0) &= 13{,}500 \text{ persons}, \\ R(0) &= 22{,}100 \text{ persons}. \end{aligned}$$

8. How many susceptibles are left after 40 days? When is the largest number of people infected? How many susceptibles are there at that time? Explain how you could determine the last number *without* using Euler's method.

9. What happens as the epidemic "runs its course"? That is, as more and more time goes by, what happens to the numbers of infecteds and susceptibles?

10. One of the principal uses of a mathematical model is to get a qualitative idea how a system will behave with different initial conditions. For instance, suppose we introduce 100 infected individuals into a population. How will the spread of the infection depend on the size of the population? Assume the same SIR differential equations that were used in the previous exercise, and draw the graphs of $S(t)$ for initial susceptible population sizes $S(0)$ ranging from 0 to 45,000 in increments of 5000 (that is, take $S(0) = 0$, 5000, 10000, ..., 45000). In each case assume that $R(0) = 0$ and $I(0) = 100$. Use these graphs to argue that the larger the initial susceptible population, the more rapidly the epidemic runs its course.

11. Draw the graphs of $I(t)$ for the same initial conditions as in the previous problem. Using these graphs you can demonstrate that the larger the susceptible population, the larger will be the fraction of the population that is infected during the worst stages of the epidemic. Do this by constructing a table displaying $I_{\max}$, $t_{\max}$, and $P_{\max}$, where $I_{\max}$ is the maximum value of $I(t)$, $t_{\max}$ is the time at which this maximum occurs (that is, $I_{\max} = I(t_{\max})$), and $P_{\max}$ is the ratio of $I_{\max}$ to the initial susceptible population: $P_{\max} = I_{\max}/S(0)$. The table below gives the first three sets of values.

$S(0)$	$I_{\max}$	$P_{\max}$	$t_{\max}$
5 000	100	0.02	0
10 000	315	0.03	> 100
15 000	2071	0.14	66
⋮	⋮	⋮	⋮

Your table should show that there is a time when over half the population is infected if $S(0) =$ 45000, while there is never a time when more than one-fourth of the population is infected if $S(0) =$ 2,0000.

Part 4: Constructing models

Systems in which we know a number of quantities at a given time and would like to know their values at a future time (or know at what future time they will attain given values) occur in many different contexts. The following are some systems for discussion. Can any of these be modelled as initial value problems? What information would you need to resolve the question? Make some reasonable assumptions about the missing information and write down an initial value problem which would model the system.

12. We deposit a fixed sum of money in a bank, and we'd like to know how much will be there in ten years.

13. We know the diameter of the mold spot growing on a cheese sandwich is 1/4 inch, and we'd like to know when its diameter will be one inch.

14. We know the fecal bacterial and coliform concentrations in a local swimming hole, and we'd like to know when they fall below certain prescribed levels (which the Board of Health deems safe).

15. We know what the temperature and rainfall is today, and we'd like to know what both will be one week from today.

16. We know what the winning lottery number was yesterday, and we'd like to know what the winning number will be the day after tomorrow.

17. We know where the earth, sun, and moon are in relation to each other now, and how fast and in what direction they are moving. We would like to be able to predict where they are going to be at any time in the future. We know the gravity of each affects the motions of the others by determining the way their velocities are changing.