The exponential function is one of the most important and widely occurring functions in physics and biology. In biology it may describe the growth of bacteria or animal populations, the decrease of the number of bacteria in response to a sterilization process, the growth of a tumor, or the absorption or excretion of a drug. (Exponential growth cannot continue forever because of limitations of nutrients, etc.) Knowledge of the exponential function makes it easier to understand birth and death rates, even when they are not constant. In physics, the exponential function describes the decay of radioactive nuclei, the emission of light by atoms, the absorption of light as it passes through matter, the change of voltage or current in some electrical circuits, the variation of temperature with time as a warm object cools, and the rate of some chemical reactions.

In this book, the exponential function will be needed to describe certain probability distributions, the concentration ratio of ions across a cell membrane, the flow of solute particles through membranes, the decay of a signal traveling along a nerve axon, and the return of some physiologic variables to their equilibrium values after they have been disturbed.

Because the exponential function is so important, and because we have seen many students who did not understand it even after having been exposed to it, the chapter starts with a gentle introduction to exponential growth (Sect. 2.1) and decay (Sect. 2.2). Section 2.3 shows how to analyze exponential data using semilogarithmic graph paper. The next section shows how to use semilogarithmic graph paper to find instantaneous growth or decay rates when the rate varies. Some would argue that the availability of computer programs that automatically produce logarithmic scales for plots makes these sections unnecessary. We feel that intelligent use of semilogarithmic and logarithmic (log–log) plots requires an understanding of the basic principles.

Variable rates are described in Sect. 2.4. Clearance, discussed in Sect. 2.5, is an exponential decay process that is important in physiology. Microbiologists often grow cells in a chemostat, described in Sect. 2.6. Sometimes there are

competing paths for exponential removal of a substance: multiple decay paths are introduced in Sect. 2.7. A very basic and simple model for many processes is the combination of input at a fixed rate accompanied by exponential decay, described in Sect. 2.8. Sometimes a substance exists in two forms, each with its own decay rate. One then must fit two or more exponentials to the set of data, as shown in Sect. 2.9.

Section 2.10 discusses the logistic equation, one possible model for a situation in which the growth rate decreases as the amount of substance increases. The chapter closes with a section on power–law relationships. While not exponential, they are included because data analysis can be done with log–log graph paper, a technique similar to that for semilog paper. If you feel mathematically secure, you may wish to skim the first four sections, but you will probably find the rest of the chapter worth reading.

## 2.1 Exponential Growth

*An exponential growth process is one in which the rate of increase of a quantity is proportional to the present value of that quantity.* The simplest example is a savings account. If the interest rate is 5 % and if the interest is credited to the account once a year, the account increases in value by 5 % of its present value each year. If the account starts out with \$ 100, then at the end of the first year, \$ 5 is credited to the account and the value becomes \$ 105. At the end of the second year, 5 % of \$ 105 is credited to the account and the value grows by \$ 5.25 to 110.25. The growth of such an account is shown in Table 2.1 and Fig. 2.1. These amounts can be calculated as follows: At the end of the first year, the original amount, $y_0$, has been augmented by $(0.05)y_0$:

$$y_1 = y_0(1 + 0.05).$$

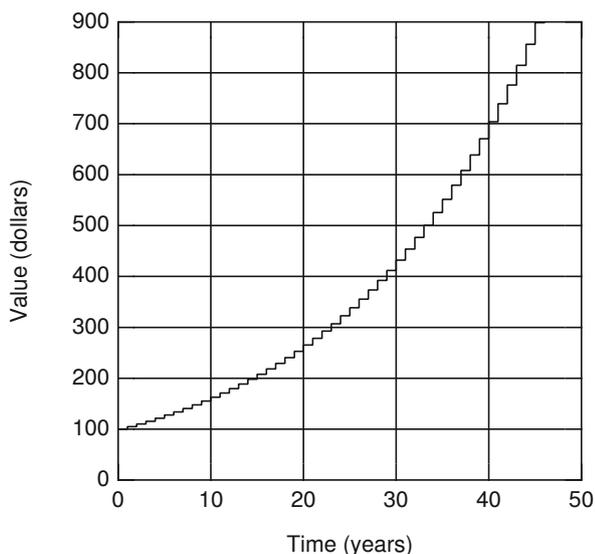During the second year, the amount $y_1$ increases by 5 %, so

$$y_2 = y_1(1.05) = y_0(1.05)(1.05) = y_0(1.05)^2.$$

**Table 2.1** Growth of a savings account earning 5 % interest compounded annually, when the initial investment is $ 100

| Year | Amount ($) | Year | Amount ($) | Year | Amount ($) |
|------|-----------|------|-----------|------|-----------|
| 1 | 105.00 | 10 | 162.88 | 100 | $1.31 \times 10^4$ |
| 2 | 110.25 | 20 | 265.33 | 200 | $1.73 \times 10^6$ |
| 3 | 115.76 | 30 | 432.19 | 300 | $2.27 \times 10^8$ |
| 4 | 121.55 | 40 | 704.00 | 400 | $2.99 \times 10^{10}$ |
| 5 | 127.63 | 50 | 1146.74 | 500 | $3.93 \times 10^{12}$ |
| 6 | 134.01 | 60 | 1867.92 | 600 | $5.17 \times 10^{14}$ |
| 7 | 140.71 | 70 | 3042.64 | 700 | $6.80 \times 10^{16}$ |
| 8 | 147.75 | 80 | 4956.14 | 800 | $8.94 \times 10^{18}$ |
| 9 | 155.13 | 90 | 8073.04 | 900 | $1.18 \times 10^{21}$ |

**Table 2.2** Amount of an initial investment of $ 100 at 5 % annual interest, with different methods of compounding

| Month | Annual ($) | Semiannual ($) | Quarterly ($) | Monthly ($) | Instant ($) |
|-------|-----------|----------------|---------------|-------------|-------------|
| 0 | 100.00 | 100.00 | 100.00 | 100.000 | 100.000 |
| 1 | 100.00 | 100.00 | 100.00 | 100.417 | 100.418 |
| 2 | 100.00 | 100.00 | 100.00 | 100.835 | 100.837 |
| 3 | 100.00 | 100.00 | 101.25 | 101.255 | 101.258 |
| 4 | 100.00 | 100.00 | 101.25 | 101.677 | 101.681 |
| 5 | 100.00 | 100.00 | 101.25 | 102.101 | 102.105 |
| 6 | 100.00 | 102.50 | 102.52 | 102.526 | 102.532 |
| 7 | 100.00 | 102.50 | 102.52 | 102.953 | 102.960 |
| 8 | 100.00 | 102.50 | 102.52 | 103.382 | 103.390 |
| 9 | 100.00 | 102.50 | 103.80 | 103.813 | 103.821 |
| 10 | 100.00 | 102.50 | 103.80 | 104.246 | 104.255 |
| 11 | 100.00 | 102.50 | 103.80 | 104.680 | 104.690 |
| 12 | 105.00 | 105.06 | 105.09 | 105.116 | 105.127 |

**Table 2.3** Numerical examples of the convergence of $(1 + b/N)^N$ to $e^b$ as $N$ becomes large

| $N$ | $b = 1$ | $b = 0.05$ |
|-----|---------|-----------|
| 10 | 2.594 | 1.0511 |
| 100 | 2.705 | 1.0513 |
| 1000 | 2.717 | 1.0513 |
| $e^b$ | 2.718 | 1.0513 |



**Fig. 2.1** The amount in a savings account after $t$ years, when the amount is compounded annually at 5 % interest

After $t$ years, the amount in the account is

$$y_t = y_0(1.05)^t.$$

In general, if the growth rate is $b$ per compounding period, the amount after $t$ periods is

$$y_t = y_0(1 + b)^t. \tag{2.1}$$

It is possible to keep the same annual growth (interest) rate, but to compound more often than once a year. Table 2.2 shows the effect of different compounding intervals on the amount, when the interest rate is 5 %. The last two columns, for monthly compounding and for "instant interest," are listed to the nearest tenth of a cent to show the slight difference between them.

The table entries were calculated in the following way: Suppose that compounding is done $N$ times a year. In $t$ years, the number of compoundings is $Nt$. If the annual fractional

rate of increase is $b$, the increase per compounding is $b/N$. For 6 months at 5 % ($b = 0.05$), the increase is 2.5, for 3 months it is 1.25, etc. The amount after $t$ units of time (years) is, in analogy with Eq. 2.1,

$$y = y_0 (1 + b/N)^{Nt}. \tag{2.2}$$

Recall (refer to Appendix C) that $(a)^{bc} = (a^b)^c$. The expression for $y$ can be written as

$$y = y_0 \left[ (1 + b/N)^N \right]^t. \tag{2.3}$$

Most calculus textbooks show that the quantity

$$(1 + b/N)^N \rightarrow e^b$$

as $N$ becomes very large. (Rather than proving this fact here, we give numerical examples in Table 2.3 for two different values of $b$.) Therefore, Eq. 2.3 can be rewritten as

$$y = y_0 e^{bt} = y_0 \exp(bt). \tag{2.4}$$

(The exp notation is used when the argument is complicated.) To calculate the amount for instant interest, it is necessary only to multiply the fractional growth rate per unit time $b$ by the length of the time interval and then look up the exponential function of this amount in a table or evaluate it with a computer or calculator. The number $e$ is approximately equal to $2.71828\ldots$ and is called the *base of the natural logarithms*. Like $\pi$ ($3.14159\ldots$), $e$ has a long history (Maor 1994).
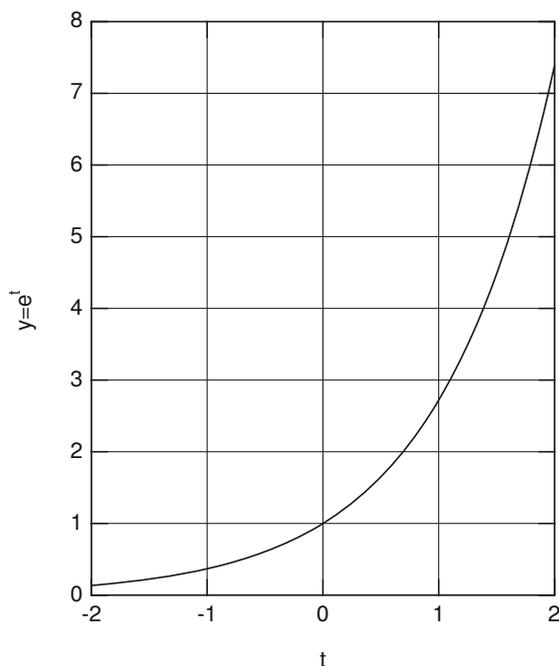
**Fig. 2.2** A graph of the exponential function $y = e^t$



**Fig. 2.3** A plot of the fraction of nuclei of $^{99m}$Tc surviving at time $t$

The exponential function is plotted in Fig. 2.2. (The meaning of negative values of $t$ will be considered in the next section.) This function increases more and more rapidly as $t$ increases. This is expected, since the rate of growth is always proportional to the present amount. This is also reflected in the following property of the exponential function:
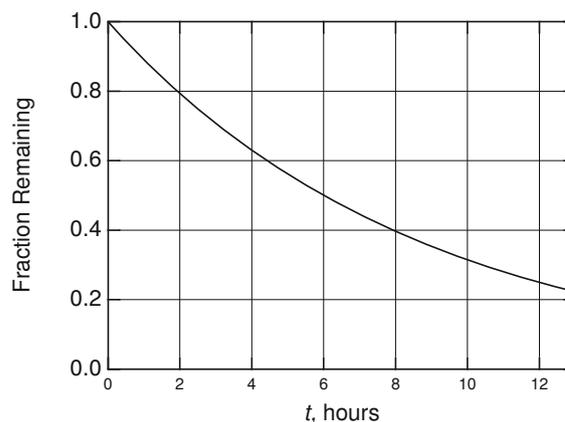
$$\frac{d}{dt}\left(e^{bt}\right) = be^{bt}. \tag{2.5}$$

This means that the function $y = y_0 e^{bt}$ has the property that

$$\frac{dy}{dt} = by. \tag{2.6}$$

*Any constant multiple of the exponential function $e^{bt}$ has the property that its rate of growth is b times the function itself.* Whenever we see the exponential function, we know that it satisfies Eq. 2.6. Equation 2.6 is an example of a *differential equation*. If you learn how to solve only one differential equation, let it be Eq. 2.6. Whenever we have a problem in which the growth rate of something is proportional to the present amount, we can expect to have an exponential solution. Notice that for time intervals $t$ that are not too large, Eq. 2.6 implies that $\Delta y = (b\Delta t)y$. This again says that the increase in $y$ is proportional to $y$ itself.

The independent variable in this discussion has been $t$. It can represent time, in which case $b$ is the fractional growth rate per unit time; distance, in which case $b$ is the fractional growth per unit distance; or something else. We could, of course, use another symbol such as $x$ for the independent variable, in which case we would have $dy/dx = by$, $y = y_0 e^{bx}$.

## 2.2 Exponential Decay

Figure 2.2 shows the exponential function for negative values of $t$ as well as positive ones. (Remember that $e^{-t} = 1/e^t$.) To see what this means, consider a bank account in which no interest is credited, but from which 5 % of what remains is taken each year. If the initial balance is $ 100, $ 5 is removed the first year to leave $ 95.00. In the second year, 5 % of $ 95 or $ 4.75 is removed. In the third year, 5 % of $ 90.25 or $ 4.51 is removed. The annual decrease in $y$ becomes less and less as $y$ becomes less and less. The equations developed in the preceding section also describe this situation. It is only necessary to call $b$ the fractional decay and allow it to have a negative value, $-|b|$. Equation 2.1 then has the form $y = y_0(1 - |b|)^t$ and Eq. 2.4 is

$$y = y_0 e^{-|b|t}. \tag{2.7}$$

Often $b$ is regarded as being intrinsically positive, and Eq. 2.7 is written as

$$y = y_0 e^{-bt}. \tag{2.8}$$

One could equally well write $y = y_0 e^{bt}$ and regard $b$ as being negative, but this can cause confusion, for example with Eq. 2.10 below.

The radioactive isotope $^{99m}$Tc (read as technetium-99) has a fractional decay rate $b = 0.1155\,\text{h}^{-1}$. If the number of atoms at $t = 0$ is $y_0$, the fraction $f = y/y_0$ remaining at later times decreases as shown in Fig. 2.3. The equation that describes this curve is

$$f = \frac{y}{y_0} = e^{-bt}, \tag{2.9}$$

where $t$ is the elapsed time in hours and $b = 0.1155\,\text{h}^{-1}$. The product $bt$ must be dimensionless, since it is in the exponent.

People often talk about the *half-life* $T_{1/2}$, which is the length of time required for $f$ to decrease to one-half. From

inspection of Fig. 2.3, the half-life is 6 h. This can also be determined from Eq. 2.9:

$$0.5 = e^{-bT_{1/2}}.$$

From a table of exponentials, one finds that $e^{-x} = 0.5$ when $x = 0.69315$. This leads to the very useful relationship $bT_{1/2} = 0.693$ or

$$T_{1/2} = \frac{0.693}{b}. \tag{2.10}$$

For the case of $^{99m}$Tc, the half-life is $T_{1/2} = 0.693/0.1155 = 6$ h.

One can also speak of a *doubling time* if the exponent is positive. In that case, $2 = e^{bT_2}$, from which

$$T_2 = \frac{0.693}{b}. \tag{2.11}$$

## 2.3 Semilog Paper

A special kind of graph paper, called *semilog paper*, makes the analysis of exponential growth and decay problems much simpler. If one takes logarithms (to any base) of Eq. 2.4, one has

$$\log y = \log y_0 + bt \log e. \tag{2.12}$$

If the dependent variable is considered to be $u = \log y$, and since $\log y_0$ and $\log e$ are constants, this equation is of the form

$$u = c_1 + c_2 t. \tag{2.13}$$

The graph of $u$ vs $t$ is a straight line with positive slope if $b$ is positive and negative slope if $b$ is negative.

On semilog paper the vertical axis is marked in a logarithmic fashion. The graph can be plotted without having to calculate any logarithms. Figure 2.4 shows a plot of the exponential function of Fig. 2.2, for both positive and negative values of $t$. First, note how to read the vertical axis. A given distance along the axis always corresponds to the same multiplicative factor. Each cycle represents a factor of ten. To use the paper, it is necessary first to mark off the decades with the desired values. In Fig. 2.4, the decades have been marked 0.1, 1, 10, and 100. The 6 that lies between 0.1 and 1 is 0.6; the 6 between 1 and 10 is 6.0; the 6 between 10 and 100 represents 60; and so forth. The paper can be imagined to go vertically forever in either direction; one never reaches zero. Figure 2.4 has two examples marked on it with dashed lines. The first shows that for $t = -1.0$, $y = 0.36$; the second shows that for $t = +1.5$, $y = 4.5$.

Semilog paper is most useful for plotting data that you suspect may have an exponential relationship. If the data plot as a straight line, your suspicions are confirmed. From the
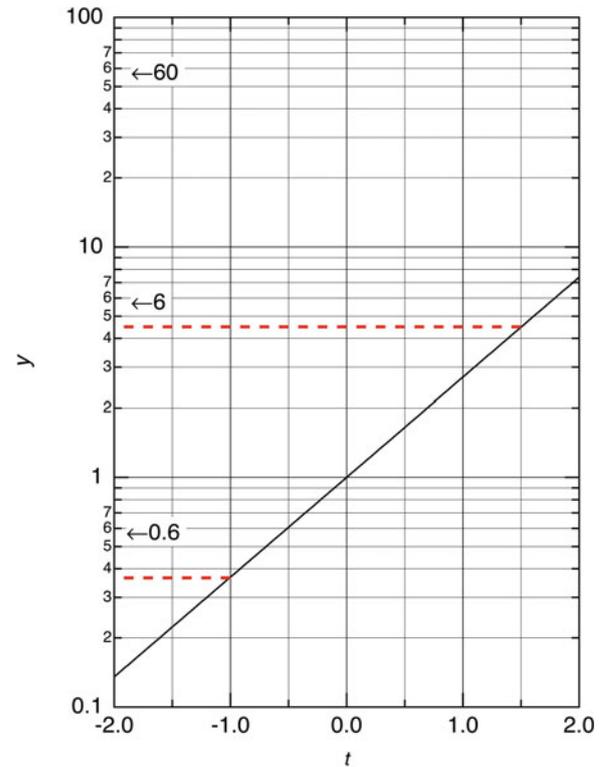


**Fig. 2.4** A plot of the exponential function on semilog paper

straight line, you can determine the value of $b$. Figure 2.5 is a plot of the intensity of light that passed through an absorber in a hypothetical example. The independent variable is absorber thickness $x$. The decay is exponential, except for the last few points, which may be high because of experimental error. (As the intensity of the light decreases, it becomes harder to measure accurately.) We wish to determine the decay constant in $y = y_0 e^{-bx}$. One way to do it would be to note (dashed line $A$ in Fig. 2.5) that the half-distance is 0.145 cm, so that, from Eq. 2.10,

$$b = \frac{0.693}{0.145} = 4.8 \text{ cm}^{-1}.$$

This technique can be inaccurate because it is difficult to read the graph accurately. It is more accurate to use a portion of the curve for which $y$ changes by a factor of 10 or 100. The general relationship is $y = y_0 e^{bx}$, where the value of $b$ can be positive or negative. If two different values of $x$ are selected, one can write

$$\frac{y_2}{y_1} = \frac{y_0 e^{bx_2}}{y_0 e^{bx_1}} = e^{b(x_2-x_1)}.$$

If $y_2/y_1 = 10$, then this equation has the form $10 = e^{bX_{10}}$ where $X_{10} = x_2 - x_1$ when $y_2/y_1 = 10$. From a table of
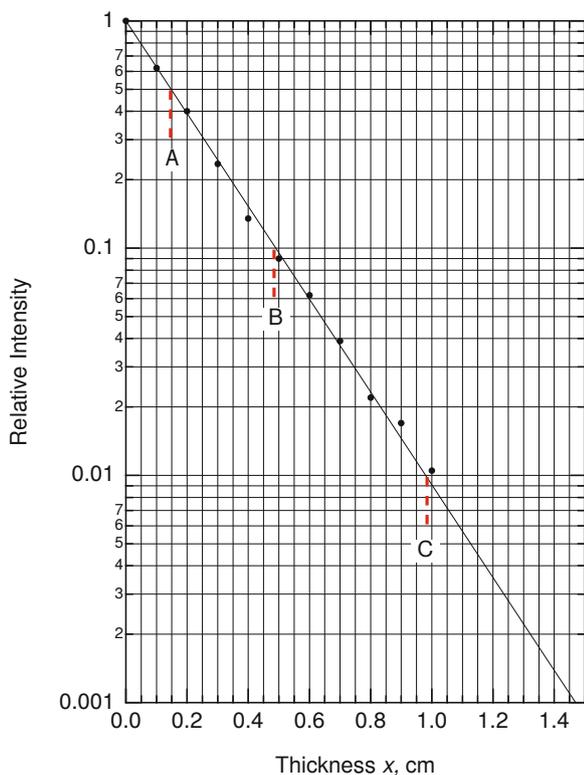
**Fig. 2.5** A semilogarithmic plot of the intensity of light after it has passed through an absorber of thickness $x$

exponentials, $bX_{10} = 2.303$, so that

$$b = \frac{2.303}{X_{10}}. \qquad (2.14)$$

The same procedure can be used to find $b$ using a factor of 100 change in $y$:

$$b = \frac{4.605}{X_{100}}. \qquad (2.15)$$

If the curve represents a decaying exponential, then $y_2/y_1 = 10$ when $x_2 < x_1$, so that $X_{10} = x_2 - x_1$ is negative. Equation 2.14 then gives a negative value for $b$. It is customary to state separately that we are dealing with decay and regard $b$ as positive.

As an example, consider the exponential decay in Fig. 2.5. Using points $B$ and $C$, we have $x_1 = 0.97$, $y_1 = 10^{-2}$, $x_2 = 0.48$, $y_2 = 10^{-1}$, $X_{10} = 0.480 - 0.97 = -0.49$. Therefore, $b = 2.303/(0.49) = 4.7$ cm$^{-1}$, which is a more accurate determination than the one we made using the half-life.

When we are dealing with real data, we must consider the fact that each measurement has an experimental error associated with it. If we make several measurements of $y$ for a particular value of the independent variable $x$, the values of $y$ will be scattered. We indicate this by the error bars in
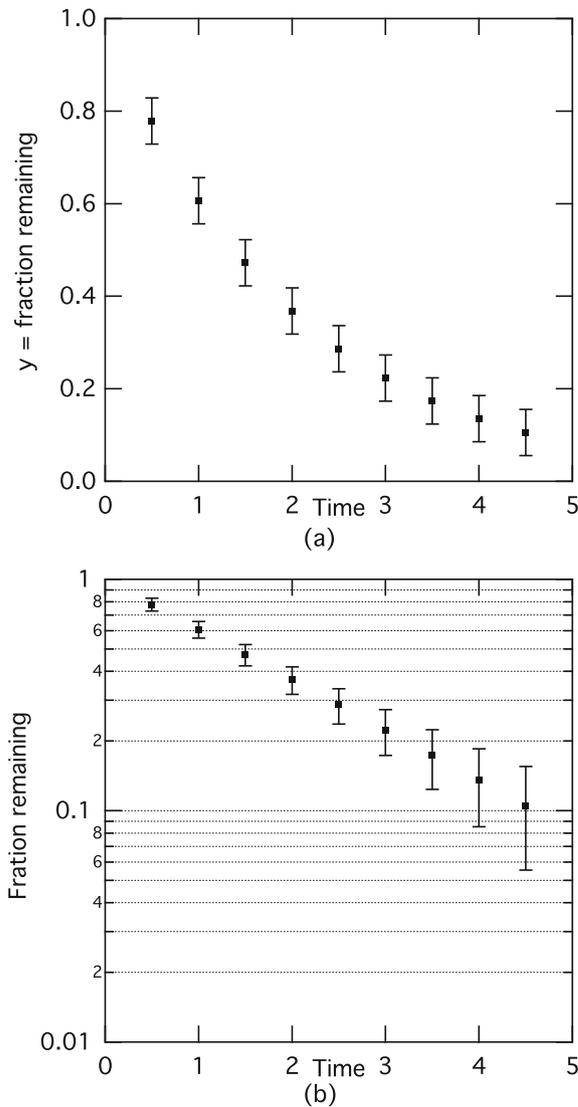


**Fig. 2.6** Plot of $y = e^{-0.5t}$ with error bars $\pm 0.05$ on linear (**a**) and semilog paper (**b**)

Fig. 2.6. (Determining the size of these error bars is discussed in Chap. 11.) The data points in Fig. 2.6 are given exactly by $y = e^{-0.5x}$, where $y$ is the fraction remaining at time $x$. There is no data point for $x = 0$, but we must make sure that our fitting line passes through the point (0,1). The error bars show an error of $\pm 0.09$. The error bars on the semilog plot are not all the same length, being much larger for long times (small values of $y$). If we do not plot the error bars before drawing our line, we will give too much emphasis to the data points for small $y$.

Equal error bars for all the points on a semilog plot correspond to the same percentage error for each point, as shown in Fig. 2.7.

(a)



(b)
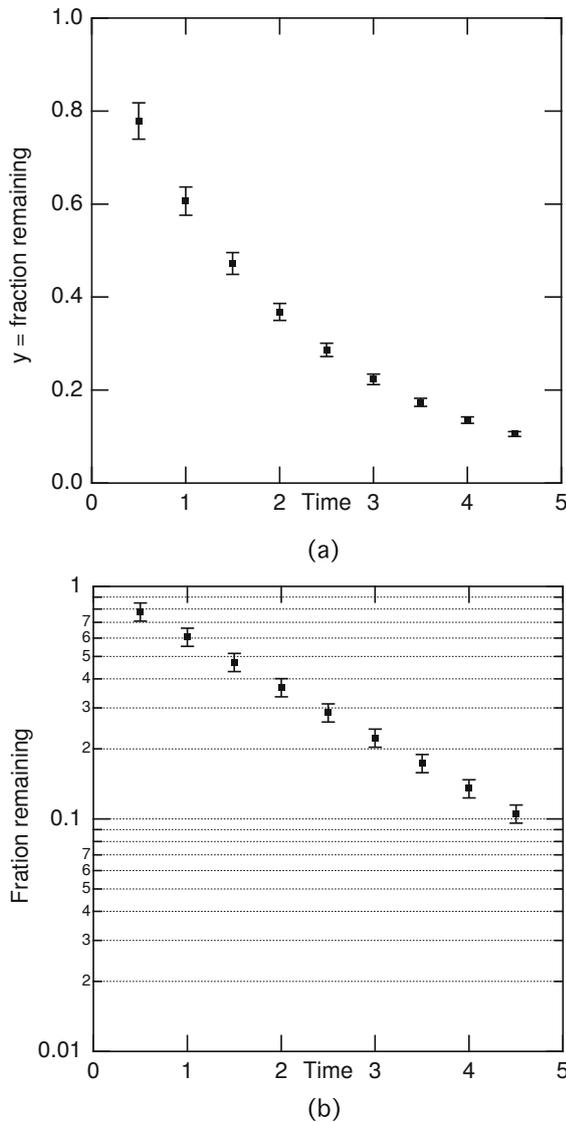
**Fig. 2.7** Plot of $y = e^{-0.5t}$ with 5 % error bars in linear (**a**) and semilog paper (**b**)

## 2.4  Variable Rates

The equation $dy/dx = by$ (or $dy/dt = by$) says that $y$ grows or decays at a rate that is proportional to $y$. The constant $b$ is the *fractional rate of growth or decay*. It is possible to define the fractional rate of growth or decay even if it is not constant but is a function of $x$:

$$b(x) = \frac{1}{y}\frac{dy}{dx}. \qquad (2.16)$$

Semilogarithmic graph paper can be used to analyze the curve even if $b$ is not constant. Since $d(\ln y)/dy = 1/y$, the
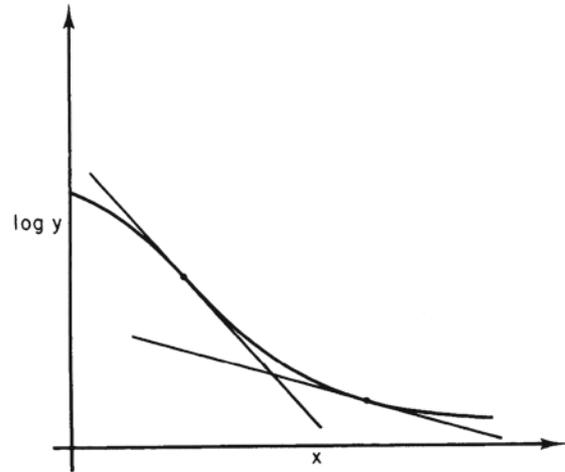


**Fig. 2.8** A semilogarithmic plot of $y$ vs $x$ when the decay rate is not constant. Each *tangent line* represents the instantaneous decay rate for that value of $x$

chain rule for evaluating derivatives gives

$$\frac{d}{dx}(\ln y) = \frac{1}{y}\frac{dy}{dx} = b.$$

This means that $b(x)$ is the slope of a plot of $\ln y$ vs $x$. A semilogarithmic plot of $y$ vs $x$ is shown in Fig. 2.8. The straight lines are tangent to the curve and decay with a constant rate equal to $b(x)$ at the point of tangency. The ordinate in Fig. 2.8 can be the log of $y$ to any base; the value of $b$ for the tangent line is determined using the methods in the previous section.
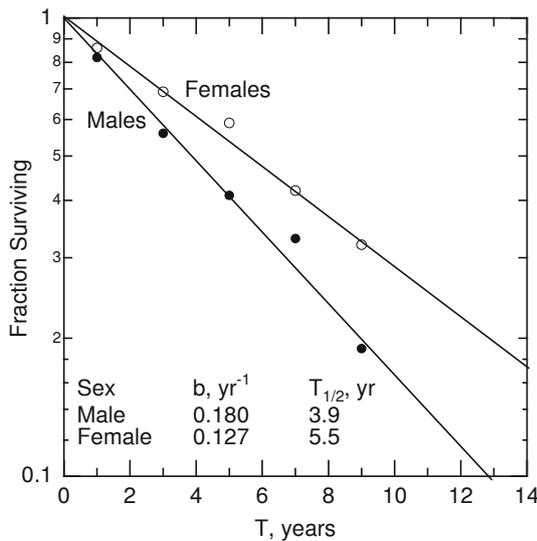
If finite changes $\Delta x$ and $\Delta y$ have been measured, they may be used to estimate $b(x)$ directly from Eq. 2.16. For example, suppose that y=100,000 people and that in $\Delta x = 1$ year there is a change $\Delta y = -37$. In this case, $\Delta y$ is very small compared to $y$, so we can say that $b = (1/y)(\Delta y/\Delta x) = -37 \times 10^{-5}\,\mathrm{y}^{-1}$. If the only cause of change in this population is deaths, the absolute value of $b$ is called the *death rate*.

A plot of the number of people surviving in a population, all of whom have the same disease, can provide information about the prognosis for that disease. The death rate is equivalent to the decay constant. An example of such a plot is shown in Fig. 2.9. Curve $A$ shows a disease for which the death rate is constant. Curve $B$ shows a disease with an initially high death rate that decreases with time; if the patient survives the initial period, the prognosis is much better. Curve $C$ shows a disease for which the death rate increases with time.

Surprisingly, there are a few diseases that have death rates independent of the duration of the disease (Zumoff et al. 1966). Any discussion of mortality should be made in terms
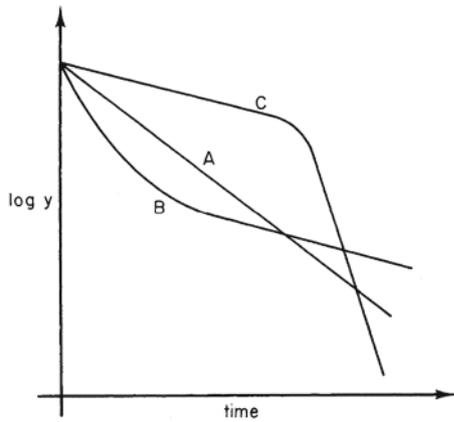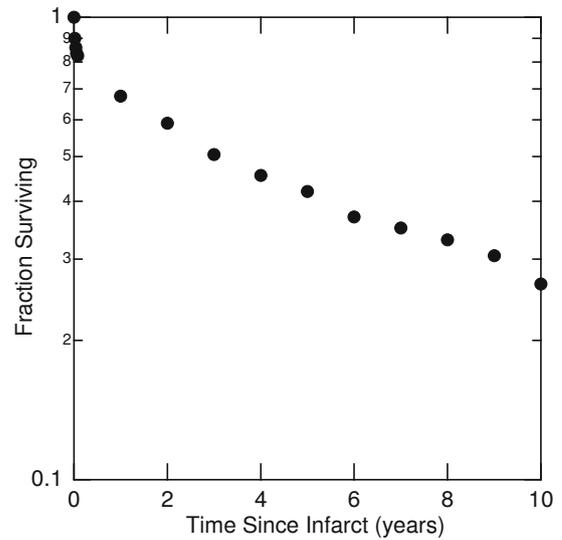
Fig. 2.9 Semilogarithmic plots of the fraction of a population surviving in three different diseases. The death rates (decay constants) depend on the duration of the disease



Fig. 2.11 The fraction of patients surviving after a myocardial infarction (heart attack) at $t = 0$. The mortality rate decreases with time. (From data in Bland and White 1941)



Fig. 2.10 Survival of patients with congestive heart failure. (Data are from McKee et al. 1971)

of the surviving population, since any further deaths must come from that group. Nonetheless, one often finds results in the literature reported in terms of the cumulative fraction of patients who have died. Figure 2.10 shows the survival of patients with congestive heart failure for a period of 9 years. The data are taken from the Framingham study (McKee et al. 1971; Levy and Brink 2005); the death rate is constant during this period. For a more detailed discussion of various possible survival distributions, see Clark (1975).

As long as $b$ has a constant value, it makes no difference what time is selected to be $t = 0$. To see this, suppose that the value of $y$ decays exponentially with constant rate: $y = y_0 e^{-bt}$. Consider two different time scales, shifted with respect to each other so that $t' = t_0 + t$. In terms of the shifted

time $t'$, the value of $y$ is

$$y = y_0 e^{-bt} = y_0 e^{-b(t'-t_0)} = \left( y_0 e^{bt_0} \right) e^{-bt'}.$$

This has the same form as the original expression for $y(t)$. The value of $y_0'$ is $y_0 e^{bt_0}$, which reflects the fact that $t' = 0$ occurs at an earlier time than $t = 0$, so $y_0' > y_0$.

If the decay rate is not constant, then the origin of time becomes quite important. Usually there is something about the problem that allows $t = 0$ to be determined. Figure 2.11 shows survival after a heart attack (myocardial infarct). The time of the initial infarct defines $t = 0$; if the origin had been started 2 or 3 years after the infarct, the large initial death rate would not have been seen.

As long as the rate of increase can be written as a function of the independent variable, Eq. 2.16 can be rewritten as $dy/y = b(x)dx$. This can be integrated:

$$\int_{y_1}^{y_2} \frac{dy}{y} = \int_{x_1}^{x_2} b(x) \, dx,$$

$$\ln(y_2/y_1) = \int_{x_1}^{x_2} b(x) \, dx,$$

$$\frac{y_2}{y_1} = \exp \left( \int_{x_1}^{x_2} b(x) \, dx \right). \qquad (2.17)$$

If we can integrate the right-hand side analytically, numerically, or graphically, we can determine the ratio $y_2/y_1$.
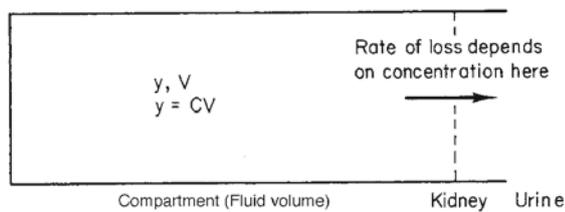
**Fig. 2.12** A case in which the rate of removal of a substance from the a fluid compartment depends on the concentration, not on the total amount of substance in the compartment. Increasing the compartment volume with the same concentration of the substance would not change the rate of removal

## 2.5 Clearance

In some cases in physiology, the amount of a substance may decay exponentially because the rate of removal is proportional to the concentration of the substance (amount per unit volume) instead of to the total amount. For example, the rate at which the kidneys excrete a substance may be proportional to the concentration in the blood that passes through the kidneys, while the total amount depends on the total fluid volume in which the substance is distributed. This is shown schematically in Fig. 2.12. The large box on the left represents the total fluid volume $V$. It contains a total amount of some substance, $y$. If the fluid is well mixed, the concentration is $C = y/V$. The removal process takes place only at the dashed line, at a rate proportional to $C$. The equation describing the change of $y$ is

$$\frac{dy}{dt} = -KC = -K\left(\frac{y}{V}\right). \qquad (2.18)$$

The proportionality constant $K$ is called the *clearance*. Its units are $m^3 s^{-1}$. The equation is the same as Eq. 2.6 if $K/V$ is substituted for $b$. The solution is

$$y = y_0 e^{-(K/V)t}. \qquad (2.19)$$

The basic concept of clearance is best remembered in terms of Fig. 2.12. Other definitions are found in the literature. It sometimes takes considerable thought to show that the definitions are equivalent. A common definition in physiology books is "*clearance is the volume of plasma from which y is completely removed per unit time.*" To see that this definition is equivalent, imagine that $y$ is removed from the body by removing a volume $V$ of the plasma in which the concentration of $y$ is $C$. The rate of loss of $y$ is the concentration times the rate of volume removal:

$$\frac{dy}{dt} = -\left|\frac{dV}{dt}\right| C. \qquad (2.20)$$

($dV/dt$ is negative for removal.) Comparison with Eq. 2.18 shows that $|dV/dt| = K$.

As long as the compartment containing the substance is well mixed, the concentration will decrease uniformly throughout the compartment as $y$ is removed. The concentration also decreases exponentially:

$$C = C_0 e^{-(K/V)t}. \qquad (2.21)$$

An example may help to clarify the distinction between $b$ and $K$. Suppose that the substance is distributed in a fluid volume $V = 18 l$. The substance has an initial concentration $C_0 = 3 mg l^{-1}$ and the clearance is $K = 2 l h^{-1}$. The total amount is $y_0 = C_0 V = 3 \times 18 = 54 mg$. The fractional decay rate is $b = K/V = 1/9 h^{-1}$. The equations for $C$ and $y$ are $C = (3 mg l^{-1})e^{-t/9}$, $y = (54 mg)e^{-t/9}$. At $t = 0$, the initial rate of removal is $-dy/dt = 54/9 = 6 mg h^{-1}$.

Now double the fluid volume to $V = 36 l$ without adding any more of the substance. The concentration falls to $1.5 mg l^{-1}$ although $y_0$ is unchanged. The rate of removal is also cut in half, since it is proportional to $K/V$ and the clearance is unchanged. The concentration and amount are now $C = 1.5 e^{-t/18}$, $y = 54 e^{-t/18}$. The initial rate of removal is $dy/dt = 54/18 = 3 mg h^{-1}$. It is half as large as above, because $C$ is now half as large.

If more of the substance were added along with the additional fluid, the initial concentration would be unchanged, but $y_0$ would be doubled. The fractional decay rate would still be $K/V = 1/18 h^{-1}$: $C = 3.0 e^{-t/18}$, $y = 108 e^{-t/18}$. The initial rate of disappearance would be $dy/dt = 108/18 = 6 mg h^{-1}$. It is the same as in the first case, because the initial concentration is the same.

## 2.6 The Chemostat

The *chemostat* is used by bacteriologists to study the growth of bacteria (Hagen 2010). It allows the rapid growth of bacteria to be observed over a longer time scale. Consider a container of bacterial nutrient of volume $V$. It is well stirred and contains $y$ bacteria with concentration $C = y/V$. Some of the nutrient solution is removed at rate $Q$ and replaced by fresh nutrient. The bacteria in the solution are reproducing at rate $b$. The rate of change of $y$ is

$$\frac{dy}{dt} = by - QC = by - \frac{Qy}{V}. \qquad (2.22)$$

Therefore the growth rate is slowed to

$$b - \frac{Q}{V}$$

and can be adjusted by varying $Q$.

## 2.7   Multiple Decay Paths

It is possible to have several independent paths by which $y$ can disappear. For example, there may be several competing ways by which a radioactive nucleus can decay, a radioactive isotope given to a patient may decay radioactively and be excreted biologically at the same time, a substance in the body can be excreted in the urine and metabolized by the liver, or patients may die of several different diseases.

In such situations the total decay rate $b$ is the sum of the individual rates for each process, as long as the processes act independently and the rate of each is proportional to the present amount (or concentration) of $y$:

$$\frac{dy}{dt} = -b_1 y - b_2 y - b_3 y - \cdots = -(b_1 + b_2 + b_3 + \cdots)y = -by.$$
(2.23)

The equation for the disappearance of $y$ is the same as before, with the total decay rate being the sum of the individual rates. The rate of disappearance of $y$ by the $i$th process *is not $dy/dt$* but is $-b_i y$. Instead of decay rates, one can use half-lives. Since $b = b_1 + b_2 + b_3 + \cdots$, the total half-life $T$ is given by

$$\frac{0.693}{T} = \frac{0.693}{T_1} + \frac{0.693}{T_2} + \frac{0.693}{T_3} + \cdots$$

or

$$\frac{1}{T} = \frac{1}{T_1} + \frac{1}{T_2} + \frac{1}{T_3} + \cdots.$$
(2.24)

## 2.8   Decay Plus Input at a Constant Rate

Suppose that in addition to the removal of $y$ from the system at a rate $-by$, $y$ enters the system at a constant rate $a$, independent of $y$ and $t$. The net rate of change of $y$ is given by

$$\frac{dy}{dt} = a - by.$$
(2.25)

It is often easier to write down a differential equation describing a problem than it is to solve it. In this case the solution to the equation and the techniques for solving it are well known. However, a good deal can be learned about the solution by examining the equation itself. Suppose that $y(0) = 0$. Then the equation at $t = 0$ is $dy/dt = a$, and $y$ initially grows at a constant rate $a$. As $y$ builds up, the rate of growth decreases from this value because of the $-by$ term. Finally when $a - by = 0$, $dy/dt$ is zero and $y$ stops growing. This is enough information to make the sketch in Fig. 2.13.

The equation is solved in Appendix F. The solution is

$$y = \frac{a}{b}\left(1 - e^{-bt}\right).$$
(2.26)

The derivative of $y$ is $dy/dt = \left(\frac{a}{b}\right)(-1)(-b)e^{-bt} = ae^{-bt}$.
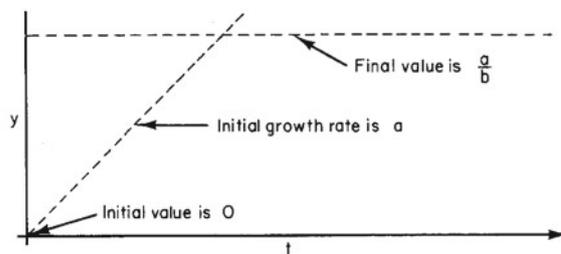


**Fig. 2.13**   Sketch of the initial slope $a$ and final value $a/b$ of $y$ when $y(0) = 0$
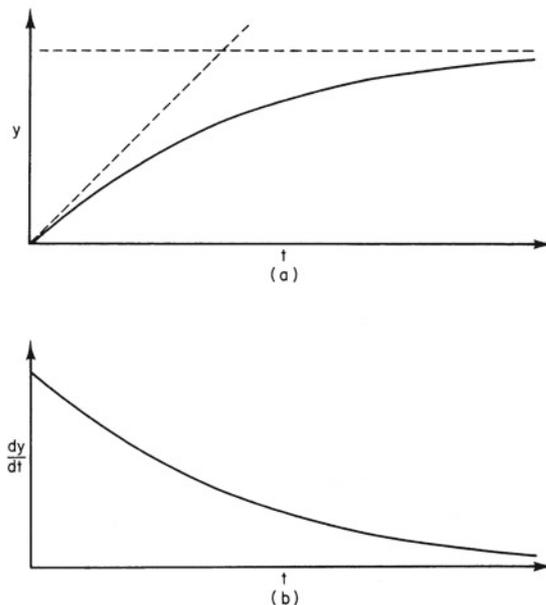


**Fig. 2.14**   **a** Plot of $y(t)$. **b** Plot of $dy/dt$

You can verify by substitution that Eq. 2.26 satisfies Eq. 2.25. The solution does have the properties sketched in Fig. 2.13, as you can see from Fig. 2.14. The initial value of $dy/dt$ is $a$, and it decreases exponentially to zero. When $t$ is large, the exponential term in $y$ vanishes, leaving $y = a/b$.

## 2.9   Decay With Multiple Half-Lives and Fitting Exponentials

Sometimes $y$ is a mixture of two or more quantities, each decaying at a constant rate. It might represent a mixture of radioactive isotopes, each decaying at its own rate. A biological example is the survival of patients after a myocardial infarct (Fig. 2.11). The death rate is not constant, and many models can be proposed to explain why. One possible model is that there are two distinct classes of patients immediately after the infarct. Each class has an associated death rate that
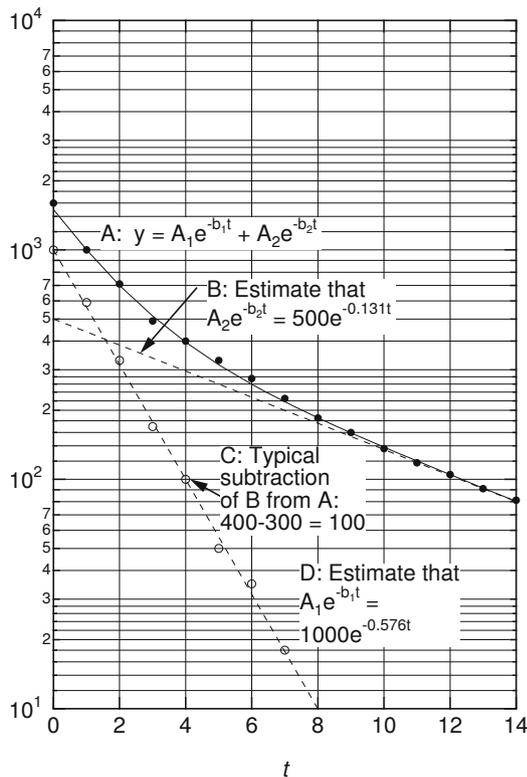
**Fig. 2.15** Fitting a curve with two exponentials

be subtracted from $y$ to give an estimate for $y_1$. For example, at point $C$ ($t = 4$), $y = 400$, $y_2 = 300$, and $y_1 = 100$. At $t = 0$, $y_1 = 1500 - 500 = 1000$. For times greater than 5 s, the curves for $y$ and $y_2$ are close together, and error in reading the graph produces considerable scatter in $y_1$. Once several values of $y_1$ have been determined, line $D$ is drawn, and parameters $A_1$ and $b_1$ are estimated.

This technique can be extended to several exponentials. However it becomes increasingly difficult to extract meaningful parameters as more exponentials are used, because the estimated parameters for the short-lived terms are very sensitive to the initial guess for the parameters of the longest-lived term. Fig. 2.6 suggests that estimating the parameters for the longest-lived term may be difficult because of the potentially large error bars associated with the data for small values of $y$. For a discussion of this problem, see Riggs (1970, pp. 146–163). A more modern and better way to fit multiple exponentials is the technique of nonlinear least squares. This is discussed in Sect. 11.2.

is constant. After 3 years, virtually none of the subgroup with the higher death rate remains. Another model is that the death rate is higher right after the infarct for all patients. This higher death rate is due to causes associated with the myocardial injury: irritability of the muscle, arrhythmias in the heartbeat, the weakening of the heart wall at the site of the infarct, and so forth. After many months, the heart has healed, scar tissue has replaced the necrotic (dead) muscle, and deaths from these causes no longer occur.

Whatever the cause, it is sometimes useful to fit a set of experimental data with a sum of exponentials. It should be clear from the discussion of survival after myocardial infarction that simply fitting with an exponential or a sum of exponentials does not prove anything about the decay mechanism.

If $y$ consists of two quantities, $y_1$ and $y_2$, each with its own decay rate, then

$$y = y_1 + y_2 = A_1 e^{-b_1 t} + A_2 e^{-b_2 t}. \qquad (2.27)$$

Suppose that $b_1 > b_2$, so that $y_1$ decays more rapidly than $y_2$. After enough time has elapsed, $y_1$ will be much less than $y_2$, and its effect on a semilog plot will be negligible. A typical plot of $y$ is curve $A$ in Fig. 2.15. Line $B$ can then be drawn through the data and used to determine $A_2$ and $b_2$. This line is extrapolated back to earlier times, so that $y_2$ can

## 2.10 The Logistic Equation

Exponential growth cannot go on forever. This fact is often ignored by economists and politicians. Albert Bartlett has written extensively on this subject. You can find several references in *The American Journal of Physics* and *The Physics Teacher*. See the summary in Bartlett (2004).

Sometimes a growing population will level off at some constant value. Other times the population will grow and then crash. One model that exhibits leveling off is the *logistic model*, described by the differential equation

$$\frac{dy}{dt} = b_0 y \left( 1 - \frac{y}{y_\infty} \right), \qquad (2.28)$$

where $b_0$ and $y_\infty$ are constants. This equation has constant solutions $y = 0$ and $y = y_\infty$. If $y \ll y_\infty$, then the equation is approximately $dy/dt = b_0 y$ and $y$ grows exponentially. As $y$ becomes larger, the term in parentheses reduces the rate of increase of $y$, until $y$ reaches the saturation value $y_\infty$. This might happen, for example, as the population begins to consume a significant fraction of the food supply, causing the birth rate to decrease or the mortality rate to increase.

If the initial value of $y$ is $y_0$, the solution of Eq. 2.28 is

$$y(t) = \frac{1}{\dfrac{1}{y_\infty} + \left( \dfrac{1}{y_0} - \dfrac{1}{y_\infty} \right) e^{-b_0 t}} \qquad (2.29)$$

$$= \frac{y_0 y_\infty}{y_0 + (y_\infty - y_0) e^{-b_0 t}}.$$
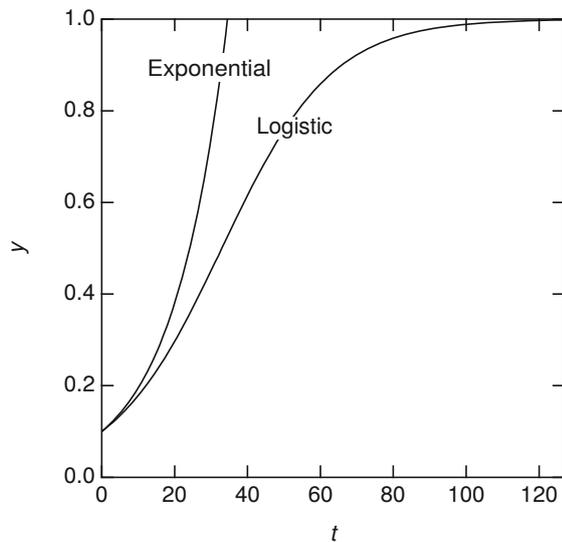
**Fig. 2.16** Plot of the solution of the logistic equation when $y_0 = 0.1$, $y_\infty = 1.0$, $b_0 = 0.0667$. Exponential growth with the same values of $y_0$ and $b_0$ is also shown



**Fig. 2.17** Log–log plots of $y = x^n$ for different values of $n$. When $x = 1$, $y = 1$ in every case

You can easily verify that $y(0) = y_0$ and $y(\infty) = y_\infty$. A plot of the solution is given in Fig. 2.16, along with exponential growth with the same value of $b_0$.

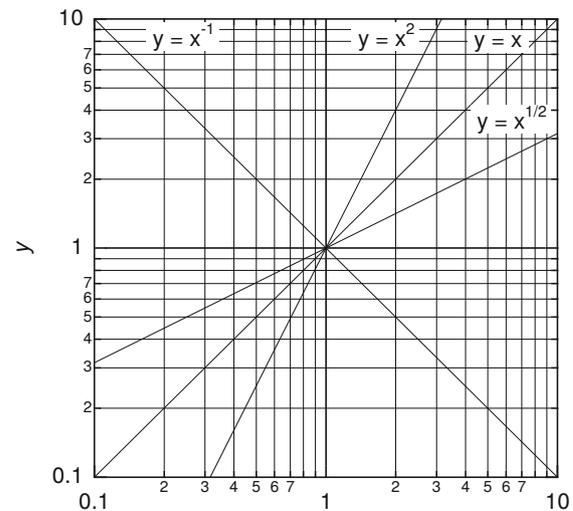Another way to think of Eq. 2.28 is that it has the form $dy/dt = b(y)y$, where $b(y) = b_0(1 - y/y_\infty)$ is now a function of the dependent variable $y$ instead of the independent variable $t$. As $y$ grows toward the asymptotic value, the growth rate $b(y)$ decreases linearly to zero. The logistic model was an early and very important model for population growth. It provides good fits in a few cases, but there are now many more sophisticated models in population biology (Murray 2001) and bacterial growth (Hagen 2010).

## 2.11 Log–log Plots, Power Laws, and Scaling

This section considers the use of plots in which both scales are logarithmic: log–log plots. They are useful when $x$ and $y$ are related by the power law

$$y = Bx^n. \tag{2.30}$$

Notice the difference between this and the exponential function: here the independent variable $x$ is *raised to a constant power*, while in the exponential case, $x$ (or $t$) is *in the exponent*. It also leads to a discussion of *scaling*, whereby simple physical arguments lead to important conclusions about the variations between species in size, shape, metabolic rate, and the like.

### 2.11.1 Log–log Plots and Power Laws

By taking logarithms of both sides of Eq. 2.30, we get

$$\log y = \log B + n \log x. \tag{2.31}$$

This is a linear relationship between $u = \log y$ and $v = \log x$:

$$u = \text{const} + nv. \tag{2.32}$$

Therefore a plot of $u$ vs $v$ is a straight line with slope $n$. The slope can be positive or negative and need not be an integer. Figure 2.17 shows plots of $y = x$, $y = x^2$, $y = x^{1/2}$, and $y = x^{-1}$. The slope can be determined from the graph by taking $\Delta u/\Delta v$. The value of $B$ is determined either by substituting particular values of $y$ and $x$ in Eq. 2.30 after $n$ is known, or by determining the value of $y$ when $x = 1$, in which case $x^n = 1$ for any value of $n$, so $n$ need not be known.

Figure 2.18 shows how the curves change when $B$ is changed while $n = 1$. The curves are all parallel to each other. Multiplying by $B$ is equivalent to adding a constant to $\log y$.

If the expression is not of the form $y = Bx^n$ but has an added term, it will not plot as a straight line on log–log paper. Figure 2.18 also shows a plot of $y = x + 1$, which is not a straight line. (Of course, for very large values of $x$, $\log(x + 1)$ becomes nearly indistinguishable from $\log x$, and the line appears straight.)

When the slope is constant, $n$ can be determined from the slope $\Delta u/\Delta v$ measured with a ruler on the log–log paper. When determining the slope in this way *one must be sure that the length of a cycle is the same in each direction on the*
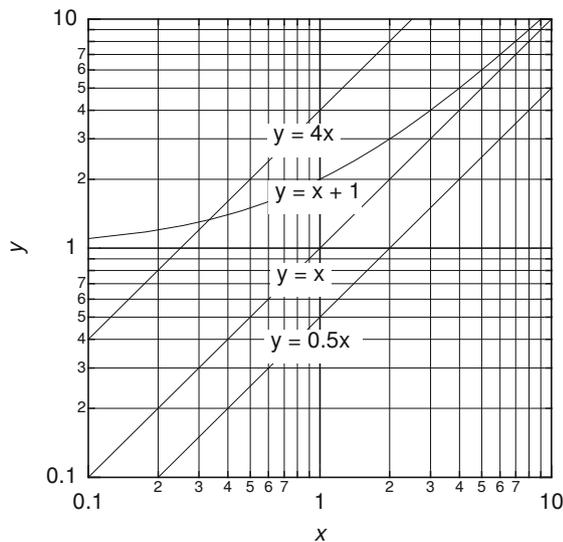
**Fig. 2.18** Log–log plots of $y = Bx$, showing how the curves shift on the paper as $B$ changes. Since $n = 1$ for all the curves, they all have the same slope. There is also a plot of $y = x + 1$ to show that a polynomial does not plot as a straight line
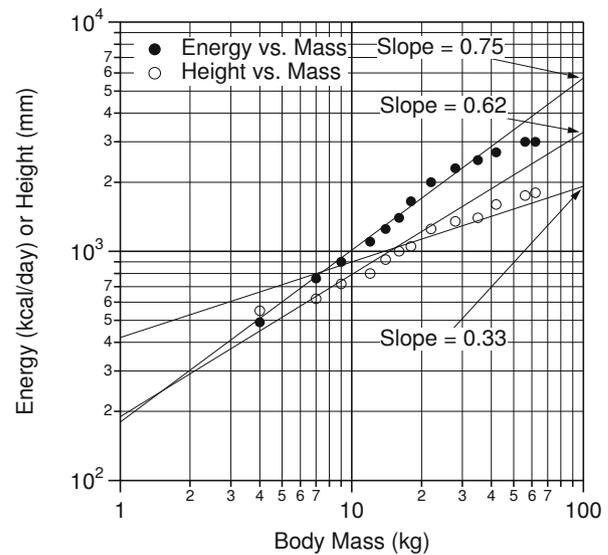


**Fig. 2.19** Plot of daily food requirement $F$ and height $H$ vs mass $M$ for growing children. (Data are from Kempe et al. 1970, p. 90)

*graph paper*. To repeat the warning: it is easy to get a rough idea of the exponent from inspection of the slope of the log–log plot in Fig. 2.17 because on commercial log–log graph paper, the distance spanned by a decade or cycle is the same on both axes. Some magazines routinely show log–log plots in which the distance spanned by a decade is not the same on both axes. Moreover, commercial graphing software does not impose this constraint on log–log plots, so it is becoming less and less likely that you can determine the exponent by glancing at the plot. Be careful!

When using a spreadsheet or other graphing software, it is often useful to make an extra column that contains the calculated variable $y_{calc} = Ax^m$ with the values for $A$ and $m$ stored in two cells of the spreadsheet. If you plot this column as a line, and your real data as points without a line, then you can change the parameters while inspecting the graph to find the values that give the best fit.

An example of the use of a log–log plot is Poiseuille flow of fluid through a tube vs tube radius when the pressure gradient along the tube is constant (Problem 39). It was shown in Chap. 1 that an $r^4$ dependence is expected.

## 2.11.2 Food Consumption, Basal Metabolic Rate, and Scaling

Consider the relation of daily food consumption to body mass. This will introduce us to simple scaling arguments. As a first model, we might suppose that each kilogram of

tissue has the same metabolic requirement, so that food consumption should be proportional to body mass. However, there is a problem with this argument. Most of the food that we consume is converted to heat. The various mechanisms to lose heat—radiation, convection, and perspiration—are all roughly proportional to the surface area of the body rather than its mass. (This statement neglects the fact that considerable evaporation takes place through the lungs and that the body can control the rate of heat loss through sweating and shivering.) If all persons were the same shape, then the total surface area would be proportional to $H^2$, where $H$ is the height. The total volume and mass would be proportional to $H^3$, so $H$ would be proportional to $M^{1/3}$. Therefore the surface area would be proportional to $(M^{1/3})^2$ or $M^{2/3}$. (See Problem 44 for a discussion of other possible dependences of surface area on mass.) Figure 2.19 plots $H$ and the total daily food requirement $F$ vs body mass $M$ for growing children (Kempe et al. 1970, p. 90).

Neither of the models proposed above fits the data very well. At early ages, $H$ is more nearly proportional to $M^{0.62}$ than to $M^{1/3}$. For older children, when the shape of the body has stopped changing, an $M^{0.33}$ dependence does fit better. This better fit occurs for masses greater than 23 kg, which correspond to ages over 6 years. The slope of the $F(M)$ curve is 0.75. This is less than the 1.0 of the model that food consumption is proportional to the mass and greater than the 0.67 of the model that food consumption is proportional to surface area.

This $\frac{3}{4}$-power dependence is remarkable because it is seen across many species, from one-celled organisms to
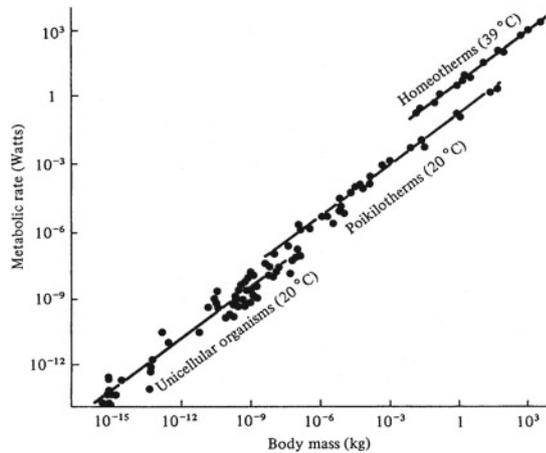
**Fig. 2.20** Plot of resting metabolic rate vs. body mass for many different organisms. (Graph is from R. H. Peters 1983. Modified from A. M. Hemmingsen 1960). Used with permission

large mammals. It is called *Kleiber's law*. Peters (1983) quotes work by Hemmingsen (1960) that shows the standard metabolic rates for many species can be fitted by the following. The standard metabolic rate is in watts and mass in kilograms. (*Standard* means as close to resting or basal as possible.) For unicellular organisms at 20 °C,

$$R_{\text{unicellular}} = 0.018M^{0.751}. \qquad (2.33a)$$

The range of masses extended from $10^{-15}$ to $10^{-6}$ kg. For *poikilotherms* (organisms such as fish whose body temperature is the same as the surroundings) at 20 °C (masses from $10^{-8}$ to $10^2$ kg),

$$R_{\text{poikilotherm}} = 0.14M^{0.751}, \qquad (2.33b)$$

and for *homeotherms* (animals that can maintain their body temperature independent of the surroundings) at 39 °C (masses from $10^{-2}$ to $10^3$ kg),

$$R_{\text{homeotherm}} = 4.1M^{0.751}. \qquad (2.33c)$$

Peters' graph is shown in Fig. 2.20.

A number of models have been proposed to explain a $\frac{3}{4}$-power dependence (McMahon 1973; Peters 1983; West et al. 1999; Banavar et al. 1999). West and his coworkers argue that the $\frac{3}{4}$-power law is universal (Brown et al. 2004; West and Brown 2004). They derive it from a model that supplies nutrients through a branching network that reaches all parts of the organism, minimizes the energy required for distribution, and ends in capillaries (or terminal xylem in plants) that are all the same size. Whether it is universal is still debated (White and Seymour 2003; Glazier 2005).

## Symbols Used in Chap. 2

| Symbol | Use | Units | First used page |
|---|---|---|---|
| $a$ | Rate of input of a substance | $s^{-1}$ | 41 |
| $b, b_0$ | Rate of growth or decay | $s^{-1}, h^{-1}$ | 33 |
| $c_1, c_2$ | Constants | | 36 |
| $f$ | Fraction | | 35 |
| $m, n$ | Exponent in power–law relationship | | 43 |
| $t$ | Time | s | 34 |
| $u$ | Logarithm of dependent variable | | 36 |
| $v$ | Logarithm of independent variable | | 43 |
| $x$ | General independent variable | | 35 |
| $y$ | General dependent variable | | 33 |
| $y$ | Amount of substance in plasma | kg, mg | 40 |
| $x_0, y_0$ | Initial value of $x$ or $y$ | | 33 |
| $y_\infty$ | Saturation value of $y$ | | 42 |
| $A$ | Constant | | 42 |
| $B$ | Constant | | 43 |
| $C$ | Concentration | kg m$^{-3}$, etc. | 40 |
| $F$ | Food requirement | kcal day$^{-1}$ | 44 |
| $H$ | Body height | m | 44 |
| $K$ | Clearance | m$^3$ s$^{-1}$ | 40 |
| $M$ | Body mass | kg | 44 |
| $N$ | Number of compoundings per year | | 34 |
| $Q$ | Flow through chemostat | m$^3$ s$^{-1}$ | 40 |
| $R$ | Standard metabolic rate | W | 45 |
| $T_{1/2}$ | Half-life | s, etc. | 35 |
| $T_2$ | Doubling time | s | 36 |
| $V$ | Volume | m$^3$ | 40 |
| $X_{10}$ | Change in $x$ for a factor-of-10 change in $y$ | | 36 |
| $X_{100}$ | Change in $x$ for a factor-of-100 change in $y$ | | 37 |

## Problems

### Section 2.1

**Problem 1.** Suppose that you are 20 years old and have an annual income of $20,000. You plan to work for 40 years. If inflation takes place at a rate of 3 % per year, what income would you need at age 60 to have the same buying power you have now? Ignore taxes. Make the calculation assuming that (a) inflation is 3 % and occurs once a year and (b) inflation is continuous but at a 3 % annual rate.

**Problem 2.** The number $e$ is defined by $\lim_{n\to\infty}(1+1/n)^n$.

(a) Calculate values of $(1 + 1/n)^n$ for $n = 1, 2, 4, 8,$ and 16.

(b) Use the binomial formula $(1 + a)^n = 1 + na + \frac{n(n-1)}{2!}a^2 + \frac{n(n-1)(n-2)}{3!}a^3 + \cdots$ to obtain a series for $e^x = \lim_{n\to\infty}(1 + x/n)^n$. [See also Appendix D, Eq. D.3.]

**Problem 3.** A child with acute lymphocytic leukemia (ALL) has approximately $10^{12}$ leukemic cells when the disease is clinically apparent.

(a) If a cell is about 8 μm in diameter, estimate the total mass of leukemic cells.

(b) Cure requires killing every single cell. The doubling time for the cells is about 5 days. If all cells were killed except for one, how long would it take for the disease to become apparent again?

(c) Suppose that chemotherapy reduces the number of cells to $10^9$ and there are no changes of ALL cell properties (no mutations). How long a remission would you expect? What if the number were reduced to $10^6$?

**Problem 4.** Suppose that tumor cells within the body reproduce at rate $r$, so that the number is given by $y = y_0 e^{rt}$. Each time a chemotherapeutic agent is given, it destroys a fraction $f$ of the cells then existing. Make a semilog plot showing $y$ as a function of time for several administrations of the drug, separated by time $T$. What different cases must you consider for the relation among $f$, $T$, and $r$?

**Problem 5.** An exponentially growing culture of bacteria increases from $10^6$ to $5 \times 10^8$ cells in 6 h. What is the time between successive cell divisions if there is no cell mortality?

**Problem 6.** The following data on railroad tracks were obtained from R. H. Romer (1991).

| Year | Miles of track |
|------|----------------|
| 1860 | 30,626 |
| 1870 | 52,922 |
| 1880 | 93,262 |
| 1890 | 166,703 |

(a) What is the doubling time?

(b) Estimate the surface area of the contiguous USA. Assume that a railroad roadbed is 7-m wide. In what year would an extrapolation predict that the surface of the USA would be completely covered with railroad track?

## Section 2.2

**Problem 7.** A dose $D$ of drug is given that causes the plasma concentration to rise from 0 to $C_0$. The concentration then falls according to $C = C_0 e^{-bt}$. At time $T$, what dose must be given to raise the concentration to $C_0$ again? What will happen if the original dose is administered over and over again at intervals of $T$?

**Problem 8.** Consider the atmosphere to be at constant temperature but to have a pressure $p$ that varies with height $y$. A slab between $y$ and $y + dy$ has a different pressure on the top than on the bottom because of the weight of the air in the slab. (The weight of the air is the number of molecules $N$ times $mg$, where $m$ is the mass of a molecule and $g$ is the gravitational acceleration.) Use the ideal gas law, $pV = Nk_B T$ (where $k_B$ is the Boltzmann constant and $T$, the absolute temperature, is constant), and the fact that the air is in equilibrium to write a differential equation for $p$ as

a function of $y$. The equation should be familiar. Show that $p(y) = Ce^{-mgy/k_B T}$.

**Problem 9.** The mean life of a radioactive substance is defined by the equation

$$\tau = \frac{-\int_0^\infty t \, (dy/dt) \, dt}{-\int_0^\infty (dy/dt) \, dt}.$$

Show that if $y = y_0 e^{-bt}$, then $\tau = 1/b$.

## Section 2.3

**Problem 10.** R. Guttman (1966) measured the temperature dependence of the current pulse necessary to excite the squid axon. She found that for pulses shorter than a certain length $\tau$, a fixed amount of electric charge was necessary to make the nerve fire; for longer pulses, the current was fixed. This suggests that the axon integrates the current for a time $\tau$ but no longer. The following data are for the integrating time $\tau$ vs temperature $T$ (°C). Find an empirical exponential relationship between $T$ and $\tau$.

| $T$ (°C) | $\tau$ (ms) |
|----------|-------------|
| 5 | 4.1 |
| 10 | 3.4 |
| 15 | 1.9 |
| 20 | 1.4 |
| 25 | 0.7 |
| 30 | 0.6 |
| 35 | 0.4 |

**Problem 11.** A normal rabbit was injected with 1 cm$^3$ of *Staphylococcus aureus* culture containing $10^8$ organisms. At various later times, 0.2 cm$^3$ of blood was taken from the rabbit's ear. The number of organisms per cm$^3$ was calculated by diluting the material, smearing it on culture plates, and counting the number of colonies formed. The results are shown below. Plot these data and see if they can be fit by a single exponential. Can you also estimate the blood volume of the rabbit?

| $t$ (min) | Bacteria (cm$^{-3}$) |
|-----------|----------------------|
| 0 | $5 \times 10^5$ |
| 3 | $2 \times 10^5$ |
| 6 | $5 \times 10^4$ |
| 10 | $7 \times 10^3$ |
| 20 | $3 \times 10^2$ |
| 30 | $1.7 \times 10^2$ |

## Section 2.4

**Problem 12.** All members of a certain population are born at $t = 0$. The death rate in this population (deaths per unit

population per unit time) is found to increase linearly with age $t$: (death rate) $= a+bt$. Find the population as a function of time if the initial population is $y_0$.

**Problem 13.** The accompanying table gives death rates (in $\text{yr}^{-1}$) as a function of age. Plot these data on linear graph paper and on semilog paper. Find a region over which the death rate rises approximately exponentially with age, and determine parameters to describe that region.

| Age | Death rate | Age | Death rate |
|-----|-----------|-----|-----------|
| 0   | 0.000 863 | 45  | 0.005 776 |
| 5   | 0.000 421 | 50  | 0.008 986 |
| 10  | 0.000 147 | 55  | 0.013 748 |
| 15  | 0.001 027 | 60  | 0.020 281 |
| 20  | 0.001 341 | 65  | 0.030 705 |
| 25  | 0.001 368 | 70  | 0.046 031 |
| 30  | 0.001 697 | 75  | 0.066 196 |
| 35  | 0.002 467 | 80  | 0.101 443 |
| 40  | 0.003 702 | 85  | 0.194 197 |

**Problem 14.** Suppose that the amount of a resource at time $t$ is $y(t)$. At $t = 0$, the amount is $y_0$. The rate at which it is consumed is $r = -dy/dt$. Let $r = r_0 e^{bt}$, that is, the rate of use increases exponentially with time. (For example, until recently the world use of crude oil had been increasing about 7 % per year since 1890.)

(a) Show that the amount remaining at time $t$ is $y(t) = y_0 - (r_0/b)(e^{bt} - 1)$.

(b) If the present supply of the resource were used up at constant rate $r_0$, it would last for a time $T_c$. Show that when the rate of consumption grows exponentially at rate $b$, the resource lasts a time $T_b = (1/b) \ln(1 + bT_c)$.

(c) An advertisement in *Scientific American*, September 1978, p. 181, said, "There's still twice as much gas underground as we've used in the past 50 years—at our present rate of use, that's enough to last about 60 years." Calculate how long the gas would last if it were used at a rate that increases 7 % per year.

(d) If the supply of gas were doubled, how would the answer to part (c) change?

(e) Repeat parts (c) and (d) if the growth rate is 3 % per year.

**Problem 15.** When we are dealing with death or component failure, we often write Eq. 2.17 in the form $y(t) = y_0 \exp\left[-\int_0^t m(t')dt'\right]$ and call $m(t)$ the *mortality function*. Various forms for the mortality function can represent failure of computer components, batteries in pacemakers, or the death of organisms. (This is not the most general possible mortality model. For example, it ignores any interaction between organisms, so it cannot account for effects such as overcrowding or a limited supply of nutrients.)

(a) For human populations, the mortality function is often written as $m(t) = m_1 e^{-b_1 t} + m_2 + m_3 e^{+b_3 t}$. What sort of processes does each of these terms represent?

(b) Assume that $m_1$ and $m_2$ are zero. Then $m(t)$ is called the *Gompertz mortality function*. Obtain an expression for $y(t)$ with the Gompertz mortality function. Time $t_{max}$ is sometimes defined to be the time when $y(t) = 1$. It depends on $y_0$. Obtain an expression for $t_{max}$.

**Problem 16.** The *incidence* of a disease is the number of new cases per unit time per unit population (or per 100,000). The *prevalence* of the disease is the number of cases per unit population. For each situation below, the size of the general population remains fixed at the constant value $y$, and the disease has been present for many years.

(a) The incidence of the disease is a constant, $i$ cases per year. Each person has the disease for a fixed time of $T$ years, after which the person is either cured or dies. What is the prevalence $p$? Hint: the number who are sick at time $t$ is the total number who became sick between $t - T$ and $t$.

(b) The patients in part (a) who are sick die with a constant death rate $b$. What is the prevalence?

(c) A new epidemic begins at $t = 0$, and the incidence increases exponentially with time: $i = i_0 e^{kt}$. What is the prevalence if each person has the disease for $T$ years?

## Section 2.5

**Problem 17.** The creatinine clearance test measures a patient's kidney function. Creatinine is produced by muscle at a rate $p\,\text{g h}^{-1}$. The concentration in the blood is $C\,\text{g l}^{-1}$. The volume of urine collected in time $T$ (usually 24 h) is $V$ l. The creatinine concentration in the urine is $U\,\text{g l}^{-1}$. The clearance is $K$. The plasma volume is $V_p$. Assume that creatinine is stored only in the plasma.

(a) Draw a block diagram for the process and write a differential equation for $C$.

(b) Find an expression for the creatinine clearance $K$ in terms of $p$ and $C$ when $C$ is not changing with time.

(c) If $C$ is constant, all creatinine produced in time $T$ appears in the urine. Find $K$ in terms of $C$, $V$, $U$, and $T$.

(d) If $p$ were somehow doubled, what would be the new steady-state value of $C$? What would be the time constant for change to the new value?

**Problem 18.** A liquid is injected in muscle and spreads throughout a spherical volume $V = 4\pi r^3/3$. The volume is well supplied with blood, so that the liquid is removed at a rate proportional to the remaining mass per unit volume. Let the mass be $m$ and assume that $r$ remains fixed. Find a differential equation for $m(t)$ and show that $m$ decays exponentially.

**Problem 19.** A liquid is injected as in Problem 18, but this time a cyst is formed. The rate of removal of mass is proportional to both the pressure of liquid within the cyst, and

to the surface area of the cyst, which is $4\pi r^2$. Assume that the cyst shrinks so that the pressure of liquid within the cyst remains constant. Find a differential equation for the rate of mass removal and show that $dm/dt$ is proportional to $m^{2/3}$.

**Problem 20.** The following data showing ethanol concentration in the blood vs time after ethanol ingestion are from Bennison and Li (1976, pp. 9–13). Plot the data and discuss the process by which alcohol is metabolized.

| $t$ (min) | Ethanol concentration (mg dl$^{-1}$) |
|:---:|:---:|
| 90 | 134 |
| 120 | 120 |
| 150 | 106 |
| 180 | 93 |
| 210 | 79 |
| 240 | 65 |
| 270 | 50 |

**Problem 21.** Consider the following two-compartment model. Compartment 1 is damaged myocardium (heart muscle). Compartment 2 is the blood of volume $V$. At $t = 0$, the patient has a heart attack and compartment 1 is created. It contains $q$ molecules of some chemical that was released by the dead cells. Over the next several days, the chemical moves from compartment 1 to compartment 2 at a rate $i(t)$, such that $q = \int_0^\infty i(t)dt$. The amount of substance in compartment 2 is $y(t)$ and the concentration is $C(t)$. The only mode of removal from compartment 2 is clearance with clearance constant $K$.

(a) Write a differential equation for $C(t)$ that may also involve $i(t)$.
(b) Integrate the equation and show that $q$ can be determined by numerical integration if $C(t)$ and $K$ are known.
(c) Show that volume $V$ need not be known if $C(0) = C(\infty)$.

## Section 2.7

**Problem 22.** The radioactive nucleus $^{64}$Cu decays independently by three different paths. The relative decay rates of these three modes are in the ratio 2:2:1. The half-life is 12.8 h. Calculate the total decay rate $b$, and the three partial decay rates $b_1$, $b_2$, and $b_3$.

**Problem 23.** The following data were taken from Berg et al. (1982). At $t = 0$, a 70-kg subject was given an intravenous injection of 200 mg of phenobarbital. The initial concentration in the blood was 6 mg l$^{-1}$. The concentration decayed exponentially with a half-life of 110 h. The experiment was repeated, but this time the subject was fed 200 g of activated charcoal every 6 h. The concentration of phenobarbital again fell exponentially, but with a half-life of 45 h.

(a) What was the volume in which the phenobarbital was distributed?

(b) What was the clearance in the first experiment?
(c) What was the clearance due to charcoal?

## Section 2.8

**Problem 24.** You are treating a severely ill patient with an intravenous antibiotic. You give a loading dose $D$ mg, which distributes immediately through blood volume $V$ to give a concentration $C$ mg dl$^{-1}$ (1 dl $= 0.1$ l). The half-life of this antibiotic in the blood is $T$ h. If you are giving an intravenous glucose solution at a rate $R$ ml h$^{-1}$, what concentration of antibiotic should be in the glucose solution to maintain the concentration in the blood at the desired value?

**Problem 25.** The solution to the differential equation $dy/dt = a - by$ for the initial condition $y(0) = 0$ is $y = (a/b)(1 - e^{-bt})$. Plot the solution for $a = 5$ g min$^{-1}$ and for $b = 0.1, 0.5$, and $1.0$ min$^{-1}$. Discuss why the final value and the time to reach the final value change as they do. Also make a plot for $b = 0.1$ and $a = 10$ to see how that changes the situation.

**Problem 26.** Derive an approximate expression for $(a/b)\left(1 - e^{-bt}\right)$ which is accurate for small times ($t \ll 1/b$). Use the Taylor expansion for an exponential given in Appendix D.

**Problem 27.** We can model the repayment of a mortgage with a differential equation. Suppose that $y(t)$ is the amount still owed on the mortgage at time $t$, the rate of repayment per unit time is $a$, $b$ is the interest rate, and the initial amount of the mortgage is $y_0$.

(a) Find the differential equation for $y(t)$.
(b) Try a solution of the form $y(t) = a/b + Ce^{bt}$, where $C$ is a constant to be determined from the initial conditions. Find $C$, plot the solution, and determine the time required to pay off the mortgage.

**Problem 28.** When an animal of mass $m$ falls in air, two forces act on it: gravity, $mg$, and a force due to air friction. Assume that the frictional force is proportional to the speed $v$.

(a) Write a differential equation for $v$ based on Newton's second law, $F = m(dv/dt)$.
(b) Solve this differential equation (hint: compare your equation to Eq. 2.25).
(c) Assume that the animal is spherical, with radius $a$ and density $\rho$. Also, assume that the frictional force is proportional to the surface area of the animal. Determine the terminal speed (speed of descent in steady state) as a function of $a$.
(d) Use your result in part (c) to interpret the following quote by J. B. S. Haldane (1985): "You can drop a mouse down a thousand-yard mine shaft; and arriving at the bottom, it gets a slight shock and walks away. A rat is killed, a man is broken, a horse splashes."

**Problem 29.** In Problem 28, we assumed that the force of air friction is proportional to the speed $v$. For flow at high Reynolds numbers, a better approximation is that the force is $-kv^2$.

(a) Write the differential equation for $v$ as a function of $t$.

(b) This differential equation is nonlinear because of the $v^2$ term and thus difficult to solve analytically. However, the terminal speed can easily be obtained directly from the differential equation by setting $dv/dt = 0$. Find the terminal speed as a function of $a$ (defined in Problem 28).

(c) Verify that $v(t) = \sqrt{mg/k} \tanh\left(\sqrt{kg/m}\,t\right)$ is a solution.

**Problem 30.** A drug is infused into the body through an intravenous drip at a rate of $100\,\mathrm{mg\,h^{-1}}$. The total amount of drug in the body is $y$. The drug distributes uniformly and instantaneously throughout the body in a compartment of volume $V = 18\,\mathrm{l}$. It is cleared from the body by a single exponential process. In the steady state, the total amount in the body is 200 mg.

(a) At noon ($t = 0$), the intravenous line is removed. What is $y(t)$ for $t > 0$?

(b) What is the clearance of the drug?

## Section 2.9

**Problem 31.** You are given the following data:

| $x$ | $y$ | $x$ | $y$ |
|---|---|---|---|
| 0 | 1.000 | 5 | 0.444 |
| 1 | 0.800 | 6 | 0.400 |
| 2 | 0.667 | 7 | 0.364 |
| 3 | 0.571 | 8 | 0.333 |
| 4 | 0.500 | 9 | 0.308 |
| | | 10 | 0.286 |

Plot these data on semilog graph paper. Is this a single exponential? Is it two exponentials? Plot $1/y$ vs $x$. Does this alter your answer?

**Problem 32.** Cells can repair DNA damage caused by x-ray exposure (see Sect. 16.9). Wang et al. (2001) found that the amount of damage is characterized by two time constants. Assume the DNA damage, $D$, as a function of time, $t$, is given by the following data

| $t$ (h) | $D(\%)$ | $t$ (h) | $D(\%)$ |
|---|---|---|---|
| 0 | 100 | 1.5 | 16 |
| 0.25 | 46 | 2 | 14 |
| 0.50 | 28 | 4 | 9.0 |
| 0.75 | 21 | 6 | 5.8 |
| 1.0 | 18 | 8 | 3.7 |

Plot the data on semilog paper. Fit the data to Eq. 2.27 by eye or using a spreadsheet and determine $A_1$, $A_2$, $b_1$, and $b_2$.

Note that the data are normalized to $100\,\%$ at $t = 0$. What does this mean in terms of $A_1$ and $A_2$?

## Section 2.10

**Problem 33.** Suppose that the rate of consumption of a resource increases exponentially. (This might be petroleum, or the nutrient in a bacterial culture.) During the first doubling time, the amount used is 1 unit. During the second doubling time, it is 2 units, the next 4, etc. How does the amount consumed during a doubling time compare to the total amount consumed during all previous doubling times?

**Problem 34.** Suppose that the rate of growth of $y$ is described by $dy/dt = b(y)y$. Expand $b(y)$ in a Taylor's series and relate the coefficients to the terms in the logistic equation.

**Problem 35.** Verify that the solution $y(t)$ in Eq. 2.29 obeys the differential Eq. 2.28.

**Problem 36.** In the logistic model (Eq. 2.28), what value of $y$ corresponds to the maximum rate of change of $y$?

**Problem 37.** The consumption of a finite resource is often modeled using the logistic equation. Let $y(t)$ be the cumulative amount of a resource consumed and $y_\infty$ be the total amount that was initially available at $t = -\infty$. Model the rate of consumption using Eq. 2.29 over the range $-\infty < t < \infty$.

(a) Set $y_0 = y_\infty/2$, so that the zero of the time axis correponds to when half the resource has been used. Show that this simplifies Eq. 2.29.

(b) Differentiate $y(t)$ to find an expression for the rate of consumption. Sketch plots of $dy/dt$ vs $t$ on linear and semilog graph paper. When does the peak rate of consumption occur?

When this model is applied to world oil consumption, the maximum is called *Hubbert's peak* (Deffeyes 2008).

**Problem 38.** Consider a classic predator–prey problem. Let the number of foxes be $F$ and the number of rabbits be $R$. The rabbits eat grass, which is plentiful. The foxes eat only rabbits. The number of foxes and rabbits can be modeled by the *Lotka–Volterra equations*

$$\frac{dR}{dt} = aR - bRF$$

$$\frac{dF}{dt} = -cF + dRF.$$

(a) Describe the physical meaning of each term on the right-hand side of each equation. What does each of the constants $a$, $b$, $c$, and $d$ denote?

(b) Solve for the steady-state values of $F$ and $R$.

These differential equations are difficult to solve because they are nonlinear (see Chap. 10). Typically, $R$ and $F$ oscillate about the steady-state solutions found in (b). For more information, see Murray (2001).

## Section 2.11

**Problem 39.** Plot the following data for Poiseuille flow on log–log graph paper. Fit the equation $i = C R_p^n$ to the data by eye (or by trial and error using a spread sheet), and determine $C$ and $n$.

| $R_p(\mu m)$ | $i(\mu m^3 s^{-1})$ |
|---|---|
| 5 | 0.000 10 |
| 7 | 0.000 38 |
| 10 | 0.001 6 |
| 15 | 0.008 1 |
| 20 | 0.026 |
| 30 | 0.13 |
| 50 | 1.0 |

**Problem 40.** Below are the molecular weights and radii of some molecules. Use log–log graph paper to develop an empirical relationship between them.

| Substance | $M$ | $R$ (nm) |
|---|---|---|
| Water | 18 | 0.15 |
| Oxygen | 32 | 0.20 |
| Glucose | 180 | 0.39 |
| Mannitol | 180 | 0.36 |
| Sucrose | 390 | 0.48 |
| Raffinose | 580 | 0.56 |
| Inulin | 5 000 | 1.25 |
| Ribonuclease | 13,500 | 1.8 |
| $\beta$-lactoglobin | 35,000 | 2.7 |
| Hemoglobin | 68,000 | 3.1 |
| Albumin | 68,000 | 3.7 |
| Catalase | 250,000 | 5.2 |

**Problem 41.** How well does Eq. 2.33c explain the data of Fig. 2.19? Discuss any differences.

**Problem 42.** Compare the mass and metabolic requirements (and hence waste output, including water vapor) of 180 people each weighing 70 kg with 12,600 chickens of average mass 1 kg.

**Problem 43.** Figure 2.19 shows that in young children, height is more nearly proportional to $M^{0.62}$ than to $M^{1/3}$. Find pictures of children and adults and compare ratios of height to width, to see what the differences are.

**Problem 44.** Consider three models of an organism. The first is a sphere of radius $R$. The second is a cube of length $L$. These are crude models for animals. The third is a broad leaf of surface area $A$ on each side and thickness $t$. Assume all have density $\rho$. In each case, calculate the surface area $S$ as a function of mass, $M$. Ignore the surface area of the edge of the leaf. (For a comparison of scaling in leaves and animals, see Reich (2001). He shows that for broad leaves, $S \propto M^{1.1}$.)

**Problem 45.** If food consumption is proportional to $M^{3/4}$ across species, how does the food consumption per unit mass scale with mass? Qualitatively compare the eating habits of hummingbirds to eagles and mice to elephants. (See Schmidt-Nielsen 1984, pp. 62–64.)

**Problem 46.** In Problem 45, you found how the specific metabolic rate (food consumption per unit mass) varies with mass. If all animal heart volumes and blood volumes are proportional to $M$, then the only way for the heart to increase the oxygen delivery to the body is by increasing the frequency of the heart rate (Schmidt-Nielsen 1984, pp. 126–150).

(a) Using the result from Problem 45, if a 70 kg man has a heart rate of 80 beats $min^{-1}$, determine the heart rate of a guinea pig ($M = 0.5$ kg).

(b) To a first approximation, all hearts beat about 800,000,000 times in a lifetime. A 30-g mouse lives about 3 years. Estimate the life span of a 3000-kg elephant.

(c) Humans live longer than what their mass would indicate. Calculate the life span of a 70-kg human based on scaling, and compare it to a typical human life span.

**Problem 47.** Let us examine how high animals can jump (Schmidt-Nielsen 1984, pp. 176–179). Assume that the energy output of the jumping muscle is proportional to the body mass, $M$. The gravitational potential energy gained upon jumping to a height $h$ is $Mgh$ ($g = 9.8\,m\,s^{-2}$). If a 3-g locust can jump 60 cm, how high can a 70-kg human jump? Use scaling arguments.

**Problem 48.** In Problem 47, you should have found that all animals can jump to about the same height (approximately 0.6 m), independent of their mass $M$.

(a) Equate the kinetic energy at the bottom of the jump ($Mv^2/2$, where $v$ is the "take-off speed") to the potential energy $Mgh$ at the top of the jump to find how the take-off speed scales with mass.

(b) Calculate the take-off speed.

(c) In order to reach this speed, the animal must accelerate upward over a distance $L$. If we assume a constant acceleration $a$, then $a = v^2/(2L)$. Assume $L$ scales as the linear size of the animal (and assume all animals are basically the same shape but different size). How does the acceleration scale with mass?

(d) For a 70-kg human, $L$ is about 1/3 m. Calculate the acceleration (express your answer in terms of $g$).

(e) Use your result from part (c) to estimate the acceleration for a 0.5-mg flea (again, express your answer in terms of $g$).

(f) Speculate on the biological significance of the result in part (e) (See Schmidt-Nielsen 1984, pp. 180–181).

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