

## Part 4: High

Let us drink and be merry, dance, joke, and rejoice,  
With claret and sherry, theorbo and voice!  
The changeable world to our joy is unjust,  
All treasure 's uncertain,  
Then down with your dust!

In frolics dispose your pounds, shillings, and pence,  
For we shall be nothing a hundred years hence.

We'll sport and be free with Moll, Betty, and Dolly,  
Have oysters and lobsters to cure melancholy:  
Fish-dinners will make a man spring like a flea,  
Dame Venus, love's lady,  
Was born of the sea;

With her and with Bacchus we'll tickle the sense,  
For we shall be past it a hundred years hence.

Then why should we turmoil in cares and in fears,  
Turn all our tranquill'ty to sighs and to tears?  
Let 's eat, drink, and play till the worms do corrupt us,  
'Tis certain, Post mortem  
Nulla voluptas.

For health, wealth and beauty, wit, learning and sense,  
Must all come to nothing a hundred years hence.

*Coronemus nos Rosis antequam marcescant* (1675), Thomas Jordan (c1612 – 1685).



Image 8.5: *The Garden of Earthly Delights* (1503 – 1504), Hieronymus Bosch (c. 1450 – 1516), Museo del Prado, Madrid. (Source: en.wikipedia.org)

## Chapter 9: Sex, drugs and rates of change

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*I met with a gal and we went on a spree  
She taught me to smoke and to drink whuskey.  
Cigareets and whuskey and wild wild women  
They'll drive you crazy, they'll drive you insane,  
Cigareets and whuskey and wild wild women  
They'll drive you crazy, they'll drive you insane.  
And now I'm feeble and broken with age  
The lines on my face make a well written page.  
I'm leavin' this story how sad but how true  
On women and whuskey and what they will do.*

Artist: Jim Croce ([www.youtube.com/watch?v=yVw96wzmZC8](http://www.youtube.com/watch?v=yVw96wzmZC8))



Image 9.1: *Skull with a burning cigarette* (c1885), Vincent van Gogh (1853 – 1890), Van Gogh Museum, Amsterdam. (Source: [en.wikipedia.org](http://en.wikipedia.org))

## 9.1 Pharmacokinetics and rates of change

### Some drug-related terminology

Broadly speaking, a **drug** is usually defined to be any externally derived chemical substance introduced into an organism that affects the function of the organism. Drugs may enhance physical or mental well-being, and include both medicinal and so-called recreational drugs.

**Pharmacology** studies the properties of drugs and their effects on living organisms.

**Pharmacokinetics** studies what happens to drugs inside the body, particularly the extent and rates of **absorption**, **distribution**, **metabolism** and **excretion**.

**Pharmacodynamics** studies the interaction of drugs with the cells of the body. (We will not cover pharmacodynamics in SCIE1000; there are many other courses in which it is studied.)

### Drug concentrations

After the administration of a drug, a key determinant of its impact on the body is the drug **concentration** in the bloodstream, which is commonly measured as mass per volume (such as mg/L).

Typically, concentrations are measured (or predicted) at various times after drug administration, and are displayed graphically using a *drug concentration curve*.

- Mathematics and functions are particularly important when modelling the *change* in drug concentrations over time, as they help to predict the *impact* of the drug and the *timing* of subsequent interventions.



## Case Study 19: Zoloft and depression

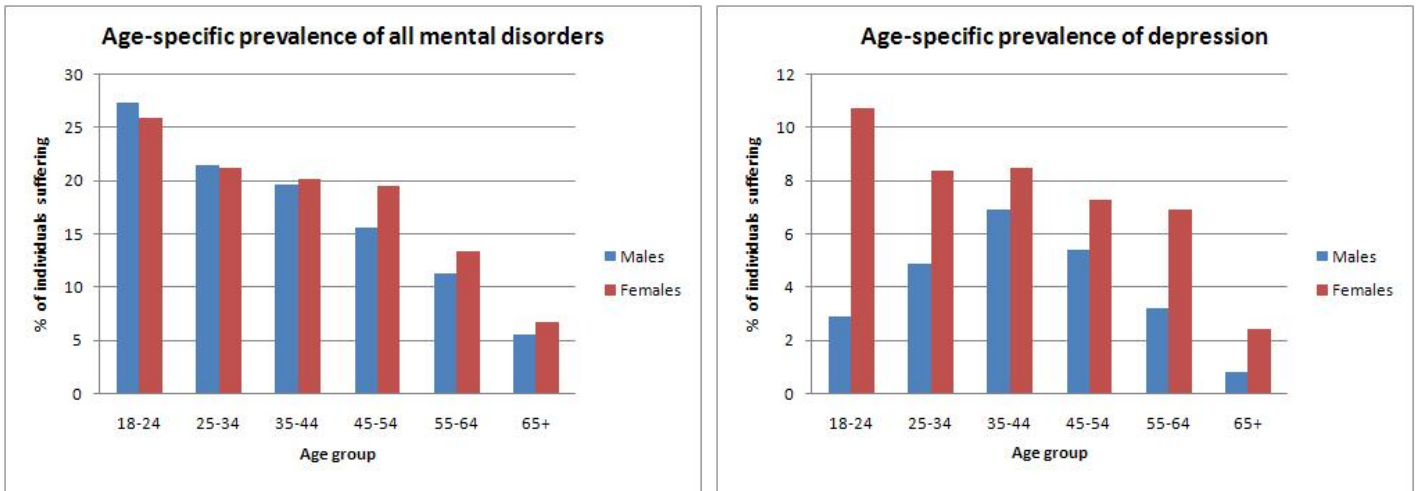


Figure 9.1: Age-specific prevalence of mental disorders and depression in Australian adults.

- *Zoloft* (and a number of generically branded equivalents) is the brand name of the drug *sertraline hydrochloride*, which is an antidepressant of the SSRI class (Selective Serotonin Reuptake Inhibitor).
- The Consumer Medicine Information fact sheet explains that SSRIs “. . . are thought to work by blocking the uptake of a chemical called serotonin into nerve cells in the brain. Serotonin and other chemicals called amines are involved in controlling mood”.
- Zoloft is the most commonly prescribed antidepressant in Australia, and one of the most prescribed drugs overall on the Australian Pharmaceutical Benefits Scheme.
- Zoloft is taken orally as a pill. The usual dosage ranges from 25 mg per day to 200 mg per day.
- Zoloft has a number of comparatively mild side effects (including insomnia, loss of appetite, and some sexual impairment), and is generally believed to be both effective and well tolerated.
- However, there has been media controversy in recent years about the possible adverse impacts of SSRIs on a small number of people.



### *Example 9.1.1*

When recommending a dosage of a therapeutic drug, pharmacologists need to consider a range of physiological factors, including:

- how rapidly the drug is absorbed;
- whether it should be taken with food;
- how often a dose needs to be administered;
- what proportion of the administered drug is absorbed;
- how quickly the drug disperses throughout the body;
- how the drug is metabolised;
- what drug concentration is required to achieve the desired effect, and for how long; and
- how rapidly the drug is excreted.

Using concentration graphs, pharmacologists will observe and measure:

- (a) the peak concentration;
- (b) the time at which peak concentration occurs;
- (c) the *half-life* of the drug, which is the time taken for the concentration to fall to half of its previous value;
- (d) the minimum effective concentration, below which the drug does not have the desired therapeutic effect;
- (e) the maximum rate of drug absorption and when it occurs;
- (f) the maximum rate of drug removal and when it occurs;
- (g) a possible “danger level” of drug concentration, above which the person may require monitoring; and
- (h) the “total exposure” of the body to the drug.

Understanding rates of change and the associated mathematical functions plays an important role in determining the best way to analyse the above factors.

**Question 9.1.2**

Figure 9.2 shows an idealised drug concentration curve (we will see later that many drugs have concentration curves with this general shape). Mark on the graph the values (or possible values) of each of (a) to (h) described in Example 9.1.1.

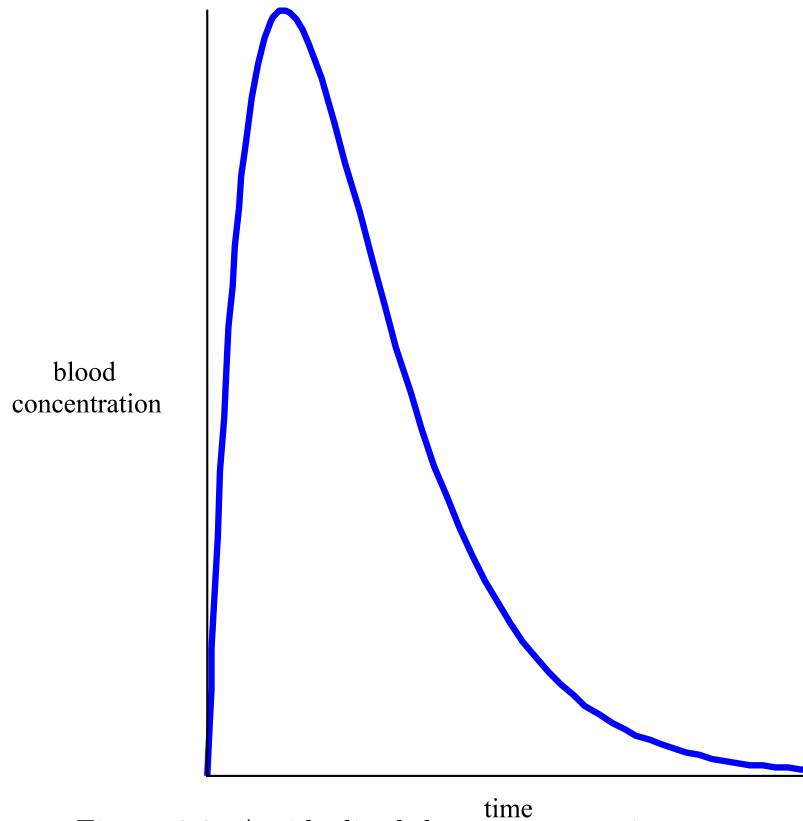


Figure 9.2: An idealised drug concentration curve.

- Compare the information on Zoloft in the following example with some of the features/observations in Example 9.1.1.

***Example 9.1.3***

(The following is taken from the sertraline fact sheet at [www.pbs.gov.au](http://www.pbs.gov.au).)

**“Pharmacokinetics:**

In humans, following oral once-daily dosing over the range of 50 to 200 mg for 14 days, mean peak plasma concentrations ( $C_{max}$ ) of sertraline occurred between 4.5 to 8.4 hours post dosing.

The average terminal elimination half-life of plasma sertraline is

*(continued over)*



**Example 9.1.3** (continued)

about 26 hours. Based on this pharmacokinetic parameter, steady-state sertraline plasma levels should be achieved after approximately one week of once-daily dosing. Linear dose-proportional pharmacokinetics were demonstrated in a single dose study in which the  $C_{max}$  and area under the plasma concentration time curve (AUC) of sertraline were proportional to dose over a range of 50 to 200 mg.

**Dosage: Adults (18 years and older)**

The usual therapeutic dose for depression is 50 mg/day. . . . patients not responding to a 50 mg/day dose may benefit from dose increases up to a maximum of 200 mg/day. Given the 24 hour elimination half-life of sertraline, dose changes should not occur at intervals of less than 1 week. The onset of therapeutic effect may be seen within 7 days . . . .

**Use in Children and Adolescents aged less than 18 years:**

Sertraline should not be used in children and adolescents below the age of 18 years for the treatment of major depressive disorder. The efficacy and safety of sertraline has not been satisfactorily established for the treatment of major depressive disorder in this age group.

**Overdosage:**

On the evidence available, sertraline has a wide margin of safety in overdose. Overdoses of sertraline alone of up to 13.5 g have been reported. Deaths have been reported involving overdoses of sertraline, primarily in combination with other drugs . . . .”

End of Case Study 19.

- Pharmacokinetics is particularly concerned with the *rate* at which the drug concentration *changes*.
- The concept of one quantity changing as another quantity changes, and the rate at which the change occurs, is crucial to understanding and modelling many processes in science, engineering, social sciences and economics.

#### *Example 9.1.4*

In addition to explaining the dynamics of drug concentrations in the body, analysing rates of change is important for solving problems such as:

- landing a space capsule on the moon with minimum fuel usage;
- predicting the spread of ash from a volcanic eruption;
- modelling earthquakes and tsunamis, and predicting which areas will be affected, and when;
- predicting future populations of two interacting species;
- estimating the impact of a vaccination program on the spread of a disease;
- predicting the impact of a constricted artery on blood flow;
- minimising risk in a share portfolio;
- determining the time taken to reach equilibrium in a chemical reaction; and
- predicting the time at which a student will attain a certain threshold level of knowledge about a topic.

- We will cover two methods for analysing rates of change:
  - *average* rates of change; and
  - *exact* rates of change.

## 9.2 Average rates of change

- The *average rate of change* measures the average change between two observed values of some phenomenon.
- In science, average rates of change are usually measured over time, such as  $60 \text{ m s}^{-1}$ .

### Average rate of change

Let  $(x_1, y_1)$  and  $(x_2, y_2)$  be two points. The **average rate of change of  $y$  with respect to  $x$**  between these points is the slope of the straight line joining the points. As we saw earlier, the slope equals the change in  $y$  values divided by the change in  $x$  values, so:

$$\frac{\text{change in } y}{\text{change in } x} = \frac{\Delta y}{\Delta x} = \frac{y_2 - y_1}{x_2 - x_1}.$$

(Note that  $\Delta$  is the Greek capital letter “Delta”, and usually means “the change in the value of”.)

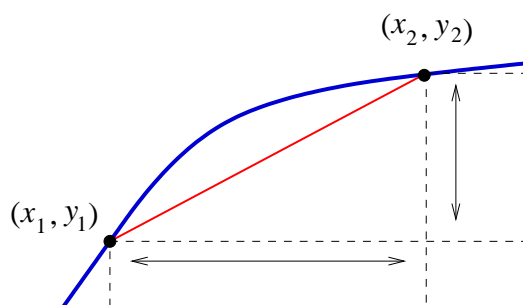


Figure 9.3: Average rate of change.

### Example 9.2.1

The concentration of atmospheric  $\text{CO}_2$  has risen by about 70 ppm over the last 50 years. Hence the average rate of change over this time is:

$$\frac{70 \text{ ppm}}{50 \text{ years}} = 1.4 \text{ ppm year}^{-1}.$$



## Case Study 20: Cigarettes



Photo 9.1: Cool, sophisticated smoker! (Source: PA.)

- Nicotine is a highly addictive, poisonous alkaloid found in a number of plants, including tobacco.
- After inhaling tobacco smoke, nicotine typically enters your blood stream within five seconds, and reaches your brain after about 10 seconds.
- In addition to nicotine, tobacco products also contain a large number of other compounds (including heavy metals, poisons and radioactive materials), many of which are toxic or known carcinogens.

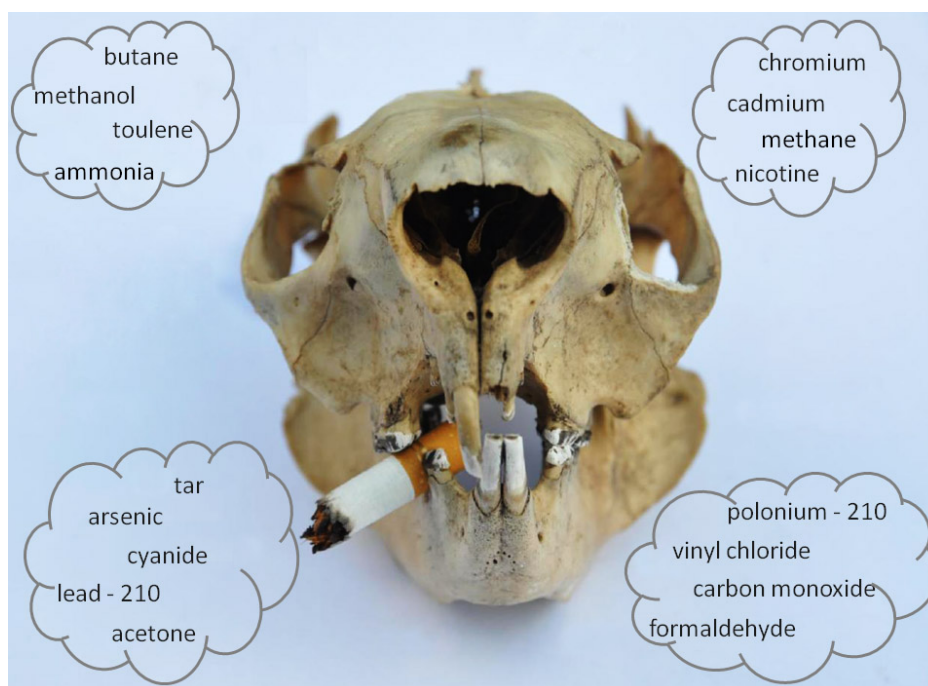


Photo 9.2: “Smoking kills”: the joy of cigarette smoke. (Source: PA.)

- Smoking is a risk factor for many types of cancer. Figure 9.4 shows the proportions of various cancers in Australians directly attributable to smoking; see [1].

Cancer site	Male %	Female %	Cancer site	Male %	Female %
Lung	89	70	Larynx	69	60
Oral cancers	52	42	Renal pelvis	51	43
Oesophagus	50	41	Anus	39	29
Bladder	38	28	Vulva	—	32
Pancreas	23	16	Penis	21	—
Kidney	17	12	Stomach	12	8

Figure 9.4: Proportions of various cancers that are directly attributable to smoking.

- From 1991 to 2001, the male incidence rate for cancers attributable to smoking fell by an average of 1.4% per year, while the rate for females rose by 0.7% per year.
- Over the same period, mortality rates fell by 1.9% per annum for males and rose by around 0.1% per annum for females.
- Smoking is also a major risk factor for morbidity and mortality from other causes.
- As we saw earlier, in 1960 the Framingham Heart Study showed that smoking increases the risk of heart disease.
- Around 17% of all deaths from heart disease are due to smoking.
- Approximately 16% of Australians smoke, and there are around 15000 smoking related deaths in Australia each year.

### *Question 9.2.2*

Figures 9.5 and 9.6 show measured blood nicotine concentrations  $N(t)$  after smoking a cigarette, starting at time  $t = 0$  minutes (see [3]). (Note that measurements were taken at discrete time intervals; we show connecting lines in the graph only for clarity.)

*(continued over)*

*Question 9.2.2 (continued)*

$t$ (min.)	0	3	6	10	14	20	35	65	95
$N(t)$ (ng/mL)	5	11	15.4	13.4	12.8	11.3	9.8	8	7

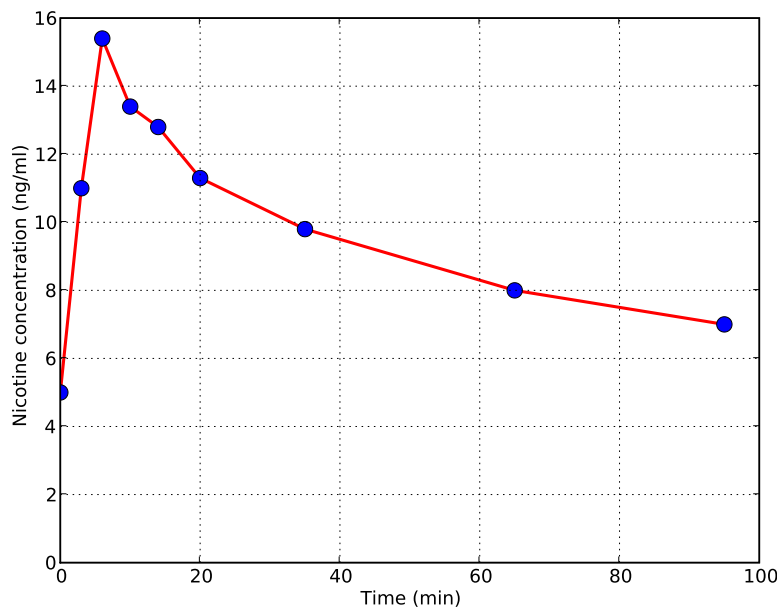
Figure 9.5: Measured blood nicotine concentrations  $N(t)$  after smoking a cigarette.

Figure 9.6: Graph of measured blood nicotine concentrations after smoking.

- (a) Describe and explain the main features of the shape of the graph.
- (b) Find the **total** change in concentration from  $t = 0$  to  $t = 95$  min.
- (c) Find the **average** rate of change in concentration from:
- (i)  $t = 0$  to  $t = 95$  min; and
  - (ii)  $t = 0$  to  $t = 10$  min.

End of Case Study 20.



## 9.3 Derivatives and rates of change

- Rather than measure the average rate of change between two points, in many situations it is more useful to measure the *exact* rate of change at a point. The mathematical term for an exact rate of change is *derivative*.
- In SCIE1000, you will not be finding derivatives (in general), but will need to interpret and use them.

### Derivatives

If  $y = f(x)$  is a function, then the derivative  $y'$  is a new function that gives the exact rate at which  $y$  is changing with respect to  $x$ .

The **value** of the **derivative** at any point describes the behaviour of the **function** at that point. At any point:

- if  $y'$  is **positive** then the function  $y$  is **increasing**;
- if  $y'$  is **negative** then the function  $y$  is **decreasing**; and
- if the function  $y$  has a **local maximum** (peak) or **local minimum** (trough) at a point, then  $y'$  **equals zero** at that point.

The *derivative of the derivative*, or *second derivative*, is denoted  $f''$ .

### Question 9.3.1

While smoking tobacco, the body absorbs many chemical compounds in addition to nicotine, including cyanide (which is highly toxic to humans). Figure 9.7 shows blood cyanide concentrations after smoking a cigarette, starting at time  $t = 0$  minutes; see [25].

$t$ (min.)	0	5	10	15	20	25	35	65
conc. ( $\mu\text{g}/\text{mL}$ )	0.11	0.43	0.21	0.16	0.14	0.15	0.125	0.1

Figure 9.7: Measured cyanide concentrations in the blood of a person after smoking a cigarette.

(continued over)

**Question 9.3.1** (continued)

The function  $C(t) = 0.1 + 0.3t^{0.6}e^{-0.17t}$   $\mu\text{g/mL}$  is a reasonable model of the measured blood cyanide concentrations. Figure 9.8 shows a plot of  $C(t)$ , along with the measured data values.

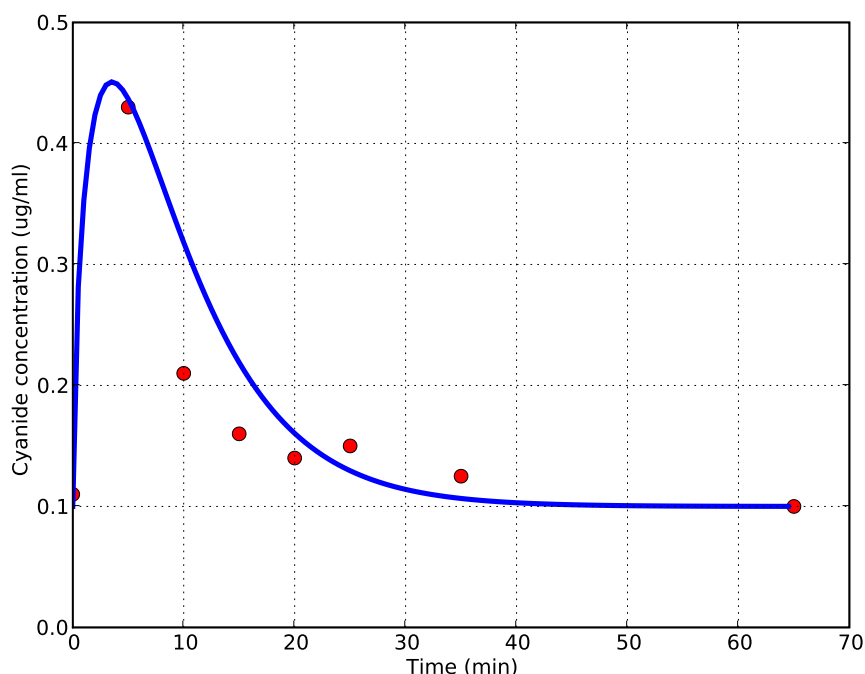


Figure 9.8: Measured and modelled blood cyanide concentrations after smoking a cigarette.

- (a) What is the physical meaning of  $C'$ ?
- (b) On the graph:
- (i) mark with a cross any points at which  $C' = 0$ ;
  - (ii) label any local maxima/minima with the word 'max'/'min';
  - (iii) identify all regions where  $C'$  is positive/negative.
- (c) What is happening physically when  $C'$  is:
- (i) positive?
  - (ii) zero?
  - (iii) negative?

## 9.4 Derivatives and Newton's method

- Derivatives have many uses, such as solving equations.

### Question 9.4.1

A function modelling blood concentration of an injected long-lasting female contraceptive (medroxyprogesterone acetate or MPA) in ng/mL is  $C(t) = 1.4t^{0.15}e^{-0.02t}$ . The graph of  $C(t)$  is:

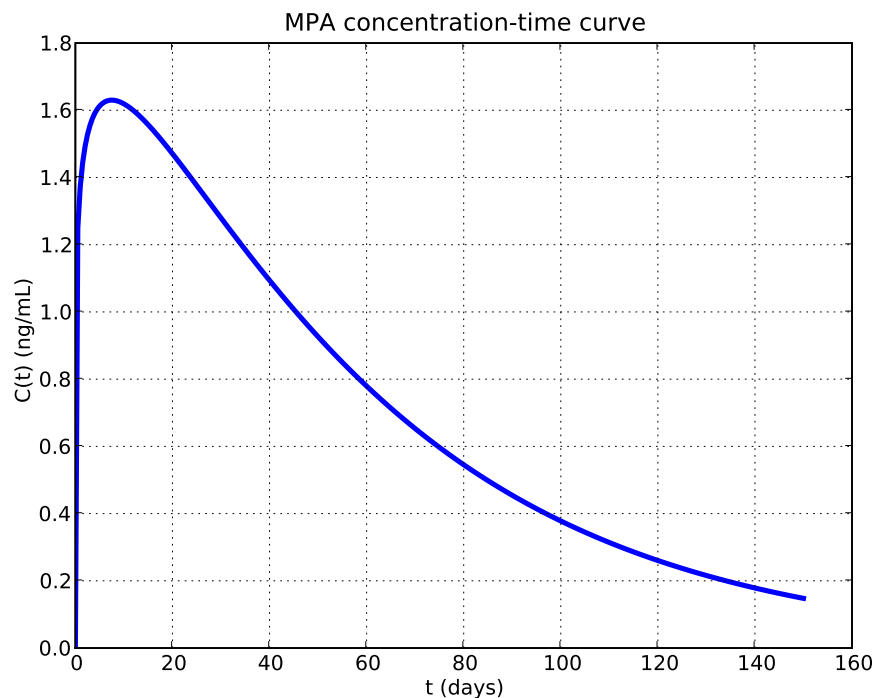


Figure 9.9: Modelled blood concentration after an injection of MPA.

- (a) The minimum blood concentration for reliable contraception is 0.3 ng/mL. Estimate from the graph the time when reliable contraception ceases. (For interest, injections are given every 12 – 13 weeks.)
- (b) Rewrite Part (a) as an equation to be solved.
- (c) How could the equation in Part (b) be solved?



- Often in science, we need to solve equations that are difficult or impossible to solve **exactly**.
- An alternative is to find an **approximate** solution, using *solution-finding* algorithms.
- Solution-finding algorithms involve repeatedly applying similar mathematical steps or *iterations*.
- Usually, a *numerical error* is associated with approximate solutions calculated by solution-finding algorithms.
- Numerical errors can often be reduced by performing more iterations.
- One iterative solution-finding algorithm is *Newton's method*, which uses
  - an initial estimate of a solution; and
  - a derivativeto find a solution of a function.
- Newton's method does not always *converge* to a solution, but will usually converge if the initial estimate is 'good enough'.

### Newton's method (informal description)

To find a solution for  $f(x)$ , that is a value of  $x$  for which  $f(x) = 0$ , Newton's method proceeds as follows:

1. Choose an initial estimate of the solution.
2. Calculate a new estimate of the solution using the old estimate and the derivative. (The new estimate is hopefully more accurate than the previous one.)
3. Stop if the new estimate is sufficiently accurate or if too many steps have been taken. Otherwise, return to Step 2.

- Note that Newton's method only solves equations of the form  $f(x) = 0$ .
- Before applying Newton's method, the equation may need rearranging into an equivalent equation with zero on the right hand side.
- For example, in Part (b) of Question 9.4.1, we rearranged the equation to  $C(t) = 0.3$ .
- To use Newton's method we instead solve  $C(t) - 0.3 = 0$ .

### Newton's method (formal description)

To find a solution for  $f(x)$ , that is a value of  $x$  for which  $f(x) = 0$ , Newton's method proceeds as follows:

1. Let  $x_0$  be an initial estimate of a solution of  $f$  that is 'sufficiently close' to an actual solution of  $f$ . At the  $i$ th iteration ( $i = 0, 1, 2, \dots$ ),  $x_i$  is the current approximation of the actual solution.
2. Calculate the next estimate: 
$$x_{i+1} = x_i - \frac{f(x_i)}{f'(x_i)}$$
3. (a) If the value of  $x_{i+1}$  is sufficiently accurate then stop;  $x_{i+1}$  is the estimated solution.  
(b) If  $x_{i+1}$  is not sufficiently accurate after a certain number of steps then stop, because the method is probably not converging to a solution. Choose a 'better' value for  $x_0$  and start again.  
(c) Otherwise, return to Step 2.

- Newton's method is based on equations of straight lines and average rates of change!
- Let the initial estimate of an unknown solution of  $f(x)$  be  $x_0$ . Newton's method calculates the next estimate  $x_1$  by extending a line from the point

$(x_0, f(x_0))$  to the  $x$ -axis, with the slope of the line equal to the value of the derivative  $f'$  at the point  $x_0$ ; see Figure 9.10.

- Rearranging the formula for the equation of a line gives Newton's method. Optional: To see how, consider the straight line joining the points  $(x_0, f(x_0))$  and  $(x_1, 0)$ .

The gradient is  $f'(x_0)$ , which must also equal  $\frac{f(x_0) - 0}{x_0 - x_1}$ .

Thus  $f'(x_0) = \frac{f(x_0)}{x_0 - x_1}$ , so  $x_1 = x_0 - \frac{f(x_0)}{f'(x_0)}$ , which is Newton's method.

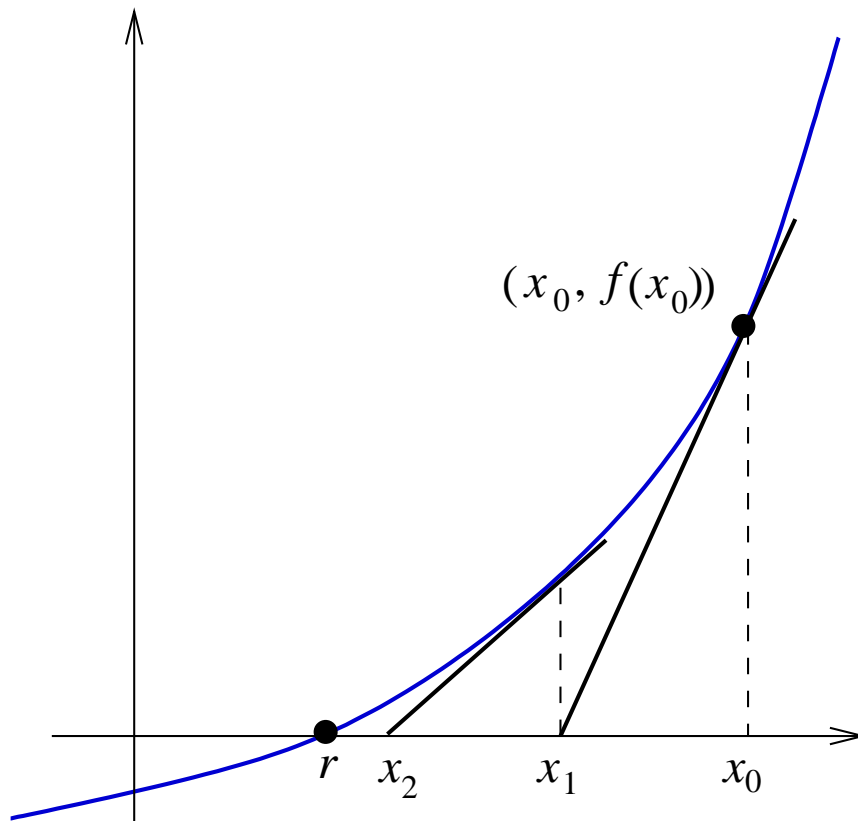


Figure 9.10: An illustration of two steps of Newton's method.

- If  $x_0$  is sufficiently close to the solution, then the new approximation  $x_1$  will be closer to the solution than  $x_0$  was.
- These steps continue until either Newton's method finds a sufficiently accurate approximation to the solution, or the process has taken too many steps without converging to a solution.

**Example 9.4.2**

Use Newton's method to estimate  $x = \sqrt{12}$ .

Let  $f(x) = x^2 - 12$ . Then solving  $f(x) = 0$  is the same as finding  $x = \sqrt{12}$ .

To apply Newton's method, we first need to find the derivative and then choose an initial estimate of the solution:

- Because  $f(x) = x^2 - 12$ , we have  $f'(x) = 2x$ .
- We know that  $\sqrt{12}$  is between 3 and 4, so we will use  $x_0 = 3$  as the initial estimate of the solution. (We could choose other estimates but  $x_0 = 3$  is likely to be "close" to the solution.)

Now we have everything we need to use Newton's method. Recall that the equation for finding the next estimate of the solution is:

$$x_{i+1} = x_i - \frac{f(x_i)}{f'(x_i)}.$$

Performing three steps of Newton's method gives the results shown in Figure 9.11, with the last column showing the sequence of approximations to the solution.

$i$	$x_i$	$f(x_i)$	$f'(x_i)$	$x_{i+1}$
0	3	-3	6	3.5
1	3.5	0.25	7	3.4642857
2	3.4642857	0.001275	6.92857	3.4641016

Figure 9.11: Three iterations of Newton's method to find  $\sqrt{12}$ .

After three steps, the estimate of  $\sqrt{12}$  is  $x_3 = 3.4641016$ . Note that:

- The estimated solution barely changed between  $x_2$  and  $x_3$ .
- The estimate of the solution is quite accurate; in fact,  $x_3$  is correct to seven decimal places.

## 9.5 Pleasures of the flesh and derivatives



Image 9.2: “Who does not love wine, wife and song will be a fool for his lifelong!”. (Kimmel and Voigt, New York, 1873. Source: en.wikipedia.org.)

- We will now study derivatives in the context of drug concentration graphs.

### Case Study 21:

### Whisky

- A standard drink contains 10 g of alcohol.
- Usually, the measure of Blood Alcohol Concentration (BAC) is the percentage of total blood volume that is alcohol (or equivalently, grams of alcohol per litre of blood). In Australia the legal blood alcohol content for driving is 0.05%, or 0.5 g/L.

- Unlike many other drugs, the rate of alcohol metabolism is roughly constant (called a *zero-order* reaction in Chemistry).
- The rate of metabolism is usually independent of the BAC because typical levels of alcohol consumption saturate the metabolising capacity of enzymes within the liver.

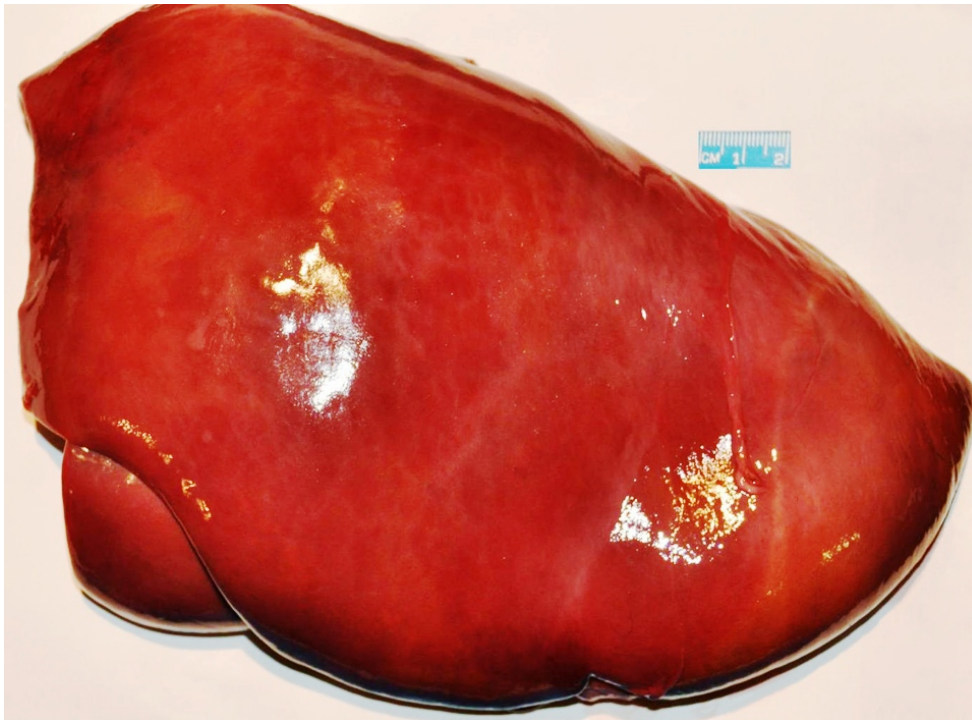


Photo 9.3: Calf liver. (Source: PA.)

- The exact rate of metabolism varies between individuals, influenced by factors such as age, mass (weight) and gender.
- A graph of BAC from the time drinking commenced will show a rapid initial rise during the absorption phase, prior to a decline in concentration during the elimination phase.
- Because the rate of alcohol metabolism tends to be constant, a graph of BAC from the time of peak concentration shows a linear decline until metabolism is almost complete.

**ALKOHOLE**

Photo 9.4: Only in Poland. (Source: PA.)



**Question 9.5.1**

Figure 9.12 shows some BAC measurements (see [46]). Let  $B(t)$  represent the straight line modelling the BAC from  $t = 1$  h to  $t = 6$  h.

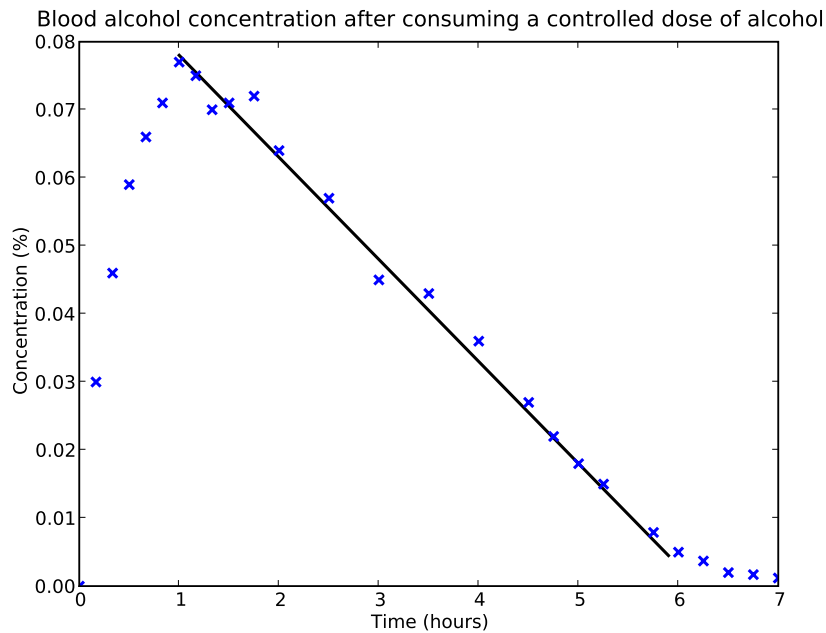


Figure 9.12: Measured blood alcohol concentrations.

- (a) Find an equation for  $B(t)$ .
- (b) Find  $B'(t)$  (include units).
- (c) Interpret, in words, what  $B'(t)$  represents.

**Question 9.5.2**

Figure 9.13 estimates the time required for the BAC of males and females of different masses (weights) to return to zero. (These values are published by the United States Government. To convert from pounds to kg, divide by 2.2.)

	num. drinks	Mass (pounds)							
		120	140	160	180	200	220	240	260
<b>Males:</b>	1	2	2	2	1.5	1	1	1	1
	2	4	3.5	3	3	2.5	2	2	2
	3	6	5	4.5	4	3.5	3.5	3	3
	4	8	7	6	5.5	5	4.5	4	3.5
	5	10	8.5	7.5	6.5	6	5.5	5	4.5
<b>Females:</b>	1	3	2.5	2	2	2	1.5	1.5	1
	2	6	5	4	4	3.5	3	3	2.5
	3	9	7.5	6.5	5.5	5	4.5	4	4
	4	12	9.5	8.5	7.5	6.5	6	5.5	5
	5	15	12	10.5	9.5	8	7.5	7	6

Figure 9.13: The time (in hours) for BACs to return to zero.

**(a)** Typically, after all (or most) alcohol has been absorbed, BACs decrease in an approximately linear fashion (see Figure 9.12). How is this apparent in Figure 9.13?

**(b)** Using the information in Figure 9.13, comment on the value of  $B'(t)$  for

*(continued over)*

**Question 9.5.2** (continued)

different genders and body masses (weights).

- (c) In an experiment, Peter used a commercial breathalyser to monitor the BACs of two females who each consumed approximately 4 standard drinks (38 g of alcohol) over an hour. Figure 9.15 shows the experimental data.



Figure 9.14: Breathalyser.  
(Source: MG.)

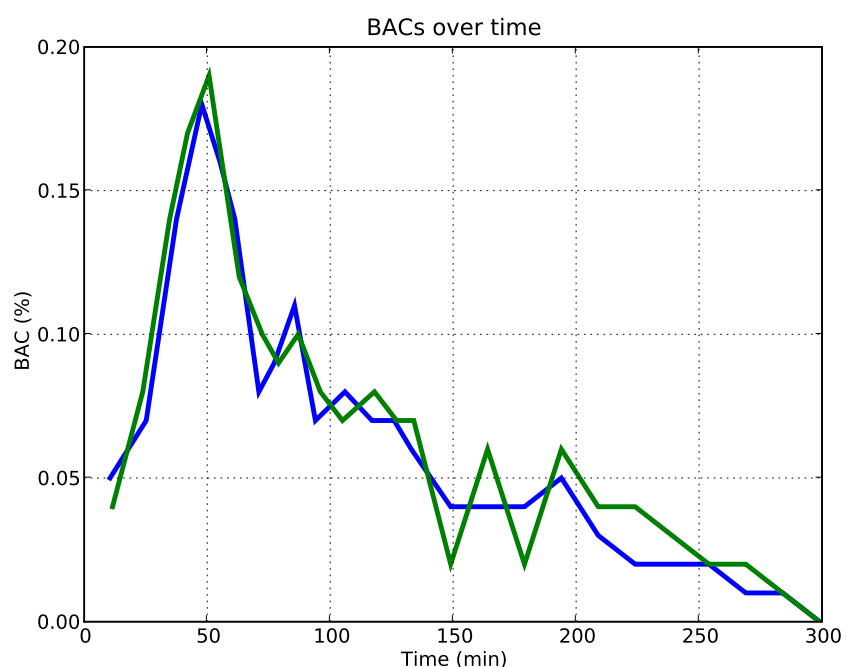


Figure 9.15: Measured blood alcohol concentrations.

Comment on the graphs in Figure 9.15, highlighting both the expected

(continued over)

***Question 9.5.2 (continued)***

and unexpected features of the shapes of the graphs.

End of Case Study 21.

**Case Study 22:**  
**Methamatics (or ‘The math of meth’).**

- The previous case study investigated the effects of alcohol, which saturates enzymes in the liver when consumed in typical doses, and is therefore metabolised at a constant rate.
- Because the lower doses of most other drugs do not saturate metabolic enzymes, they are therefore typically metabolised by the body at a rate proportional to the current concentration of the drug in the bloodstream (called *first-order* reactions in Chemistry).
- Hence the typical blood concentration functions of such drugs are exponentials, and it is useful to talk about their half-lives.
- Figure 9.16 shows the approximate half-lives of some substances.

drug	$t_{1/2}$	drug	$t_{1/2}$
caffeine (coffee)	5 h	nicotine (cigarettes)	2 h
codeine (analgesic)	3 h	progesterone (oral contraceptive)	40 h
adrenaline	2 min	3,4-Methylenedioxymethamphetamine (ecstasy)	8 h
testosterone	3 h	$\gamma$ -Hydroxybutyric acid (GHB)	40 min
diacetylmorphine (heroin)	8 min	morphine	2.5 h
sertraline (Zoloft)	26 h	sildenafil (Viagra)	3 h

Figure 9.16: Some common drugs and hormones, and their approximate half-lives.

**Question 9.5.3**

The synthetic central nervous system stimulant methamphetamine (also known as ‘ice’, ‘speed’ and ‘meth’) is a relatively common recreational drug that is typically smoked, ‘snorted’, injected, swallowed orally or taken as a rectal suppository. It also has approved medical uses, for example in the treatment of attention-deficit hyperactivity disorder, ADHD.

Methamphetamine causes the release of chemicals such as *dopamine* and

*(continued over)*

**Question 9.5.3** (continued)

*serotonin* in the brain, leading to feelings of intense excitement and euphoria, intensified emotions, increased energy levels, reduced appetite, increased libido and a general feeling of extreme well-being. The ‘high’ can last from 2 to 12 hours.

Methamphetamine is highly addictive, leading to depression, psychosis, extreme risk taking, and damage to almost every major organ system in the body.

Methamphetamine can be synthesised from *pseudoephedrine*, which is a common nasal decongestant in medications for allergies and colds. Australia now heavily regulates the sale of such preparations to prevent their use in the production of methamphetamine.

In [7], researchers administered methamphetamine to study participants, and recorded the subsequent blood concentrations of the drug. A model for the blood concentration (in ng/mL) of one participant at time  $t$  hours after dosing followed the equation  $M(t) = 47e^{-0.06t}$  where  $t > 3$  for the model to apply; see Figure 9.17.

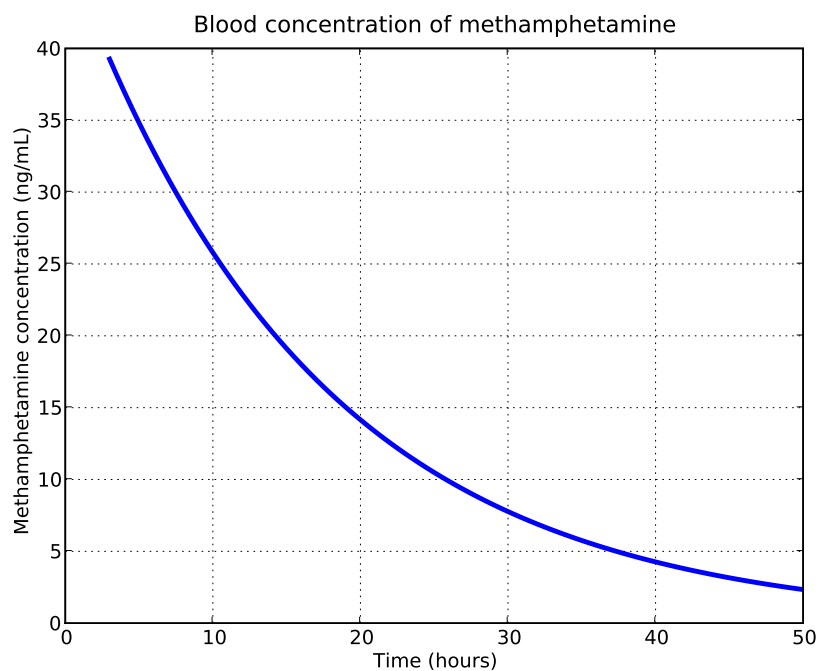


Figure 9.17: Modelled blood concentration of methamphetamine.

(continued over)



**Question 9.5.3** (continued)

- (a) Find the units of  $M'(t)$ .
- (b) What do you notice about the functions  $M$  and  $M'$ ? What is the significance of your observation? (Hint:  $M'(t) = -0.06 \times 47e^{-0.06t}$ .)
- (c) Estimate the half-life of methamphetamine for this person.

End of Case Study 22.

## Case Study 23: Wild, wild women

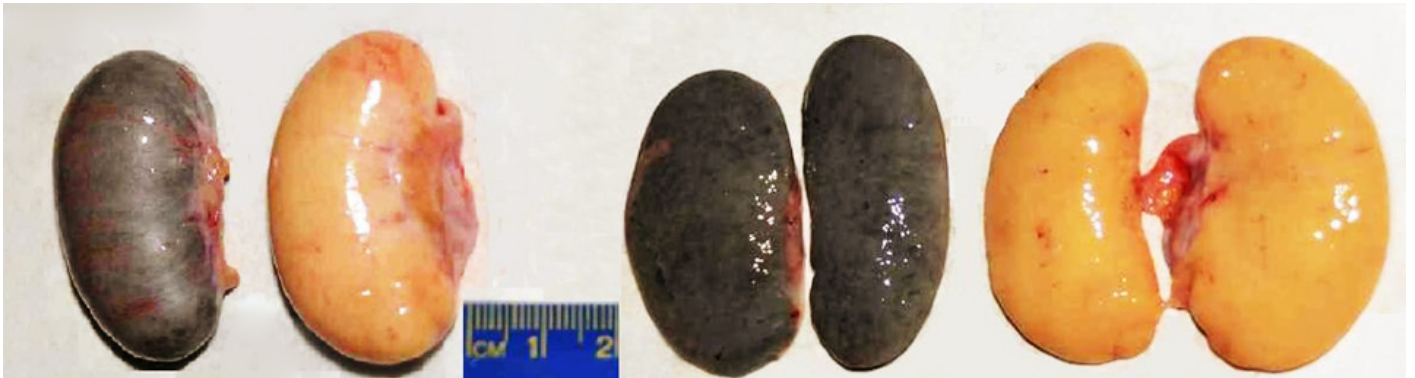


Photo 9.5: A pair of paltry testes, before and after dissection. (Source: PA. (Just the photo!))



Photo 9.6: Various types of contraceptive including: oral contraceptive, condoms, injected contraceptives and traditional herbal methods. (Source: PA.)

- Each of the many different methods of contraception has advantages and disadvantages.
- Figure 9.18 compares the effectiveness of various methods of contraception, based on data given in [11].

Method	Typical use	Ideal use	1-year
Chance	85	85	
Spermicides	26	6	40
Periodic Abstinence	25	1 – 9	63
Cap			
Parous Women	40	26	42
Nulliparous Women	20	9	56
Sponge			
Parous Women	40	20	42
Nulliparous Women	20	9	56
Diaphragm	20	6	56
Withdrawal	19	4	
Condom	14	3	61
Oral pill	5	0.1	71
IUD	0.1 – 2.0	0.1 – 1.5	80
Depo-Provera IM 150 mg	0.3	0.3	70
Female Sterilisation	0.5	0.5	100
Male Sterilisation	0.15	0.10	100

Figure 9.18: The expected percentage of women who will experience an unintended pregnancy when using various methods of contraception for a year, through either typical use or ideal (very careful) use. Also shown is the average percentage of women continuing to use that method of contraception after one year.



Photo 9.7: Fireworks, Hong Kong. (Source: PA.)

- Depo-subQ Provera 104 is a long-term female contraceptive administered as an injection every 12 – 13 weeks.
- The active ingredient in a standard 0.65 mL dose is 104 mg of the artificial female hormone medroxyprogesterone acetate (MPA), which is similar to progesterone.

- The contraceptive works by inducing changes to the female reproductive system, inhibiting egg release and creating a hostile environment to sperm.
- It is 99.7% effective, which is very high when compared to many other forms of contraception.
- Commonly quoted benefits are convenience and reliability.
- Studies have identified some side effects, including breakthrough bleeding, reduced libido, weight gain and potentially, reduced bone density.

### *Example 9.5.4*

Figure 9.19 shows some pharmacokinetic parameters of MPA after a single subcutaneous injection of Depo-SubQ Provera 104 in healthy women. The data are based on results in [11], with a sample size of  $n = 42$  women.

	$C_{max}$ (ng/mL)	$t_{max}$ (day)	$C_{91}$ (ng/mL)	$AUC_{0-91}$ (ng day/mL)	$AUC_{0-\infty}$ (ng day/mL)	$t_{1/2}$ (day)
Mean	1.56	8.8	0.402	66.98	92.84	43
Min	0.53	2.0	0.133	20.63	31.36	16
Max	3.08	80.0	0.733	139.79	162.29	114

Figure 9.19: Pharmacokinetic parameters of MPA.

In Figure 9.19:

- $C_{max}$  = peak blood concentration;
- $t_{max}$  = the time at which  $C_{max}$  occurs;
- $C_{91}$  = blood concentration at 91 days;
- $AUC_{0-91}$  = the area under the concentration-time curve over 91 days;
- $AUC_{0-\infty}$  = the area under the concentration-time curve over an indefinite time period; and
- $t_{1/2}$  = half-life of MPA.

**Example 9.5.5**

A patient has an injection of Depo-subQ Provera 104. After the dose, the concentration  $C(t)$  of MPA in her blood (in ng/mL at time  $t$  in days) is modelled by  $C(t) = 1.4t^{0.15}e^{-0.02t}$ . Figure 9.20 shows the graph of  $C(t)$ .

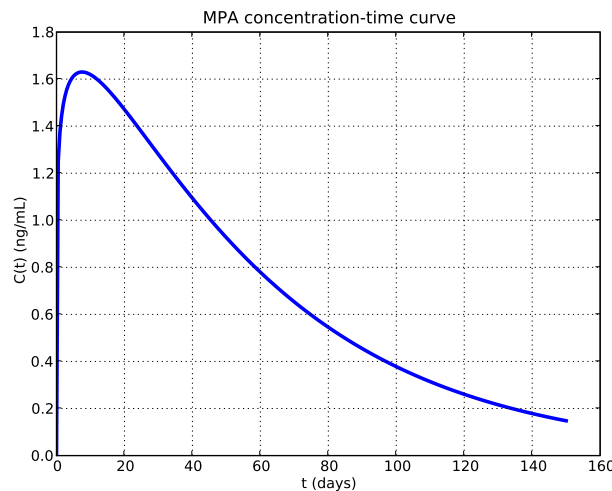


Figure 9.20: A model of the blood concentration of MPA.

**Surge functions**

In a **surge** function, the value initially surges rapidly before falling off exponentially over time. A general equation for a surge function is

$$f(t) = at^pe^{-bt}$$

where the values of  $a$ ,  $p$  and  $b$  depend on the phenomenon. For Depo-subQ Provera 104,  $C(t) = 1.4t^{0.15}e^{-0.02t}$ , so  $a = 1.4$ ,  $p = 0.15$  and  $b = 0.02$ .

**Question 9.5.6**

Explain mathematically why surge functions  $f(t) = at^pe^{-bt}$  have the general shape demonstrated in Example 9.5.5.



- Now we will demonstrate how to use derivatives and Newton's method to determine the timing of a follow-up injection.

*Example 9.5.7*

The minimum blood concentration level of MPA necessary for reliable contraception is 0.3 ng/mL. Calculate the time in days after which contraception ceases to be reliable. (Your answer should be accurate to 3 decimal places.)

**Answer:** we have  $C(t) = 1.4t^{0.15}e^{-0.02t}$ . The equation that requires solving is  $C(t) = 0.3$ .

Hence if we let  $f(t) = C(t) - 0.3$  then we can solve  $f(t) = 0$  by using Newton's method, as follows:

$$f(t) = 1.4t^{0.15}e^{-0.02t} - 0.3, \quad \text{so}$$

$$f'(t) = 1.4e^{-0.02t} (0.15t^{-0.85} - 0.02t^{0.15})$$

Finally, we use  $t_0 = 50$  as the initial estimate for the solution.

After substituting  $f$ ,  $f'$  and  $t_0$  into Newton's method and iterating, on the fifth step the estimate of the solution is

$$t_5 \approx 112.440.$$

Further iterations do not change the value significantly, so the blood concentration of MPA decreased to 0.3 ng/mL at around 112 days, which is about 16 weeks.

For reference, the time recommended by the manufacturer for follow-up injections is 12–13 weeks, which provides a reasonable safety margin.

Now we can develop a computer model.

**Program specifications:** Write a program that uses Newton's method to find the time (in days) at which the MPA concentration decreases to 0.3 ng/mL.



## Program 9.1: Newton's method

```

1 # Program to use Newton's method to solve an equation.
2 from __future__ import division
3 from pylab import *
4
5 # Define the function for Newton's method. Here it is
6 # the blood concentration of MPA.
7 def func(t):
8     return 1.4 * t**0.15 * exp(-0.02*t) - 0.3
9
10 # Define the derivative of the function for Newton's method.
11 def funcDash(t):
12     return 1.4 * exp(-0.02*t) * (0.15*t**-0.85 - 0.02*t**0.15)
13
14 # Initialise variables
15 ctr = 0
16 newEst = 50
17 prevEst = 0
18 tolerance = 0.001
19 # Loop through steps of Newton's method.
20 while abs(newEst - prevEst) > tolerance:
21     ctr = ctr + 1
22     prevEst = newEst
23     newEst = prevEst - func(prevEst) / funcDash(prevEst)
24     print ctr, round(newEst, 3)

```

Here is the output from running the above program:

```

1 89.769
2 108.467
3 112.302
4 112.44
5 112.44

```

End of Case Study 23.

## 9.6 Forensic toxicology

- *Forensic science* is concerned with applying scientific techniques to gather evidence relevant to legal cases.
- *Forensic toxicology* is the branch of forensic science that investigates drugs, poisons and other substances in the body.
- Many legal actions rely on evidence from forensic science/toxicology.
- One of the most common drugs of interest is alcohol, particularly in connection with accidents and violent crimes.
- Forensic toxicology units often analyse blood, tissue or urine samples, from crime victims and suspected perpetrators. They are also asked to extrapolate measured readings to earlier times.

### Question 9.6.1

In practice (particularly in legal cases), models of BAC use the *Widmark formula*, developed in 1932. The equation is:

$$B = \frac{A}{rM} \times 100\% - Vt$$

where  $B$  is the BAC at any time  $t$  since commencing drinking,  $A$  is the amount of alcohol consumed in g,  $V$  is the rate at which the body eliminates alcohol measured in % per time period,  $M$  is the body mass in g and  $r$  is the *Widmark factor* which estimates the proportion of body mass that is water. The precise value of  $r$  depends on factors such as gender, age and percentage body fat. Reasonable estimates are  $r \approx 0.7$  for men and  $r \approx 0.6$  for women.

(a) What is the physical meaning of the term  $rM$ ?

(continued over)

**Question 9.6.1** (*continued*)

- (b) Why is the value of  $r$  for women typically less than for men?
- (c) Verify that the units in the Widmark formula are consistent.
- (d) Justify the Australian government guideline that suggests: to remain below the legal driving BAC limit, within the first hour “men should drink at most two drinks and women at most one”.
- (e) Find  $B'$  and comment on your answer.

**Question 9.6.2**

In the Widmark formula, the absorption term assumes that the body absorbs alcohol **immediately** after consumption. The following variation, from [33], takes into account absorption time.

$$B = \frac{A}{rM} \times (1 - e^{-kt}) \times 100\% - Vt$$

where  $k$  is the rate at which the body absorbs alcohol.

(a) The “standard” Widmark formula is:  $B = \frac{A}{rM} \times 100\% - Vt$ . Explain the difference between the two versions.

(b) If  $t$  is measured in hours, what are the units of  $k$ ?

(c) What factors could influence the value of  $k$  for:

(i) a given person, at different times?

(ii) different people?

*(continued over)*

**Question 9.6.2** (continued)

(d) Find an expression for the time  $t_{max}$  in hours at which the value of  $B$  reaches its maximum. (Hint:  $B'(t) = \frac{100Ak}{rM}e^{-kt} - V$ .)

(e) When consuming alcohol with food in the stomach, a typical value for  $k$  is 2.3. When consuming alcohol on an empty stomach,  $k \approx 6$ . Find  $t_{max}$  for an 80 kg male consuming 4 standard drinks, both on an empty stomach and after eating.

Now we can develop a computer model of food consumption and BACs.

**Program specifications:** Write a program that plots BAC graphs for 6 hours after alcohol consumption on both a full and empty stomach, for men or women of varying masses and with various levels of alcohol consumption.

## Program 9.2: BACs and food consumption

```

1 # Program to compare BACs for men and women of varying masses
2 # and levels of alcohol consumption, on full and empty stomachs
3 from __future__ import division
4 from pylab import *
5
6 alcohol = input("How much pure alcohol is consumed (in g)? ")
7 mass = input("What is the person's mass (in kg)? ")
8 gender = input("Type 1 if male, anything else for female: ")
9 if gender == 1:
10     r = 0.7
11 else:
12     r = 0.6
13 times = arange(0,6.1,0.1)
14 BAC1 = arange(0,6.1,0.1)
15 BAC2 = arange(0,6.1,0.1)
16 ka1 = 6
17 ka2 = 2.3
18 mult = alcohol / (r * mass * 1000) * 100
19
20 # Apply the equation for the required number of steps.
21 i = 0
22 while i < size(times):
23     t = times[i]
24     BAC1[i] = mult * (1 - exp(-t * ka1)) - 0.015 * t
25     BAC2[i] = mult * (1 - exp(-t * ka2)) - 0.015 * t
26     if BAC1[i] < 0:
27         BAC1[i] = 0
28     if BAC2[i] < 0:
29         BAC2[i] = 0
30     i = i + 1
31 plot(times, BAC1, 'b-', linewidth=3)
32 plot(times, BAC2, 'k-', linewidth=3)
33 grid(True)
34 xlabel("Time (hours)")
35 ylabel("BAC (%)")
36 title("BAC curve for a full stomach versus an empty stomach")
37 text(0.7, 0.041, "Full stomach")
38 text(1.1, 0.06, "Empty stomach")
39 show()

```



Figure 9.21 shows the output from running the above program for an 80 kg male consuming four standard drinks:

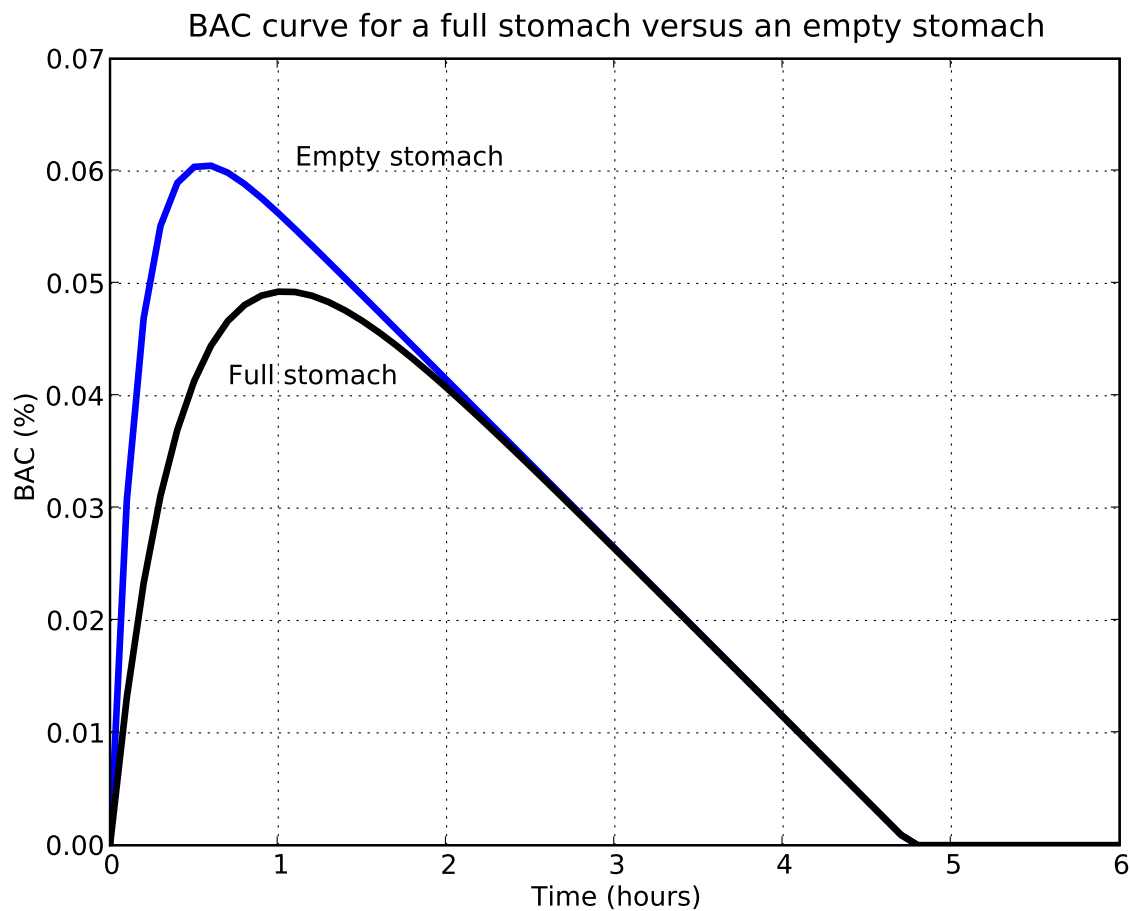


Figure 9.21: Predicted BACs when consuming alcohol on a full stomach compared to an empty stomach.

***Question 9.6.3***

Briefly discuss the implications of the graph in Figure 9.21.

## Case Study 24: CSI UQ



Image 9.3: Nicole Richie mug-shot, (Source: en.wikipedia.org).

### Question 9.6.4

Previously we saw that reasonable estimates for the value of  $r$  (the *Widmark factor*) are  $r \approx 0.7$  for men and  $r \approx 0.6$  for women. Some researchers propose alternate formulae for more accurate estimations of  $r$  for different individuals. For a female with height  $H$  in m and mass  $M$  in kg, [39] estimates  $r$  as

$$r = 0.31223 - 0.006446M + 0.4466H.$$

(For interest, the formula for males is  $r = 0.3161 - 0.004821M + 0.4632H$ .) Why is it reasonable that the coefficient of  $M$  is negative and the coefficient of  $H$  is positive?

**Question 9.6.5**

In 2006, police charged actress Nicole Richie with DUI (driving under the influence) after she drove the wrong way down a highway in Los Angeles. The charge sheet recorded her height as 1.55 m and mass (weight) as 38.5 kg.

- (a) Would you expect her value of  $r$  to be more or less than 0.6 (which is the 'standard' value for women)? Why?
- (b) Calculate her value of  $r$  using  $r = 0.31223 - 0.006446M + 0.4466H$  and comment on your answer.
- (c) If she rapidly consumed 2.5 standard drinks on an empty stomach, would she remain under the legal Californian BAC driving limit of 0.08%? (Use  $r = 0.6$  and also the value of  $r$  calculated in Part (b).)

End of Case Study 24.

## 9.7 Space for additional notes

## Chapter 10: A good area for drugs

---

*Lily the Pink she turned to drink  
she filled up with paraffin inside  
and despite her medicinal compound  
sadly pickled-Lily died.*

*Up to heaven her soul ascended  
all the church bells they did ring  
she took with her medicinal compound  
hark the herald angels sing.*

*We'll drink a drink a drink  
to Lily the Pink the Pink the Pink  
the saviour of the human race  
for she invented medicinal compound  
most efficacious in every case.*

Artist: The Scaffold ([www.youtube.com/watch?v=8QHOdA400wM](http://www.youtube.com/watch?v=8QHOdA400wM))



Image 10.1: *The Drunks* (1629), Diego Velázquez (1599 – 1660), Museo del Prado, Madrid. (Source: en.wikipedia.org)

## 10.1 Integration and the indefinite integral

- All semester we have stressed the importance of *change*. The *rate at which a function is changing* can be calculated by *differentiating* the function.
- Often, the ability to answer the **reverse** question is useful: given the rate at which something is changing, can we find a function for it?
- To answer the reverse question we use a process called *integration*.

### Integration

A function  $F$  is an *indefinite integral* or *antiderivative* of another function  $f$  if the derivative of  $F$  is  $f$ ; that is,  $F'(x) = f(x)$ . The process of finding an integral is called **integration**.

- In SCIE1000, you will not (generally) need to find integrals, but it is essential to understand *why* integrals are important and **how** they are used.

### The integral sign

Let  $f(x)$  be a function with integral  $F(x)$ . The indefinite integral of  $f$  is:

$$\int f(x) dx = F(x) + C$$

where  $C$  is the arbitrary constant of integration.

The symbol  $\int$  is the **integral sign**, and  $dx$  means that integration is with respect to the variable  $x$ .

### Example 10.1.1

The integral of  $f(x) = 3x^2$  is  $F(x) = x^3 + C$ , where  $C$  is an arbitrary constant. (You can check the answer by differentiating  $F$ .)

- Sometimes, extra information, called a **boundary condition**, allows the value of the constant  $C$  to be found.

**Question 10.1.2**

Earlier, we saw that the rate of alcohol metabolism is about 0.015% per hour. Let  $B(t)$  be the BAC (in %) of a person at any time  $t$  (in hours).

- (a) Write an expression for  $B'(t)$ .
- (b) Find an expression for  $B(t)$ .
- (c) Researchers administer a controlled dose of alcohol to an individual. At time  $t = 1$ , absorption is essentially complete and the recorded BAC attains its maximum value of 0.077%. Find an expression for  $B(t)$  after  $t = 1$ .
- (d) Estimate the time at which the BAC will first be legal:
- (i) for driving on an open licence.
  - (ii) for driving on a provisional licence.
- (e) Comment on the likely accuracy of your answers to Part (d).

*(continued over)*



**Question 10.1.2** (continued)

(f) Figure 10.1 shows measured BACs after researchers administered four different controlled doses of alcohol to study participants (see [46]). Relate your answers for Parts (a) to (e) to Figure 10.1.

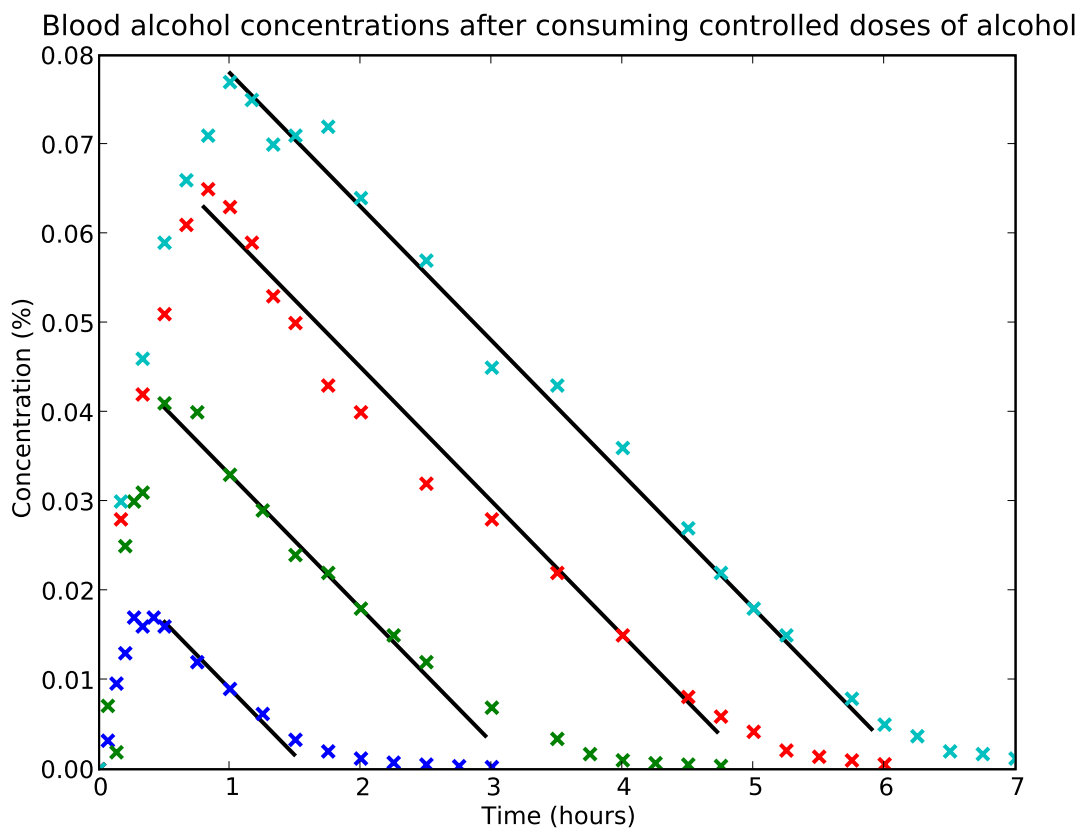


Figure 10.1: Measured BACs after administration of four different controlled doses of alcohol.

## 10.2 Areas and definite integrals

- Given an equation modelling some phenomenon, the area between the curve and the  $x$ -axis often has an important and useful physical meaning.

### *Question 10.2.1*

A person with a BAC of 0.077% at time  $t = 1$  hr metabolises alcohol at a constant rate of  $V = 0.015\% \text{ hr}^{-1}$ .

- (a) Assuming that all alcohol has been absorbed by time  $t = 1$ , calculate the **total** change in BAC between times  $t = 1$  hr and  $t = 6$  hr; include units.
- (b) Draw a rough sketch of the graph of  $-V$  between those times.
- (c) Calculate the area between the graph of  $V$  and the  $x$ -axis between those times; include units.
- (d) Compare your answers from Parts (a) and (c).

- Given a graph, the area under the curve or AUC of that graph is the area bounded by that curve, the  $x$ -axis and two time points on the  $x$ -axis.
- AUCs are positive (above the  $x$ -axis) or negative (below the  $x$ -axis).

- Often, the AUC of a graph has very useful practical applications. The precise meaning of the area depends on what the graph represents.
- For example, given the graph of a rate of change of some phenomenon, the AUC between two time points is equal to the total change in the value of the phenomenon between those points.

### Question 10.2.2

Figure 10.2 shows a graph with a line fitted to some measured blood alcohol concentrations (see [46]).

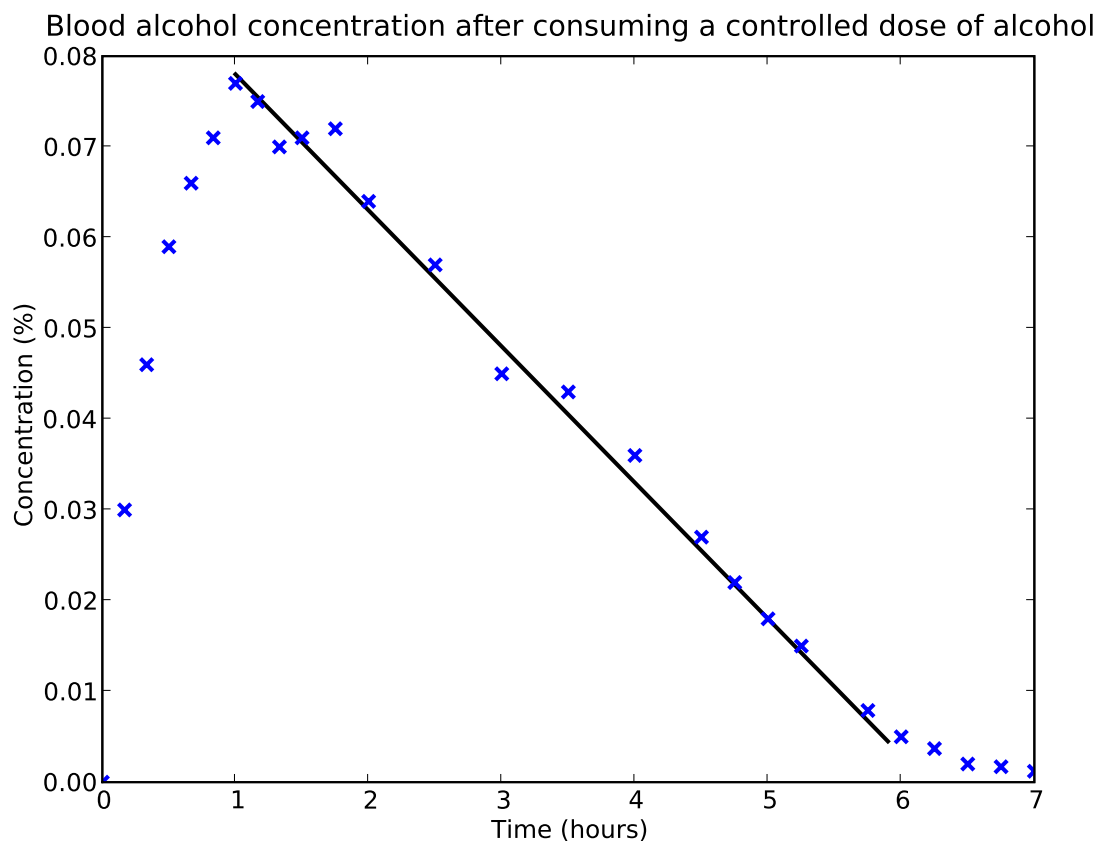


Figure 10.2: A graph of measured BACs.

- (a)** What are the units of the AUC in the graph?
- (b)** What does the AUC represent?

*(continued over)*

**Question 10.2.2** (continued)

(c) Why is the AUC significant?

(d) Calculate the AUC between  $t = 1$  hr and  $t = 6$  hr.

- Areas under curves are so useful that they have a special name and notation.

**Definite integrals**

Given a function  $f(x)$ , the AUC from the point  $x = a$  to the point  $x = b$  is called the *definite integral of  $f(x)$  from  $a$  to  $b$* , written as

$$\int_a^b f(x) dx.$$

**Example 10.2.3**

In Question 10.2.1 we calculated  $\int_1^6 -0.015 dt$ .

- Recall from school that if a function  $f(x)$  is known, then there is an easy way to find areas mathematically (we will cover this later).
- In practice, usually  $f(x)$  is unknown; instead, the only known information is measured data values.
- Hence, the area is estimated approximately, by summing the areas of geometric shapes of “narrow” width, such as rectangles (called Riemann sums), or trapezoids (called the trapezoid rule).

- Note that summing areas of shapes is used to estimate AUCs predominantly when a function is **not known** but some data values **have been measured**.
- At school, you probably encountered problems such as “Let  $f(x) = x^2$ . Use rectangles to estimate the AUC of this function.”
- Such problems are artificial: in reality, if we know the function, then the alternate mathematical approach is usually easier and more accurate.

### Question 10.2.4

Figure 10.3 shows a rectangle, a trapezoid and a composite shape.

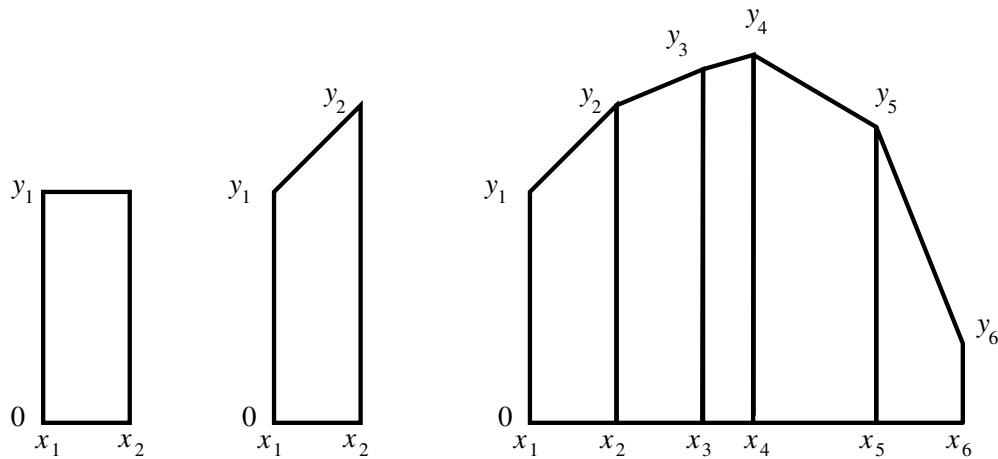


Figure 10.3: A rectangle (left), trapezoid (centre) and composite shape (right).

- (a) Derive expressions for the areas of the rectangle and the trapezoid.
- (b) Show how to find the area of the composite shape.

**Question 10.2.5**

Let  $N(t)$  be an unknown function representing the blood nicotine concentration of a person after smoking a cigarette. Figure 10.4 shows some concentrations, measured experimentally (see [3]).

$t$ (min.)	0	3	6	10	14	20	35	65	95
Value (ng/mL)	5	11	15.4	13.4	12.8	11.3	9.8	8	7

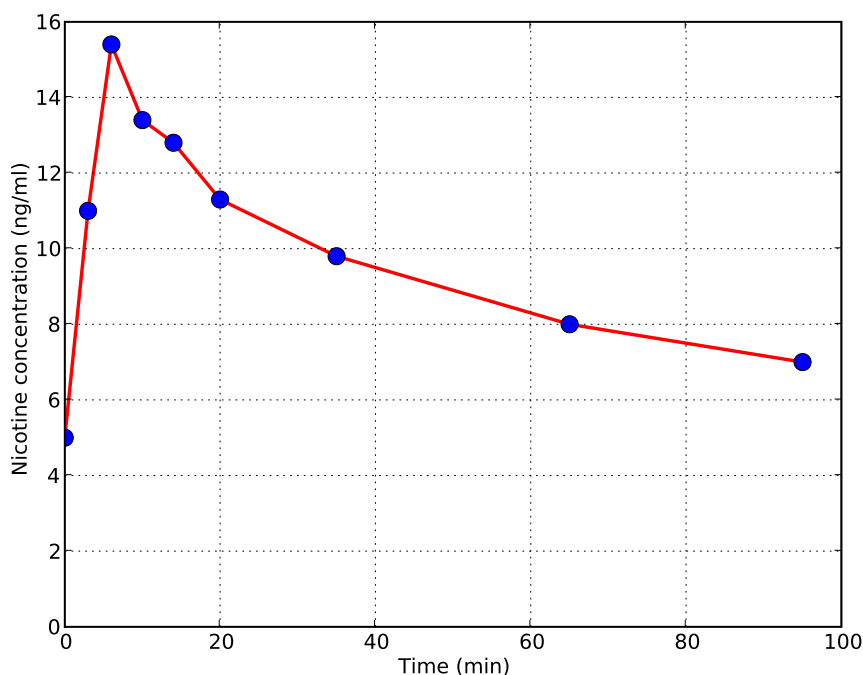


Figure 10.4: Measured blood nicotine concentrations after smoking.

Use Riemann sums to **estimate** the AUC of the unknown function  $N(t)$ ; that is, estimate  $\int_0^{95} N(t) dt$ .

**Question 10.2.6**

Repeat Question 10.2.5 but instead use the trapezoid rule.

$t$ (min.)	0	3	6	10	14	20	35	65	95
Value (ng/mL)	5	11	15.4	13.4	12.8	11.3	9.8	8	7

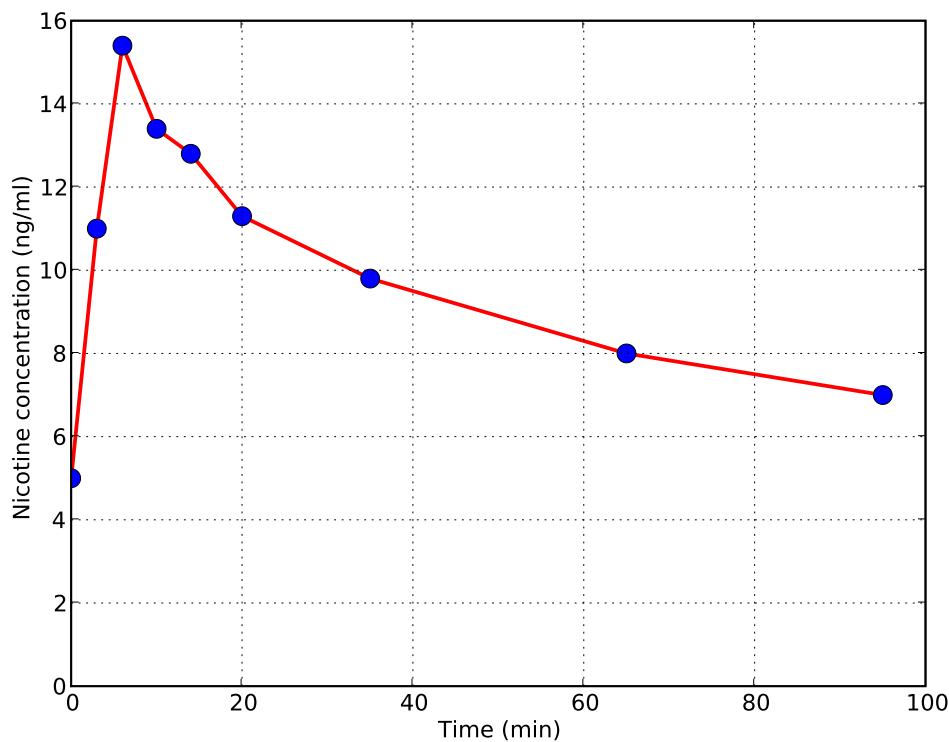


Figure 10.5: Measured blood nicotine concentrations after smoking.

Now we can develop a computer model.

**Program specifications:** Write a Python program that estimates the AUC for  $N(t)$  using Riemann sums or the trapezoid rule. The program must output the total AUC and draw a graph showing the shapes used in the sums.

## Program 10.1: Nicotine

```

1 # Program to use Riemann sums or the trapezoid rule to
2 # estimate the area under a nicotine concentration curve.
3 from __future__ import division
4 from pylab import *
5
6 # Initialise variables
7 type = input("Type: 1 for Riemann sum, 2 for trapezoid: ")
8 t = array([0, 3, 6, 10, 14, 20, 35, 65, 95])
9 concs = array([5, 11, 15.4, 13.4, 12.8, 11.3, 9.8, 8, 7])
10 area = 0
11
12 # Sum the areas in each shape
13 i = 1
14 while i < size(t):
15     width = t[i] - t[i-1]
16     if type == 1:
17         height = concs[i-1]
18         shapeX = array([t[i-1], t[i-1], t[i], t[i]])
19         shapeY = array([0, height, height, 0])
20     else:
21         height = (concs[i-1] + concs[i])/2
22         shapeX = array([t[i-1], t[i-1], t[i], t[i]])
23         shapeY = array([0, concs[i-1], concs[i], 0])
24     area = area + height * width
25 # Plot each shape
26 plot(shapeX, shapeY, 'k-', linewidth=2)
27 i = i + 1
28
29 # Give the output.
30 print "The estimated AUC is", area, "ng min / mL"
31
32 plot(t, concs, 'bo', markersize=8)
33 xlabel("Time (mins)")
34 ylabel("Nicotine concentration (ng/mL)")
35 if type == 1:
36     title("Blood concentration of nicotine (rectangles)")
37 else:
38     title("Blood concentration of nicotine (trapezoids)")
39 show()

```



Here is the output from running the above program twice:

```

1 Type: 1 for Riemann sum, 2 for trapezoid: 1
2 The estimated AUC is 943.5 ng min / mL
3
4 Type: 1 for Riemann sum, 2 for trapezoid: 2
5 The estimated AUC is 896.15 ng min / mL

```

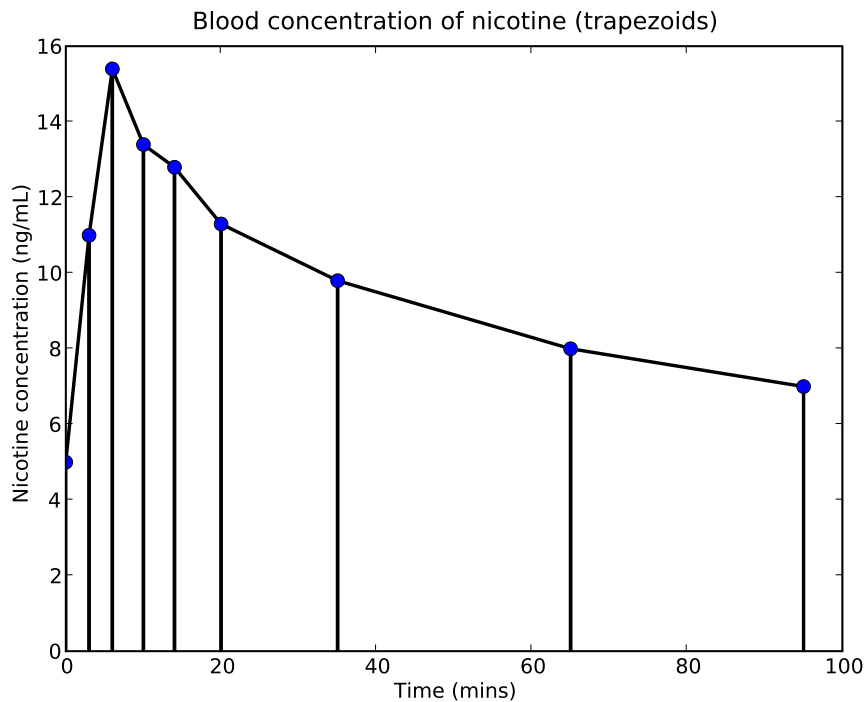
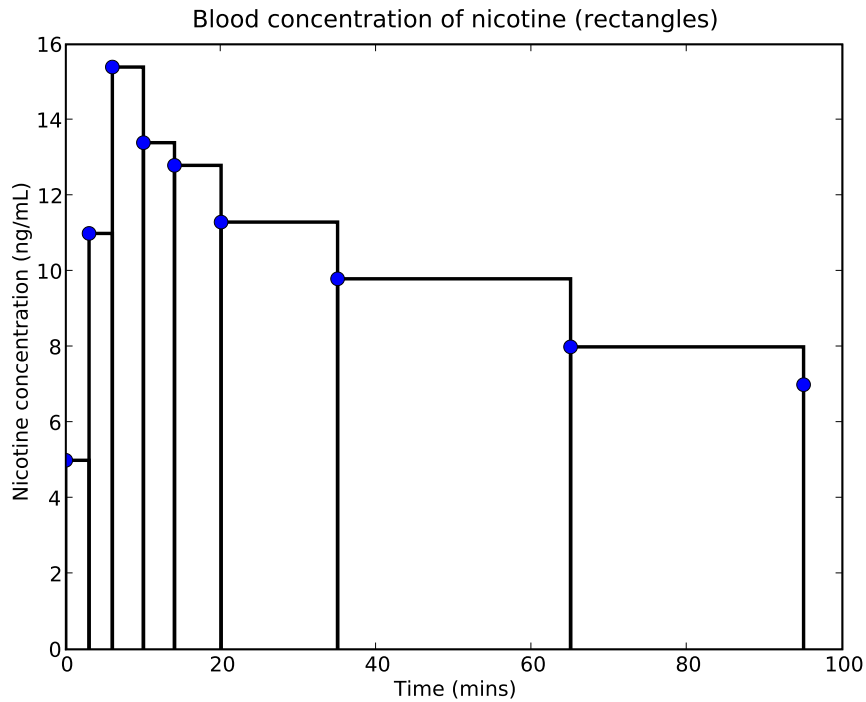


Figure 10.6: Program output using the Riemann sum (top) and trapezoid rule (bottom).

## 10.3 To the Fundamental

- In the last few sections we have covered:

(1) indefinite integrals,  $\int f(x) dx$ , which are solved using antiderivatives; and

(2) definite integrals,  $\int_a^b f(x) dx$ , which are calculated by measuring AUCs.

- These two concepts are useful precisely because they represent a range of important physical phenomena. For example:
  - velocity is the antiderivative of acceleration, and displacement is the antiderivative of velocity; and
  - the area under the concentration curve measures the overall exposure of the body to a drug.
- Our discussions so far do not suggest any apparent links between indefinite integrals and definite integrals. However, a very important theorem demonstrates a very close link.

### The Fundamental Theorem of Calculus

The **definite integral** of the **rate of change** of a function  $F$  between two points equals the **net change** in the **value** of  $F$  between the two points. That is:

$$\int_a^b F'(x) dx = F(b) - F(a)$$

### Significance of the Fundamental Theorem

The Fundamental Theorem is important and useful for the following reason. Consider some phenomenon, and let  $f$  be a function that models that phenomenon. Then we can often calculate the area under the curve between two points without needing to sum the areas of rectangles. Instead, find an antiderivative of  $f$ , substitute the values of the points into the antiderivative, and then subtract.

#### Example 10.3.1

Some examples include:

- (1) Let  $V(t)$  be the volume of water in a reservoir at time  $t$ , so  $V'(t)$  is the rate of inflow/outflow at any time. Then

$$\int_{t_1}^{t_2} V'(t) dt = V(t_2) - V(t_1)$$

is the net change in total volume from time  $t_1$  to time  $t_2$ .

- (2) If the population size of a bacterial colony changes at a rate of  $P'(t)$  (allowing for births, deaths and migration), then

$$\int_{t_1}^{t_2} P'(t) dt = P(t_2) - P(t_1)$$

is the net change in population from time  $t_1$  to time  $t_2$ .

- (3) Let  $[C](t)$  be the unknown concentration of the product  $C$  of a chemical reaction at time  $t$ , so  $[C]'(t)$  is the rate of reaction. Then

$$\int_{t_1}^{t_2} [C]'(t) dt = [C](t_2) - [C](t_1)$$

is the net change in concentration from time  $t_1$  to time  $t_2$ .

### Question 10.3.2

In Question 10.2.2 Part (d) we used the area of a triangle to calculate the AUC between  $t = 1$  hr and  $t = 6$  hr for the line shown in Figure 10.7.

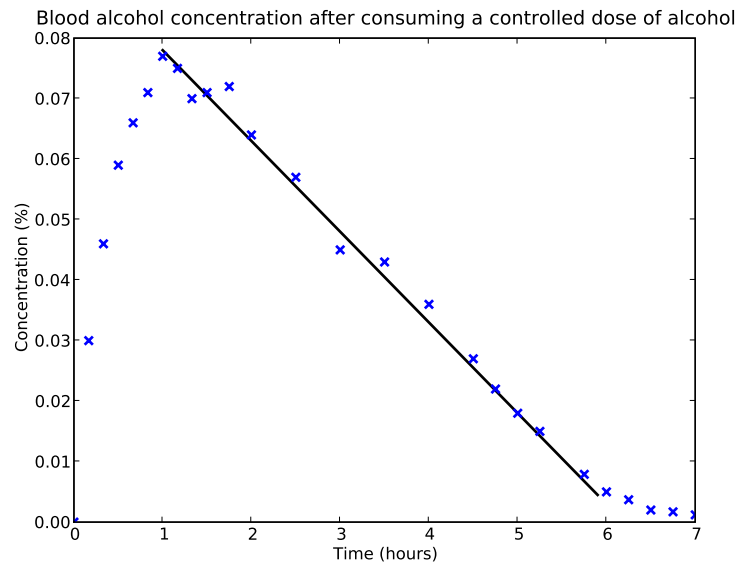


Figure 10.7: Blood alcohol concentrations.

**(a)** Rewrite Question 10.2.2 Part (d) as a definite integral.

**(b)** Evaluate the expression in Part (a).

**(c)** Compare your answer to Part (b) with your answer to Question 10.2.2 Part (d).

## Case Study 25: Dying for a drink



Photo 10.1: Left: mellow and yellow. Right: better red than dead. (Source: DM.)

- In addition to the immediate risks associated with alcohol consumption (such as accidents), the risk of many negative long-term health effects is increased by both the frequency and volume of consumption.

### *Question 10.3.3*

In Question 9.6.1, we estimated BACs using the Widmark formula. For a 70 kg man drinking  $n$  standard drinks (each containing 10 grams of alcohol), his estimated BAC % at time  $t$  in hours since commencing drinking is

$$B = \frac{10n}{490} - 0.015t.$$

- (a) At what time will his BAC return to 0?

*(continued over)*

**Question 10.3.3** (*continued*)

(b) Define the *total exposure to alcohol*  $E$  as the AUC of  $B$  from  $t = 0$  until the BAC reaches 0 again. Find an expression for  $E$ .

(c) Assume that long-term damage to internal organs from consumption of alcohol is proportional to the total exposure to alcohol  $E$  (which is simplistic, but not unreasonable). Discuss the impact on  $E$  of “one extra drink for the road”.

(*continued over*)

**Question 10.3.3** (*continued*)

- (d) A man with mass 70 kg consumes two standard drinks every day. A second man with the same mass consumes 14 standard drinks once a week, but does not drink at any other time. Estimate the weekly value of  $E$  for each.

(*continued over*)



**Question 10.3.3** (*continued*)

- (e) Comment on your results to Part (d). What are some ramifications of these results (for example, for binge drinking)?
- (f) Earlier we stated that it was “simplistic but not unreasonable” to assume that long-term organ damage from alcohol is proportional to  $E$ . What are some of the simplifying assumptions in the statement?

Now we can develop a computer model.

**Program specifications:** Write a Python program that uses the Widmark formula to graph the total exposure to alcohol for a 70 kg man consuming 0 to 15 standard drinks, and also prints out the relative exposure to alcohol compared with consuming 2 drinks.

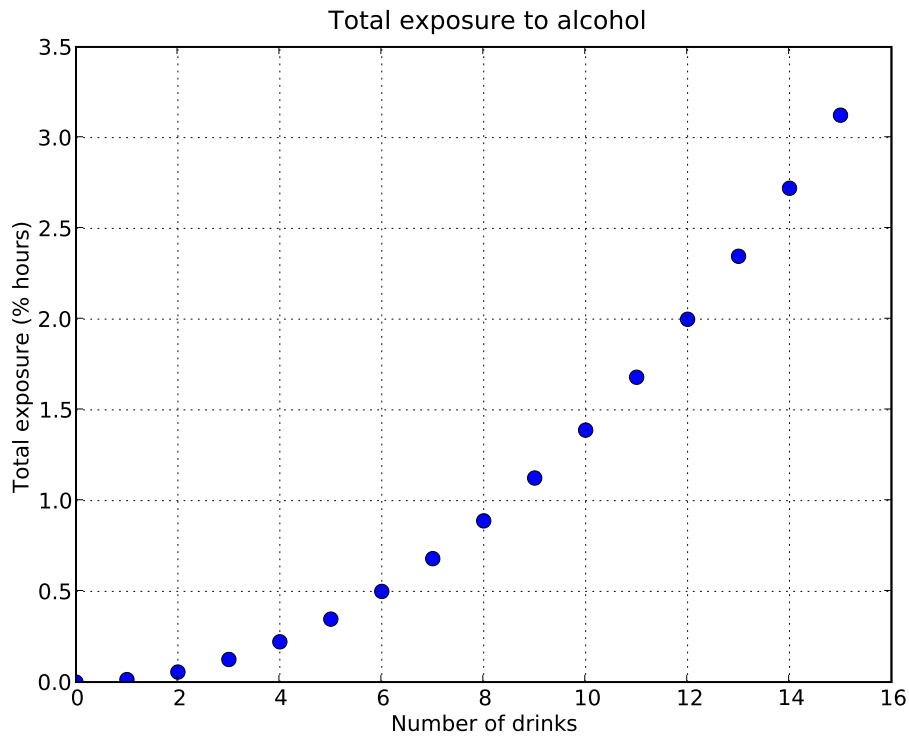
**Program 10.2: Wilful exposure (to alcohol)**

```

1 # Find the "exposure to alcohol" for a person of chosen gender
2 # and mass, consuming 0 to 15 drinks, and also print
3 # the relative total exposure compared to consuming 2 drinks.
4 from __future__ import division
5 from pylab import *
6
7 # Initialise variables
8 mass = input("Enter the person's mass in kg: ")
9 gender = input("Select 1 for male, anything else for female: ")
10 mass = mass * 1000
11 drinks = arange(0,16)
12 areas = 1.0 * arange(0,16)
13 if gender == 1:
14     water = mass * 0.7
15 else:
16     water = mass * 0.6
17
18 # Estimate E for each number of drinks and draw the graph.
19 nd = 0
20 while nd < 16:
21     tBAC0 = 1000 * nd / (0.015 * water)
22     areas[nd] = 1000 * nd * tBAC0 / water - 0.0075 * tBAC0**2
23     nd = nd + 1
24 plot(drinks, areas, 'bo', markersize=8)
25 grid(True)
26 xlabel("Number of drinks")
27 ylabel("Total exposure (% hours)")
28 title("Total exposure to alcohol")
29
30 # Output the relative exposure compared with 2 drinks
31 print "Num      Exposure relative to 2 drinks"
32 nd = 0
33 while nd < 16:
34     ratio = areas[nd] / areas[2]
35     print nd, "      ", round(ratio,1)
36     nd = nd + 1
37 show()

```

Figure 10.8 shows the output from running the above program.



```

1 Enter the person's mass in kg: 70
2 Select 1 for male, anything else for female: 1
3 Num    Exposure relative to 2 drinks
4 0      0.0
5 1      0.3
6 2      1.0
7 3      2.3
8 4      4.0
9 5      6.3
10 6     9.0
11 7    12.3
12 8    16.0
13 9    20.3
14 10   25.0
15 11   30.3
16 12   36.0
17 13   42.3
18 14   49.0
19 15   56.3
    
```

Figure 10.8: Exposure to alcohol.

End of Case Study 25.

## 10.4 You, me and AUC

### Case Study 26: Sweet P's



Photo 10.2: Left: sweet pea. Right: sweet pee. (Source: PA. (Not just the photo!))

- *Diabetes mellitus* is a group of chronic diseases in which sufferers have high levels of blood glucose.
- There are three main types of diabetes: *type 1* (insulin-dependent diabetes), *type 2* (non-insulin-dependent diabetes) and *gestational diabetes*.
- Typical signs of diabetes include:
  - *polyuria* (excessive urination, often with a sweet taste)
  - *polydipsia* (excessive thirst)
  - *polyphagia* (excessive hunger).
- Once type 1 or type 2 diabetes becomes established in an individual, it is typically permanent.

- Diabetes is increasingly common in societies with a “western lifestyle”: it affects around one million Australians, only about half of whom are aware they have the disease.
- Data from the Framingham heart study (which we saw early in semester) show that diabetes significantly reduces life expectancy (by around 7.5 years for men aged over 50, and by 8.2 years for women).
- Untreated diabetes can cause blindness, kidney failure and cardiovascular disease including blockages in small arteries. Some patients require amputations after blocked peripheral circulation causes the death of soft tissue.
- An *Oral Glucose Tolerance Test* (OGTT) is a common test for diabetes.
- Prior to taking the test, the patient fasts for around 12 hours. During the test, the patient is administered a measured oral dose of glucose, with blood samples taken immediately prior to ingestion of the glucose and at various intervals for 2 hours afterwards.
- The graph in Figure 10.9 compares the measured blood glucose levels for a non-diabetic person with those from a hypothetical diabetic person.

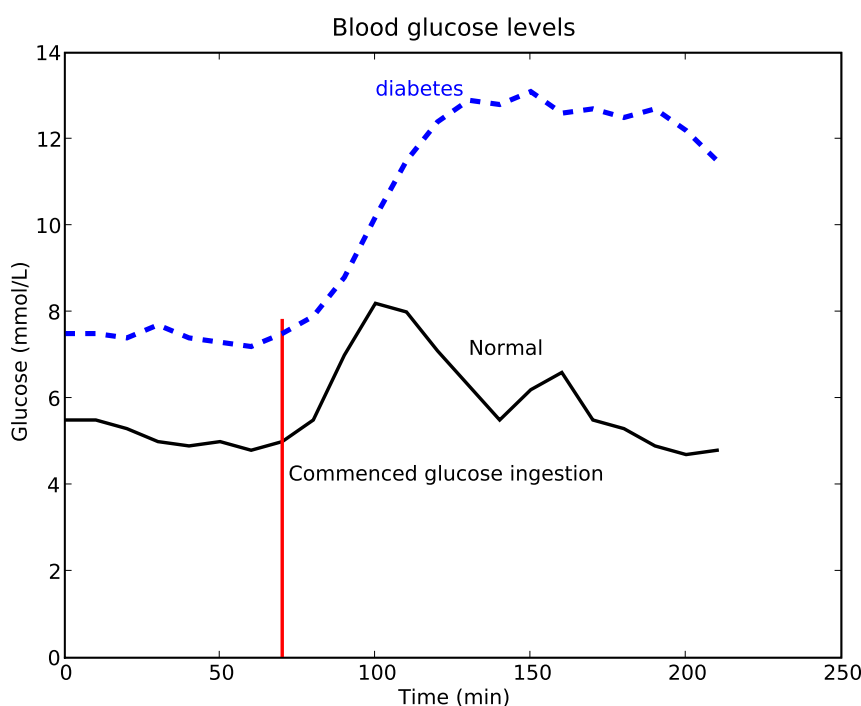


Figure 10.9: Normal blood glucose levels (solid line) and levels indicative of diabetes (dashed line).

- Figure 10.10 shows the World Health Organisation guidelines for blood glucose levels indicating various stages of health or disease.

	Normal		IFG		IGT		DM	
Levels	$t = 0$	$t = 2$	$t = 0$	$t = 2$	$t = 0$	$t = 2$	$t = 0$	$t = 2$
mmol/L	< 6.1	< 7.8	$\geq 6.1, < 7.0$	< 7.8	< 7.0	$\geq 7.8$	$\geq 7.0$	$\geq 11.1$

Figure 10.10: World Health Organisation guidelines for blood glucose levels as indicators of: Impaired Fasting Glycaemia (IFG); Impaired Glucose Tolerance (IGT or *pre-diabetes*); and Diabetes Mellitus (DM).



Photo 10.3: Left: bloody finger. Right: measured blood glucose concentration. (Source: PA.)

### Question 10.4.1

The graph in Figure 10.11 shows 22 blood glucose level measurements, taken from Peter at ten minute intervals between 6 am and 9:30 am. He had not eaten for 10 hours prior to testing, and at 7:10 am he commenced eating breakfast.

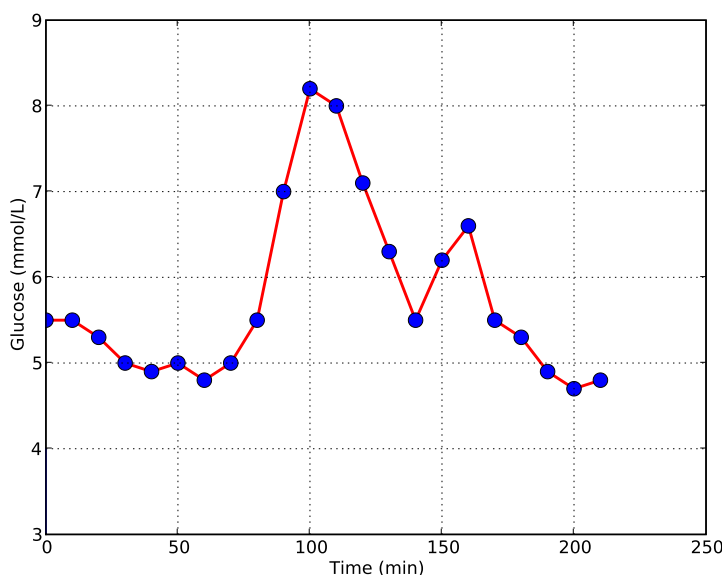


Figure 10.11: A graph of Peter's measured blood glucose levels. Time is given in minutes after 6 am.

*(continued over)*

**Question 10.4.1** (*continued*)

- (a) Comment on the graph and the measured values.
- (b) Estimate the total mass of glucose (molar mass 180.16 g/mol) in Peter's blood at the time of peak concentration.

- A blood glucose measurement shows the concentration of glucose in the blood at a specific instant in time.
- It is possible that the level might be within the normal range at that instant, but outside the normal range over a longer time period.
- AUCs allow analysis of the values over a longer time period.
- For example, the paper [20] studies a group of patients with type 1 diabetes who have normal fasting glucose levels but very high levels after an OGTT.

**Question 10.4.2**

Figure 10.12 shows measured blood glucose levels for a diabetic group and a control group, adapted from [20].

*(continued over)*



*Question 10.4.2 (continued)*

time (mins)	0	30	60	90	120
diabetic group (mmol/L)	5.3	10	13	14.4	14.2
control group (mmol/L)	5.1	8.2	8.2	7.1	6.5

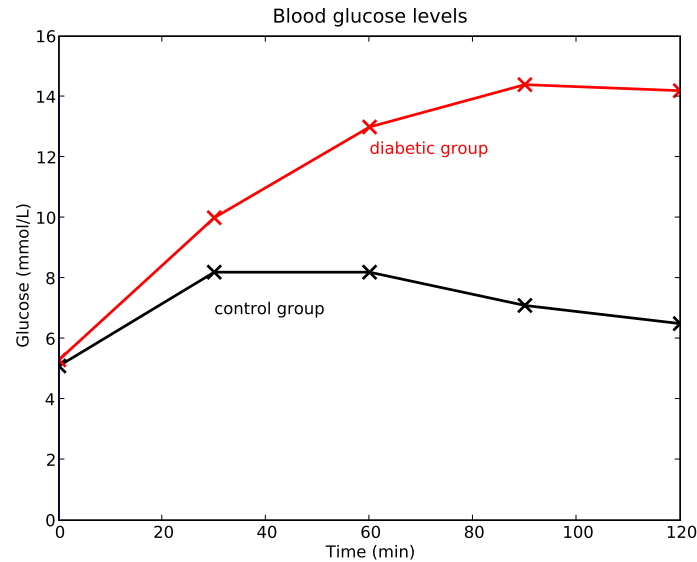


Figure 10.12: Mean blood glucose levels for a diabetic group and a control group.

The paper [20] found that the AUC for the diabetic group is around 779 mmol/L/min, and for the control group is around 265 mmol/L/min. Comment on the units and justify these results.

End of Case Study 26.

## Case Study 27:

### Hi GI!

- The *Glycaemic Index* or GI of foods is often mentioned in marketing campaigns and in association with dietary health claims.
- The definition of GI is the **ratio of the AUCs for two blood glucose curves**, one for the food of interest and the other for pure glucose.
- GIs range between 0 and 100, and indicate the relative extent by which blood glucose levels rise after the consumption of a food.
- Hence, GI scores are only valid for foods containing carbohydrates.
- Researchers classify foods into the following GI categories.
  - *Low GI* – when the GI is 55 or lower, the digestion of carbohydrates is slow, producing a slow rise and lower peak in blood sugar level. Examples of Low GI foods include cherries, skim milk, apples, chick peas, oranges and carrots.
  - *Medium GI* – when the GI is between 56 and 69, the digestion of carbohydrates occurs at a moderate rate. Examples of Medium GI foods include include boiled potato, honey, ice cream and sultanas.
  - *High GI* – when the GI is 70 or higher, the digestion of carbohydrates is fast, leading to a rapid rise and high peak in blood sugar level. Examples of High GI foods include mashed potato, white bread, cornflakes, watermelon and steamed white rice.
- The many claimed health benefits of Low GI diets include weight loss and improved weight control, improved management of diabetes, reduced risk of cardiovascular disease and increased physical stamina.
- Researchers calculate the GI of a food in the following way:
  - Ten healthy people fast overnight. In the morning, each person consumes a controlled dose of the test food, with known total carbohydrate content (typically 50 g).

- Over a 2 hour period, researchers measure the increase in the blood glucose level above baseline for each participant, produce a graph, and then calculate the AUC of the test food for each individual using the trapezoid rule.
  - On a separate day, participants undergo the same procedure, but consume a glucose solution which contains the same amount of total carbohydrate. Researchers calculate the AUC for glucose (the reference food) for each individual.
  - The formula for calculating the GI is: the AUC for the test food divided by the AUC for glucose, multiplied by 100%. An average of the individual GI scores represents the overall GI for the test food.
- Criticisms of focusing on GIs as a dietary tool include:
    - GIs can vary greatly for a given food, depending on how ripe it is, and how it is processed, stored and cooked;
    - the GI of a food may be less important than the actual *quantity* consumed; and
    - measured GIs may not be very exact or reliable. For example, if the GI of a given food is measured at different times of the day then the results can differ quite substantially.

### **Question 10.4.3**

Consider a certain test food for which the GI is to be calculated. Let  $F(t)$  and  $G(t)$  be the increase (above baseline) in blood glucose levels in mmol/L measured while calculating the GI, with  $F(t)$  corresponding to the test food and  $G(t)$  corresponding to glucose.

- (a)** Write a mathematical expression for the GI of the test food.

*(continued over)*

**Question 10.4.3** (continued)

(b) Draw a diagram illustrating your answer to Part (a).



Photo 10.4: Nut sandwich. (Source: PA.)

**Question 10.4.4**

The paper [23] compared the GI of meals containing bread and almond nuts to the GI of meals containing bread only. Figure 10.13 shows the study data.

The GI of the the ‘bread only’ meal is about 70. Estimate the GI of the ‘bread and almonds’ meal.

(continued over)

*Question 10.4.4 (continued)*

time (mins)	0	15	30	45	60	90	120
'bread only' group (mmol/L)	4.7	5	6.5	7	6.8	5.5	4.8
'bread and almonds' group (mmol/L)	4.7	4.7	5.5	5.8	5.3	4.8	5.1

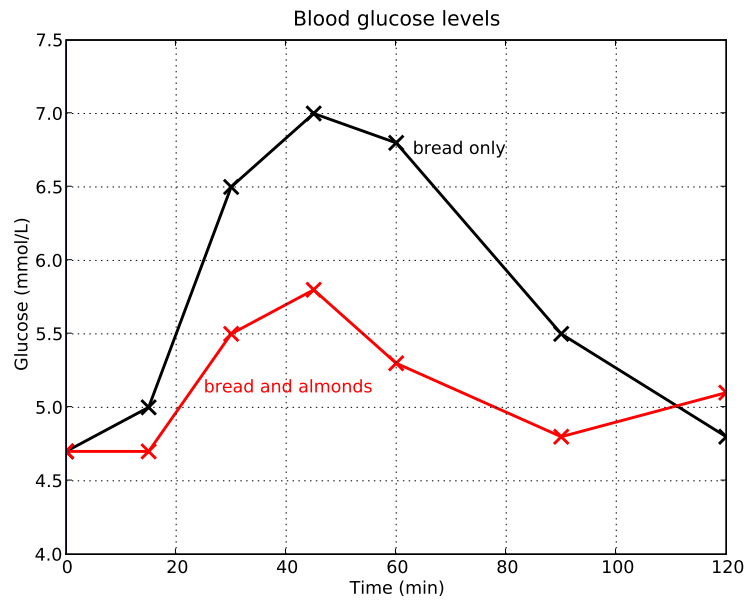


Figure 10.13: Mean blood glucose levels.

End of Case Study 27.

## Case Study 28:

### Bioavailability of drugs

- Drugs are administered via many routes, including:
  - orally, such as the contraceptive pill;
  - as a gas, such as nicotine from a cigarette;
  - through the skin, such as a nicotine patch;
  - intravenously, such as chemotherapy drugs for treating cancer;
  - sublingually, such as nitroglycerin used to treat angina;
  - through the rectum, such as a paracetamol suppository.
- Different routes of drug delivery are required depending on the drug type and the condition of the patient. Oral administration is often most convenient, but other routes may be more convenient for drugs that cause nausea or vomiting, or for patients undergoing cancer treatment, who often develop severe, painful mouth ulcers.
- After administration of a drug, it typically needs to pass through a number of stages before it enters general circulation and has a chance to act.
- For example, the amount of an oral drug which enters circulation is influenced by the following factors, collectively called *first pass effects*:
  - how readily the drug is liberated from the tablet;
  - how readily and rapidly the drug dissolves in the digestive tract;
  - whether the drug is damaged by acidic stomach contents;
  - whether the drug is partially metabolised by bacteria in the gut;
  - how much of the drug is absorbed across the intestinal wall;
  - the digestive health of the individual (for example, vomiting or diarrhoea causes mechanical expulsion of the drug);
  - whether the drug is partially metabolised while being transported in the blood; and
  - how much drug is metabolised in the liver prior to entering general circulation (because blood travels from the small intestine to the liver).

- After administering a drug by a given route, its **bioavailability**  $F$  is the fraction of the dose which enters general circulation compared to a dose of the same size administered intravenously.

### Definition of bioavailability

Let  $R(t)$  be the measured blood concentration after administration by some route a dose of size  $D_R$ , and let  $I(t)$  be the measured concentration after intravenous administration of a dose of size  $D_I$ . Then the bioavailability of the drug administered via this route is:

$$F = \frac{\int_0^{\infty} R(t) dt}{\int_0^{\infty} I(t) dt} \times \frac{D_I}{D_R}.$$

### Question 10.4.5

(a) Explain the meaning of each term in the expression for  $F$ .

(b) Relate the concepts of bioavailability and GI.

### Question 10.4.6

In [34], patients were administered 1000 mg of the analgesic paracetamol intravenously, and then had their subsequent blood paracetamol levels measured. In the paper, researchers modelled the measured blood concentration in  $\mu\text{g}/\text{mL}$  at time  $t$  in hours after dosing with  $I(t) = 13.8e^{-2.55t} + 13e^{-0.28t}$ .

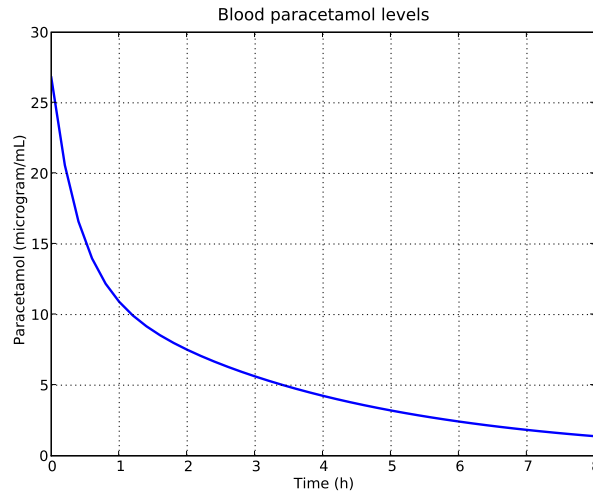


Figure 10.14: The graph of  $I(t)$ , modelling blood concentrations after patients were administered intravenous doses of 1000 mg of paracetamol.

- (a) Calculate the AUC from  $t = 0$  to  $t = \infty$  for  $I(t)$ , with units. (Hint:  $\int ae^{kt} dt = \frac{a}{k}e^{kt} + C$ .)

*(continued over)*



**Question 10.4.6** (*continued*)

- (b) Researchers also administered paracetamol orally. Find the AUCs if the bioavailability of a 500 mg oral dose is 0.63, and 1000 mg is 0.9.
- (c) In [28], researchers administered 1000 mg rectal doses of paracetamol in aqueous solution. They monitored blood concentrations for 6 hours, and then calculated the AUC from time  $t = 0$  h to  $t = 6$  h, denoted  $AUC_{0-6}$ , using the trapezoid rule. The researchers then estimated the AUC until  $t = \infty$  using the following equation (quoted from [28]):

$$AUC_{0-\infty} = AUC_{0-6} + C_{t=6} \times t_{1/2} \times \frac{1}{0.69}$$

where  $C_{t=6}$  is the measured concentration 6 hours after the dose was administered and  $t_{1/2}$  is the half life of paracetamol. Illustrate the equation with a diagram and justify it mathematically.

(*continued over*)

**Question 10.4.6** (*continued*)

- (d) The paper [28] found that the AUC for the 1000 mg **oral** paracetamol dose is around 2540  $\mu\text{g}/\text{mL}/\text{min}$  and the 1000 mg **rectal** mg dose is around 2290  $\mu\text{g}/\text{mL}/\text{min}$ . Deduce the relative bioavailability of a 1000 mg **rectal** dose compared with a 1000 mg **oral** dose. (Also, comment on the units for the AUCs given in [28] and reproduced above.)

(*continued over*)

**Question 10.4.6** (continued)

(e) The model for blood concentration after administration of 1000 mg rectal doses of paracetamol, using the data given in [28], is

$$R(t) = 14t^{0.5}e^{-0.5t}$$

where the units for  $R(t)$  are  $\mu\text{g}/\text{mL}$  and  $t$  is the number of hours since administration. Figure 10.15 shows the graph of  $R(t)$ .

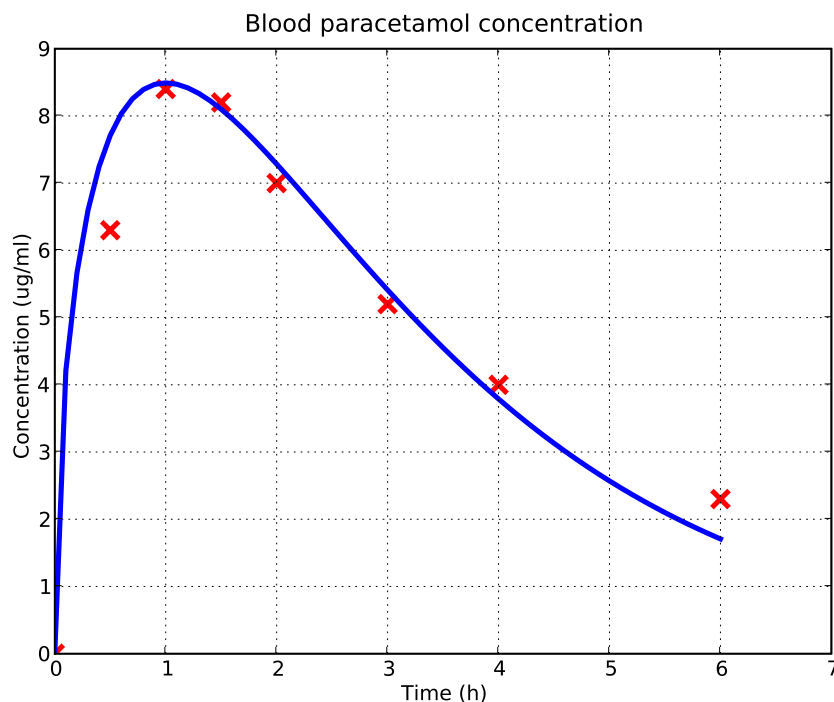


Figure 10.15: Modelled blood paracetamol concentrations for patients after administration of 1000 mg rectal doses.

On the above graph, draw a curve which is likely to model (roughly) the concentration after a 1000 mg oral dose. Also indicate how the equation modelling the curve would differ from  $R(t)$ . (Hint: absorption after an oral dose is more rapid than for a rectal dose.)

End of Case Study 28.

## 10.5 Space for additional notes

## Part 5: Life and Death

“O sweeter than the marriage-feast,  
'Tis sweeter far to me,  
To walk together to the kirk  
With a goodly company!

To walk together to the kirk,  
And all together pray,  
While each to his great Father bends,  
Old men, and babes, and loving friends,  
And youths and maidens gay!

Farewell, farewell! but this I tell  
To thee, thou Wedding-Guest!  
He prayeth well, who loveth well  
Both man and bird and beast.

He prayeth best, who loveth best  
All things both great and small;  
For the dear God who loveth us,  
He made and loveth all.”

The Mariner, whose eye is bright,  
Whose beard with age is hoar,  
Is gone; and now the Wedding-Guest  
Turned from the bridegroom's door.

He went like one that hath been stunned,  
And is of sense forlorn:  
A sadder and a wiser man  
He rose the morrow morn.

*The Rime of the Ancient Mariner* (1797 – 98),  
Samuel Taylor Coleridge, (1772 – 1834).



Image 10.2: *The three ages of Man and Death* (c1510), Hans Baldung (c. 1484 – 1545), Museo del Prado, Madrid. (Source: commons.wikimedia.org).



## Chapter 11: Populations

---

*All things bright and beautiful,  
All creatures great and small,  
All things wise and wonderful,  
The Lord God made them all.  
Each little flower that opens,  
Each little bird that sings,  
He made their glowing colours,  
He made their tiny wings.*

Artist: Cecil Alexander ([www.youtube.com/watch?v=KLfkL8uDuc8](http://www.youtube.com/watch?v=KLfkL8uDuc8))



Image 11.1: *The Entry of the Animals into Noah's Ark* (1613), Jan Brueghel the Elder (1568 – 1625), The J. Paul Getty Museum, Los Angeles. (Source: [en.wikimedia.org](http://en.wikimedia.org).)

## 11.1 Introduction to differential equations

- If we can write an equation representing the rate at which a phenomenon is changing, mathematical techniques can be used to predict future values.

### *Example 11.1.1*

The acceleration due to gravity on Earth is  $g = -9.8 \text{ m/s}^2$ . Let  $v(t)$  be the unknown velocity of a ball dropped at time  $t = 0 \text{ s}$ . Acceleration is the rate of change of velocity, so  $v'(t) = -9.8$ . We can then use integration to solve for  $v$ , giving  $v(t) = -9.8t \text{ m/s}$  at any time  $t$  in seconds.

- In Example 11.1.1, we started with an equation for the rate at which the function  $v$  is changing, and used integration to find the value of the function.
- Integration was easy, because **the rate at which  $v$  is changing is only dependent on the value of  $t$** .
- In nature, many phenomena do not only change according to time. Instead, their rate of change may be influenced by the **value they currently have**, or to the **value that some other phenomenon has**, or even the rate at which the other phenomenon is changing.
- Equations that relate rates of change to the value of a function (and possibly other factors) are called *differential equations*.

### **Differential equations**

If  $y$  is an unknown function of  $t$ , then a **differential equation**, or **DE**, is an equation that involves a combination of  $t$ ,  $y$  and/or the derivatives of  $y$ .

If the DE is true when a particular function  $y$  and its derivative(s) are substituted into the DE, then  $y$  is a **solution** to the DE.

- In all of the examples we will study, the DE will be of the form  $y' = \dots$ . A **solution** to the DE will be **another function** that, when **substituted** into the DE, makes the DE **true**.

## 11.2 DEs and exponential growth

- Earlier we studied exponential growth and decay. On Page 133 we stated “Any phenomenon that has a rate of change proportional to the current amount follows an exponential function”.
- This occurs precisely because such phenomena satisfy simple DEs whose solutions are exponential functions.
- Many populations satisfy exponential functions.
- Note that we can measure the size of a population in multiple ways, such as the total number of individuals, the density of individuals, or the total biomass of the population.

### Case Study 29: Algal blooms



Figure 11.1: Algal bloom in the Atlantic Ocean. (Source: commons.wikimedia.org.)

Photo 11.1: Close-up view of algae. (Source: DM.)

- Most microscopic algae reproduce asexually, with each *mother* cell splitting to form two *daughter* cells.
- Under normal conditions, factors such as predation and limited resources keep algal populations under control.
- However, sometimes uncontrolled reproduction occurs, leading to an **algal bloom** in which the population can reach  $10^6$  individuals per mL of water.



- Some blooms are harmful to humans, producing dangerous biotoxins that pass down food chains. Many algal blooms result directly or indirectly from human activities, such as an excess of nutrients in water.
- Researchers expect that the frequency and severity of algal blooms will increase due to further environmental degradation.
- Because the rate at which algae reproduce is often proportional to the current population size, algal populations follow exponential functions for some time periods.

**Question 11.2.1**

Consider a population of algae growing at 2% per hour. If  $N(t)$  is the population of algae per mL of water at time  $t$  in hours then the population size satisfies the DE  $N' = 0.02N$ .

**(a)** Explain carefully, in words, what the DE is saying.

**(b)** Show that  $N(t) = Ae^{0.02t}$  is a solution to the DE, where  $A$  is a constant.

**(c)** If we know that the population at time  $t = 0$  hours is 500 algae per mL of water, find the population at any time  $t$ .

### DE for exponential growth and decay

Any function  $N(t)$  with a rate of change proportional to the value of  $N$  (at any time), and a change constant equal to  $r$  per time period, follows the DE  $N' = rN$ .

The solution to the DE is  $N(t) = N_0e^{rt}$ , where  $N_0$  is the value of  $N$  at time 0.

### Question 11.2.2

Demonstrate mathematically *why* the solution to the DE  $N' = rN$  is the exponential function.

### Case Study 30:

### Poo



Photo 11.2: Steaming heap of panda poo. (Source: PA.)

- *Escherichia coli* (usually shortened to *E. coli*) are bacteria commonly found in the lower intestine of warm-blooded animals, including humans.

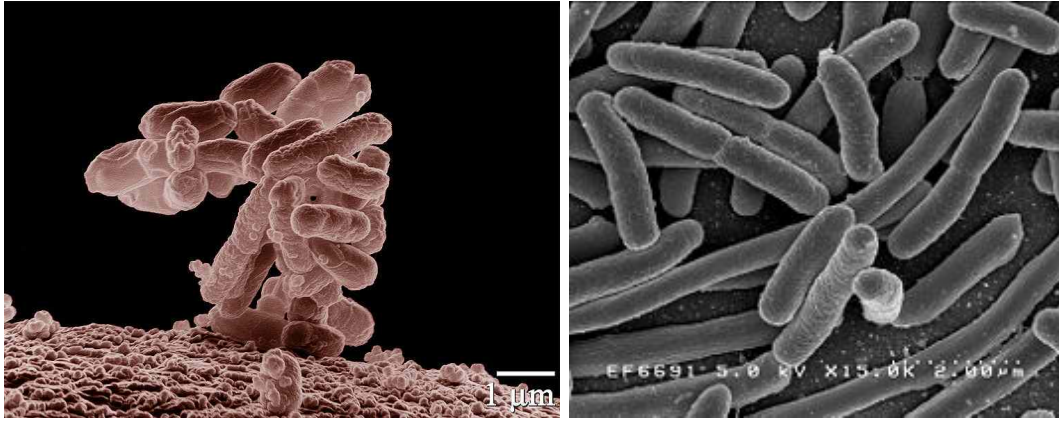


Image 11.2: Left: Low-temperature electron micrograph of *E. coli*, magnified 10,000 times. Right: Scanning electron micrograph of culture-grown *E. coli*. (Source: en.wikipedia.org.)

- Most strains of *E. coli* are harmless in the digestive system, or even beneficial to the host. However, some strains produce toxins, and can cause food poisoning, gastrointestinal infections and urinary tract infections.
- One such strain is *O157:H7*, which caused outbreaks of illness in Washington and California in 1994, and probably came from contaminated salami.
- Because *E. coli* can survive outside the body for some time, tests for *E. coli* are often used to identify faecal contamination in environmental samples or foods during hygiene checks.
- Under simplifying assumptions (such as relatively unlimited resources) the rate of increase of a population of *E. coli* at any time is proportional to the population size at that time.
- Hence the population follows an exponential function, and it makes sense to discuss the *doubling time* of the population.
- Under favourable conditions, the doubling time for a population of *E. coli* may be an hour, or even shorter.
- The rapid growth rate is one reason why good hygiene standards are important in food preparation.
- When studying populations of bacteria, microbiologists commonly count *colony-forming units* (CFU), which is the number of *live* bacterial cells. (Direct counts of individuals include both dead and living cells.)

**Question 11.2.3**

A population of *E. coli* in a contaminated food sample increases with a growth constant of  $r = 1$  per hour. Assume there are  $10^3$  CFU/g at time 0.

(a) Write a DE for the population size  $E(t)$  in CFU/g after  $t$  hours.

(b) Solve the DE in Part (a).

- A recent paper [40] investigates *E. coli* contamination of pre-cooked meat products (specifically ham) during the slicing process.
- The study models two sources of contamination:
  - from a slicing blade infected with *E. coli* to clean ham; and
  - from infected ham, to a clean slicing blade, then to clean ham.

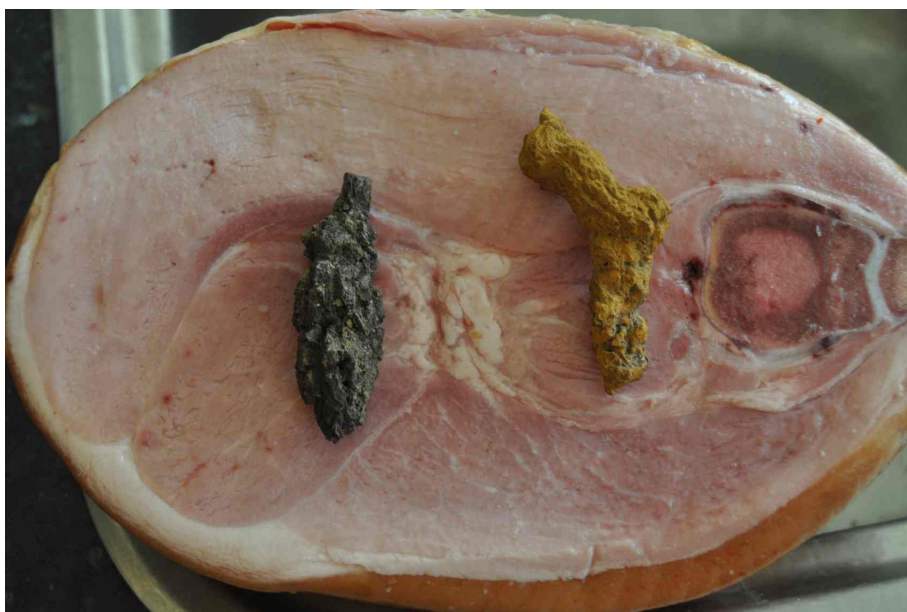


Photo 11.3: Ham with (subtle) faecal contamination. (Source: PA.)

One of the research experiments involved:

- inoculating (infecting) ham with “7 log CFU of O157:H7 *E. coli*” (that is,  $10^7$  CFU);
- using a clean blade to slice the inoculated ham;
- using that blade to cut 100 slices of clean ham; and
- counting the number of CFU on each of the 100 slices.

**Question 11.2.4**

If  $x$  is the number of a ham slice from 1 to 100, then  $\log_{10}$  of the number of CFU on each slice  $Y(x)$  is modelled by

$$Y = 2.793 \times e^{-0.0105x}.$$

- (a) Roughly how many CFU were on Slice 1 and on Slice 100?
- (b) Find an expression for the number of CFU on any slice of ham after any number of hours, assuming the slices are stored under ideal growing conditions for *E. coli*.

- Given a DE that models a phenomenon, the general solution to the DE (together with initial conditions) predicts the values of the phenomenon at various times.
- Scientists are often interested in *stable points*.

### Stable points

The general solution  $y$  to a DE **may** have one or more *stable points* (also called *equilibrium values*), which are points at which  $y' = 0$ . If the value of the phenomenon ever reaches a stable point, it remains equal to that value indefinitely.

### Question 11.2.5

Why are stable points important scientifically?

### Question 11.2.6

In Question 11.2.3 we considered a population of *E. coli* bacteria that satisfied the DE  $E' = E$ .

- (a) Find all stable population sizes.
- (b) Interpret your answer to Part (a).

End of Case Study 30.

- Many other phenomena satisfy exponential DEs, including temperature change and alcohol absorption.

**Question 11.2.7**

When we move an object with one temperature to an environment with a different temperature, the temperature of the object changes according to *Newton's Law of Cooling*. Assume we place a small object in a room with temperature equal to a constant  $T$ . Let  $y(t)$  be the temperature of the object at any time  $t$ .

**(a)** Derive a DE for the rate of change of temperature of the object.

**(b)** Your equation should include a constant, say  $k$ . What physical factors would determine the value of  $k$ ?

*(continued over)*

**Question 11.2.7** (*continued*)

In Question 6.2.5 we studied how the temperature changed in hot water placed in a room with temperature 25 °C. We modelled the temperature  $y(t)$  in °C at any time  $t$  in minutes with

$$y(t) = 60e^{-0.05t} + 25.$$

**(c)** Show that the equation is the solution to the DE  $y' = -0.05(y - 25)$  and relate the solution to Newton's Law of Cooling.

**(d)** Find all stable points and explain your answer.



**Question 11.2.8**

Alcohol is mostly absorbed into the bloodstream via the small intestine. The rate of absorption is proportional to the amount of alcohol that is present in the digestive tract at any time.

(a) Assume an individual consumes  $A$  grams of pure alcohol. Write a DE for the rate of change of the amount of alcohol  $D$  in the digestive system at any time, and solve the DE.

(b) Find an expression for the **total** amount of alcohol *absorbed by the body at any time*, ignoring elimination.

(c) Find an expression for blood alcohol content (BAC) if the drinker has

*(continued over)*

**Question 11.2.8** (*continued*)

mass  $M$  g, and a fraction  $r$  of their mass is water. (Hint: ignore elimination, and remember to convert BAC to a percentage.)

**(d)** If the body can eliminate alcohol at a constant rate of  $V$  % per hour, find an expression for the BAC at any time  $t$  in hours.

**(e)** Compare your answer to the equation given in Question 9.6.2.

## 11.3 Limited scope for growth

- Exponential growth is *unconstrained*; that is, it continues growing indefinitely. Unconstrained growth is unrealistic over extended time periods.

### *Question 11.3.1*

Let  $N(t)$  be the size of a fish population in a certain lake at any time  $t$  in months. If the natural rate of increase of the fish population is 10% per month, then  $N(t)$  satisfies the differential equation  $N' = 0.1N$ . Assume that at time 0 there are 30 fish.

- (a) Draw a rough sketch of the predicted population versus time.

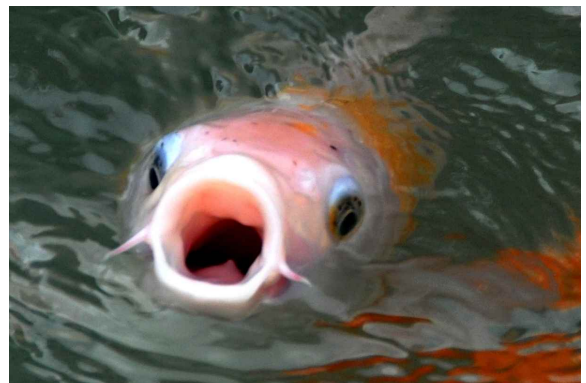


Photo 11.4: Pucker up. (Source: PA.)

- (b) Environmental analysis has shown that the maximum fish population the lake can support is 1000. What is a more realistic rough sketch of  $N(t)$  over time?

- During unconstrained exponential growth, the proportional rate of increase is constant at all times, irrespective of the population size.
- A constant proportional rate of increase is often quite accurate over some time periods.
- However, in most cases populations cannot continue to show unconstrained growth: environmental conditions and limited availability of resources restricts growth to a **maximum** population size.

### Carrying capacity

The **carrying capacity** of an ecosystem is the maximum population size of a particular organism that can be supported by resources within the ecosystem. Resources may include food, water, shelter and sunlight.

A population size below the carrying capacity will typically increase towards the carrying capacity, whereas a population size above the carrying capacity will typically decrease to the carrying capacity.

- The carrying capacity for a particular organism often changes over time; for simplicity, we will assume it remains constant.
- In more sophisticated population models than the exponential model, the **rate of change** in the population will:
  - **increase** as the population size gets bigger and there are more individuals who can reproduce; and
  - **decrease** as the population size gets closer to the carrying capacity and individuals compete for scarce resources.
- One such model that reflects these features is the *logistic model*.
- The power of the logistic model is the interaction between the two opposing growth and competition factors.

**Question 11.3.2**

The logistic DE is

$$N' = r N \left( \frac{K - N}{K} \right),$$

where  $N(t)$  is an unknown function (such as a population),  $r$  is the unconstrained growth rate and  $K$  is the carrying capacity.

Explain carefully, in words, what the DE is saying.

In particular, what is the significance of the term  $\left( \frac{K - N}{K} \right)$ ?

- Just as it is possible to solve the exponential DE, it is also possible to find a solution to the logistic DE.

### Solution to the logistic DE

Any function  $N(t)$  that changes at a rate proportional to its value (with unconstrained growth rate  $r$ ), **and also** in reverse proportion to how close the value is to a carrying capacity  $K$ , is modelled by the logistic DE

$$N' = r N \left( \frac{K - N}{K} \right).$$

If  $N_0$  is the value of  $N$  at time 0 then the solution to the DE is

$$N(t) = \frac{K N_0}{N_0 + (K - N_0)e^{-rt}}$$

### Question 11.3.3

From the equation for  $N'$ , explain why the solution to the logistic DE displays the following properties. If the initial population is:

- (a) much less than the carrying capacity, then the population initially grows approximately exponentially.
- (b) close to the carrying capacity, then the population grows slowly towards the carrying capacity.
- (c) more than the carrying capacity, then the population declines approximately exponentially towards the carrying capacity.

## Case Study 31: Very fishy

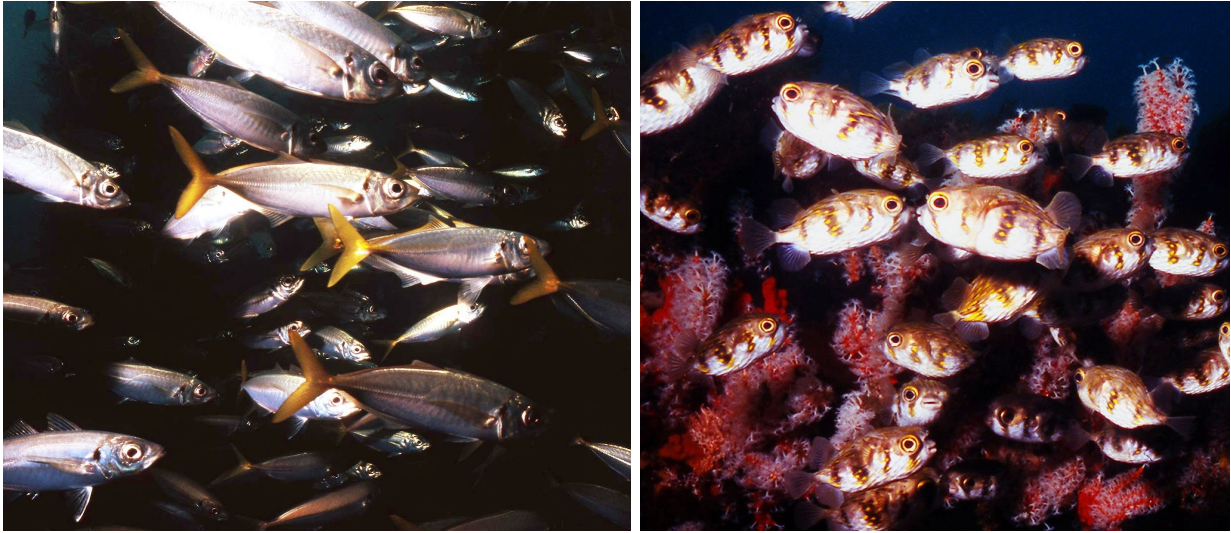


Photo 11.5: Left: Southern Yellowtail Scad (*Trachurus novaezelandiae*). Right: Globe Fish (*Diodon nichthemerus*). (Source: DM.)

- The logistic model applies to many populations. A common use is fish population modelling, including harvest rates and stock management.

### *Example 11.3.4*

A fish species with an unconstrained population growth rate of 10% per month lives in a reef with a carrying capacity of  $K=1000$  fish. Assume that growth is logistic, and that the initial population is  $N_0 = 30$  fish.

The function for the fish population  $N(t)$  at time  $t$  months satisfies the DE

$$N' = 0.1 N \left( \frac{1000 - N}{1000} \right).$$

Substituting  $N_0$ ,  $r$  and  $K$  in the solution for the logistic DE gives the following function for the number of fish at time  $t$  months:

$$\begin{aligned} N(t) &= \frac{1000 \times 30}{30 + (1000 - 30)e^{-0.1t}} \\ &= \frac{30000}{30 + 970e^{-0.1t}} \end{aligned}$$

*(continued over)*



*Example 11.3.4 (continued)*

- Figure 11.2 shows the population for a period of 80 months. Note the typical *sigmoidal* “S”-shaped logistic curve.
- Because the initial population is much less than the carrying capacity, the population initially rises close to exponentially, then the (actual) growth rate slows and the population gradually approaches the carrying capacity.
- For comparison, Figure 11.3 shows the resulting graph when the initial population is  $N_0 = 1500$ . Here, the population rapidly decreases towards the carrying capacity.

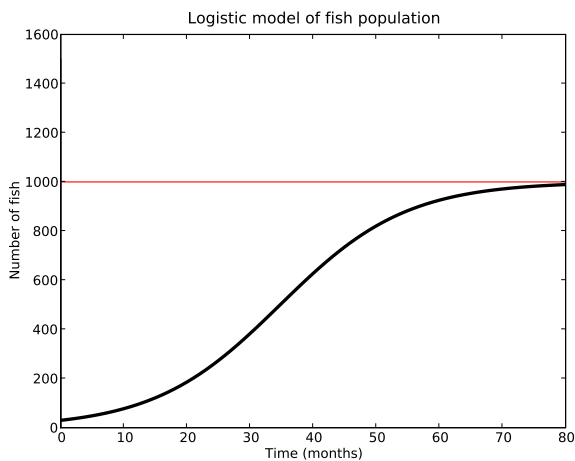


Figure 11.2: Logistic model with initial population 30.

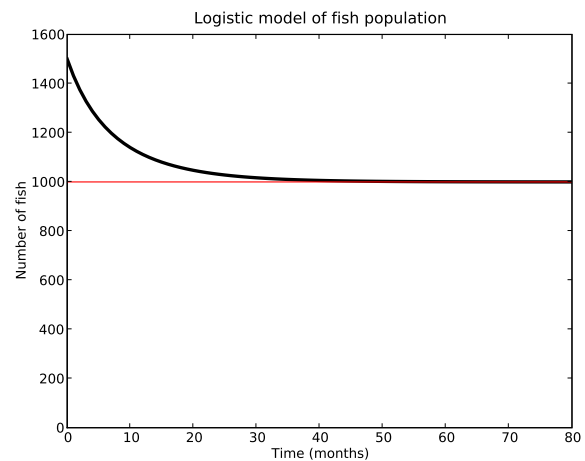


Figure 11.3: Logistic model with initial population 1500.



Photo 11.6: Left: Moonlighter (*Tilodon sexfasciatus*). Right: Five-line Snapper (*Lutjanus quinquelineatus*) and Black-spot Snapper (*Lutjanus fulviflammus*). (Source: DM.)

End of Case Study 31.



### Example 11.3.5

The logistic DE can also model the size or mass of individual organisms. (Organisms are effectively populations of cells.)

- In [26], researchers studied a particular species of North-Queensland bird, the Yellow-bellied Sunbird *Nectarinia jugularis*, to predict the expected masses and growth rates of hatchlings.
- Researchers visited a number of nests for 14 days, weighing individually marked nestlings. The data show that when sunbirds hatch, they:
  - typically weigh around  $0.92 \pm 0.13$  g;
  - initially grow by about 0.62 g per day;
  - ultimately weigh around  $8.92 \pm 1.14$  g (males) or  $8.12 \pm 1.11$  g (females) as adults.
- Researchers modelled the mass  $M$  (in g) of nestling sunbirds  $t$  days after birth with the equation

$$M = \frac{8.6}{1 + e^{-0.37(t-5.8)}}.$$

- Figure 11.4 shows a graph of the measured data and the model.

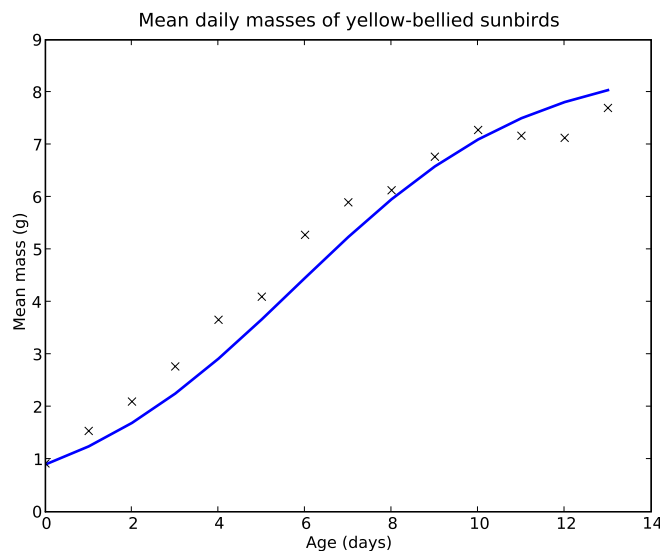


Figure 11.4: Mean daily masses of yellow-bellied sunbirds, as measured and as modelled.

## Case Study 32: Overfishing annoys an oyster



Photo 11.7: Oysters. (Source: MG.)

- Chesapeake Bay is a large estuary on the east coast of the United States, near the states of Virginia and Maryland.
- It has a surface area of more than 11000 km<sup>2</sup>, with a shoreline length of more than 18000 km.
- More than 150 watercourses enter the bay, including the Potomac River, which runs through Washington.
- In the past, the bay supported a diverse range of flora and fauna, including an abundant shellfish population, most notably oysters.
- However, the bay has experienced serious environmental degradation due to over-use, overfishing, and polluted runoff from agriculture, urban areas and industry.
- Substantial *marine dead zones*, which are areas of water so low in oxygen that they are unable to support life, are often found within the bay.
- These dead zones often result from large algal blooms, and are clearly disastrous to the ecosystem.

- Harvesting oysters is a long-term commercial industry in Chesapeake Bay, however, the size of the population (and hence the harvest) has drastically reduced, due to overharvesting and environmental damage; see Figure 11.5.
- The total current biomass of the oyster population is less than 0.5% of the previous, long-term, pre-harvesting total.
- Between 1982 and 2008, the value of the oyster harvest reduced by 88%.
- Considerable time, research, money and education are being devoted to developing and implementing a more sustainable, comprehensive management strategy.
- The paper [45] studied the population of market-sized oysters in the Maryland part of the Chesapeake Bay.
- Using data from 1994 – 2007, researchers found that the effective unconstrained growth rate of market-sized oysters is around  $r = 0.133$  per year.
- The estimated carrying capacity of the Maryland part of the bay is around  $5 \times 10^9$  market-sized oysters.

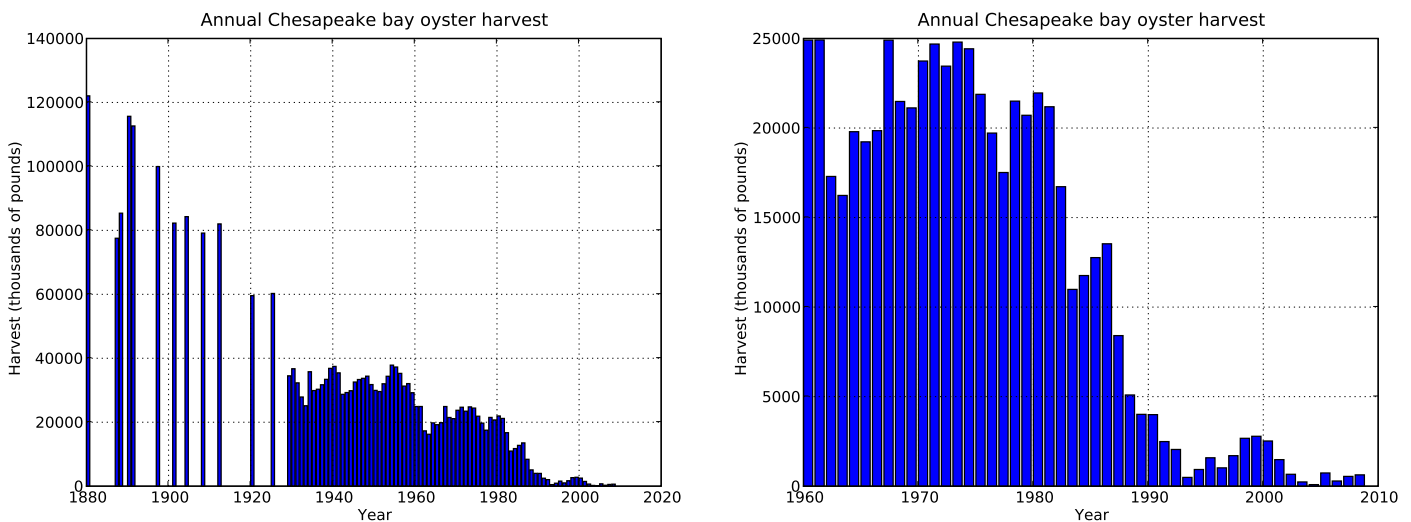


Figure 11.5: Annual Chesapeake Bay oyster harvests. Left: 1880 – 2008. Right: 1960 – 2008.

**Question 11.3.6**

The logistic DE model for the population  $N(t)$  of market-sized oysters is

$$N' = 0.133 N \left( \frac{5 \times 10^9 - N}{5 \times 10^9} \right).$$

**(a)** Find all stable population sizes.

**(b)** Interpret your answer to Part (a).

**(c)** In 2007, around  $50 \times 10^6$  oysters were harvested. Assuming a constant catch size every year, write a new DE for  $N(t)$ , and explain your answer.

*(continued over)*

**Question 11.3.6** (*continued*)

**(d)** Find all new stable population sizes.

**(e)** Interpret your answer to Part (d).

*(continued over)*

**Question 11.3.6** (*continued*)

- (f) In resource management (especially fisheries management) the *Maximum Sustainable Yield* (MSY) is the largest harvest size that can be maintained indefinitely. Find the MSY for the population. (Hint: first find the population at which the MSY occurs.)

(*continued over*)

**Question 11.3.6** (*continued*)

- (g) The current population of market-sized oysters is  $81 \times 10^6$ . How sustainable is the 2007 harvest and how achievable is the MSY?
- (h) Often, harvest rates are a fixed *percent* of the population, rather than a fixed *number* of individuals. From 1994–2007, the average annual rate was around 28% of the population. Write a new DE for  $N(t)$ .
- (i) Explain why an exponential DE can approximate the above DE quite accurately. Estimate the oyster population in the year 2107 if conditions remain unchanged and current harvest rates are maintained.

(*continued over*)

**Question 11.3.6** (continued)

(j) Would you expect your answer to Part (i) to occur in reality? Why?

(k) Make some brief recommendations to assist the government with long-term oyster stock management.



Photo 11.8: Over-exploited? (Source: MG.)

End of Case Study 32.



## 11.4 Euler's method

- We can solve many DEs *analytically*; that is, using integration and algebra, it is possible to find an exact solution to the equation.
- All of the DEs we have studied so far can be solved analytically.
- However, for more complex cases, especially with systems of DEs, it is not possible to find exact solutions.
- We can find approximate solutions using numerical algorithms (recall the use of Newton's method for approximately solving equations).
- One of the simplest techniques for solving DEs approximately is *Euler's method*.
- We will describe how to use Euler's method to solve a simple DE as an illustration of how the method works. In practice, you would not use Euler's method on this DE, as there is an exact solution.

### Euler's method (informal description)

To approximate an unknown function  $y$ :

1. Choose a small *stepsize*  $h$ , and start at the given initial point.
2. Use the DE to calculate the (estimated) slope of the function at the current point.
3. Approximate the unknown function as a short **straight line**, starting from the current point, with:
  - **width** equal to the stepsize  $h$ ;
  - **slope** equal to the estimated slope of the function calculated using the expression for the derivative; and hence
  - **height** equal to width multiplied by slope.
  - Advance the current point to the end point of the straight line.
4. If finished then stop, otherwise return to Step 2.

**Euler's method (semi-formal description)**

Given a DE  $y' = \dots$  and an initial value  $(x_0, y_0)$ :

1. Choose a small *stepsize*  $h$ , and start at  $(x, y) = (x_0, y_0)$ .
2. Substitute the current values of  $x$  and  $y$  into the DE to estimate an approximate value for  $y'$ .
3. Set  $y = y + h \times y'$  and  $x = x + h$ .

The new point  $(x, y)$  is the next approximate function value.

4. If  $x$  has reached the desired value then stop, else return to Step 2.

**Question 11.4.1**

Draw a diagram illustrating Euler's method.

**Example 11.4.2**

Use Euler's method to find an approximate solution to the DE  $y' = 0.1y$ , with initial condition  $y_0 = 100$  when  $x_0 = 0$ . Estimate  $y$  when  $x = 5$ , using a stepsize of  $h = 1$ .

*(continued over)*

*Example 11.4.2 (continued)*

(Note that the above DE is exponential, so has an exact solution. In practice, we would not use Euler's method to solve it; this is for illustration.)

**Answer:** With a stepsize of  $h = 1$ , to find the approximate value of  $y$  when  $x = 5$  we proceed as shown in Figure 11.6. (Remember that at each step, the new value of  $x$  equals the previous value of  $x$  plus  $h$ .)

Step	$x$	$y$	$y' = 0.1y$	$h \times y'$	new $x$	new $y$
0	0	100	10	10	1	110
1	1	110	11	11	2	121
2	2	121	12.1	12.1	3	133.1
3	3	133.1	13.31	13.31	4	146.41
4	4	146.41	14.641	14.641	5	161.051

Figure 11.6: Five steps of Euler's method.

So when  $x = 5$ ,  $y \approx 161.051$ .

Figure 11.7 shows a graph of the approximate solution. The five  $y$  values from the last column of the above table are marked as circles, with straight lines approximating the function between these points.

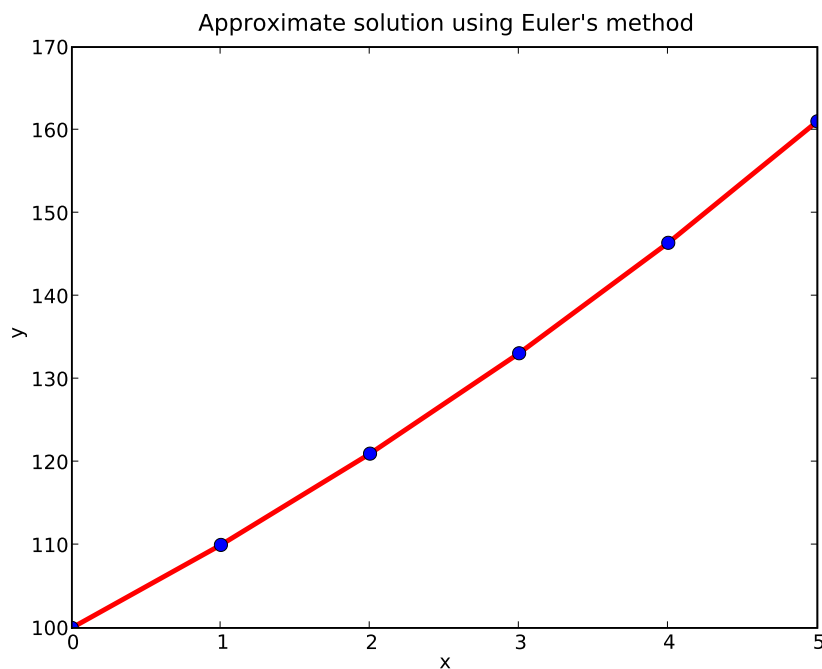


Figure 11.7: Approximate solution to the DE  $y' = 0.1y$  with  $y(0) = 100$ .

There are some important things to know about Euler's method.

- It gives an **approximate** solution, not an exact solution. There will be numerical inaccuracies in the answer.
- The choice of stepsize is very important: smaller values will give a more accurate answer, but take longer to calculate.
- The method can result in large numerical inaccuracies if used over a very large range of  $x$  values.
- Despite these limitations, the method can give very good approximate solutions to quite difficult problems.

### *Example 11.4.3*

In Example 11.4.2 we used a stepsize of  $h = 1$  to solve  $y' = 0.1y$ .

Figure 11.8 shows approximate solutions with a stepsize of  $h = 2.5$  (bottom curve),  $h = 1$  (middle curve) and the exact solution (top curve).

As  $h$  becomes smaller, the solution becomes more accurate (that is, moves closer to the top curve).

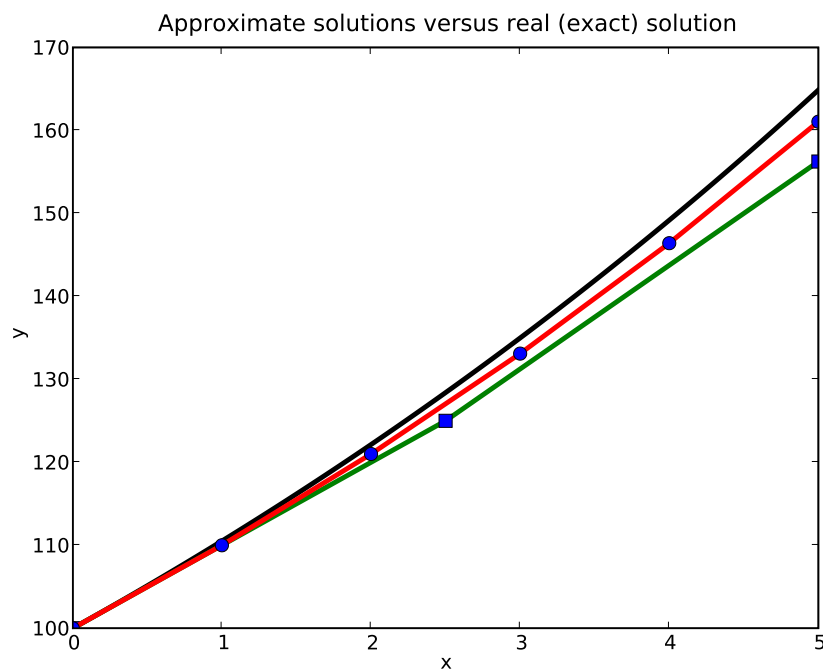


Figure 11.8: Approximate and exact solutions to the DE  $y' = 0.1y$  with  $y(0) = 100$ .

## Case Study 33: Cancer

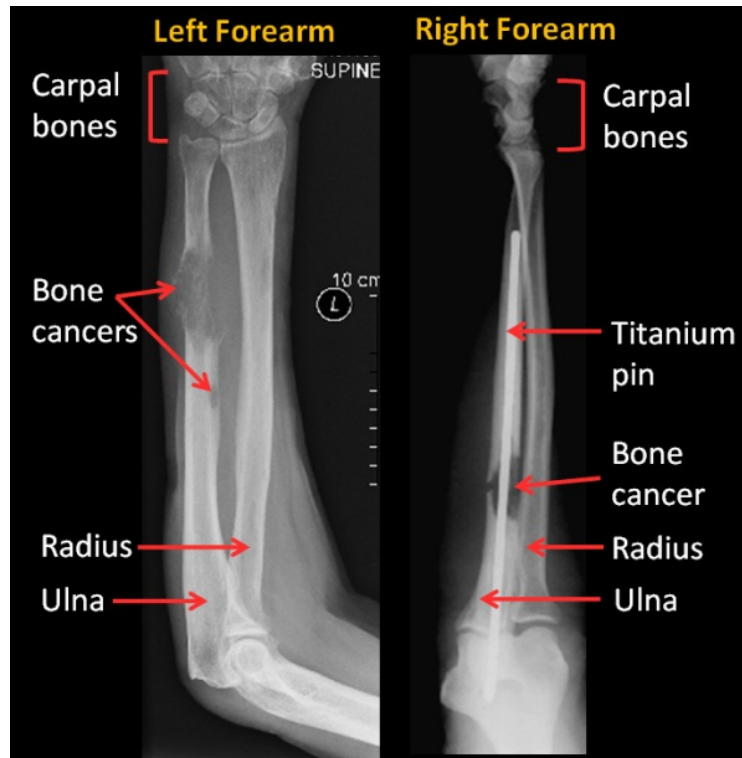


Photo 11.9: Left: x-ray of left forearm showing the destruction of bone due to cancer in the ulna. Right: x-ray of right forearm (different patient) showing a titanium pin stabilising the pathological fracture through the weakened bone. (Source: Qld Health and DM.)

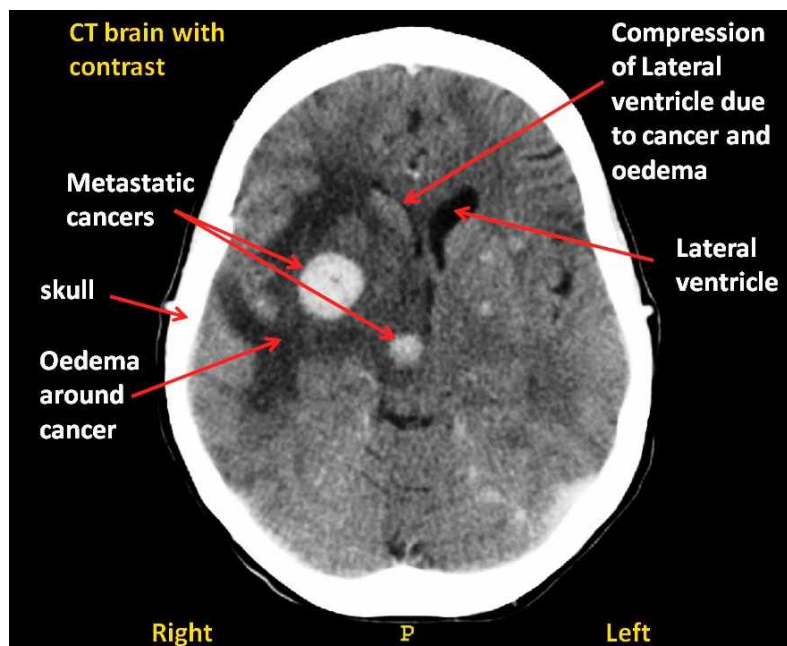


Photo 11.10: Axial CT image with contrast shows enhancing metastatic cancers with associated vasogenic oedema (swelling) within the brain. The metastases are due to breast cancer. (Source: Qld Health and DM.)

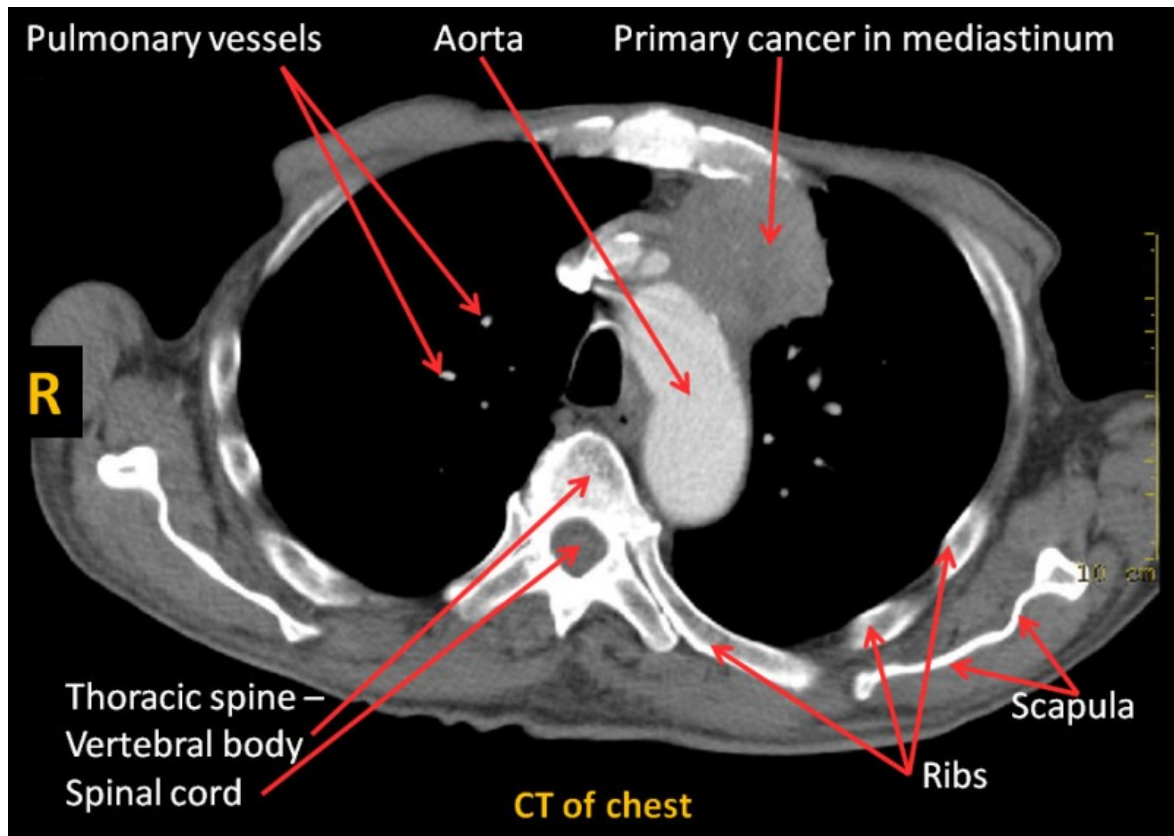


Photo 11.11: An axial CT image of the chest illustrates a primary cancer within the mediastinum extending to the anterior chest wall. (Source: Qld Health and DM.)

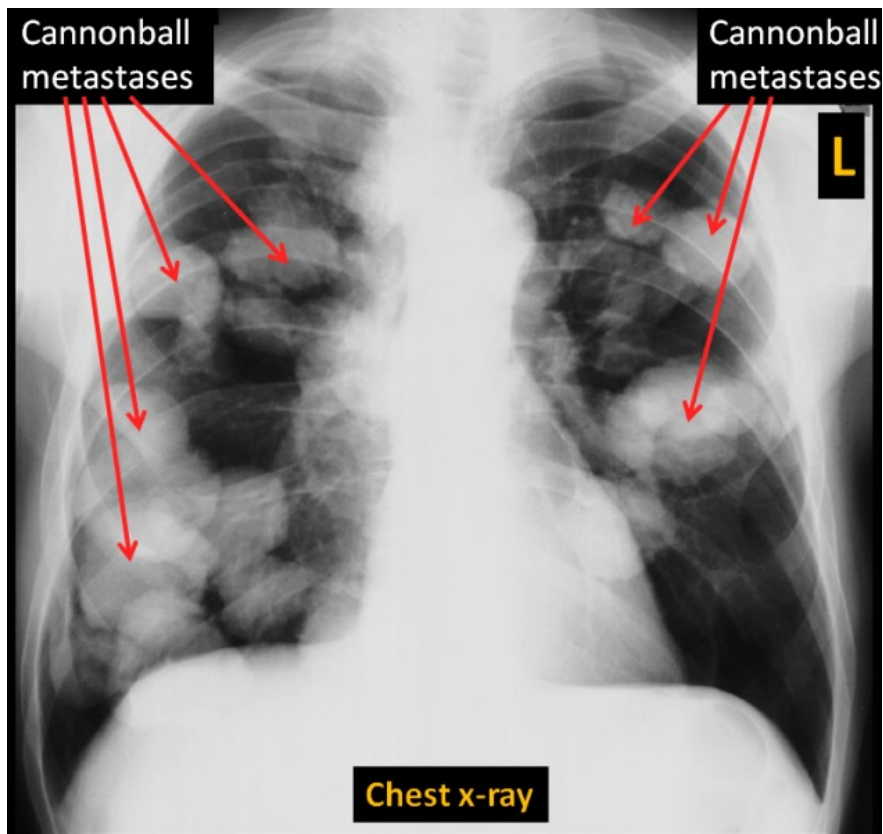


Photo 11.12: X-ray of a chest displaying many classic “cannonball” metastases. (Source: Qld Health and DM.)





Photo 11.13: Tumour from a rooster. (Source: PA.)

- Cancer comprises a large range of diseases, affecting many different parts of the body. It arises from the uncontrolled, rapid growth of abnormal cells that interfere with usual body function.
- Cancerous cells can *metastasise*, spreading to other parts of the body.
- Common cancers include cancers of the lung, prostate (males), breast (mostly females), colon, skin, bladder, kidney and blood (leukaemia).
- Smoking and excessive alcohol consumption are major risk factors.
- Cancer is a leading cause of death in humans. Figure 11.9 lists all leading causes of death for Australians, by gender.

Cause of death	M	Cause of death	F
Ischaemic heart disease	12444	Ischaemic heart disease	11221
Lung/trachea cancer	5025	Stroke	7246
Stroke	4727	Dementia/Alzheimer disease	5464
Chronic lower respiratory disease	3387	Lung/trachea cancer	2921
Prostate cancer	3031	Chronic lower respiratory disease	2868
Dementia/Alzheimer disease	2707	Breast cancer	2774
Colon/rectal cancer	2230	Diabetes	2050
Blood/lymph cancer	2220	Heart failure	2034
Diabetes	2141	Colon/rectal cancer	1890
Suicide	1709	Kidney/urinary disease	1756

Figure 11.9: Leading causes of death in Australians in 2008. (Source: Australian Bureau of Statistics.)

- Common cancer treatments include:
  - *Chemotherapy*, which involves the infusion of highly toxic chemicals into the body, killing rapidly dividing cells. (Recall that rapid division is a common characteristic of cancerous cells.)
  - *Radiation therapy*, which involves exposing cells to radiation and hence damaging their DNA, leading to cell death.
  - *Surgery*, which involves removing cancerous tissue from the individual.
  - *Stem cell transplants* (or *bone marrow transplants*), which involves infusing healthy stem cells into an individual with cancer.
- All of these treatments can have minor to major side effects, including fatigue, nausea, mouth ulcers, hair loss, cognitive problems, infection, anaemia, infertility, graft-versus-host disease, radiation burns or death.
- Determining the precise treatment regime and dosages involves a trade-off between the beneficial impact of reducing tumour size and the (often severe or life-threatening) side-effects resulting from the treatment.
- A large amount of research is ongoing, trying to understand different forms of cancer, including the search for better methods of management, treatment and cure.
- An important component of cancer research is developing better models of tumour growth and treatment.
- For example, the paper [43] discusses various models of tumour growth, including the logistic model. (Tumours are essentially populations of cells.)
- Tumours cannot grow indefinitely; their maximum size is determined by the physiology of the sufferer and by the need for tumour cells to receive nutrients (such as oxygen).
- The maximum possible tumour size corresponds to the carrying capacity  $K$  in the logistic DE.



**Example 11.4.4**

*Multiple myeloma* is a cancer of the blood plasma cells, which are an integral part of the immune system. It is one of the more common blood cancers, affecting 4 people per 100,000. Average age at diagnosis is around 60, and researchers are yet to identify the cause or any clear risk factors. Multiple myeloma is incurable, but treatment with high-dose chemotherapy and stem cell grafts has extended life expectancy (which is currently around 60 months if diagnosis is early).

**Question 11.4.5**

The paper [43] models multiple myeloma tumour growth using the logistic equation. A newly diagnosed, early-stage tumour will typically have: a size of around  $10^9$  cells; a doubling time of about 61 days so the growth rate is  $r \approx 0.0114$  per day; and a maximum size of about  $4 \times 10^{12}$  cells.

(a) Write a DE for the rate of change of the size  $C(t)$  of the tumour.

Hint: the logistic DE is  $C' = r C \left( \frac{K - C}{K} \right)$ .

(b) Assume that the rate at which chemotherapy kills cancerous cells is proportional to the tumour size. (This is a **very** rough model.) Write a new DE for the rate of change of the size  $C(t)$  of a tumour undergoing treatment.

*Example 11.4.6*

One treatment regime for multiple myeloma involves 12 cycles of chemotherapy, at intervals of six weeks, with the drugs melphalan, prednisone and thalidomide administered on Days 1 to 4 of each cycle.

Figure 11.10 shows modelled multiple myeloma tumour sizes with no treatment (left) and with treatment destroying 10% of the cancer cells per day for the four days of treatment **and the two subsequent days**, on each treatment cycle. The treatment graph was produced using Euler's method.

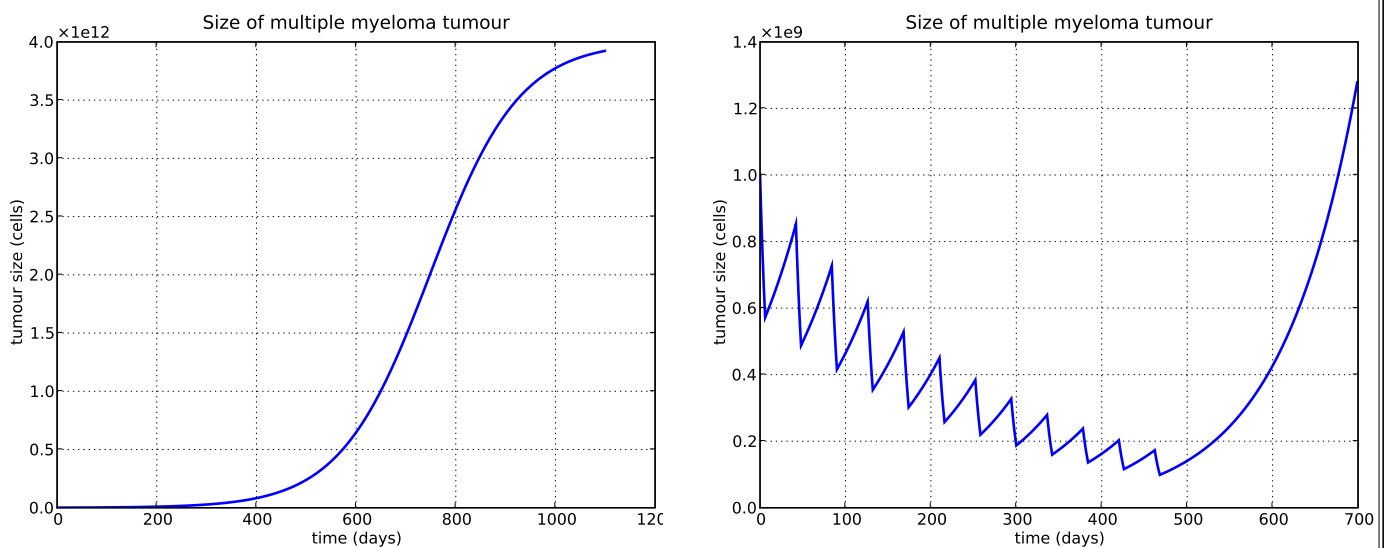


Figure 11.10: Modelled multiple myeloma tumour size with no treatment (left) and treatment (right).

*Question 11.4.7*

Comment on the graphs in Figure 11.10. In particular, comment on the benefit of the modelled treatment.

End of Case Study 33.

## 11.5 Space for additional notes

## Chapter 12: Systems of DEs

---

*On the farm, every Friday  
On the farm, it's rabbit pie day.  
So, every Friday that ever comes along,  
I get up early and sing this little song  
Run rabbit - run rabbit - Run! Run! Run!  
Don't give the farmer his fun! Fun! Fun!  
He'll get by  
Without his rabbit pie  
So run rabbit - run rabbit - Run! Run! Run!*

Artist: Flanagan and Allen ([www.youtube.com/watch?v=SVdoZNxtL8k](http://www.youtube.com/watch?v=SVdoZNxtL8k))



Image 12.1: *The wild hunt: Åsgårdsrei* (1872), Peter Nicolai Arbo (1831 – 1892), Nasjonalgalleriet, Oslo. (Source: en.wikipedia.org)



## 12.1 Introduction to systems of differential equations

- The DE models we have studied so far have all modelled a single, distinct phenomenon.
- Often, multiple factors interact, requiring more sophisticated models.
- For example:
  - in predator-prey relationships, changes in population sizes of *two* species are interrelated;
  - in species with multiple distinct life stages, changes in the population sizes within each stage depend on the numbers in other stages; and
  - the rates at which epidemics spread through populations are influenced by the number of infected individuals **and also** by the number of susceptible individuals.
- Typically, models for these more complex situations use a *system* of DEs (that is, more than one DE).
- Just as with single DEs, analytical solutions exist for some systems of DEs, but other systems require approximate solution.
- Euler’s method can be used to solve a system of DEs approximately, by applying a single iteration to each equation in turn, and then repeating.



Photo 12.1: Predators: Siberian tigers, *Panthera tigris altaica*. (Source: PA.)

## 12.2 Going through a difficult stage

- We previously modelled populations using exponential and logistic DEs. In each case we assumed that populations were *homogeneous*; that is, every individual in the population had an identical impact on population growth.
- Many organisms have different life stages with substantial differences in typical survival rates and reproduction rates.
- For example, in many species, small juveniles have a low survival rate and do not reproduce, whereas mature individuals have a high survival rate and typically do reproduce.
- Hence, simple models based on single DEs are inaccurate for more advanced organisms, particularly those with long life spans. In such cases, systems of DEs give rise to better models.
- In one type of model, populations are classified into groups based on their *life stages*, such as *juvenile* or *breeding adult*.
- Rather than applying a constant growth rate to every individual in the population, a system of DEs includes:
  - the *distribution* of the population within the distinct groups;
  - differing rates of reproduction and death within groups; and
  - the transitions of individuals between groups.
- *Life-cycle diagrams* are useful aids to writing the equations in a system of DEs. These diagrams show the rates of *transition* between stages.

### Life-cycle diagram

**Life-cycle diagrams** represent all possible transitions between stages in the life-cycle of an organism. Each stage is represented as a circle in the diagram, with a directed arrow joining Stage *A* to Stage *B* whenever it is possible for an individual to transition from Stage *A* to Stage *B*. Each arrow has an associated number, which is the *rate* of transition.

- The general form of a stage in a life-cycle diagram is shown in Figure 12.1. Not all stages will have all of these arrows, as some particular transitions may not be possible.

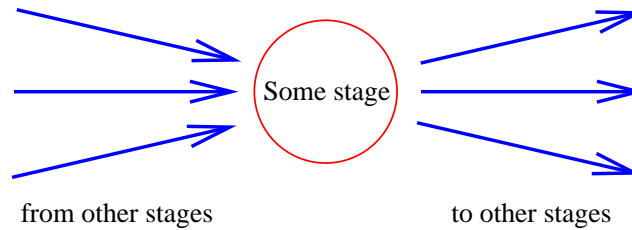


Figure 12.1: A stage in a life-cycle diagram, showing some transitions.

- In order to draw the life-cycle diagram for an organism, we need to know:
  - the number of stages;
  - all possible transitions to and from each stage, including:
    - \* reproduction;
    - \* transitions due to the passage of time, or other factors; and
    - \* deaths.
  - the number associated with each possible transition.
- Once we have drawn a life-cycle diagram, it is usually easy to write a system of DEs for the number of individuals in each stage.

### **Question 12.2.1**

Consider an idealised fish species with two distinct life stages: juvenile and adult. Each month, on average:

- Juveniles do not breed, have a 50% probability of surviving to adulthood, and a 50% probability of dying.
- Adults produce 5 offspring, and then die.

*(continued over)*

*Question 12.2.1 (continued)*



Photo 12.2: Bighead Gurnard Perch (*Neosebastes pandus*). (Source: DM.)

- (a) Draw a life-cycle diagram for this fish, with two stages.
- (b) Let the populations of juveniles and adults at any time be  $J(t)$  and  $A(t)$ . Write a system of DEs for these populations.

*(continued over)*



**Question 12.2.1** (*continued*)

(c) Assume that a specific population comprises 20 juveniles and 2 adults at time  $t = 0$  months. Use Euler's method and a stepsize of one month to estimate the number of fish in each stage at time  $t = 2$  months.

(d) Sometimes it is convenient to include death as a stage in a life-cycle diagram. Draw a life-cycle diagram with three stages, including death.

(*continued over*)

**Question 12.2.1** (*continued*)

- (e) Write a DE for  $D(t)$ , the total number of dead fish at any time.
- (f) Assume that a specific population comprises 20 juveniles, 2 adults and no dead fish at time  $t = 0$  months. Use Euler's method and a stepsize of one month to estimate the number of **dead** fish at time  $t = 2$  months.

## Case Study 34: Total turtle turmoil.



Image 12.2: Loggerhead sea turtle.  
(Source: en.wikipedia.org.)



Photo 12.3: Sea turtle species. (Source: DM.)

- The loggerhead sea turtle (*Caretta caretta*) is a large marine turtle, reaching a length of around 1 m and a mass of more than 100 kg.
- The species is distributed throughout temperate, subtropical and tropical regions, and nests in a number of countries, including Australia.
- Individuals often live for more than 50 years.
- The species is listed as threatened, largely due to human activity, so is likely to become endangered within the foreseeable future.
- Ecologists have studied these turtles in detail, in order to better understand how populations change over time, to investigate possible management strategies and predict the impacts of further environmental change and human activity.
- Researchers in [5] and [8] identified that the life-cycle of these turtles could be divided into seven distinct stages, and developed a population model based on these seven stages.
- (For interest, the researchers used a matrix model rather than a system of DEs. However, such models are equivalent to using a system of DEs and Euler's method with a stepsize of 1.)

- We will study a simplified version of their model, with the seven stages collapsed into three for ease of calculation.
- Figure 12.2 shows the life stages used for the simplified model, along with the estimated proportion of the total turtle population, and the global number of individuals, in each stage.

Stage	Description	Age (years)	Proportion	Global population
A	hatchlings	< 1	0.20651	1445570
B	youth	1 – 23	0.79097	5536790
C	breeding adult	24 – 54	0.00252	17640

Figure 12.2: Loggerhead sea turtles classified into three life stages.

- Each year, individuals transition between stages with the following probabilities:
  - Hatchlings become youths (with probability 0.6747) or die.
  - Youths become breeding adults (probability 0.0004335), remain in the youth stage (probability 0.76888), or die.
  - Breeding adults produce new hatchlings (77.36 per adult), and either remain as breeding adults (probability 0.8089) or die.
- Researchers estimated that the global population across all life stages was 7 million.

### *Question 12.2.2*

- (a)** Draw a life-cycle diagram for the loggerhead sea turtle, with three stages.

*(continued over)*

**Question 12.2.2** *(continued)*

- (b)** Write a system of DEs for the turtle population.
- (c)** Use Euler's method with a stepsize of 1 year to estimate the turtle population in each stage after one year.
- (d)** Find the total turtle population after one year. What does this mean?

*(continued over)*

**Question 12.2.2** (*continued*)

- (e) Find the **proportion** of the population in each life stage after one year, and compare your answer with the proportions in the initial population. What does this mean?
- (f) Researchers and authorities have proposed various conservation strategies for the sea turtle. Briefly discuss some possible strategies, and explain how the population model would change to reflect them.

A computer model is a convenient way of studying the population for an extended time period.

**Program specifications:** Develop a Python program that uses Euler's method with a stepsize of 1 to model the turtle population for 30 years.

## Program 12.1: Turtles

```
1 # Uses Euler's method to model the turtle population.
2 from __future__ import division
3 from pylab import *
4
5 # Initialise variables.
6 maxt = 30
7 Apops = zeros(maxt+1)
8 Bpops = zeros(maxt+1)
9 Cpops = zeros(maxt+1)
10 Apops[0] = 1445570
11 Bpops[0] = 5536790
12 Cpops[0] = 17640
13 stepsize = 1
14
15 # Step through Euler's method for 30 years.
16 i = 1
17 while i < (maxt+1):
18     dA = -Apops[i-1] + 77.36 * Cpops[i-1]
19     dB = 0.6747 * Apops[i-1] - 0.23112 * Bpops[i-1]
20     dC = 0.0004335 * Bpops[i-1] - 0.1911 * Cpops[i-1]
21     Apops[i] = Apops[i-1] + stepsize * dA
22     Bpops[i] = Bpops[i-1] + stepsize * dB
23     Cpops[i] = Cpops[i-1] + stepsize * dC
24     i = i + 1
25
26 # Output the graph.
27 times = arange(0, maxt+1)
28 plot(times, Apops, "bx", mew=3)
29 plot(times, Bpops, "rx", mew=3)
30 plot(times, Cpops, "gx", mew=3)
31 plot(times, Apops+Bpops+Cpops, "kx", mew=3)
32 xlabel("Time (years)")
33 ylabel("Number of turtles")
34 title("Turtle population")
35 text(10.3, 4100000, "Total")
36 text(1, 4000000, "Stage B")
37 text(1, 1400000, "Stage A")
38 text(5.5, 100000, "Stage C")
39 grid(True)
40 # show()
```



- Figure 12.3 shows the output from running the program.

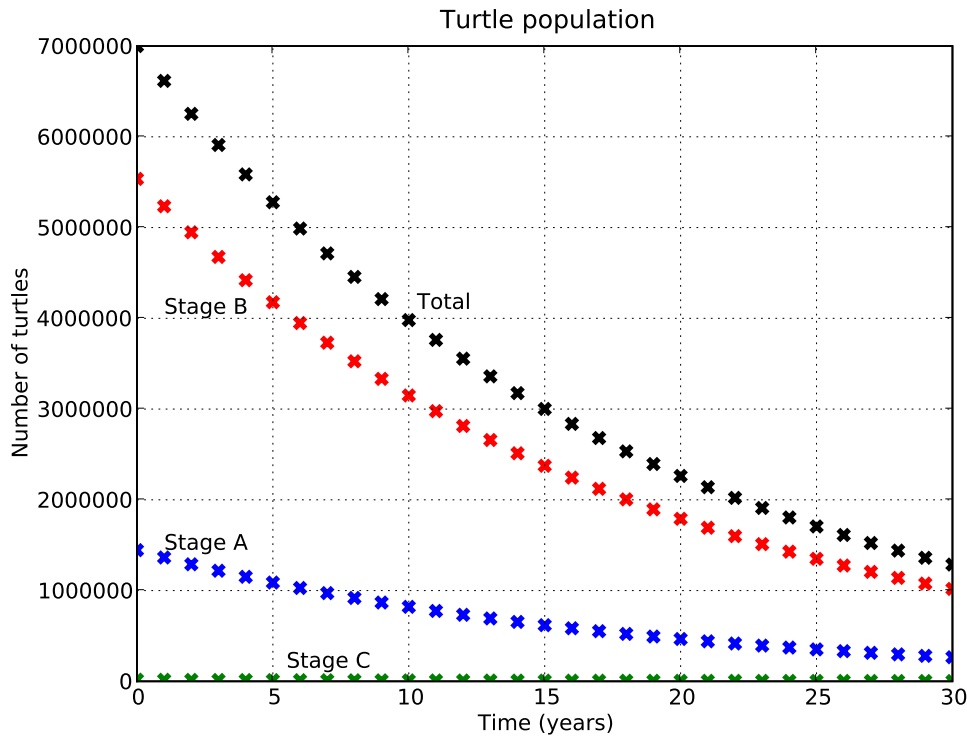


Figure 12.3: Turtle population modelled using Euler's method.

**Question 12.2.3**

The model predicts that after 30 years, the total population will be 1.36 million, with 280600 hatchlings, 1077300 youths, and 3430 breeding adults.

(a) Find the proportion of the total population in each stage, and comment.

(b) Predict the total population after 30 **more** years (60 years from now).

End of Case Study 34.

## 12.3 Eat or be eaten



Photo 12.4: Left: skeleton of *Tyrannosaurus rex*. Right: skeleton of *Triceratops horridus*. (Source: PA.)

- Systems of DEs can model interactions between multiple species.
- In laboratory situations there is control over these interactions. In nature, inter-species interactions are highly complex.
- The classical *predator/prey* problem in ecology considers what happens to the populations of two species if one preys on the other.
- We will first investigate a controlled example, then model a real interaction.

### Case Study 35: Frogs and crickets

- One method of predicting what may happen in a real-world situation is to simulate it in a laboratory.
- Unpredictable phenomena complicate and impact predator/prey interactions in nature. However, controlled laboratory simulations can give valuable insight into real situations.
- Consider a controlled, time-compressed laboratory experiment simulating the effects of immigration, emigration, births and deaths on populations of frogs (predators) and crickets (prey).

- Initially the experiment comprises 60 frogs and 400 crickets. Each day:
  - 15 crickets are introduced into the experiment (modelling immigration and birth of crickets);
  - 25% of the frogs each eat a cricket (death of crickets);
  - 12 frogs are removed (modelling emigration and death of frogs); and
  - for each 25 crickets present, one new frog is introduced (modelling birth and immigration of frogs based on available food resources).



Photo 12.5: Left: Striped burrowing frog, *Litoria alboguttata*. Right: cricket. (Source: DM.)

### *Question 12.3.1*

Let  $F(t)$  and  $C(t)$  be the populations of frogs and crickets at time  $t$  in days.

(a) Write a DE for the rate of change of **each** of the populations.

*(continued over)*

**Question 12.3.1** (*continued*)

(b) Show that the following equations are solutions to the DEs. (Hint: if  $y = \sin kt$  then  $y' = k \cos kt$ . If  $y = \cos kt$  then  $y' = -k \sin kt$ .)

$$F = 40 \sin 0.1t + 60$$

$$C = 100 \cos 0.1t + 300.$$

(*continued over*)

**Question 12.3.1** (continued)

(c) Draw a rough sketch of the populations of frogs and crickets, and briefly interpret the graphs.

- The above model of inter-species predator/prey interactions between frogs and crickets is very simple, but it is not completely unreasonable.



Photo 12.6: Left: genuine KTF. Right: fossilised cricket. (Source: PA.)

End of Case Study 35.



- There are many models of predator/prey relationships. Standard assumptions are that:
  - the prey species has no other predators, and the predator species has no other prey; and
  - the prey species breeds rapidly and individuals do not compete with each other, but the predator species breeds more slowly and individuals compete with each other.



Photo 12.7: Left: gray wolf (*Canis lupus*). Right: elk (*Cervus canadensis*). (Source: PA.)

### *Question 12.3.2*

Let  $P$  and  $Q$  be populations of predators and prey (respectively). How do the values of  $P$  and  $Q$  influence the *rate of change* of each of  $P$  and  $Q$ ? In each case, identify whether the impact is positive or negative.

(a) Factors influencing  $P'$ :

(b) Factors influencing  $Q'$ :

- The best-known predator/prey model is the **Lotka-Volterra** model.

### Lotka-Volterra model

Let  $P(t)$  and  $Q(t)$  be the sizes of populations of a predator and prey species respectively, at any time  $t$ . The *Lotka-Volterra model* represents the population movements in the following system of DEs:

$$Q' = aQ - bPQ$$

$$P' = -cP + dPQ$$

where  $a, b, c$  and  $d$  are positive constants whose values depend on the particular species being modelled.



Photo 12.8: Left: red fox (*Vulpes vulpes*). Right: cottontail rabbit (*Sylvilagus sp.*) (Source: PA.)

### Question 12.3.3

Carefully explain the meaning of each term in the Lotka-Volterra equations. In particular, explain the physical relevance of the terms involving  $PQ$ .

It is not possible to find a general solution to the Lotka-Volterra equations; however, we can find approximate solutions using Euler's method.

### Case Study 36: Snowshoe hares and Canadian lynx



Image 12.3: Canadian lynx chasing a snowshoe hare. (Source: [www.animalspedia.com](http://www.animalspedia.com).)

- The Canadian lynx, *Lynx canadensis*, is a member of the feline family distributed predominantly in Canada and Alaska.
- Lynx are carnivorous, with individuals weighing 8 to 15 kg, and living for up to 15 years.
- The primary food source of the Canadian lynx is the snowshoe hare (or varying hare), *Lepus americanus*. The hare has large hind feet (for moving on snow) and turns white in winter.
- People have hunted these species for their fur for many years. Records of hare and lynx harvests dating from the 1730s allow population estimates over an extended time.
- Figure 12.4 shows a graph of these data over 90 years. Clearly, there is a continuing series of reasonably regular fluctuations in the sizes of both populations.
- The graph is similar to the periodic population movements in the laboratory-controlled predator/prey relationship between frogs and crickets.



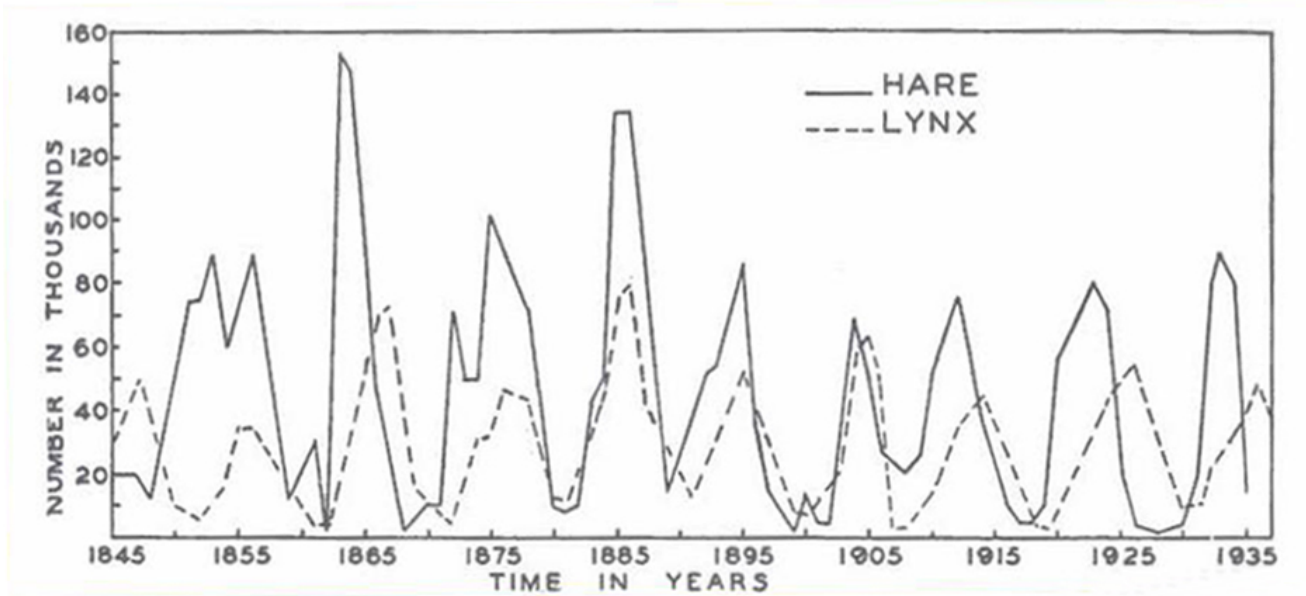


Figure 12.4: Numbers of Canadian lynx and snowshoe hares. (Source: [27].)

- Of course, interactions in nature are much more complex than those in controlled experiments; hares and lynx interact with other species as well.
- Figure 12.5 illustrates major dietary links within the food web of the Canadian boreal forest in which lynx and hare live. (Links that directly influence Snowshoe hares are highlighted.)

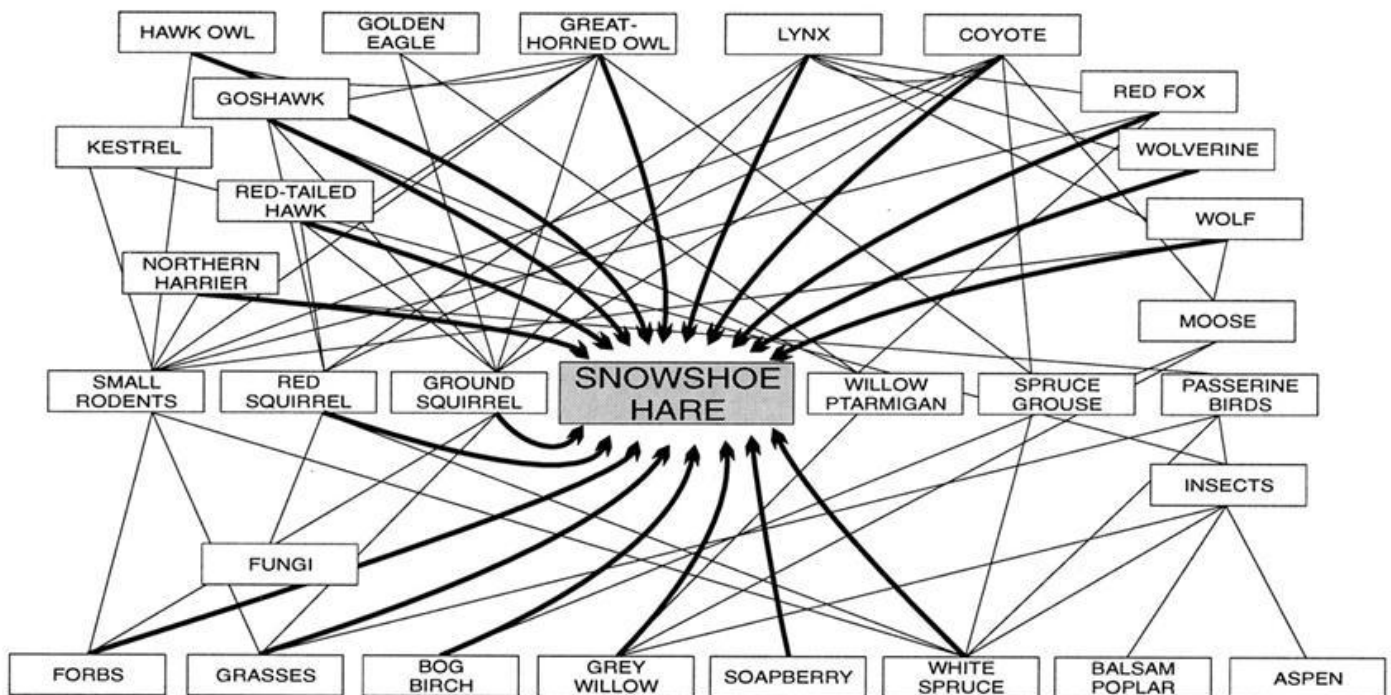


Figure 12.5: Major dietary interactions (food web) of the Canadian boreal forest. (Source: [42].)

- Figure 12.5 (which is itself a model of reality) shows that many food-related factors influence the populations of hares and lynx.
- However, the hare typically forms a dominant component of the food source for lynx (up to 95%).
- Hence it is not unreasonable to model the populations of both species as a simple interaction in which lynx prey on hares.

### *Question 12.3.4*

Let  $L(t)$  and  $H(t)$  be the populations of lynx (predators) and hares (prey) respectively, **measured in thousands**. The Lotka-Volterra equations are:

$$H' = aH - bHL \qquad L' = -cL + dHL$$

- (a) How would “lynx become extinct” be written mathematically?
- (b) If all lynx died suddenly from disease, what does the model predict will happen to the population of hares, and why?
- (c) Is your answer to Part (b) biologically realistic? What would probably happen in reality?

*(continued over)*

**Question 12.3.4** (*continued*)

(d) If  $a = 0.0484$ ,  $b = 0.028$ ,  $c = 1$  and  $d = 0.032$ , find all pairs of stable population sizes and interpret your answer.

### Example 12.3.5

Data from the Canadian Government and the Hudson's Bay Company estimated the populations of hare and lynx in part of their range from 1900 to 1920. Figures 12.6 and 12.7 show the data. (All population units are in thousands.)

Year	Hares	Lynx	Year	Hares	Lynx	Year	Hares	Lynx	Year	Hares	Lynx
1900	30	4	1905	20.6	41.7	1910	27.1	7.4	1915	19.5	51.1
1901	47.2	6.1	1906	18.1	19	1911	40.3	8	1916	11.2	29.7
1902	70.2	9.8	1907	21.4	13	1912	57	12.3	1917	7.6	15.8
1903	77.4	35.2	1908	22	8.3	1913	76.6	19.5	1918	14.6	9.7
1904	36.3	59.4	1909	25.4	9.1	1914	52.3	45.7	1919	16.2	10.1
									1920	24.7	8.6

Figure 12.6: Populations of lynx and hares (in thousands).

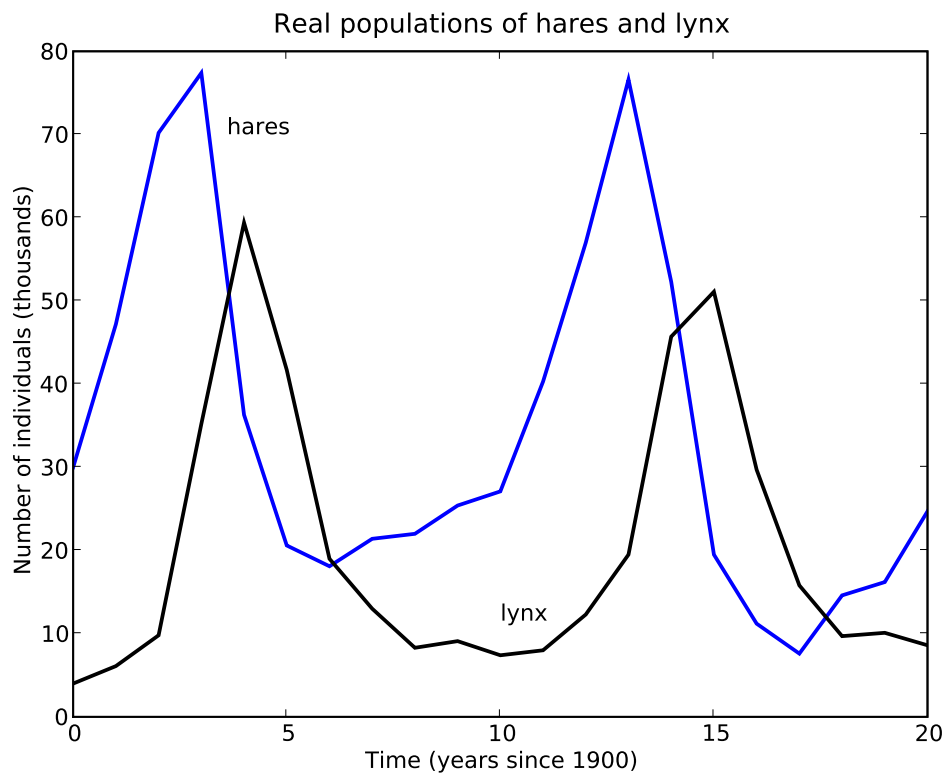


Figure 12.7: Graph of the populations of lynx and hares (in thousands).

We can use Euler's method to model the population sizes.

**Program specifications:** Develop a Python program that uses Euler's method with a stepsize of 0.1 year to model the populations of lynx and hares. Assume that  $a = 0.0484$ ,  $b = 0.028$ ,  $c = 1$  and  $d = 0.032$  (in the correct units).

**Program 12.2: Lotka-Volterra model of hares and lynx.**

```
1 # Uses Euler's method and Lotka-Volterra equations to model
2 # populations of lynx and hare from 1900 to 1920.
3 from __future__ import division
4 from pylab import *
5
6 # Initialise variables for Euler's method.
7 ss=0.1
8 time=arange(0,20.1,ss)
9 a = 0.484
10 b = 0.028
11 c = 1
12 d = 0.032
13 H = zeros(size(time))
14 L = zeros(size(time))
15 H[0] = 30.0
16 L[0] = 4.0
17 nn=size(time)
18
19 # Step through Euler's method with stepsize ss.
20 # Repeatedly calculate derivatives then update the 'next'
   values.
21 i = 0
22 while i < nn-1:
23     dH = a*H[i] - b*H[i]*L[i]
24     dL = -c*L[i] + d*H[i]*L[i]
25
26     H[i+1] = H[i] + ss*dH
27     L[i+1] = L[i] + ss*dL
28     i = i+1
29
30 # Output graphs.
31 text(4,7,"H(t)")
32 text(15.1,60,"L(t)")
33 xlabel("Time (years since 1900)")
34 ylabel("Number of individuals (thousands)")
35 title("Modelled populations of hares and lynx")
36 plot(time, H, "b-", linewidth=3)
37 plot(time, L, "k-", linewidth=3)
38 show()
```

### Example 12.3.6

- At time  $t = 0$  years (corresponding to year 1900), data show that there were 30 (thousand) hares and 4 (thousand) lynx in the monitored region.
- The program was used to model population movements over the next 20 years.
- Figure 12.8 shows the predicted movements in both population sizes during that time.
- Figures 12.9 and 12.10 compare the predicted populations with the real (measured) data for each population.

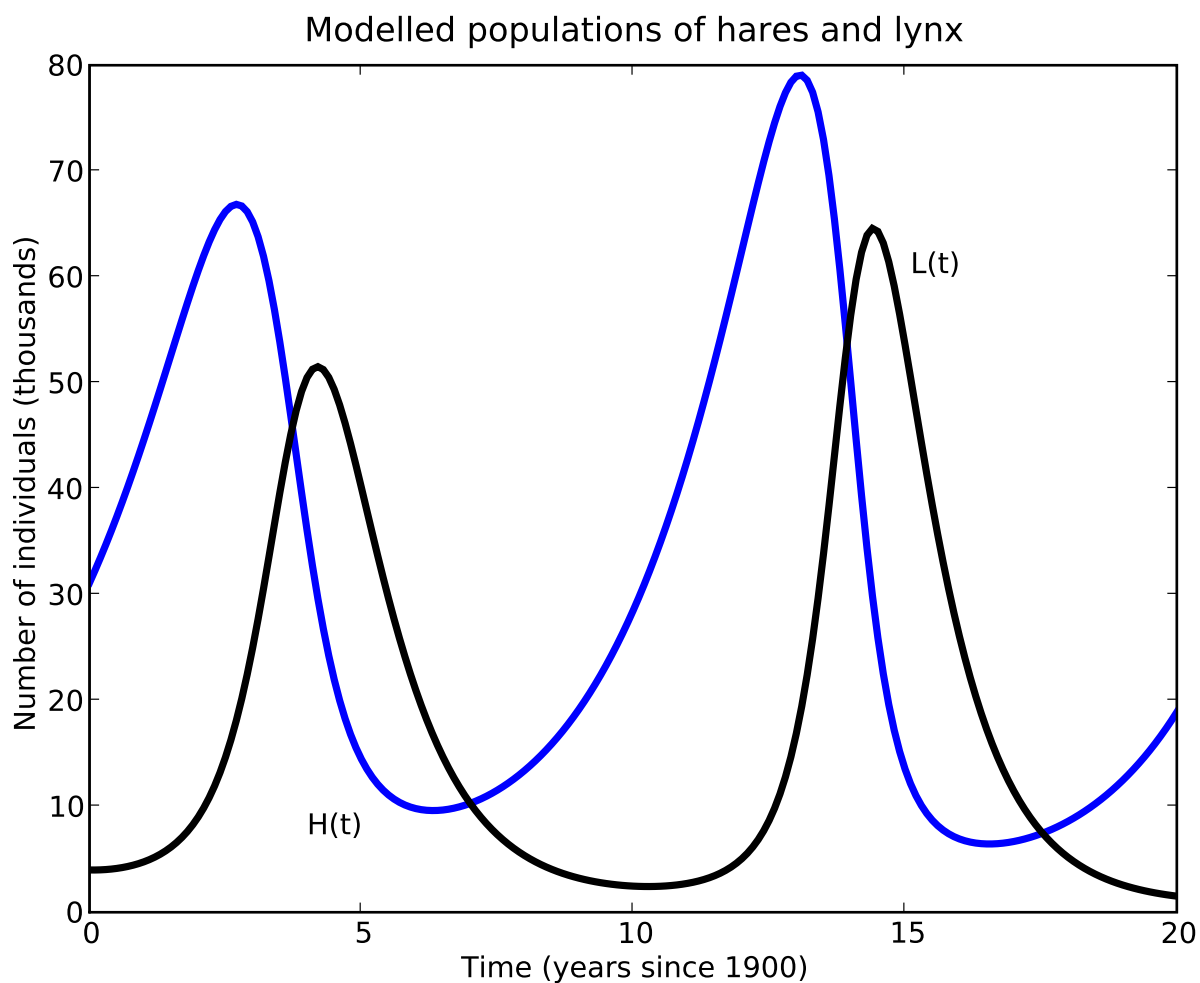


Figure 12.8: Modelled populations of hare and lynx.

(continued over)

*Example 12.3.6 (continued)*

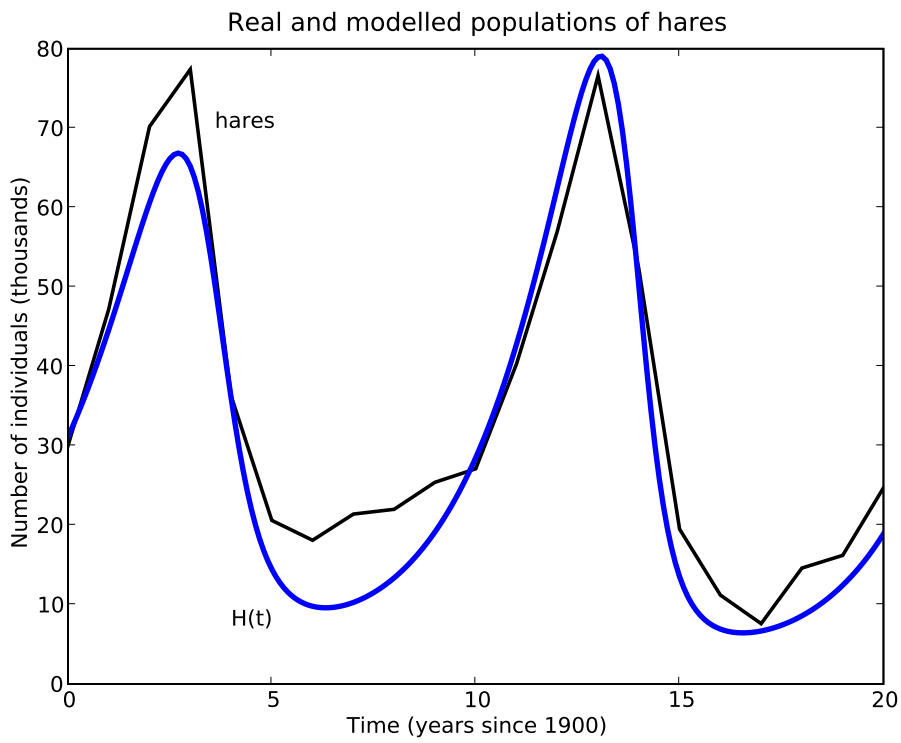


Figure 12.9: Real and modelled hare populations.

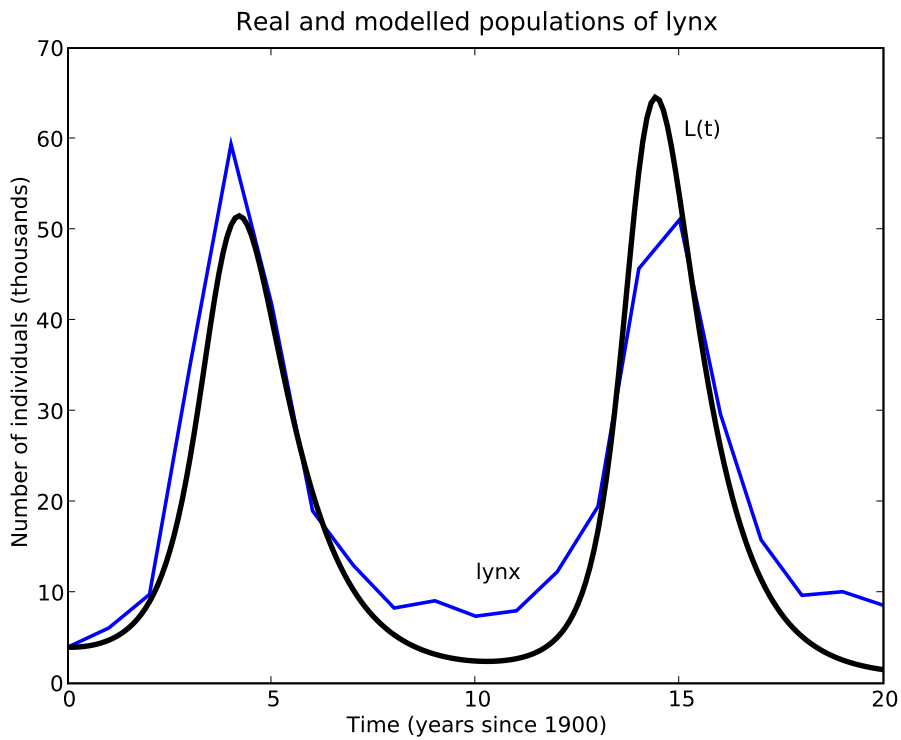


Figure 12.10: Real and modelled lynx populations.



**Question 12.3.7**

(a) Comment on the results in Example 12.3.6.

(b) Critically evaluate the following possible media statement:

*A survey has shown that the populations of lynx and snowshoe hares are both in decline. We need to act promptly or else one or both species will become extinct.*

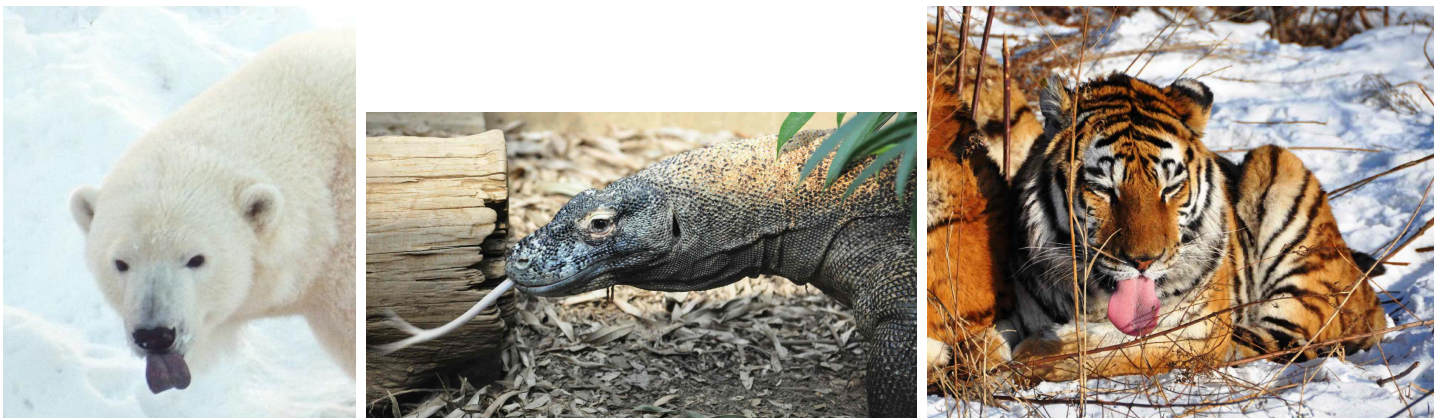


Photo 12.9: Three top predators. Left: polar bear, *Ursus maritimus*. Centre: Komodo dragon, *Varanus komodoensis*. Right: Siberian tiger, *Panthera tigris altaica*. (Source: PA.)

End of Case Study 36.

## 12.4 Space for additional notes

## Chapter 13: Fully sick

*From New Delhi to Darjeeling I have done my share of healing,  
and I've never yet been beaten or outboxed.*

*I remember that with one jab of my needle in the Punjab  
how I cleared up beriberi and the dreaded dysentery,  
but your complaint has got me really foxed.*

*Oh doctor, touch my fingers.*

*Well, goodness gracious me.*

*You may be very clever but however, can't you see,  
my heart beats much too much at a certain tender touch,  
it goes boom boody-boom boody-boom boody-boom  
boody-boom boody-boom boody-boom-boom-boom.*

Artist: Peter Sellers and Sophia Loren ([www.youtube.com/watch?v=gKMy15O1tCw](http://www.youtube.com/watch?v=gKMy15O1tCw))



Image 13.1: *The Triumph of Death* (1562), Pieter Bruegel the Elder (c. 1525 – 1569), Museo del Prado, Madrid. (Source: commons.wikimedia.org.)



## 13.1 Epidemics and SIR models

- In this section we discuss the use of systems of DEs to model the large-scale spread of infectious disease through a population over time.

### Epidemic

A large-scale occurrence of disease in a human population is called an **epidemic** if new cases of the disease arise at a rate that “substantially exceeds what is expected” in a given time period. Localised occurrences are called **outbreaks**, and global occurrences are often called **pandemics**.

- Modelling diseases is an important aid to understanding their spread, and how their impact can be mitigated through approaches such as quarantine, vaccination and public health campaigns.

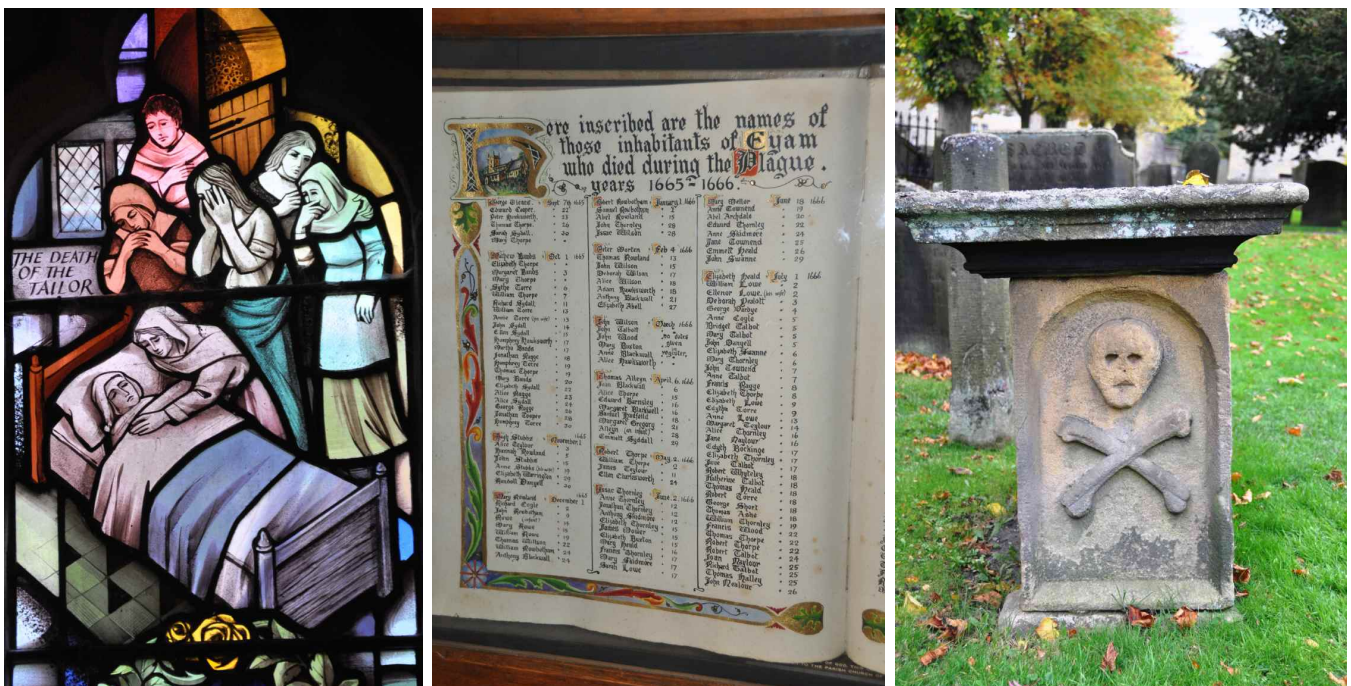


Photo 13.1: Images commemorating the bubonic plague in Eyam, the “Plague Village”, UK. Left: stained glass ‘Plague Window’. Centre: first page of the list of names of villagers who died from plague in 1665–1666. Right: tombstone. (Source: PA.)

- Modelling the spread of a disease often commences with estimating the number of secondary infections typically arising from an individual with the disease, and the rate at which individuals recover from the disease.

### Basic reproduction number

The **basic reproduction number** of a disease, written  $R_0$ , is the average number of secondary infections caused by a single infected individual in a completely susceptible population, in the absence of any preventive interventions. The value of  $R_0$  is determined by factors including how infectious the disease is, how homogeneously the population mixes and the duration of the infectious period.

### Infectious period

The **infectious period** of a disease is the average length of time during which an infected individual can pass the disease on to a susceptible individual. Many diseases are infectious before symptoms are apparent.

- Figure 13.1 shows some well-known infectious diseases along with their values of  $R_0$ , transmission methods and infectious periods.

Disease	Transmission method	$R_0$	Infectious period
Rubella	Airborne droplet	$\approx 5$	14 days
Measles	Airborne droplet	12 – 18	10 days
Pertussis	Airborne droplet	12 – 17	21 days
Mumps	Airborne droplet	4 – 7	14 days
Swine flu	Airborne droplet	1.4 – 1.6	6 days
Seasonal influenza	Airborne droplet	2 – 3	6 days
Smallpox	Social contact	5 – 7	20 days
HIV/AIDS	Sexual contact	2 – 5	unlimited
Syphilis	Sexual contact	$\approx 1.5$	up to 2 years
Human papillomavirus	Sexual contact	1 – 3	very variable
Pneumonic plague	Airborne droplet	$\approx 1.3$	2 days (100% death rate)

Figure 13.1: Some infectious diseases along with their basic reproduction numbers and infectious periods.

- When modelling disease spread, it is useful to define the following two additional concepts:
  - the **infection rate**, which equals the basic reproduction number divided by the infectious period; and

- the **recovery rate**, which equals 1 divided by the infectious period.
- For example, the infection rate for rubella is  $5/2$ , which equals 2.5 per week, and the recovery rate is 0.5 per week.
- These concepts make sense: a person infected with rubella will typically be ill for two weeks, and will infect five additional people during that time. Hence the individual infects 2.5 people per week, and each week “half recovers”.
- Researchers, governments and the medical community use a variety of models when studying epidemics.
- We will commence our study of epidemics with a simple model, known as the SIR (**S**usceptible, **I**nfectious, **R**emoved) model.
- The SIR model is used to model many diseases, including rubella, measles, cholera, swine flu and bubonic plague.

### SIR model of epidemics

The *SIR* epidemic model classifies a population into three distinct **compartments** or groups. At any time  $t$ :

- (1) The *susceptible* compartment  $S(t)$  is the group of people who are susceptible to the disease.
- (2) The *infective* compartment  $I(t)$  is the group of people who have the disease and can infect susceptible people.
- (3) The *removed* compartment  $R(t)$  is the group of people who cannot catch the disease, either because they have permanently recovered, are naturally immune, or have already died from the disease.

The SIR model uses a system of DEs to model the changes in the number of people in each compartment over time.



- The SIR model assumes that:
  - a susceptible person can become infected;
  - an infected person can become removed;
  - there are no births, or deaths from other causes, so the population size is constant (apart from disease-related deaths);
  - the population mixes homogeneously, so susceptible, infected and removed individuals mix equally.

*Question 13.1.1*

Draw a “life-cycle diagram” for the SIR model.

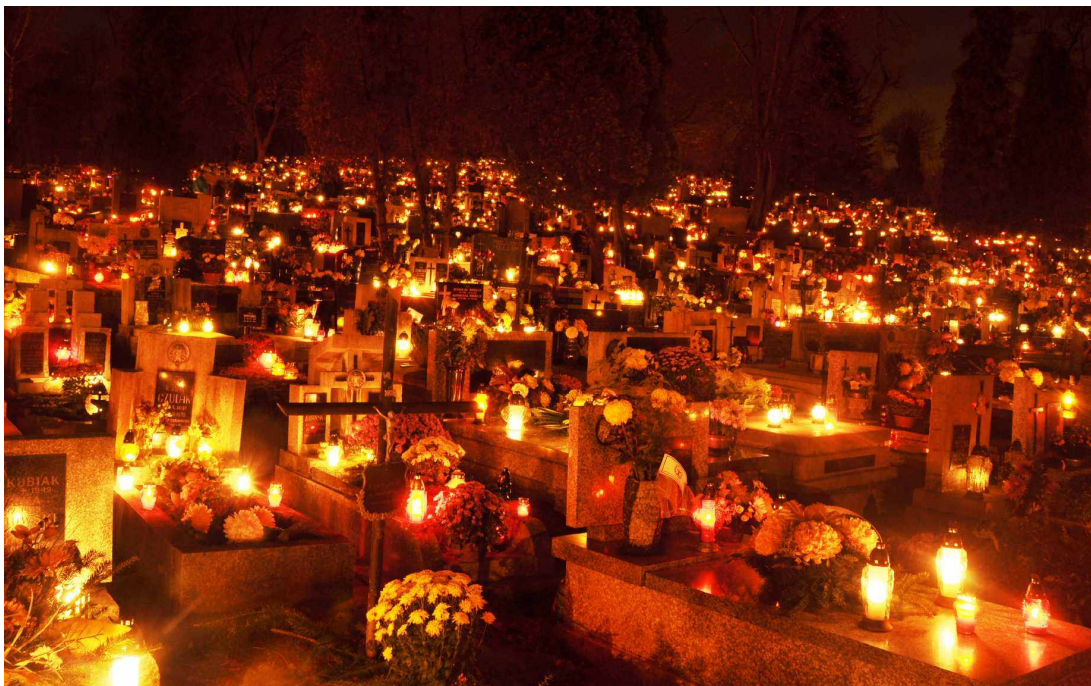


Photo 13.2: Night view of New Podgorski cemetery, Krakow, Poland, on All Saints' Day. (Source: PA.)



**The equations for the SIR model**

If a population of  $N$  people at time  $t$  is divided into three compartments, susceptible  $S(t)$ , infected  $I(t)$  and removed  $R(t)$ , then the SIR model states:

$$S' = -\frac{a}{N} SI$$

$$I' = \frac{a}{N} SI - bI$$

$$R' = bI$$

where  $a$  is the infection rate and  $b$  is the recovery rate.

**Question 13.1.2**

Explain what each of the terms in each of the SIR equations represents.

- Note that the SIR equations maintain the same total population size  $N$  at all times, because the rates at which people move between compartments always balance.
- An epidemic occurs if introducing a group of infected people into a population causes an increase in the number of infectives in the population.
- The SIR model predicts that an epidemic will occur if at  $t = 0$ ,  $I' > 0$  (that is, the number of infectives is increasing).
- Simple algebra shows that  $I' > 0$  at time 0 if the fraction of the total population that is susceptible is more than  $b/a$ .
- (This is identical to saying that the proportion of susceptibles in the population is more than  $1/R_0$ , where  $R_0$  is the basic reproduction number.)

***Question 13.1.3***

Explain intuitively **why** an epidemic will occur if a fraction of more than  $1/R_0$  of a population is susceptible.

***Question 13.1.4***

What is the purpose of mass public vaccination?

- Some people are opposed to vaccinations, claiming either that there are no benefits, or that the risks outweigh any benefits.
- However, each time someone remains unvaccinated, there is an increase in the number of susceptibles in the population, resulting in an increased risk of an epidemic occurring. This in turn increases the risk to all susceptibles, including those who are unvaccinated for unavoidable reasons, including migrants, babies, or people with health problems that preclude vaccination.

### *Example 13.1.5*

In 1998, a paper published in the *Lancet*, with primary author Dr Andrew Wakefield, found a link between the MMR (Measles, Mumps and Rubella) vaccine and autism in children. The findings had a large impact on the public perception of the vaccination. As a result, more than 3 million young people in the UK were not fully vaccinated.

In recent years, the study linking MMR vaccines with autism has been completely discredited. In fact, Wakefield was found to have committed scientific fraud by falsifying data, to have acted dishonestly and irresponsibly, and to have a conflict of interest. A number of his research papers were retracted by the journals that had previously published them, and in 2010 he was struck off the UK medical register.

From 1996 to 2005 there was a total of 1621 confirmed cases of measles in England and Wales. In 2006 and 2007 there were more than 1700 confirmed cases. Around 95% of the population need to be vaccinated to protect against a measles epidemic, but the rate in England and Wales is around 85%. In 2008, the UK government launched a campaign to raise MMR vaccination rates.

### *Example 13.1.6*

In early 2011, Queensland Health issued a measles warning after an infected man came into contact with people at a Brisbane shopping centre.

- The SIR model can also be applied when some individuals have been vaccinated against a disease, so are not susceptible.
- Vaccinated people are placed in the removed compartment at time 0, rather than in the susceptible compartment.
- We can then use the model to investigate the impact of different vaccination rates on the potential spread of disease.

***Question 13.1.7***

The SIR model predicts that an epidemic will occur whenever the proportion of susceptibles in a population is greater than  $b/a$ , where  $b$  is the recovery rate and  $a$  is the infection rate. Suggest some strategies that might be used to prevent an epidemic or reduce its severity or duration, and explain how each strategy impacts on the values of  $b$ ,  $a$  and  $b/a$ .

## Case Study 37:

### Rubella

- **Rubella** (or **German measles**) was (and in some countries, still is) a common disease, particularly in childhood.
- In most cases, symptoms are very mild, and may even pass unnoticed. However, if a woman is infected during the first 20 weeks of pregnancy then spontaneous abortion can occur (in about 20% of cases), or the child may be born with congenital rubella syndrome (CRS), which is a range of incurable conditions including deafness, blindness and mental retardation.
- There was a rubella epidemic in the USA between 1962 and 1965. Health authorities estimate that there were well over 10 million infections, leading to 30,000 still births and 20,000 children born with CRS.
- A rubella vaccine was introduced in 1969 and is routinely administered in many countries. In Queensland, the Department of Health recommends all children have combined MMR (measles, mumps and rubella) vaccines at the ages of 12 months and 4 years.
- Vaccination campaigns have greatly reduced the incidence of rubella and the frequency of outbreaks. The Centers for Disease Control and Prevention announced that rubella was eliminated from the USA in 2004.
- In January 2008, at least four babies in Sydney became infected with rubella. All were less than 12 months old, so were under the age for administering the MMR vaccine.
- Earlier, we saw that for rubella:

$$\begin{aligned} \text{the infection rate } a &= 2.5 \text{ week}^{-1}; \text{ and} \\ \text{the recovery rate } b &= 0.5 \text{ week}^{-1}. \end{aligned}$$

- The fraction  $b/a = 0.5/2.5 = 0.2$ . (Alternately,  $1/R_0 = 1/5 = 0.2$ .)  
Hence if more than 20% of a population is susceptible to rubella and infectives enter the population then an epidemic is expected to occur.

**Example 13.1.8**

Assume that a population of 10000 people contains 10 rubella infectives, and that everyone else is susceptible. Using the values of  $a$  and  $b$  from above, the SIR equations for rubella are:

$$S' = -\frac{2.5}{10000} SI$$

$$I' = \frac{2.5}{10000} SI - 0.5I$$

$$R' = 0.5I$$

where  $I(0) = 10$ ,  $S(0) = 9990$  and  $R(0) = 0$ .

**Question 13.1.9**

Use Euler's method and a stepsize of one week to estimate the number of people in each category after one week.

Now we can develop a computer model.

**Program specifications:** Write a Python program that uses Euler's method and the SIR model to predict the spread of rubella when 10 infectives are in a population of 10000 people, with vaccination proportions between 0 and 1.

**Program 13.1: SIR model of rubella.**

```

1 # Uses Euler's method and the SIR equations to model the spread of rubella
2 # in a population with a vaccination proportion between 0 and 1.
3 from __future__ import division
4 from pylab import *
5
6 # Input parameters for the model.
7 maxt = input("Over how many weeks should the model run? ")
8 vacc = input("Enter proportion vaccinated (0..1):")
9
10 # Initialise variables for rubella; values of a and b are per week.
11 N = 10000
12 a = 2.5
13 b = 0.5
14
15 # Initialise variables for Euler's method. The stepsize is 0.1 week.
16 ss = 0.1
17 time=arange(0, maxt+0.1, ss)
18 nn=size(time)
19 SA = zeros(nn)
20 IA = zeros(nn)
21 RA = zeros(nn)
22
23 # Set the initial number of people in each category.
24 IA[0] = 10
25 SA[0] = N * (1.0 - vacc) - IA[0]
26 RA[0] = N - SA[0] - IA[0]
27
28 # Step through Euler's method with stepsize ss.
29 i = 0
30 while i < nn-1:
31     dS = -a * SA[i] * IA[i]/N
32     dI = a * SA[i] * IA[i]/N - b * IA[i]
33     dR = b * IA[i]
34     SA[i+1] = SA[i] + ss*dS
35     IA[i+1] = IA[i] + ss*dI
36     RA[i+1] = RA[i] + ss*dR
37     i = i+1
38
39 # Output
40 xlabel("Time (days)")
41 ylabel("Number of people")
42 title("SIR model of rubella")
43 plot(time, SA, "b-", linewidth=3)
44 plot(time, IA, "k-", linewidth=3)
45 plot(time, RA, "r-", linewidth=3)
46 text(3.5,8000,"S(t)")
47 text(7.4,2000,"I(t)")
48 text(6.3,6000,"R(t)")
49 show()

```



*Example 13.1.10*

Figure 13.2 shows the output from the Python program using a period of 14 weeks, and with no vaccinations.

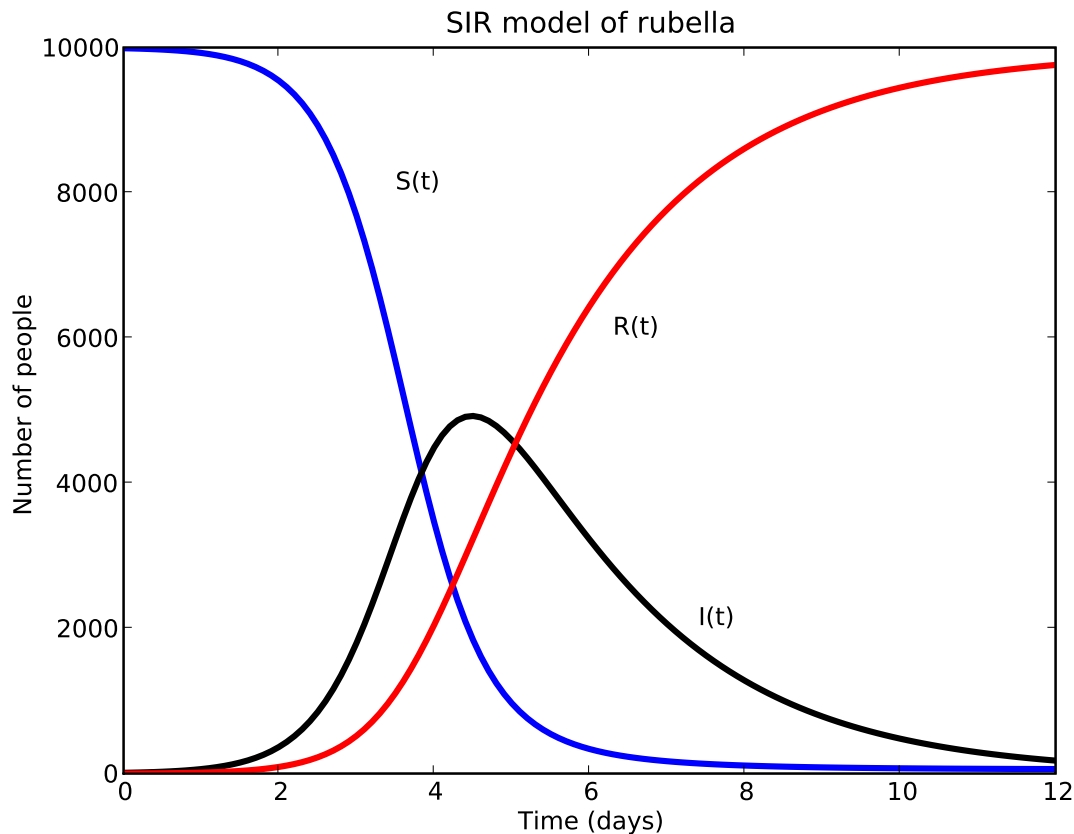


Figure 13.2: A rubella epidemic, as modelled by Euler's method, showing the numbers of susceptibles  $S(t)$ , infectives  $I(t)$  and removed people  $R(t)$ .

Figure 13.2 shows that:

- An epidemic occurs. (This is expected, as the initial proportion of susceptibles is more than 0.2).
- The epidemic lasts for about 14 weeks.
- The peak number of infectives at any time is 4925, which occurs about 4.4 weeks after the infectives entered the population.
- Almost everybody becomes infected over time, although a small number never become infected.

### *Example 13.1.11*

Consider a population of 10000 people with 10 infectives. The graphs in Figure 13.3 show the predicted values of  $S(t)$ ,  $I(t)$  and  $R(t)$  for two different vaccination rates.

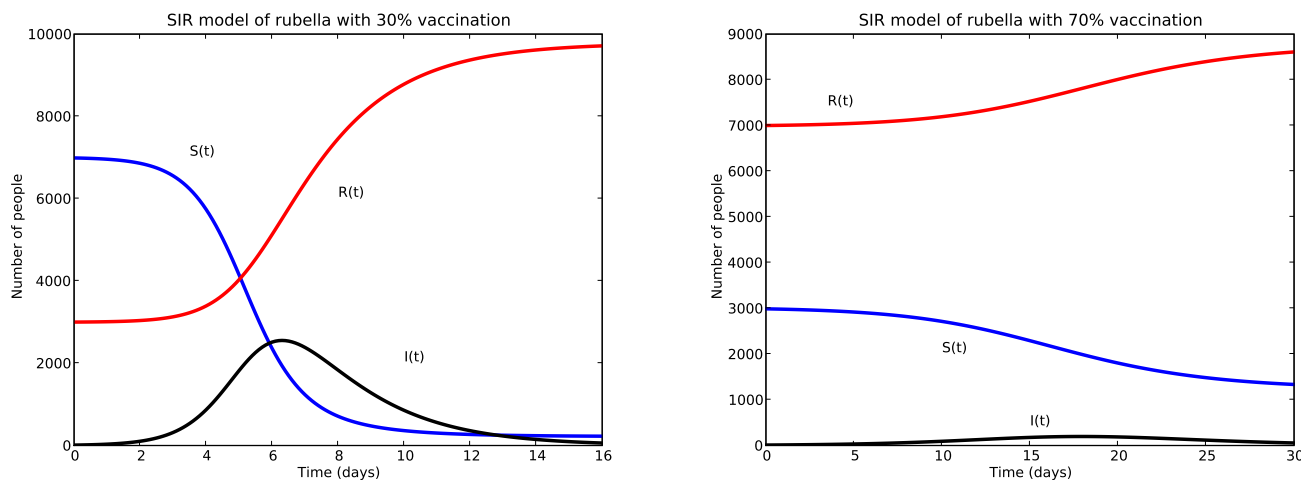


Figure 13.3: Models of rubella with 30% vaccination (left; over 16 weeks) and 70% (right; 30 weeks).

### *Question 13.1.12*

Describe the key differences between the predicted rubella outbreaks with vaccination rates of 0% (Example 13.1.10), 30% and 70% (Example 13.1.11). What are some practical benefits of achieving high vaccination rates?

Now we can develop a computer model of the impact of different vaccination rates on a (possible) rubella epidemic.

**Program specifications:** Write a Python program that uses Euler’s method and the SIR model to predict possible rubella epidemics, with vaccination rates ranging from 0% to 80%.

**Program 13.2: Impact of vaccinations on rubella epidemics.**

```

1 # Uses Euler’s method and the SIR equations to model the spread of rubella
2 # in populations with a range of vaccination rates. Prints out information
3 # about the vaccination rates and the resulting spread of disease.
4 from __future__ import division
5 from pylab import *
6
7 # Initialise variables. Run the model for a "long" time with stepsize 0.1.
8 N = 10000
9 a = 2.5
10 b = 0.5
11 maxt = 200
12 ss = 0.1
13
14 # Choose different vaccination rates from 0 to 0.8.
15 vacc = 0
16 while vacc <= 0.8:
17 # Set the initial number of people in each category.
18     I = 10
19     S = N * (1.0 - vacc) - I
20     R = N - S - I
21     R0 = R
22     Ipeak = 0
23 # Step through Euler’s method with stepsize ss.
24     t = 0
25     while t < maxt:
26         dS = -a * S * I/N
27         dI = a * S * I/N - b * I
28         dR = b * I
29         S = S + ss*dS
30         I = I + ss*dI
31         R = R + ss*dR
32         if I > Ipeak:
33             Ipeak = I
34             tpeak = t
35         t = t + ss
36
37 # Print output for this vaccination rate.
38     print vacc, round(Ipeak), round(tpeak,1), round(10000-R0-S), round(S)
39     vacc = vacc + 0.1

```

*Example 13.1.13*

Figure 13.4 presents some output from the program. In the figure,  $V$  is the percentage of the population vaccinated,  $I_{peak}$  is the peak number of infectives at any time,  $t_{peak}$  is the time at which this occurs,  $I_{tot}$  is the total number who **ever** become infected, and  $S_{final}$  is the number of susceptible people who **never** become infected.

$V$ (%)	$I_{peak}$ (people)	$t_{peak}$ (weeks)	$I_{tot}$ (people)	$S_{final}$ (people)
0	4925	4.4	9944	56
30	2554	6.2	6781	219
40	1841	7.3	5662	338
50	1190	8.9	4481	519
60	626	11.7	3202	798
70	197	17.8	1764	1236
80	10	0	194	1806

Figure 13.4: Predicted impact of different vaccination rates on a rubella outbreak.

Figure 13.4 shows that, as expected, epidemics of varying severity occur until the vaccination rate reaches 80%. Figure 13.5 shows the peak and total numbers of infectives for a range of vaccination rates.

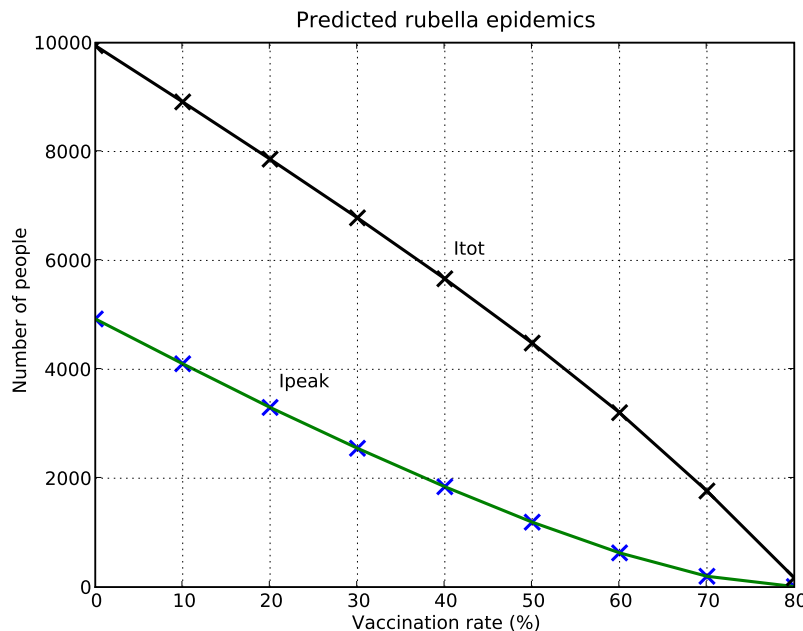


Figure 13.5: Peak and total numbers of rubella infectives for various vaccination rates.

End of Case Study 37.

## 13.2 Catastrophes



Photo 13.3: Bones of plague victims (and others). Left: Sedlec ossuary, Kutna Hora, Czech Republic. Right: Capela dos Ossos, Evora, Portugal. (Source: PA.)

- Many governments conduct *catastrophe planning*, modelling potential impacts of disastrous events, such as nuclear explosions, terrorist strikes, tsunamis, earthquakes and pandemics. Much of this work is highly secret, partly for security reasons, but also because some of the predicted outcomes are too frightening for public release.
- History contains many severe pandemics. In 2009, the Australian government spent \$200 million responding to the (very mild) swine flu pandemic.

### *Example 13.2.1*

In terms of numbers of fatalities, three of the four worst catastrophes in (European) Australian history are diseases. These four events are:

- Spanish influenza in 1918–19, causing more than 12000 deaths;
- a polio epidemic in 1946–55, causing more than 1000 deaths;
- a naval battle in the Second World War, causing 727 deaths; and
- a bubonic plague epidemic in 1900–1910, causing 550 deaths.

In addition, thousands of indigenous Australians died from diseases introduced by European settlement.



### *Example 13.2.2*

In the 1300s, the bubonic plague or *Black Death* killed around 20 million Europeans in six years, which was about one third of the population. In the worst-affected urban areas, around half of the population died.

The plague returned regularly over the next 400 years, with around 100 epidemics occurring. The social, economic, humanitarian and psychological costs and disruption arising from these pandemics are incalculable, and unimaginable today.



Photo 13.4: Plague monuments. Left: Brno, Czech Republic. Centre: Vienna, Austria. Right: Plzen, Czech Republic. (Source: PA.)

### *Example 13.2.3*

A Spanish Flu pandemic occurred in 1918–1919. Within six months the death toll was 25 million, statistical life expectancy in the USA dropped by 10 years and it is generally accepted that more people died from the disease than from combat in the First World War. The flu was so virulent and deadly that it ‘burnt itself out’, disappearing completely within 18 months.

The following is a quote from a letter written by Professor N R Grist in a camp infected by the disease, 29 September 1918.

“These men start with what appears to be an ordinary attack of LaGrippe

*(continued over)*

*Example 13.2.3 (continued)*

or Influenza, and when brought to the Hosp. they very rapidly develop the most viscous type of Pneumonia that has ever been seen. Two hours after admission they have the Mahogany spots over the cheek bones, and a few hours later you can begin to see the Cyanosis extending from their ears and spreading all over the face, until it is hard to distinguish the coloured men from the white. It is only a matter of a few hours then until death comes, and it is simply a struggle for air until they suffocate. It is horrible. One can stand it to see one, two or twenty men die, but to see these poor devils dropping like flies sort of gets on your nerves. We have been averaging about 100 deaths per day, and still keeping it up. There is no doubt in my mind that there is a new mixed infection here, but what I don't know. My total time is taken up hunting Rales, rales dry or moist, sibilant or crepitant or any other of the hundred things that one may find in the chest, they all mean but one thing here – Pneumonia – and that means in about all cases death.

... It takes special trains to carry away the dead. For several days there were no coffins and the bodies piled up something fierce, we used to go down to the morgue (which is just back of my ward) and look at the boys laid out in long rows. It beats any sight they ever had in France after a battle...



Photo 13.5: Snow sculpture of Death, Harbin, China. (Source: PA.)



## Case Study 38: Avian influenza

- The World Health Organisation (WHO) has warned that:
  - the risk of an influenza pandemic is high;
  - H5N1 (avian) influenza is endemic in many bird populations;
  - bird-to-human transmission has already caused fatalities; and
  - there is a serious risk that the virus could mutate and become human-to-human transmissible. This is sometimes called a “nightmare scenario” (although there has not yet been a verified case of this occurring).
- A major focus of international catastrophe planning is identifying and planning actions that can be taken in order to minimise the impact of a pandemic.



Photo 13.6: Feathered fiends? (Source: PA.)

- We will use the SIRD model to investigate the potential impact of a catastrophe caused by human-transmissible avian influenza. The SIRD model classifies the population into **four** distinct compartments: Susceptible,  $S(t)$ ; Infected,  $I(t)$ ; Recovered,  $R(t)$ ; and Dead,  $D(t)$ .
- The only possible movements of people *between* compartments are:
  - a susceptible person can become infected; and
  - an infected person can either recover or die.

**Question 13.2.4**

Draw a “life-cycle diagram” for the SIRD model.

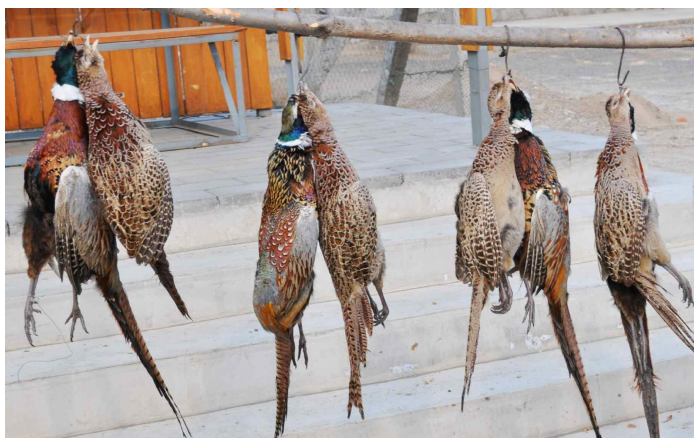


Photo 13.7: Ring-necked pheasants, *Phasianus colchicus*, China. (Source: PA.)



Photo 13.8: Painted Desert National Park, USA. (Source: PA.)

- Because there has never been a verified case of human-to-human transmission of avian influenza, the model is hypothetical. When building such models, it is important to choose reasonable values for all parameters.
- Researchers estimate the following values for the Spanish Flu pandemic in 1918–1919. We will use these values in our catastrophe model.

$$\begin{array}{lll}
 a & = & \text{infection rate} & b & = & \text{recovery rate} & c & = & \text{mortality rate} \\
 & = & 1.9 \text{ week}^{-1}; & & = & 1.4 \text{ week}^{-1}; & & = & 0.065 \text{ week}^{-1}.
 \end{array}$$



Photo 13.9: Spanish bird: nativity facade, Sagrada Familia, Barcelona, Spain. (Source: PA.)

**Example 13.2.5**

The equations of the SIRD catastrophe model are:

$$S' = -a \frac{S}{(N - D)} I$$

$$I' = a \frac{S}{(N - D)} I - (c + b) I$$

$$R' = b I$$

$$D' = c I$$

where  $N$  is the total initial population size, so  $N = S + I + R + D$ .

**Question 13.2.6**

In the SIRD model, the equations for  $S'$  and  $I'$  include the ratio  $S/(N - D)$ . In the SIR model, the ratio was  $S/N$ . Explain why the ratios are different.

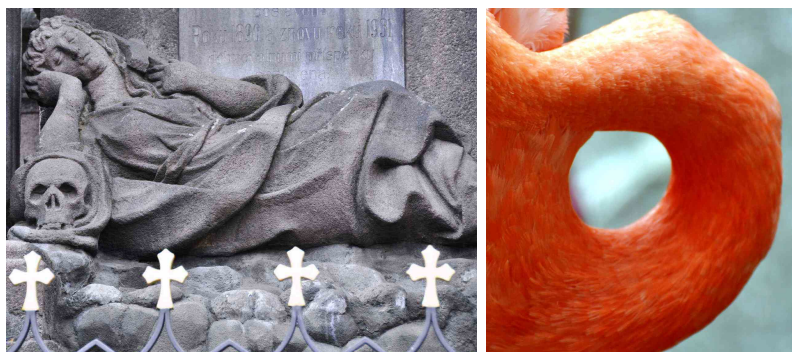


Photo 13.10: Left: Plague monument, Plzen, Czech Republic. Right: ring of pestilence? (Source: PA.)

- Now we can use Euler's method and our model to investigate various scenarios in a city such as Brisbane with  $N = 10^6$ .



### Example 13.2.7

An infective enters a city in which  $N = 10^6$  and everyone is susceptible.

**Results:** The results are shown in Figure 13.6. The model predicts that the disease outbreak will last for about 45 weeks, around 435,000 people will become ill, the largest number of infected people at any time will be about 29,800, and that approximately 19,200 people will die.

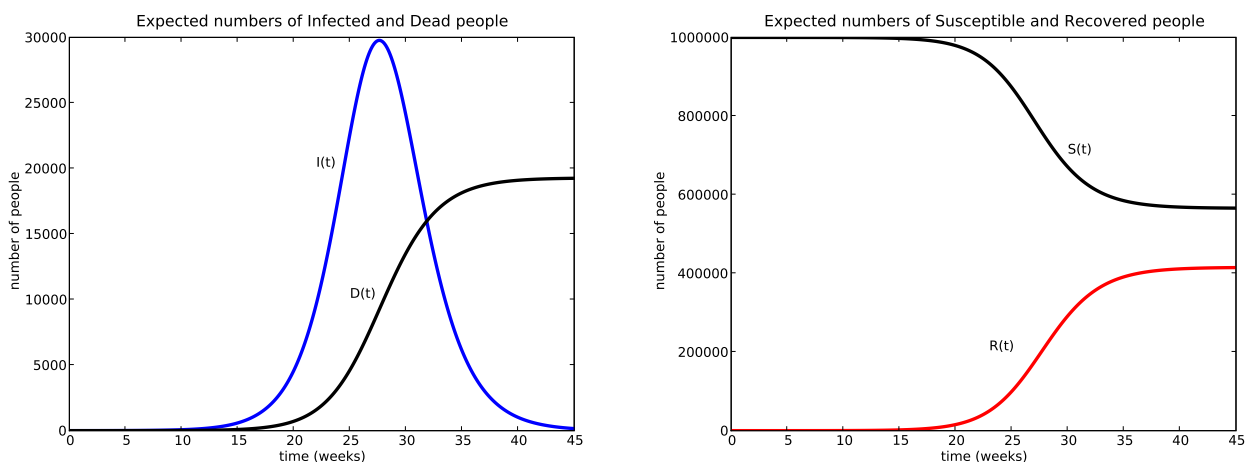


Figure 13.6: The impact of a possible human-transmissible avian influenza epidemic on a city of one million people, as modelled by Euler's method.



Photo 13.11: Marabou Stork, *Leptoptilos crumeniferus*. (Source: PA.)

- Of course, this catastrophe model is speculative. Is it realistic?

- For comparison, Figure 13.7 shows some mortality rates during the Spanish flu pandemic. The graphs are of similar shape to those in our catastrophe model.

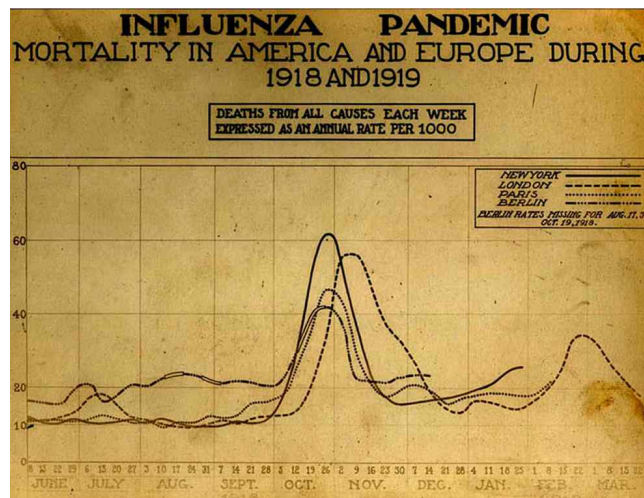
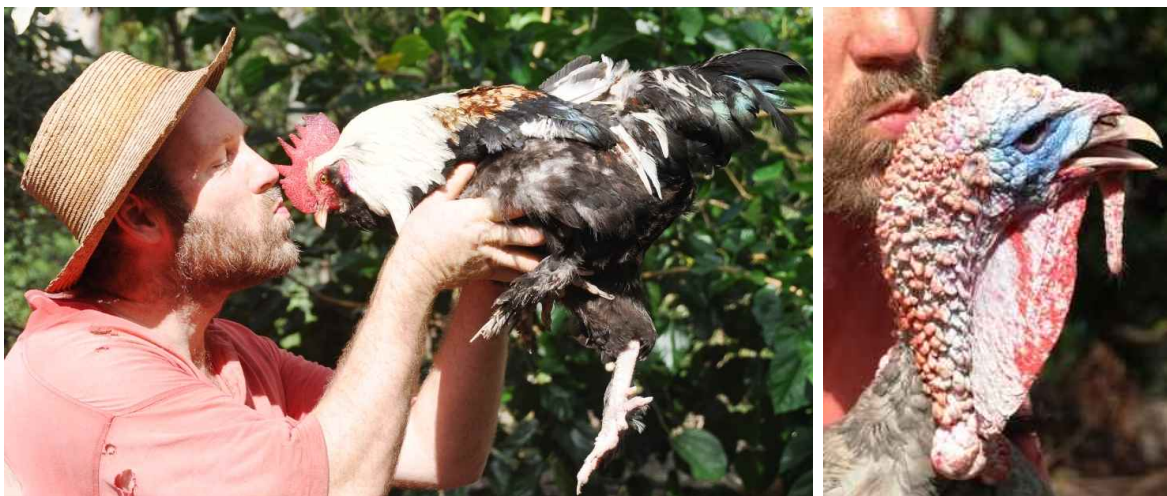


Figure 13.7: Mortality rates (per thousand population) for the Spanish flu in several cities in 1918–1919.

- Our catastrophe model predicts an overall infection rate of 45% and a mortality rate of 4.2% of infected people.
- For the Spanish flu, infection rates reached around 50%, with mortality rates ranging from 2% to 5%.
- Comparison of both scenarios shows that the catastrophe model that we have presented is (at least) plausible.
- Perhaps we all should be very, very afraid? At least, stop kissing poultry!



End of Case Study 38.

## 13.3 Space for additional notes

## A.1 Introduction to Python

### A.1.1 Using this manual

The purpose of this chapter of the notes is to help you learn how to use Python to represent models and answer questions in science. These notes are designed to be used in conjunction with your weekly computer lab sheets. Each week you will be told when to read which sections of these Python notes. In this way, you will be reading the material in these notes, then doing lab activities to reinforce your learning.

If you are keen to learn Python more rapidly, feel free to read ahead in these notes. The best way to learn computer skills is often to play around. Try things out, see what you can do, and challenge yourself!

### A.1.2 Installing Python at home

You may want to install Python at home so that you can try out some of this exciting stuff on your own. You can download the installation files from the course website, which also gives some instructions on what to do. To complete all the activities we will be doing in this course, you will need to install Python, NumPy and matplotlib (in that order).

For more information about Python, see <http://www.python.org/>.

If you would like to find out more about the packages we are using, or to find installations for MacOS or linux, the following links might also be useful:

- **ActivePython** is the distribution of Python which we will be using in this course. For more information see <http://www.activestate.com/Products/activepython/>.
- **NumPy** provides mathematical tools for Python, and is needed to use matplotlib. See <http://numpy.scipy.org/>.
- **matplotlib** provides graphing capabilities for Python, and can be found at <http://matplotlib.sourceforge.net/>.



### A.1.3 Getting started

In this course we will be using Python through a program called **IDLE**, which is an Integrated Development Environment (IDE) for Python. An IDE typically consists of an editor (which often uses colours to highlight features of the language) and other tools to aid in software development and maintenance.

#### Opening IDLE

To open IDLE, go to the Start Menu and choose:

Programs → ActiveState ActivePython 2.5 → idle.

If you need to do something different from this in order to start IDLE, your tutor will give you instructions.

The screen in **IDLE** will probably look something like Image A.1, although there may be some variations, depending on which version of Python you are running. This window is the main Python window. All output from your program and any error messages will appear in this screen. (You can also type Python commands directly into this window, but we will not usually do that in SCIE1000.)

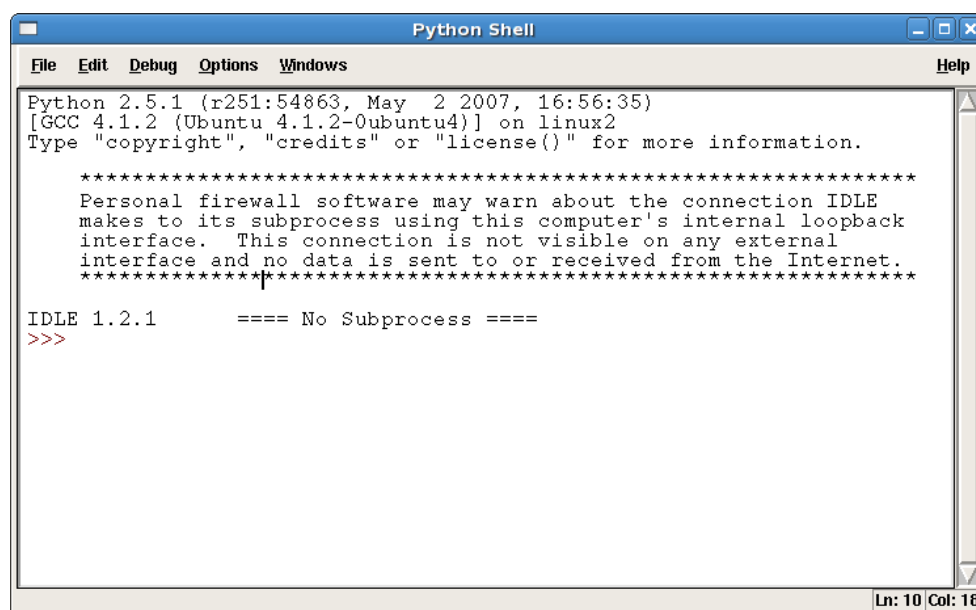


Image A.1: The IDLE window.

## A.2 Basic use of Python

We will be writing and running Python programs throughout semester. In this section we first describe in general what a program is, how to write and save programs, and how to run programs. Then we will cover some Python commands that can be included in your programs.

### A.2.1 Programming

#### What is a program?

A *program* is simply a set of instructions which a computer is able to interpret and carry out. You may be familiar with programs such as Firefox or Microsoft Word. Even the Python programming language is itself a program.

When we have a problem to solve computationally, we usually want to write a sequence of Python commands, save them to a file, and then run them.

Advantages of doing this include:

- Programs can be run multiple times, and in multiple places.
- Programs can be debugged more easily. For example, once a section of a program has been thoroughly checked (or even proved to be correct) then it does not need to be checked again.
- Teams of people can design and write different parts of the program.
- Problems of much greater complexity can be solved.

#### Writing and saving programs

To create and save a program:

- In IDLE's "Python Shell" window, select **File** → **New Window**. This will open a new window, called an *editor* window, in which you can enter your code.
- Type in the Python commands that you want in your program. When you type the commands, they will not run straight away. This allows you to enter multiple lines, and go back to fix any errors you make before you run the program.

- Do not include any spaces or tabs at the start of your lines; we will see why later.
- When you have finished choose **File** → **Save As** in the editor window. You may like to save your program in a special Python programming folder (which you will need to create the first time you want to use it).

To open an existing program, select **File** → **Open** and choose the file.

### Naming your programs

Python programs are conventionally named

`something.py`

where **something** is a name that explains the purpose of the program. The `.py` extension is well-recognised for Python programs.

### Running a program

To run a program that is in an editor window, select **Run** → **Run Module** from that editor window. This will load your commands into the main Python window and run them, as if you had typed them directly into the window. (If you have changed the program since you last saved it, you will be prompted to save it again.)

When you run your program, you will notice that the Python window shows the following message:

```
>>> ===== RESTART =====
```

This tells you that Python is clearing the values of any variables you have previously created. This means that earlier calculations do not interfere with your current work, but also that you cannot use values from previous calculations. Any output from your program will appear under that message.

## A.2.2 Comments in Python programs

Any lines in a Python program that starts with a `#` are *comments*, and will be ignored by Python. You should use comments to explain what your program is doing, which will help anyone reading your program to understand what is happening. Always try to use comments where appropriate.

## A.2.3 Importing modules

Like most computer languages, Python provides access to a large collection of mathematical functions and other useful operations. These functions are organised into *modules*. In SCIE1000 we will be using the mathematical functions defined in the module called `pylab`. This module contains many useful functions, and we will be using it all of the time.

To instruct Python to allow us to access all of the functions defined in the `pylab` module (as well as to avoid some odd behaviour when dividing integers), use the following commands (which should appear at the top of all of your Python programs):

```
from __future__ import division
from pylab import *
```

## A.2.4 Printing to the screen

The next Python command we will see is the *print* command, which outputs text and the results of calculations to the screen.

### Printing text

To print something to the computer screen, use the `print` command.

The `print` command may be used in a number of ways. If you want to print a blank line to the screen, use:

```
print
```

To print a message to the screen, use:

```
print "message"
```

The message must be enclosed in quotation marks. You may use either single quotes 'like this', or double quotes "like this". You may not mix the two. These two symbols occur on the same key of your keyboard.

Note that if you open quotation marks in a command, **you must close them**. If you try to enter a command without closing your quotation, the command will not be complete. Python will open a new blank line and will not run the command until you close the quotation and then press enter.

To evaluate a mathematical expression and print the answer, use:

```
print expression
```

Note that there are no quotation marks in this case. If you use quotation marks, whatever is *within* the quotation marks will be printed *exactly as it is*, whereas anything that is not inside quotation marks will be evaluated as an expression, and the *answer* will be printed. Note that if you open quotation marks in a command, **you must close them**. If you want to print multiple items (this may include a mixture of expressions and messages), you can separate the items by commas.

The following example is a simple Python program that demonstrates these uses of the **print** command. Note that the line numbers and vertical line at the left have been added into these notes for ease of reference. They are not a part of the program. (If you like, you can type this program into a Python edit window, then save it and run it. Take care to type the brackets and quotation marks exactly as they appear.)

Program A.1: My first program

```
1 from __future__ import division
2 from pylab import *
3
4 # Print some messages.
5 print "This is a message"
6 print "This is also a message!"
7 print "This is first", "and this is second"
8
9 # Print the result of a calculation.
10 print 3+4
```

Here is the output from running the program:

```

1 This is a message
2 This is also a message!
3 This is first and this is second
4
7

```

Note that Lines 4 and 9 of the program contain comments. Also, you can use blank lines (like Lines 3 and 8) to make your program more readable.

### A.2.5 Numerical calculations

As suggested by Line 10 of the previous program, Python can use standard mathematical operations. The following table summarises the Python symbols for a number of these operations. (In each case, the letters  $a$  and  $b$  represent numbers.)

Operation	Mathematical representation	Python spelling
Addition	$a + b$	<code>a+b</code>
Subtraction	$a - b$	<code>a-b</code>
Multiplication	$a \times b$	<code>a*b</code>
Division	$a \div b$	<code>a/b</code>
Exponentiation	$a^b$	<code>a**b</code>
Brackets	$(...)$	<code>(...)</code>
Remainder	$a \bmod b$	<code>a % b</code>

#### Important note

You may have seen  $a^b$  used to represent  $a^b$  on your calculator. In Python `a^b` means something completely different so be careful to use `a**b`.

The following example is a simple Python program that demonstrates some mathematical operations.

## Program A.2: Python as a calculator

```
1 from __future__ import division
2 from pylab import *
3
4 print 12/4
5 print -6*4
6 print 10%6
7 print 10%5
8
9 # Python correctly applies order of operations:
10 print 2+3*4
11 print (2+3)*4
12 print 2**5
13
14 # You can combine text and calculations in print commands.
15 print "All up, 10 cows have",10*4," legs"
```

Here is the output from running the program:

```
1 3
2 -24
3 4
4 0
5 14
6 20
7 32
8 All up, 10 cows have 40 legs
```

### Permission to experiment and play

**Important:** Do not be afraid of experimenting and trying something new. If you type something into Python and it does not work, you will not destroy modern civilisation. You will not even crash the computer.

In the examples above, none of the expressions which we typed contained spaces. In Python, you can add spaces into an expression anywhere you like, provided that the expression still makes sense. Adding spaces to your expressions in sensible places can make them easier to read and understand, particularly when you start to write more complicated expressions. The following example demon-



strates writing expressions with sensible spacing.

### Program A.3: Spacing

```
1 from __future__ import division
2 from pylab import *
3
4 # Adding one space between numbers and symbols is reasonable.
5 print 6 + 4
6
7 # You normally do not use space between brackets and numbers.
8 print (2 + 3) * (6 - 4)
9
10 # Sometimes spaces are used to show order of operations.
11 print 2 + 3*4 + 5*6
```

When putting spaces into your expressions, remember that your main concern is *communication*. There is no one correct answer. Use your judgment.

## A.2.6 Integers and real numbers

Internally, computers store values in binary. That is, they use 1s and 0s to represent them. Depending on the kind of value, computers may represent values in different ways.

- **integers** can be represented exactly in binary.
- **real numbers** usually cannot be exactly represented using binary. Instead, the computer stores a very close approximation to the number. The term *floating point* number refers to a number which is not stored as an exact integer, but is stored as a real number instead.

Because computers cannot always store real numbers exactly, calculations can sometimes result in numbers which are not exactly what you expect. The errors are usually so small that they can be ignored.

Python uses the symbol **e** to represent scientific notation. So for instance, Python would represent  $6.02 \times 10^{23}$  as **6.02e+023**, and  $3 \times 10^{-4}$  as **3e-04**.

Most programming languages can only store integers in a certain range. Python has the added feature that it can store arbitrarily large integers. Python shows

that a number is stored in large integer format by appending the letter **L** to the number.

## A.3 Variables and mathematical functions

### A.3.1 Variables

A powerful feature of computers and programming languages is their ability to “remember” values. This is done by *assigning values* to *variables*.

#### Variable names

Every variables has a name, which is used to access it. A variable name:

- is made up of one or more letters, digits and underscores.
- must begin with a letter or an underscore.
- is **case sensitive**. For example, **sideLen**, **SideLen** and **SIDELEN** are all different variables.

When writing programs, always remember that someone else may need to read your program later. You should always choose *meaningful* variable names which tell the reader what the variables are used for.

#### Assigning to variables

To assign a value to a variable use the command

```
variable = expression
```

where **variable** is the name of the variable, and **expression** is either a value (such as **3** or **-2.25**), or an expression (such as **2 + 4**). If you use an expression, Python will calculate the result of the expression and assign that value to the variable.

Once you have assigned a value to a variable, you can use that variable name in subsequent calculations. You can even assign its value to another variable.

## Accessing variables

Once a variable has been created, it is accessed using its name. So, to print the value of a variable named `bob` to the screen you can use the command:

```
print bob
```

Remember that if you were to write `print "bob"` (notice the quotes), then Python would print the word “bob” to the screen. Because the command above does not use quotes, Python accesses the variable *named* `bob`.

You can also use variable names in calculations. For example:

### Program A.4: Using variables

```
1 width = 20
2 height = 45
3 print width, height
4 print width * height
5 perimeter = 2 * width + 2 * height
6 print "The perimeter is", perimeter
```

Here is the output from running the program:

```
1 20 45
2 900
3 The perimeter is 130
```

If you try to access a variable that does not yet have a value, you will get an error message.

### A.3.2 Functions and parameters

As in mathematics, many Python functions act on one or more values (called *arguments*), and produce some output.

**Arguments** (also known as **parameters**) are values that are passed in to a function. An argument can be a variable, a value or a mathematical expression. To use a Python function to calculate the result of a mathematical function, type

```
functionName(argument)
```

where `functionName` is the name Python gives to the function and `argument` is the argument to the function. For example:

## Program A.5: Python functions

```
1 from __future__ import division
2 from pylab import *
3 B = 9
4 SqB = sqrt(B)
5 print "The square root of ",B," is ",SqB
6 print "The square root of 64 is",sqrt(64)
```

Here is the output from running the program:

```
1 The square root of 9 is 3
2 The square root of 64 is 8
```

### Common mathematical functions

Here is a list of some mathematical functions in Python. In this list, ... represents an argument.

- `sqrt(...)` which gives the square root of the argument.
- `sin(...)` which gives the sine of the argument (where the argument is given in radians).
- `cos(...)` gives the cosine of the argument (where the argument is in radians).
- `tan(...)` gives the tangent of the argument (where the argument is in radians).
- `exp(...)` gives  $e$  raised to the given power.
- `log(...)` gives  $\ln$  of the given argument.
- `log10(...)` gives  $\log_{10}$  of the given argument.

Python also includes the constant `pi`, which (approximately) equals  $\pi$ .

All of the trigonometric functions in Python operate on angles measured in radians. Any angles measured in degrees must first be converted to radians, by multiplying the angle by  $2\pi$  and dividing by 360 (or, equivalently, multiplying by  $\pi$  and dividing by 180).

The following example demonstrates the use of mathematical functions.

## Program A.6: Mathematical functions in Python

```
1 from __future__ import division
2 from pylab import *
3 # Access the constant pi
4 print pi
5
6 print sin(pi/2)
7 print exp(1)
8 print log10(1000)
9 # Evaluate sin of 90 degrees. We first need to convert degrees
   to radians.
10 print sin(90*pi/180)
11 print "45 degrees = ", 45*pi/180, " radians"
```

Here is the output from running the program:

```
1 3.1415926535897931
2 1.0
3 2.71828182846
4 3.0
5 1.0
6 45 degrees = 0.785398163397 radians
```

### A.3.3 The input command

Often when writing programs it is useful to be able to ask the user for some input values. To do this, we use the `input` command. In Python, `input` acts in a similar way to other functions. There are two ways to use it:

To read a value from the user and store that value into the variable `var`, use the command

```
var = input()
```

When reading a value from the user, you can instruct Python to write some message to the screen as a prompt. Suppose that the message prompt you wish to write to the screen is `prompt`. To do this you would use the command

```
var = input("prompt")
```

The command above will write the prompt to the screen, then input a value and store it in the variable `var`.

The following example program shows how to use the `input` command.

### Program A.7: Inputting values into Python programs

```
1 from __future__ import division
2 from pylab import *
3
4 a = input("Tell me a number: ")
5 b = input("Tell me another number: ")
6
7 c = a + b
8 d = a * b
9
10 print a, "+", b, "=", c
11 print a, "x", b, "=", d
```

Here is the output from running the program twice:

```
1 >>>
2 Tell me a number: 8
3 Tell me another number: 7
4 8 + 7 = 15
5 8 x 7 = 56
6
7 >>>
8 Tell me a number: 987
9 Tell me another number: 654
10 987 + 654 = 1641
11 987 x 654 = 645498
```

#### A.3.4 Software errors and bugs

Even the best computer programmers will sometimes (even often) make errors or *bugs* in their programs. A key skill in programming is minimising the number of errors, and then identifying and fixing any that occur. There are many different types of error, including incomplete problem description, design faults in the software, unanticipated ‘special cases’, coding errors and logic errors.

In SCIE1000 the result of any errors will be minor. You will probably get a bit frustrated and might even need to ask for help, but no lasting damage will occur. In real life, the consequences arising from programming errors can be very serious: for example, they have caused planes to crash, rockets to explode and entire transport systems to fail. As a result, there is an entire branch of

computer science devoted to techniques for minimising errors, and even proving that software is correct.

In SCIE1000 we will not be giving you control of aeroplanes, rockets or entire transport systems. If your program has an error, you should learn from it and try to fix the problem. You probably will not have killed anyone important.

### Avoiding errors

When writing programs, make sure that you:

- Make sure you understand the question **before** you start programming.
- Think about the best and most logical way to solve the problem.
- Consider planning your program on paper first.
- Put comments in your program so you know what you are trying to do.
- Test your programs on a range of data;
- Check some output carefully to make sure it is correct; and
- Pay attention to any error messages!

A Python error message is shown in the following example:

```
1 Traceback (most recent call last):  
2   File "<pyshell#243>", line 1, in <module>  
3     2/0  
4 ZeroDivisionError: integer division or modulo by zero
```

The Python error message may be a bit confusing, but on Line 4 it clearly identifies the kind of error (in this case, trying to divide by zero). In general, the last line of a Python error message will tell you what kind of error occurred. This will help you to diagnose the problem.

### Fear not!

Do not be afraid of error messages! Never let the fear of error messages stop you from playing around with Python and trying different commands.

*(continued over)*



## Fear not! *(continued)*

Getting an error message **does not** mean that you will fail the course. If it helps you to figure out what you did wrong, then you have learned something!

Equally important, do not ignore error messages. They give you useful advice about what is going wrong.

A common error message is:

```
SyntaxError: invalid syntax
```

This message means that Python cannot make sense of your instruction. This might be because you have forgotten a bracket or accidentally used a symbol which does not mean anything in Python.

### A.3.5 What did I do wrong?

Previously we found out how to use a Python error message to find out what *kind* of error occurred. Now we will look at how we can work out *where* in your program an error occurred.

#### Program A.8: Errors in Python programs

```
1 from __future__ import division
2 from pylab import *
3
4 a = input("Tell me a number: ")
5 b = input("Tell me another number: ")
6
7 c = a + b
8 d = a * bb
9
10 print a, "+", b, "=", c
11 print a, "x", b, "=", d
```

Here is the output from running the program:

```
>>>
1 Tell me a number: 8
2 Tell me another number: 7
```

```
4  
5 Traceback (most recent call last):  
6   File "example.py", line 7, in <module>  
7     d = a * bb  
8 NameError: name 'bb' is not defined
```

To help you to identify the error, you should:

1. Look at the last line of the error message to identify the kind of error. In this case, we see

```
NameError: name 'bb' is not defined
```

2. Look at the third last line of the error message (line 10 in the example above). This will tell you *where* the error was detected.

```
File "example.py", line 9, in <module>
```

This tells us the file and the line where the error occurred. You should look very carefully at this line of your program and try to see where you made a mistake. If you look at line 9 of the program in the example above, you will see that the programmer has accidentally typed `'bb'` instead of `'b'`.

To help you find a certain line number in a Python program, the editor window tells you in the bottom-right corner the number of the line where your cursor is currently located. You can also use **Edit** → **Go to Line** to move to a specific line.

If you know what line the error is in, but you cannot figure out exactly what the problem is, see if you can think of a way of rephrasing your instruction a bit. Try something a little bit different and see what it does. This can help you to diagnose the problem.

If a program contains more than one error, Python will display the message for the first one which it encounters. So after you have found and fixed an error, you may be given a different error message. *This is usually a good sign.* It often means that you have fixed the first error and can move on to fixing the next one.

Some common types of errors are:

<b>Error</b>	<b>Explanation and possible causes</b>
<b>SyntaxError</b>	The command is not understood by Python. Perhaps: <ul style="list-style-type: none"> <li>• You have used incorrect bracket types (e.g. ( ) instead of [ ])</li> <li>• You have forgotten a bracket</li> <li>• Your indentation is incorrect (wrong number of spaces at start of line)</li> </ul>
<b>NameError</b>	There is no variable with the given name. Perhaps: <ul style="list-style-type: none"> <li>• You have mistyped the name of a variable.</li> <li>• You have forgotten to set a starting value for a variable.</li> </ul>
<b>ImportError</b>	A module to be imported does not exist. Perhaps: <ul style="list-style-type: none"> <li>• You mistyped the name of the module to import.</li> </ul>
<b>OverflowError</b>	The answer is too large or too small to calculate.
<b>ValueError</b>	One of the arguments you have given is not valid for this function.
<b>IndexError</b>	You have used an invalid index to an array or sequence.
<b>TypeError</b>	One of the arguments you have given is not the correct type— for instance, you may have put quotation marks around a number in a numerical calculation.

Some of these errors you will probably not see until later on. For example, an **IndexError** will not make much sense until you have learned about arrays. These errors are included in the table so that you can use this table as a reference later on.

## A.4 Conditionals

Sometimes when programming, you want the computer to behave in a different way depending on whether a certain condition is true or false. For example, if you had written a program to simulate the metabolism of alcohol by the body, you might want to print a different message depending on the answer to the question “is the blood alcohol content greater than 0.05% after three hours?”

### A.4.1 Boolean values

A *Boolean* value is a value which is either true or false, but cannot be both at

the same time. Examples of statements which can be either true or false (but not both) are:

All frogs are green    4 is greater than 3     $x \leq y$ , for given values of  $x$  and  $y$ .

Python uses the special values **True** and **False** to represent boolean values.

### A.4.2 Evaluating conditions

Python has a number of operations which will always result in Boolean values when the operations are used on two numbers.

Operation	Mathematical representation	Python representation
Greater than	$a > b$	<code>a &gt; b</code>
Less than	$a < b$	<code>a &lt; b</code>
Greater than or equal	$a \geq b$	<code>a &gt;= b</code>
Less than or equal	$a \leq b$	<code>a &lt;= b</code>
Equal to	$a = b$	<code>a == b</code>
Not equal to	$a \neq b$	<code>a != b</code>

You can use these operations in Python in the same way that we used mathematical operations such as  $+$  or  $-$ .

Notice that the operator for checking whether two things are equal in Python is `==` and not just a single `=` sign. We have already seen that the single `=` sign is used to assign a value to a variable.

### A.4.3 Combining conditions

Boolean values can also be combined using **and**, **or**, **not**, in the following ways:

- **x and y**    is true if and only if both  $x$  is true and  $y$  is true.
- **x or y**    which is true if  $x$  is true or  $y$  is true, or both  $x$  and  $y$  are true.
- **not x**    which is true if and only if  $x$  is false.

The effects of these conditions are illustrated in the following Python program.

## Program A.9: Booleans

```
1 from __future__ import division
2 from pylab import *
3 x = 4
4 y = 5
5 print x>4
6 print x>=4
7 print x==4
8 print x==4 and y==5
9 print x==5 or y==4
```

Here is the output from running the program:

```
1 False
2 True
3 True
4 True
5 False
```

### A.4.4 Conditional statements

Now that we can evaluate conditions, we can use them to write statements which are only performed if a given condition is true.

#### The if statement

Simple conditional statements are written in the following way:

```
1 if condition:
2     actions
```

This statement will run **actions**, but only if **condition** is true. Note that the **indentation is important**. Python uses the indentation so it can tell which actions to perform only if the condition is met. If the condition is **not** true, the next command that runs is the **first** command **after** the indented lines.

The following program inputs a driver's blood alcohol content and prints a message if it is illegal to drive in Queensland.

## Program A.10: BAC, conditionals and driving 1

```
1 from __future__ import division
2 from pylab import *
3
4 # This program inputs your blood alcohol content BAC
5 # and prints a message if you are over the legal limit.
6
7 BAC = input("What is your blood alcohol content? ")
8
9 if BAC >= 0.05:
10     print "You are over the legal limit!"
```

Here is the output from running the program twice:

```
1 What is your blood alcohol content? 0.07
2 You are over the legal limit!
3
4 What is your blood alcohol content? 0.04
```

Note that in the second case there is no message printed, as it is legal to drive with a blood alcohol content of 0.04.

### The else statement

In the previous example, the program outputs a message if it is illegal to drive, but gives no output if it is legal to drive. The program would be more useful if it printed out a different message if it is legal to drive.

When programming, it is often the case that we have **two** possible situations, with a need to execute one or other of the cases depending on the value of some Boolean condition. This is done in the following way.

The following program inputs a driver's blood alcohol content and prints a message stating whether it is legal to drive in Queensland.

## Program A.11: BAC, conditionals and driving 2

```
1 from __future__ import division
2 from pylab import *
3
4 # This program inputs your BAC and prints a message
5 # indicating whether or not it is legal to drive.
6
7 BAC = input("What is your blood alcohol content? ")
8
9 if BAC >= 0.05:
10     print "You are over the legal limit!"
11 else:
12     print "You are legal to drive!"
```

Here is the output from running the program twice:

```
1 What is your blood alcohol content? 0.07
2 You are over the legal limit!
3
4 What is your blood alcohol content? 0.04
5 You are legal to drive!
```

If there are multiple different conditions to check then the following approach is used:

```
1 if condition1:
2     action1
3 elif condition2:
4     action2
5 elif condition3:
6     action3
7 else:
8     other_action
```

The command **elif** is short for “else if”, and means that Python should do these actions if the previous conditions are not true, but this condition is. The **else** section is only run if none of the other conditions is true.

Once again, we can use this new form to extend our example.



## Program A.12: BAC, conditionals and driving 3

```
1 from __future__ import division
2 from pylab import *
3 # This program inputs your BAC and prints a message
4 # indicating whether it is legal to drive, or BAC = 0.
5
6 BAC = input("What is your blood alcohol content? ")
7
8 if BAC >= 0.05:
9     print "You are over the legal limit!"
10 elif BAC == 0:
11     print "Your BAC is zero; go for it!"
12 else:
13     print "You are legal to drive UNLESS you are on"
14     print "a Learner's permit or a Provisional licence."
```

Here is the output from running the program three times:

```
1 What is your blood alcohol content? 0.07
2 You are over the legal limit!
3
4 What is your blood alcohol content? 0.04
5 You are legal to drive UNLESS you are on
6 a Learner's permit or a Provisional licence.
7
8 What is your blood alcohol content? 0
9 Your BAC is zero; go for it!
```

## A.5 Loops

### A.5.1 Why loops?

In all of the programming which we have done so far, each of the lines of code in the program were executed once in the order in which they were written (except for lines inside an `if` statement). Solving problems often requires the program to execute a sequence of code multiple times.

For instance, suppose we were modelling population growth in a predator-prey system. We might write a few lines of programming to describe how the number of predators and number of prey interact over a year. If we wanted to simulate

a population over 50 years, it would be inconvenient to have to repeat the same programming 50 times. The programming concept which allows lines of code to execute multiple times in succession is called a *loop*.

## A.5.2 While loops

Different programming languages have different kinds of loop. In this section we will focus on *while* loops in Python. A *while* loop in Python is constructed in the following way:

```
1 while condition:  
2     actions
```

Here, **condition** is a Boolean condition (an expression that can either be true or false) and **actions** is an indented sequence of instructions forming the loop *body*. The **condition** may include any of the boolean operations which we looked at in the last section. Once again, it is important that the loop body is indented. When Python executes a *while* loop, it will:

1. Check whether **condition** is true.
2. If **condition** is not true, jump to step 4.
3. If **condition** is true, execute the **actions** in the loop body, then return to step 1.
4. Run the rest of the program, recommencing from the **first** line **after** the loop body.

### Program A.13: Loops

```
1 from __future__ import division  
2 from pylab import *  
3 # Using a loop to calculate and print square and cubic numbers.  
4  
5 i = 1  
6 while i <= 5:  
7     print i, i*i, i*i*i  
8     i = i + 1  
9 print "Done."
```

The output of this program is:

```
1 1 1 1
```

```
2 2 4 8
3 3 9 27
4 4 16 64
5 5 25 125
6 Done.
```

The events in the program are carried out in the following sequence:

- In Line 4, `i` is set to 1.
- Python tests the condition `i <= 5` (Line 5) and finds that it is true.
- Python executes the loop body (Lines 6 and 7), which:
  - Prints 1,  $1^2$  and  $1^3$ .
  - Sets `i` to equal 2.
- Python tests the condition in Line 5 again and finds that `i <= 5` is still true.
- Python executes the loop body again, which:
  - Prints 2,  $2^2$  and  $2^3$ .
  - Sets `i` to equal 3.
- Python tests the condition in Line 5 again.
- This process continues until `i` is 5.
- Python tests the condition in Line 5 and finds that `i <= 5` is still true.
- Python executes the loop body which:
  - Prints 5,  $5^2$  and  $5^3$ .
  - Sets `i` to equal 6.
- Python tests the condition in Line 5 and finds that `i <= 5` is now **false**.
- The program resumes at the first line after the loop body (Line 8), which prints the word “Done.”.

### A.5.3 Loop forever...

A *while* loop will continue to run the commands in the loop body until the condition is no longer met. This means that you have to be very careful that you choose a condition which will cause the loop to stop at some stage.

Consider the following loop:

Program A.14: Infinite loop

```
1 from __future__ import division
2 from pylab import *
3 x = 3
4 while x < 10:
5     print "forever ..."
```

Notice that there is nothing within the body of the loop that changes the value of **x**. This means that the condition **x < 10** will always be true, so the loop will never terminate. This is called an *infinite loop*. Take care to avoid infinite repetition when writing loops.

#### Stopping infinite loops

If you run a Python program and it seems to be taking a long time, it **may** contain an infinite loop. If you suspect that a running program contains an infinite loop, you can terminate it by pressing **Ctrl+C**.

### A.5.4 Nested loops

Sometimes it may become necessary to have loops within loops. For instance, in a neuroscience model you might want to have one loop which goes through all the neurons in your model, and use this *within* a loop which steps through time to calculate how the system changes over time. This is called *nesting*—one loop is said to be *nested* within the other.

To accomplish this in Python, you can simply put one loop inside the body of another loop. Remember that the body of the **inner** loop must be **double** indented.

### Program A.15: Nested loops

```
1 # This program demonstrates nested loops.
2 from __future__ import division
3 from pylab import *
4
5 a = 1
6 while a <= 3:
7     b = 1
8     while b <= a:
9         print "a =", a, " and b =", b
10        b = b + 1
11    a = a + 1
```

In this program:

- Line 4 contains the condition for the outer loop.
- Lines 5 to 9 form the body of the outer loop.
- Line 6 contains the condition for the inner loop.
- Lines 7 and 8 form the body of the inner loop.
- Line 9 is part of the body of the outer loop, but not part of the inner loop.

When the condition of the inner loop is false, the program will resume at the next line which is not part of the body of that loop: line 9. This *is* however part of the body of the outer loop.

This program generates the following output:

```
1 a = 1 and b = 1
2 a = 2 and b = 1
3 a = 2 and b = 2
4 a = 3 and b = 1
5 a = 3 and b = 2
6 a = 3 and b = 3
```

You can also nest conditional (**if**) statements inside loops and vice versa. By combining loops and conditionals, you can create very powerful algorithms to solve scientific problems.

## A.6 Arrays

We have already used Python to store individual data values in variables such as **x** or **y**. Often we need to store many related items of data. In these cases, using an individual variable for each value can make things cumbersome.

Programming languages provide different mechanisms for storing lots of data. In general, a **data structure** is a way of storing and accessing data in a computer program.

A key component of good programming is choosing a data structure that is appropriate to the problem being solved. Choosing a good data structure can allow algorithms to run much more quickly or to make more efficient use of the available computer memory.

Probably the most common data structure is the *array*.

### A.6.1 What is an array?

An array is a group of data items, and may be thought of as a list or table of data. The position of an entry in an array is given by one or more *indices*.

The **number of indices** needed to specify the positions of each element in an array is called the **dimension** of the array. For example in a one-dimensional array, each value in the array can be accessed using a single index, such as 1 or 5 or 16. The number of elements in an array is called the **size** of the array. We will only cover one-dimensional arrays in SCIE1000.

### A.6.2 Printing arrays

To print the contents of an entire array, you can use the **print** command as we have seen before. Python will print the array on the screen in a neat format. For instance, suppose **A** is an array containing the three elements 10, 20, 30. If you were to write **print A** in a program, Python would print `[10 20 30]`. The square brackets around the entries indicate that the thing being printed is an array.

### A.6.3 Creating arrays

There are two common ways to create arrays in Python. These are outlined below with examples of their use. Always remember that you need to import the module **pylab** before you can use arrays.

## Creating an array from values

The `array` command is used to create an array containing a given list of values.

### Creating arrays with a list of values

To create a one-dimensional array containing a list of values, use:

```
A = array([...])
```

where `...` lists the **values of the entries** in the array, separated by commas. It is important to type the square brackets `[ ]` and round brackets `( )` as shown or the command will not work correctly.

The following program illustrates this method of creating arrays.

#### Program A.16: Creating arrays from lists

```
1 # This example creates an array from a list of values.  
2 from __future__ import division  
3 from pylab import *  
4  
5 # Create a new array with the given values.  
6 A = array([2, 4, 6, 8, 10])  
7 print A
```

The output from running this program is:

```
1 [ 2  4  6  8 10]
```

## Creating an empty array

### Creating arrays of a given size

To create an array of a given size, with all entries equal to zero, use:

```
A = zeros(...)
```

where `...` gives the **size** of the new array.

This is illustrated in the following program:



### Program A.17: Creating an empty array

```
1 # This example illustrates how to create an empty array.
2
3 from __future__ import division
4 from pylab import *
5 # Create a new array containing five 0s.
6 B = zeros(5)
7
8 # Create an array containing seven 0s.
9 C = zeros(7)
10
11 print B
12 print C
```

The output from running this program is:

```
1 [0 0 0 0 0]
2 [0 0 0 0 0 0 0]
```

## A.6.4 Arrays and indices in Python

### Accessing arrays

In Python, arrays are given names just like any other variables, and an entire array can be accessed by giving its name. To access **specific elements** in an array, you must give the name of the array, immediately followed by the appropriate index surrounded by square brackets. For example, if **A** is an array, then **A[i]** will give the value of the element at position **i**.

### Accessing array elements

To access **specific elements** in an array, you must give the name of the array, immediately followed by the appropriate index surrounded by square brackets.

### Array indices

The index of an element refers to the position of that element in the array. In Python, the **first** entry in an array has index **0**. This is potentially confusing, but it is important to remember. This is also true in many (but not all!) other computer languages. Let **A** be an array which contains  $n$  entries. The valid values of the index are from  $0$  to  $n - 1$  (inclusive).

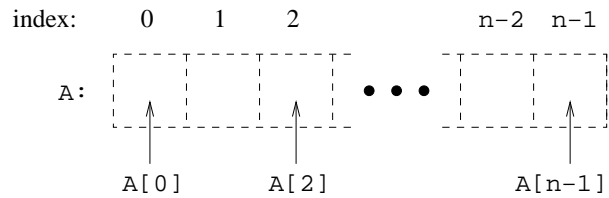


Figure A.1: Indexing elements in a one-dimensional array  $A$  with  $n$  entries

## Array indices

In Python, the **first** element in an array has index **0**.

The following example illustrates creating an array and assigning values to its elements.

### Program A.18: Assigning values to array entries

```

1 from __future__ import division
2 from pylab import *
3
4 # First create an array called A with 5 entries.
5 A = zeros(5)
6 print "Step one:", A
7
8 # Now assign the value 2 to the first element of A.
9 A[0] = 2
10 print "Step two:", A
11
12 # Assign the value 10 to the last element of A.
13 A[4] = 10
14 print "Step three:", A
15
16 # Access the values we have just assigned and save them in x.
17 x = A[0] + A[4]
18 print "Step four, x =", x
19
20 # Assign the value 40 to A[1].
21 A[1] = 2 * A[4] * A[0]
22 print "Step five:", A

```

The output from running this program is:

```

1 Step one: [0 0 0 0 0]
2 Step two: [2 0 0 0 0]

```

```
3 Step three: [ 2 0 0 0 10]
```

```
4 Step four, x = 12
```

```
5 Step five: [ 2 40 0 0 10]
```

After running the above program, the array **A** will look as follows:

index:	0	1	2	3	4
A:	2	40			10

Figure A.2: Assigning and accessing values in an array *A* with five entries

### A.6.5 Copying an existing array

If **oldA** is an array and you want to copy it into a new array named **newA**, use:

```
newA = oldA.copy()
```

Do **not** use **newA = oldA** as this does not create a new copy. (Instead, both **oldA** and **newA** will refer to the **same** data.)

#### Program A.19: Copying arrays

```
1 # This program demonstrates copying an array.  
2 from __future__ import division  
3 from pylab import *  
4  
5 A = array([5,10,15])  
6 B = A.copy()  
7 print B
```

The output of this program is:

```
1 [ 5 10 15]
```

## A.6.6 Operations on entire arrays

Many of the Python commands we have already seen can act element-by-element on entire arrays at once, producing new arrays as their output. The operations `+` `-` `*` `/` act on **two** arrays  $A$  and  $B$  **of the same size**, and the output is an array (of the same size) resulting from applying the given operation to corresponding pairs of elements from  $A$  and  $B$ .

The Python functions `sqrt`, `sin`, `cos`, `tan`, `exp`, `log` and `log10` all act on single arrays, with the output an array (of the same size) resulting by applying the operation to each element. For instance, consider look through the following program and its output:

Program A.20: Functions and arrays

```
1 # This example program shows Python operating on entire arrays.
2 # First, create an array with 5 elements, then create a new
3 # array containing the squares of these elements.
4 A = array([5, 10, 5, 0, 20])
5 B = A * A
6
7 # Create a new array.
8 C = array([1, 4, 9, 16, 25, 36])
9
10 # Display combinations of these arrays.
11 print B
12 print A + B
13 print sqrt(C)
```

The output of this program is:

```
1 [ 25 100  25   0 400]
2 [ 30 110  30   0 420]
3 [ 1.  2.  3.  4.  5.  6.]
```

## A.7 Graphs

### A.7.1 Drawing a graph

One of the major uses of computers in modelling is data visualisation. The simplest type of visualisation is a graph. Graphs usually involve plotting points, given their  $x$ - and  $y$ -coordinates. To draw a graph in Python, you need an array

of  $x$ -coordinates and an array of  $y$ -coordinates. These arrays must be the same size. To plot a graph, we use the command `plot(A, B)`. Python pairs up the values in the two arrays to form points of  $(x, y)$ , and then plots the points. (To draw multiple plots on the same graph, use the `plot(...)` command more than once.) The command `show()` displays all plotted graphs on the screen.

### Graphing in Python

Suppose  $A$  is an array containing the  $x$ -coordinates of  $n$  points, and  $B$  is an array containing the  $y$ -coordinates of the  $n$  points, **in the same order**. To draw a graph of the points with lines joining the consecutive points, use the following commands.

```
plot(A, B)
show()
```

Note that you must type the brackets in `show()` or the command will not work as expected. The `show()` command should only be used once in a program, and should be the **last** command in your program.

The following example shows how to use Python to plot  $x^2$  versus  $x$  for integer values of  $x$  from 0 to 9 inclusive.

#### Program A.21: Graphing

```
1 # This program plots x**2 vs x for x ranging from 0 to 9 and
2 # connects the consecutive points.
3 from __future__ import division
4 from pylab import *
5 A = array([0,1,2,3,4,5,6,7,8,9])
6 B = A * A
7 plot(A, B)
8 show()
```

Here is the output from running the program:

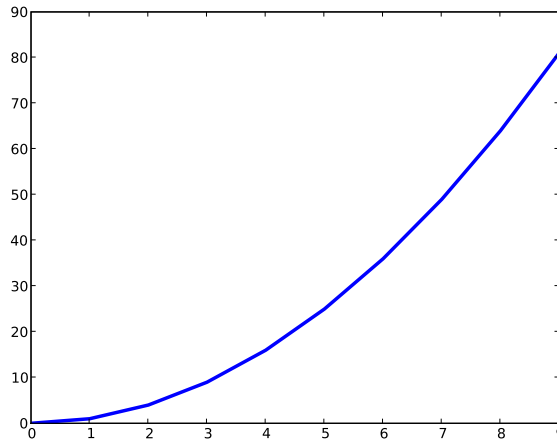


Figure A.3: A graph with values shown as a curve.

## A.7.2 Plotting separate points

Sometimes you may want to plot discrete points rather than a curve.

### Changing the style of plotting

To select the colour and style when plotting, type

```
plot(X, Y, 'style')
```

where **style** is replaced by letters representing the colour and marker to use. Valid colours are **b g r c m y k w**. Valid marker styles are **+ , o . s v x < > ^**. To connect the dots, include the **-** character with the settings, for example `plot(A,B,'ro-')`, which plots the points in red, marked by circles and joined with a line.

The following example shows how to plot a graph using crosses.

#### Program A.22: Graphing

```

1 # Plot x**2 vs x as discrete points with x between 0 and 9.
2 from __future__ import division
3 from pylab import *
4 A = array([0, 1, 2, 3, 4, 5, 6, 7, 8, 9])
5 B = A * A
6 # Note the additional parameter 'bx' to the plot command.
7 # This indicates that blue crosses should be used.
8 plot(A,B, 'bx', markeredgewidth=3)
9 show()
```

Here is the output from running the program:

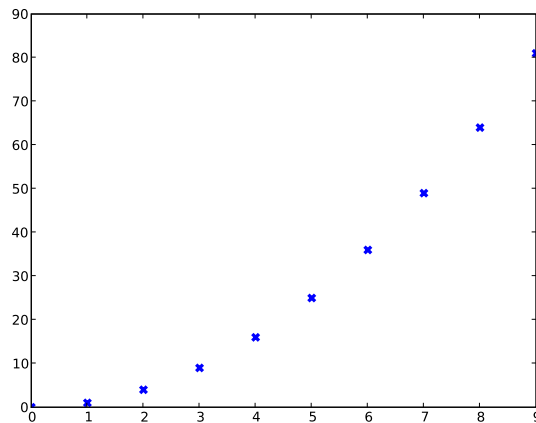


Figure A.4: A graph with values shown as discrete points.

### A.7.3 Graphing mathematical functions

When drawing graphs, you most likely either want to graph measured values (perhaps from an experiment), or a mathematical equation. Previously we plotted measured data points. To plot an equation, you want the computer to draw a smooth curve. Computers cannot actually draw smooth curves: instead, they approximate smooth curves by drawing straight line segments joining points that are very close together. (If you look at the graph in Example A.3 you may be able to see some straight line segments.) The more data points you have, the smoother your curve will look. The exact number of points that you will need will be different for different problems.

#### How to graph an equation

To plot a mathematical equation in Python, you first need to calculate some points which lie on the curve. The usual approach is to:

- Create an array with the  $x$ -coordinates of “appropriate” points.
- Create an array of the corresponding  $y$ -coordinates by applying the equation to each  $x$ -coordinate.
- Plot the graph.
- If the graph is not sufficiently smooth, edit your program so that it uses more data points.



Suppose you are attempting to plot a mathematical equation. Let  $X$  represent an array of  $x$ -coordinates, and  $Y$  be the array of corresponding  $y$ -coordinates. Once you have created  $X$  you can easily create  $Y$  by applying the function to  $X$ . In order to create  $X$  you could type each of the  $x$ -coordinates, but this takes a long time, especially if you need a lot of data points to make the graph look smooth.

When plotting graphs on computers, it is very common to choose points whose  $x$ -coordinates are *equally spaced*. This means that the difference between the  $x$ -coordinates of consecutive points is a constant, and this distance is chosen to be sufficiently small for the plots to look smooth. Python has a command `arange` to easily create an array of equally spaced points.

### Equally spaced values in Python

To create an array  $X$  of equally spaced values in Python, use this command:

```
X = arange(a,b,s)
```

This creates an array of points with values starting at **a**, increasing by an equally spaced step of **s** each time, and stopping at the **last value less than b**.

**Take care here:** the final value in the array is **always strictly less than b**. So, for example,

```
X = arange(0,1,0.2)
```

does not include the value 1, so

```
X=array([0.,0.2,0.4,0.6,0.8]).
```

The command `arange` is very useful for graphing. If the graph is not sufficiently smooth then use `arange` to create more points.

This example demonstrates using the `arange` function to help with plotting  $\sin x$  versus  $x$  for values of  $x$  from 0 to 5.

### Program A.23: Plotting functions

```
1 # This program uses arange() to help plot sin(x) vs x for
2 # values of x ranging from 0 to 5.
3 from __future__ import division
4 from pylab import *
5 # Plot with the x-coordinates separated by 0.5.
6 X = arange(0.0, 5.1, 0.5)
7 B = sin(X)
8 plot(X, B)
9 show()
```

Upon examining the graph produced by this program (shown at the left, below), we might decide that there are too few points. In an effort to produce a smoother graph, we might modify the program as follows:

### Program A.24: Plotting functions smoothly

```
1 # This program uses arange() to help plot sin(x) vs x for
2 # values of x ranging from 0 to 5.
3 from __future__ import division
4 from pylab import *
5 # Plot with x-coords separated by .1 to make graph smoother.
6 X = arange(0.0, 5.1, 0.1)
7 B = sin(X)
8 plot(X, B)
9 show()
```

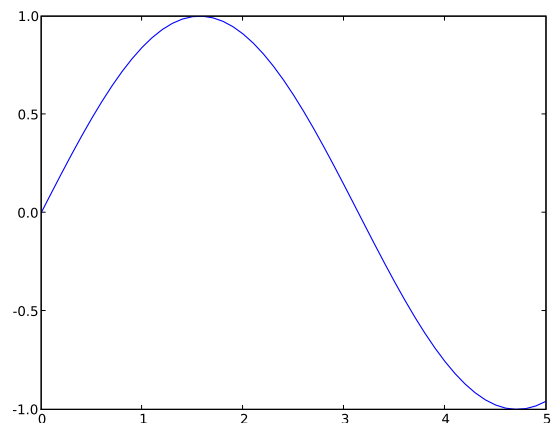
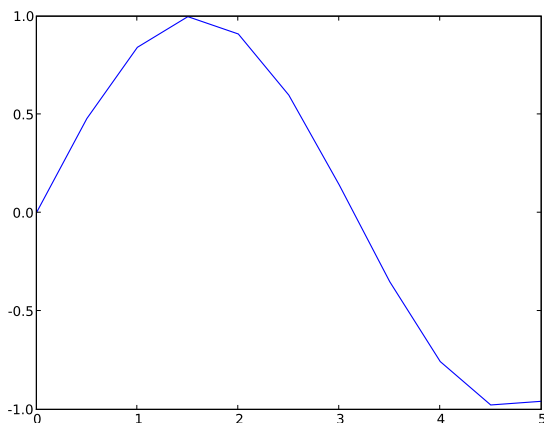


Figure A.5: Two sin graphs, plotted by the above programs. The graph on the right plots more points, and hence is smoother.

## A.7.4 Titles and axes

On any scientific graph it is important to title the graph and label the axes. This can be done in Python using the following commands:

- `title("Graph Title")` – sets the graph title.
- `xlabel("Time (s)")` – sets the label on the horizontal axis.
- `ylabel("Heart rate (bpm)")` – sets the label on the vertical axis.

### Program A.25: Formatting graphs

```
1 # This program uses the title(), xlabel() and ylabel()
2 # commands to draw "pretty" graphs.
3 from __future__ import division
4 from pylab import *
5 # Create an array using arange then define the function.
6 x = arange(0.0, 10.1, 0.2)
7 y = 2 * exp(0.4 * x)
8
9 # Draw the graph with title and labels.
10 plot(x, y, linewidth=3)
11 title("Graph of Student Interest in Free BBQ")
12 xlabel("Time after first sausage is cooked (min)")
13 ylabel("Number of students")
14 show()
```

The output from running this program is:

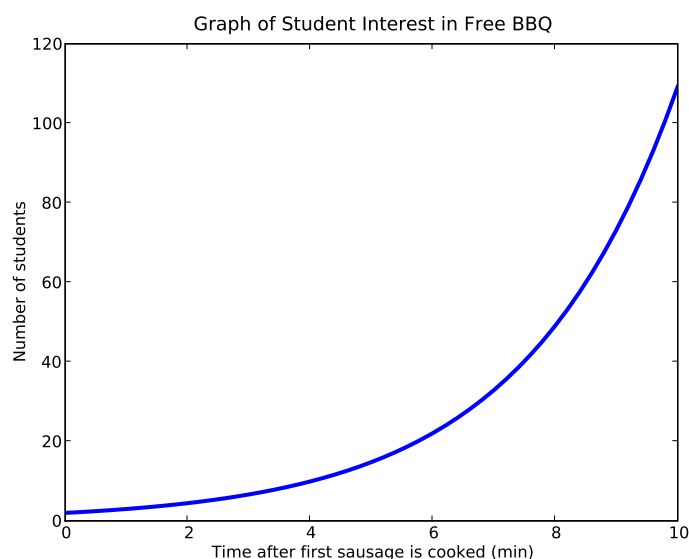


Figure A.6: A graph with a title and labels on the axes.

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