DATA HANDLING SKILLS

BSc Biochemistry
BSc Biological Science
BSc Bioinformatics

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1 Introduction

We make the world around us comprehensible through our cognitive skills, making use of our senses and the mind to reason about phenomena and to answer questions. As animals we are limited in our perception and conception and for anything that goes beyond common experience, in the areas of science and engineering, we complement common sense with technologies and methodologies. For example, molecular systems are usually not directly observable and properties not directly measurable. Experimentation, helped by instrumentation, generates data we can analyse to explain the phenomenon under consideration. Raw data, i.e., a list of numbers usually does not reveal a relationship or pattern by itself. Mathematics helps us to reveal, explain and represent (model) principles for which the data may provide evidence.

Like for anything else it takes time to learn the tricks of the trade. You should enjoy learning math as you like to acquire skills with the latest technology. The advantages over technology are obvious: it is cheap – paper and pencil to start with; it is safe – equations don't bite but most of all it is generic – it works in different contexts, it lasts a lifetime.

Data handling, the analysis of data for the purpose of model building, hypothesis testing and decision making is central to all sciences. To be a good scientist, being able to answer questions, you need to be able to *ask* questions. Questioning is as important in learning math as it is in the natural sciences. For this course, the most important advice I can give to you is that if you get stuck, treat the math like a wet-lab experiment:

- Ask *why?* and *how?* questions!
- Help yourself with a pen and paper
  - visualise the question,
  - keep a record of the answering process.
- Remember: Repeated trials are essential to gain confidence...

These lecture notes have extra large margin to encourage you to make comments. Use this space!

Finally, for the given exercises, if you compare your results with those of others, please make sure that you don't just compare the final result but also the steps that lead to the solution. For most problems in mathematics there are several valid ways of reaching a solution! This should not confuse you but by comparing and "playing" with alternatives you will improve your problem-solving skills. I also recommend that you quickly read or "scan" the notes before the lecture. This will help you memorise new ideas and concepts. Some time after the lecture you should again read the notes but this time try to understand all the material and do the exercises.

ENJOY YOUR EXPERIMENTS IN MATHEMATICS!

2 Simple Powers

Most people who have no particular interest in mathematics find it difficult that in mathematics many things can be written, or arrived at, in different ways. Mathematicians enjoy this aspect, because, like using a natural language, this allows for creativity and by introducing new concepts, notation or representations one can enrich the 'vocabulary'. You should not get confused by notation and alternative representations. Although not always obvious a lot of equivalent representations are for convenience. Honestly!

Multiplication of powers:

$$\boxed{a^n \cdot a^m = a^{n+m}}$$

Positive *powers* are a convenient shorthand for repeated multiplications. For example, for $4 \cdot 4$ we write 4^2 ("square") or in general

$$a^n = \underbrace{a \cdot a \cdot a \cdot \ldots \cdot a}_{n \quad \text{times}}$$

where a is called the **base** and n is referred to as the exponent, **power** or index. Let us see what happens when we multiply powers of the *same* base together:

$$6^2 \cdot 6^3 = (6 \cdot 6) \cdot (6 \cdot 6 \cdot 6) = 6^5 \quad \text{or} \quad 6^2 \cdot 6^3 = 6^{2+3} = 6^5 \ .$$

It does not matter whether the base is a number or letter

$$x^3 \cdot x^5 = (x \cdot x \cdot \cdot x) \cdot (x \cdot x \cdot x \cdot x \cdot x) \quad \text{or} \quad x^3 \cdot x^5 = x^{3+5} = x^8 \ .$$

An example for powers occurring in biology are processes that double in time, for instance, cell division. Imagine you start with two cells, at the next stage you have $2 \cdot 2$ cells and thereafter $2 \cdot 2 \cdot 2$ etc. PCR amplification is an important biological tool that serves as an example. PCR produces an amount of DNA that doubles in each cycle of DNA synthesis. For example, three PCR cycles of reactions produce $8 (= 2 \cdot 2 \cdot 2)$ DNA chains. We are going to consider mathematical representations of such "exponentially increasing processes" in greater detail in Sections 12 to 16.

PRACTICE. *The rule is: When **multiplying** powers of the* same *base, **add** the powers. Try simplifying the following:*

1. $7^2 \cdot 7^5 \cdot 7^9 =$

2. $4^2 \cdot 16^2 =$

3. $a^4 \cdot a^5 \cdot a^7 =$

4. $a^2 \cdot b^2 =$

If we replace a and/or n by zero and one, we obtain a few special cases

$$\boxed{1^n = 1 \ , \qquad a^1 = a \ , \qquad a^0 = 1}$$

and some familiar examples:

$$
\begin{aligned}
10^2 &= 100 && \text{hundred}\\
10^3 &= 1000 && \text{thousand}\\
10^6 &= 1\,000\,000 && \text{million.}
\end{aligned}
$$

Let us see what happens when we divide powers of the *same* base:

$$\frac{3^5}{3^2} = \frac{3\cdot 3\cdot 3\cdot 3\cdot 3}{3\cdot 3} = 3\cdot 3\cdot 3 = 3^3$$

The same result could be obtained by subtracting the indices

$$\frac{3^5}{3^2} = 3^{5-2} = 3^3$$

Likewise

Division of powers:

$$\boxed{\frac{a^n}{a^m} = a^{n-m}}$$

$$
\begin{aligned}
\frac{7^{12}}{7^5} &= 7^{12-7} = 7^7\\
\frac{a^4}{a^3} &= a^{4-3} = a^1 = a\ .
\end{aligned}
$$

PRACTICE. *The rule is: When* ***dividing*** *powers of the* same *base,* ***subtract*** *the powers. Try the following without a calculator.*

1. $\dfrac{5^7}{5^3} =$

2. $\dfrac{7^3\cdot 7^4\cdot 7^8}{7^5\cdot 7^6} =$

3. $\dfrac{a^8}{a^5} =$

4. $\dfrac{y^2\cdot y^7}{y^4} =$

Next we try to answer what the value of $\left(3^3\right)^2$ is. One way is to proceed as follows:

Powers of powers:

$$\boxed{\left(a^b\right)^c = a^{(b\cdot c)}}$$

$$\left(3^3\right)^2 = 3^3{\cdot}3^3 = 3^{3+3} = 3^6 \quad \text{similarly} \quad \left(2^2\right)^3 = 2^2{\cdot}2^2{\cdot}2^2 = 2^{2+2+2} = 2^6\,.$$

The same result could be obtained if the indices were multiplied together, i.e.,

$$
\begin{aligned}
\left(3^3\right)^2 &= 3^{3\cdot 2} = 3^6\\
\left(2^2\right)^3 &= 2^{2\cdot 3} = 2^6\ .
\end{aligned}
$$

PRACTICE. *The rule is: When* ***raising the power*** *of a number to a power,* ***multiply*** *the indices together.*

1. $\left(5^7\right)^3 =$

2. $\left(x^2\right)^4 =$

3. $\left(a^{-2}\right)^3 =$

4. $\left(x^{-1}\right)^{-2} =$

5. $\left(3^2 \cdot 7^4\right)^3 =$

6. $\left(\frac{5^7}{3^5}\right)^4 3 =$

Negative indices arise when we simplify expression such as

$$\frac{4^3}{4^6} = \frac{4 \cdot 4 \cdot 4}{4 \cdot 4 \cdot 4 \cdot 4 \cdot 4 \cdot 4} = \frac{1}{4 \cdot 4 \cdot 4}$$

Applying the division rule

$$\frac{4^3}{4^6} = 4^{(3-6)} = 4^{-3}$$

Hence

$$4^{-3} = \frac{1}{4^3}$$

A negative index therefore indicates a **reciprocal**. We return to this in the next section. Other examples are

$$2^{-3} = \frac{1}{2^3}\ , \quad a^{-5} = \frac{1}{a^5}\ , \quad x^{-1} = \frac{1}{x}\ .$$

PRACTICE. *Rewrite the following expressions.*

1. $3^{-1} =$

2. $5 \cdot 2^{-2} =$

3. $x^{-2} =$

4. $3 \cdot a^{-2} =$

Powers of fractions:

$$\left(\frac{a}{b}\right)^c = \frac{a^c}{b^c}$$

Our number system uses base ten and each digit in decimal numbers such as 9023.4056 can therefore be represented by its *place value*. The place value of each digit in a base ten number is determined by its position with respect to the decimal point. Each position represents multiplication by a power of ten. For example, in 324, the 3 means 300 because it is 3 times 10^2 ($10^2 = 100$). The 2 means 20 because it is 2 times 10^1 ($10^1 = 10$), and the 4 means 4 times one because it is 4 times 10^0 ($10^0 = 1$). There is an invisible decimal point to the right of the 4. In 5.82 the 8 means 8 times one tenth because it is 8 times 10^{-1} ($10^{-1} = 0.1$). Summarised for the number 9023.4056 we have:

9 0 2 3 . 4 0 5 6

- 9: Thousands, 10^3
- 0: Hundreds, 10^2
- 2: Tens or Units, 10^1
- 3: Ones or Units, 10^0
- 4: Tenth, 10^{-1}
- 0: Hundredth, 10^{-2}
- 5: Thousands, 10^{-3}
- 6: Ten-thousands, 10^{-4}

Powers of ten are a convenient way to manipulate very large or very small numbers. Molecular biologists frequently deal with 'extreme numbers', they handle milliliters (10^{-3}L) and count in there a million (10^6) bacteria. (More on this when we introduce measurement units in Section 9). For example,

$$\frac{30\,000 \cdot 0.02}{0.006 \cdot 10} = \frac{3\times10^4 \cdot 2\times10^{-2}}{6\times10^{-3} \cdot 1\times10} = \frac{6\times10^2}{6\times10^{-2}} = 10^2 \cdot 10^2 = 10^4$$

Scientific notation:

$$a \times 10^n$$

Scientific notation (or standard form) is the convention used for placing a decimal after the first non-zero digit of a number, and then multiplying it by the appropriate power of 10. In this way, large numbers such as $3,690,000,000$ are more conveniently represented as 3.69×10^9. Likewise, very small numbers such as 0.00000573 are reported as 5.73×10^{-6}.

PRACTICE. *Try these questions without a calculator.*

1. $\dfrac{0.0006}{2000} =$

2. $\dfrac{0.05 \cdot 200}{0.002} =$

3. $\dfrac{0.0009}{7000} \cdot \dfrac{1}{30} \cdot \dfrac{4.9\times10^5}{0.1} =$

4. $(0.0005)^2 =$

5. *Although biologists deal with big numbers, astro-physicists probably break the records. For example, the speed of light in empty space is approximately* $301,000,000$ *m/s. Stars are so far away that their distance from Earth is measured in terms of how long the light has taken to reach us. The light from our nearest star, Alpha Centauri takes* 4.3 *years to reach us. How far is this in meters?*

Negative exponents are dealt with in the next section and before then we only briefly note that for very large numbers, much greater than one, we obtain the scientific notation as follows. To express $4\,500\,000$ in standard form $a \times 10^n$, we must first identify the value of a which is a number between 1 and 10. In this example $a = 4.5$ and $4\,500\,000 = 4.5 \times 1\,000\,000 = 4.5 \times 10^6$. An alternative method is first to consider the position of the decimal point. For example, write $2\,756\,000\,000$ in standard form. Place the decimal point and to find n count the number of places to the right. So $n = 9$ and hence $2\,756\,000\,000 = 2.756 \times 10^9$. To practise the standard notation, invent three examples!

> **Remark:** Powers are useful for a number of reasons. In biology, cell division or the growth of microbiological cultures are examples. On the other hand, our number system is "base ten", that is, a number like 25.3 is actually a short form of $2 \cdot 10^1 + 5 \cdot 10^0 + 3 \cdot 10^{-1}$.

For subsequent sections, I try to encourage you to treat the exercises like a laboratory experiment. In a laboratory environment it is natural to try ("experiment") with different tools and to ask questions when something doesn't work. For maths, many of us feel that a solution should appear instantly or never. This is a mistake and the ability to question and experiment in maths is in fact a sign of skill rather than weakness.

The exercises required some knowledge of how to deal with fractions and bracketed expressions. We will address these issues in the following sections.

3 Fractions

A fraction is a mathematical concept used to describe *proportions*, *ratios*, and *rates*. Fractions consist of two parts, the **numerator** and the **denominator**:

$$\frac{\text{num}}{\text{den}}, \quad \text{for example} \quad \frac{3}{4} \qquad \text{(read this as `three over four')} .$$

An equivalent way to write the example is

$$3 \cdot \frac{1}{4} \qquad \text{(`three fourth')}$$

which highlights the fact that a whole is divided into 4 parts and what we have is 3 parts or "three quarters" in this particular case. Probably the most frequently used case are 'hundreds' or as it is more commonly known as: *percent*. It even has its own symbol: %. More about percentages below. Sometimes fractions are equivalent, even this is not obvious at

Equivalent fractions

first glance:

$$\frac{3}{4} = \frac{6}{8} = \frac{9}{12} = \frac{12}{16} = \frac{15}{20}$$

Cancelling fractions

To find a fraction in its lowest terms (with numbers on top and bottom lines that are as small as possible) we *cancel down*:

$$\frac{27}{63} \overset{\div 9}{\underset{\div 9}{=}} \frac{3}{7}$$

Division of fractions:

$$\boxed{\frac{\frac{a}{b}}{\frac{c}{d}} = \frac{a}{b} \cdot \frac{d}{c}}$$

Dividing numerator and denominator by the **same** number, simplifies the expression but doesn't change its value. To check this, we write the operation out in detail:

$$\frac{27}{63} = \frac{\frac{27}{9}}{\frac{63}{9}} = \frac{27 \cdot \cancel{9}}{63 \cdot \cancel{9}}. \qquad \text{Try this:} \quad \frac{24}{54} =$$

Multiplication of fractions:

$$\boxed{\frac{a}{b} \cdot \frac{c}{d} = \frac{a \cdot c}{b \cdot d}}$$

Cancelling fractions involves the division of fractions. In general, to divide two fractions you multiply the first fraction by the **reciprocal** of the second fraction:

$$\frac{\frac{3}{8}}{\frac{1}{4}} = \frac{3}{8} \cdot \frac{4}{1} = \frac{3 \cdot 4}{8 \cdot 1} = \frac{12}{8} = \qquad \text{(cancel)}$$

Substraction of fractions:

$$\boxed{\frac{a}{b} - \frac{c}{d} = \frac{a \cdot d - c \cdot b}{b \cdot d}}$$

The reciprocal of a fraction is therefore found by turning the fraction upside down. The reciprocal of a/b is b/a. To multiply two fractions we multiply the numerators and denominators. The following example shows how cancelling down, before multiplication, can simplify the operation:

$$\frac{7}{\cancel{4}^{1}} \cdot \frac{\cancel{12}^{3}}{5} = \frac{7}{1} \cdot \frac{3}{5} = \frac{21}{5}$$

Addition of fractions:

$$\boxed{\frac{a}{b} + \frac{c}{d} = \frac{a \cdot d + c \cdot b}{b \cdot d}}$$

To subtract or add two fractions, we first have to ensure that the denominators of both fractions are the same. A simple way to find a common multiple is to multiply the denominators. To find the common denominator you can use the *lowest common multiple* of the two denominators. To work out $\frac{7}{8} - \frac{1}{4}$, we multiply the numerator and denominator with the factor that makes the denominator equivalent to the lowest common multiple $8 \cdot 4 = 32$:

$$\frac{7}{8} \overset{\times 4}{\underset{\times 4}{=}} \frac{28}{32} \qquad \frac{1}{4} \overset{\times 8}{\underset{\times 8}{=}} \frac{8}{32}$$

such that

$$\frac{28}{32} - \frac{8}{32} = \frac{28-8}{32} = \frac{20}{32} = \qquad \text{(cancel)}$$

Note: Although multiplying or dividing the numerator **and** denominator with the **same** number does not change the value of the fraction, this is not true for adding or subtracting numbers:

$$\frac{a+3}{b+3} \text{ is } \textit{not} \text{ the same as } \frac{a}{b}. \qquad \text{Similar} \qquad \frac{a^2}{b^2} \neq \frac{a}{b} \text{ !}$$

Comparing fractions, it is often difficult to see the difference, say, whether $4/5$ is greater or less than $1/2$ by just looking at the numbers. However, basic fractions can be "visualised" by 'sharing a cake' or by colouring a rectangle. For example, use the following rectangles to fill in the fraction next to it. (Do it **NOW**):

$\frac{3}{8}$ $\qquad$ $\frac{2}{4}$

$\frac{1}{2}$ $\qquad$ $\frac{3}{6}$

If we consider the basic fraction a/b, we can think of some special cases, setting $b = a$, a or b equal to one or zero. This leads to the following rules:

$$\boxed{a = \frac{a}{1}\ , \qquad \frac{0}{a} = 0\ , \qquad \frac{a}{a} = 1\ , \qquad \frac{1}{a} = a^{-1} \quad (a \geq 1)}$$

Negative indices:

$$\boxed{\frac{1}{a^n} = a^{-n}}$$

For $1/a$ and $a \geq 1$ the fraction gives a number which is smaller than one. In Section 2, on positive exponents such as a^n and $n \geq 1$, we observed that a number such as 250 can be expressed as 2.5×10^2 and since $10^2 = 100$, the exponent 2 means effectively that we shift the decimal point by two positions to the right to get 250. Negative exponents are very much the same only that we move in the opposite direction. For example, 0.025 is the same as 2.5×10^{-2}. We can therefore generalise the case $1/a = a^{-1}$ to any negative exponent:

$$\frac{1}{a^n} = a^{-n}$$

For $a = 10$ we obtain something familiar:

$$\begin{aligned}
10^{0} &= 1/1 &&= 1 \\
10^{-1} &= 1/10 &&= 0.1 \\
10^{-2} &= 1/100 &&= 0.01 \quad \textit{(one hundredth or a percent)} \\
10^{-3} &= 1/1000 &&= 0.001 \\
10^{-4} &= 1/10\,000 &&= 0.0001 \\
10^{-5} &= 1/100\,000 &&= 0.00001 \\
10^{-6} &= 1/1\,000\,000 &&= 0.000\,001
\end{aligned}$$

Describing one portion as $4/5$ and another as $1/2$ is not very convenient if we want to compare the two. Percentages are fractions with a denominator of 100. Dividing a cake, hundred percent, written 100%, is the whole, while 25% is a quarter. We are usually familiar with percentages, i.e., have an intuition about them and therefore it is often useful to convert a fraction to a percentage we multiply a fraction by 100:

$$\frac{4}{5} \cdot 100 = 80 \quad \text{therefore} \quad \frac{4}{5} = 80\%$$

Converting decimals to fractions

More on calculating with percentages follows further on. In the list above, we found that the fraction $1/100$ in **decimals** is 0.01. To convert any decimal, say 0.473, to a fraction we notice that from above

$$0.473 = \frac{4}{10} + \frac{7}{100} + \frac{3}{1000} = \frac{400}{1000} + \frac{70}{1000} + \frac{3}{1000} = \frac{473}{1000}$$

Convert the following decimals **NOW** – can you see the pattern?

$$0.12 =$$

$$0.3044 =$$

Ratios vs rates

A **ratio** is a comparison between two like quantities (e.g. 'you receive two, I keep three') while a **rate** is a comparison of two unlike quantities ('the limit is 25 miles per hour). A ratio is often written 2 : 3, read 'two to three'. Receiving 'two' out of five means you get 2/5. Notice the relation between a ratio and the fraction: the denominator of the fraction must be the total number of parts involved. Rates are similar to ratios. The units show the quantities being compared. For example,

$$\text{speed} = \frac{\text{distance}}{\text{time}}$$

For instance, take a car travelling at an average speed of 30 mph (miles per hour). It will take 20 mins to go 10 miles. If the average speed increases to 40 mph, how long will it take to cover 10 miles? The car travels

$$\begin{aligned} 40 \text{ miles} \quad &\text{in} \quad 1 \text{ hour} = 60 \text{ mins} \\ 1 \text{ mile} \quad &\text{in} \quad \frac{60}{40} \text{ mins} \\ 10 \text{ miles} \quad &\text{in} \quad \frac{60}{40} \cdot 10 \text{ mins} \\ &= 15 \text{ mins} \end{aligned}$$

As the speed increases, the time will decrease (inverse proportion).

PRACTICE. *Try these questions without a calculator.*

1. *Which two fractions are equivalent?*

$(a)\ \frac{3}{10} \quad \frac{4}{9} \quad \frac{24}{54}$ $\qquad (b)\ \frac{6}{7} \quad \frac{12}{13} \quad \frac{12}{14}$

2. *Write down* 20*p as a fraction of* £1.

3. *Work out* $\frac{2}{7}$ *of* 105 *millimeters.*

4. *Convert* $\frac{4}{5}$ *to a percentage.*

5. *Convert* 34% *to a fraction.*

6. *Out of* 24*, how many percent are* $\frac{1}{3}$ *and* $\frac{5}{8}$.

7. $\frac{12}{5} + \frac{3}{4} =$

8. $\frac{2}{5} \cdot \left(\frac{1}{3} + \frac{2}{5}\right) =$

9. $\left(\frac{\frac{a}{b}}{c}\right) \cdot \frac{e}{f} =$

10. *Divide* 0.00034 *by* 0.7.

11. *If a car can travel* 35 *miles per gallon of petrol, how much petrol (to the nearest gallon) would it need to go* 100 *miles?*

12. *What is the length of* 3/4 *of a piece which is* 2/3 *metres long?*

Remark: If you wonder how you can best remember all the concepts and ideas mentioned so far, I recommend you go through all framed boxes, most of which are in the margin, and devise an example for each 'rule'. Probably the best way of learning math is 'learning by doing'.

4 Percentages

A percentage represents a fraction of 100. Percent therefore means "out of 100" or "per 100". We describe quantities in % because they are more intuitive than decimal numbers. Percents can be written as fractions by placing a number over 100 and simplifying or reducing. For example,

$$30\% = 30 \cdot \frac{1}{100} = \frac{30}{100} = \left(\frac{3}{10}\right)$$

If we say that $\frac{3}{4}$ ("three quarters") of a given material is used, we mean that

$$\frac{3}{4} \times 100\% = \frac{3}{4} \cdot \frac{100}{1} = \frac{300}{4} = 75\%$$

of the available material is used. Therefore, fractions can be changed to percents by writing them with denominators of 100. The numerator is then the percent number:

To convert a decimal or fraction to a percentage, multiply it by 100.

$$\frac{3}{5} = \frac{3 \cdot 20}{5 \cdot 20} = \frac{60}{100} = 60\%$$

If we ask: What is 7% of 30?

$$7\% = \tfrac{7}{100} \text{ so } 7\% \times 30 = \tfrac{7}{100} \cdot \tfrac{30}{1} = \tfrac{7}{10} \cdot \tfrac{3}{1} = \tfrac{7 \cdot 3}{10} = \tfrac{21}{10} = 2.1$$

100 and 30 have the common factor 10.

To change a percent to a decimal number move the decimal point 2 places to the left because percent means "out of 100" and *decimal* numbers with two digits behind the decimal point also mean "out of 100". For example,

Conversion of % to decimal.

$$45\% = 0.45\,, \qquad 125\% = 1.25$$

$$6\% = 0.06\,, \qquad 3.5\% = 0.035$$

Note that because the 5 was already behind the decimal point and therefore does not count as one of the digits in the "move two places". To change a decimal number to a percent move the decimal point two places to the right:

$$0.47 = 47\%\,, \qquad 3.2 = 320\%\,, \qquad 0.205 = 20.5\%$$

Although they are related to fractions and decimals, percentages are used and manipulated in different ways. Typical problems involving percentages can be illustrated using our 'shopping instincts': Imagine you are asked to purchase the material needed for your experiments. Prices in catalogues are often given excluding VAT (Value Added Tax), so that must be added to find the actual cost. For example, your cultures are priced at £2000 + VAT (at 17.5%). The actual cost can be found in more than one way:

VAT = 17.5% of £2000

$£2000 \cdot \frac{17.5}{100} = £350$

Final price = £2000 + 350 = £2350

Price = 117.5% of £2000

$£2000 \cdot \frac{117.5}{100} = £2350$

A colleague tells you that he paid £1950 with a 15% reduction. What was the original price?

You should not find it necessary to use the calculator's % function. (I can never remember how to use it). However, in case you want a kind of algorithm: Any problems that are or can be stated with percent and the words "is" and "of" can be solved using this formula:

$$\frac{\%}{100} = \frac{\text{“is” number}}{\text{“of” number}}$$

or "of" means multiply and "is" means equals.

"IS" and "OF" formula :

$$\boxed{\frac{\%}{100} = \frac{\text{“is” number}}{\text{“of” number}}}$$

Example 1: What percent **of** 125 **is** 50?

$$\frac{\mathbf{n}}{100} = \frac{50}{125} \,.$$

Or $\mathbf{n} \cdot 125 = 50$, in either case the percent = 40%

Example 2: What number **is** 125% **of** 80?

$$\frac{125}{100} = \frac{\mathbf{n}}{80} \,.$$

Or $1.25 \cdot 80 = \mathbf{n}$. In either case the number = 100.

If you are not confident with the rearrangement of algebraic equations, return after you read Section 8.

PRACTICE. *Try these questions without a calculator.*

1. *What is* 15% *of* 70*?*
2. *A DNA fragment of* 35 *kilobases is digested by an exonuclease. The enzyme degrades seven kilobases. What percentage of the DNA is degraded?*
3. *You counted* 10,000 *cells three weeks ago and* 12,000 *today, what is the % increase?*

Problem Solving Strategies

Read the following section in your own time and reflect upon questions questions related to percentages.

Reflective thinking

It is important to acknowledge that, in general, there is more than one way to obtain a solution. The following example is taken from [9] and illustrates strategies for mathematical problem solving. One of the main conclusions is: getting STUCK is a natural state of affairs:

> A company offers you a 30% discount but you must pay 15% tax. Which would you prefer to have calculated first, discount or tax?

The natural response is to start by trying some specific cases. Say, we try it with an item priced at £100.

DO SO NOW IF YOU HAVE NOT ALREADY

Surprised by the result? Now, will the same happen for a price of say £120?

TRY IT AND SEE!

Write down your calculations and your insights. It is the only way to develop your thinking skills. There should be a pattern in the special cases you have tried.

TRY EXAMPLES UNTIL YOU ARE SURE!

Specialisation, which means turning to examples to learn, is as important as trying to vary your way of thinking. With any luck you will have found that

1. subtracting 20% from a price is the same as paying 80%, that is, you pay 0.8 times the price.

2. adding 15% to a price is the same as paying 115% of it, that is you pay 1.15 times the price.

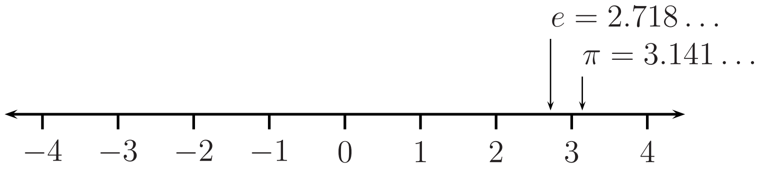
Then for any initial price of say £x, calculating

discount first: you pay $1.15 \cdot (0.80 \cdot £x)$
tax first: you pay $0.80 \cdot (1.15 \cdot £x)$

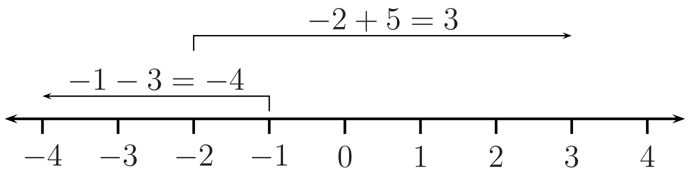
By writing the calculation in this form you can see that the order of calculation does not matter and, indeed, you pay the same in both cases.

5 Real Numbers

Like biologists classify species, mathematicians distinguish different kinds of numbers. (Well, it is not quite the same but there are certainly some unusual species on the real line...) A **rational number** is any number which can be expressed exactly as a fraction $\frac{a}{b}$ where a and b are **integers** ('whole numbers', i.e., $\ldots -3, -2, , 0, 1, 2, 3 \ldots$). An **irrational number** is any number which cannot be expressed exactly as a fraction in this form. For example, $\sqrt{4} = \frac{2}{1}$ is rational while $\sqrt{2} = 1.4142135\ldots$ is not. Positive integers $\{1, 2, 3, \ldots\}$ are also called **natural numbers**. Measurements are often assumed to be **real numbers**, i.e., any numerical value we can represent on the *number line*:



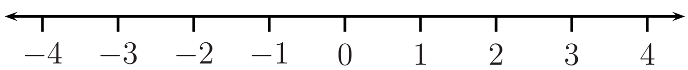
Negative numbers are written to the left of zero. The further a number is to the right, the bigger it is. Addition indicates that you move to the right, while substraction takes you to the left:



Use the number line below to demonstrate the following properties of real numbers:

Use drawings and examples to illustrate and memorise abstract concepts or rules.

1. **Addition**
   (a) is **associative**, i.e., $(a + b) + c = a + (b + c)$
   (b) is **commutative**, i.e., $a + b = b + a$
2. **Subtraction**
   (a) is **NOT commutative**, i.e, $a - b \neq b - a$
   (b) is **NOT associative**, e.g., $(5 - 2) - 1 = 3 - 1 = 2$ but $5 - (2 - 1) = 4 - 1 = 3$



What we cannot illustrate so easily with the number line is that

1. **Division**
   (a) is **NOT commutative**: $\frac{a}{b} \neq \frac{b}{a}$, i.e., we cannot divide in any order and get the same answer.
   (b) is **NOT associative**: e.g., $\frac{\frac{12}{6}}{2} = \frac{2}{2} = 1$ but $\frac{12}{\frac{6}{2}} = \frac{12}{3} = 4$.
2. **Multiplication**
   (a) is **commutative**: $a \cdot b = b \cdot a$

(b) is **associative**: $(a \cdot b) \cdot c = a \cdot (b \cdot c)$

We should also remember that multiplying or dividing numbers of the same sign gives a positive number, while if any one of the two numbers is negative, the result is negative. Take the following examples:

$$3 \cdot 4 = (+3) \cdot (+4) = 12 \qquad 3 \cdot (-4) = -12$$
$$(-4) \cdot (-5) = 20 \qquad \frac{-9}{3} = -\frac{9}{3} = \frac{9}{-3} = -3$$

6 Logarithms

A logarithm is the **exponent** or power to which a base must be raised to yield a given number. In the previous section we considered powers like $10^2 = 100$ or more generally given the base, 10, and index n, we asked $10^n = ?$ On the other hand, given a number, say 100, and a base, say 10, we can ask for index n. In other words, what is the power that 10 is raised to, to give 100? This question has its own notation:

The logarithm of a number gives an exponent:

$$\boxed{\log_b a = n \text{ where } b^n = a}$$

$$\log_{10} 100 = 2 \qquad \text{such that} \qquad 10^2 = 100\ .$$

Try the following for yourself:

$$\log_{10} 10\,000 = \qquad \log_3 9 = \qquad \log_2 64 = \qquad \log_{10} 0.0001 =$$

There are three bases that are most relevant to science and engineering, base 10 (**common logarithm**), base 2 and base e. The latter is called **natural logarithm**[1] (or *Napierian log*), denoted $\log_e$ or ln:

Logarithm of a product:

$$\boxed{\log(a \cdot b) = \log a + \log b}$$

$$\log_e a = n \qquad \text{such that} \qquad e^n = a\ .$$

In general, i.e., for logarithms with any base, we find that

Logarithm of a fraction:

$$\boxed{\log\left(\frac{a}{b}\right) = \log a - \log b}$$

$$\log 1 = 0 \qquad \text{since} \qquad a^0 = 1\ .$$

Logarithm of a power:

$$\boxed{\log\left(a^b\right) = b \cdot \log a}$$

PRACTICE. *Use a calculator to solve the following:*

1. $\log_{10} 3 =$

2. $\log_{10} 30 =$

3. $\log_{10} 300 =$

4. $\log_{10} 3000 =$

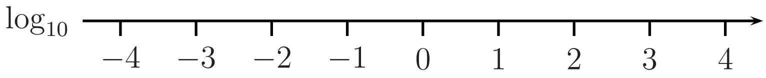
5. $\log_{10} 0.3 =$

[1] Many calculators will use log to denote the logarithm to base 10 while ln is used to denote the natural logarithm.

6. $\log_{10} 0.03 =$

7. $\log_{10} 0.003 =$

There are many uses for logarithms. In the biosciences or specifically for the analysis of experimental data, it is often more convenient to use a log-scale of the number line:



We notice that the distances between tick marks are equal although the difference in value increases rapidly. Obvious? Write the difference out on the number line above! Another way to see what the logarithm does to a given number is to produce a table:

Notation:

$\ln x \equiv \log_e x \equiv \log_e(x)$

Number	$\log_{10}$
$1/10,000$	-4
$1/1,000$	-3
$1/100$	-2
$1/10$	-1
$1/1$	0
10	1
100	2
$1,000$	3
$10,000$	4
$100,000$	5

Create tables to experiment with a new concept.

The table above is the first step towards the concept of a *function*. The example also suggests a method to use logarithms for "scaling" a graph (cf. Fig. 12.8). The use and usefulness of logarithms becomes clearer when we introduce this concept fully in Section 12.

If $\log_{10}(a) = n$, then $10^n = a$

PRACTICE. *A number of rules for operating with logarithms are shown in the margins. Below are exercises to practice these rules. More exercises can be found in Section 19. Try the following questions (without a calculator or computer).*

1. *Show that* $10^{(a-b)} \cdot 10^{(b-a)} = 1$

2. *Show by example that* $\left(a^b\right)^c = a^{(b \cdot c)}$

3. *Simplify* $10^a \cdot 10^a \cdot 10^a \cdot 10^a \cdot 10^a \cdot 10^a =$

4. *Simplify* $(10^a)^3 \cdot (10^a)^{-4}$

5. $\log (a \cdot b^2) - 2 \cdot \log b =$

6. $\log \left(\frac{a^2}{b^2} \right) + 2 \cdot b =$

7. $\log (3^2) - \log 3 - \log 18 =$

Remark: Logarithm were *invented* by the Scotsman John Napier in the late sixteenth century. Because multiplication of large numbers is cognitively more complicated than to add them, Napier developed this concept. How products turn into sums is clear from the rule $\log(a \cdot b) = \log a + \log b$. Our parents are more appreciative of his efforts: the slide rule they used before pocket calculators came to our rescue, work on this principle.

7 Variables and Constants

When we introduced fractions, we *generalised* an example, say $\frac{3}{4} \cdot \frac{2}{5} = \frac{3 \cdot 2}{4 \cdot 5}$ by replacing the integers with letters:

$$\frac{a}{b} \cdot \frac{c}{d} = \frac{a \cdot c}{b \cdot d}$$

In dealing with more complex scientific equations, a quantity that varies is said to be a **variable**. If the symbol represents a fixed value and is not multiplied by any variables, then this is termed a **constant**. **Coefficients** are numbers that are multiplied by one or more variables. In $-4xy$, -4 is a coefficient and in $-4xy + 3$, '3' is a constant. Which letter is used for variables and which for coefficients or constants is arbitrary. For example, in $-4xy + b$, b may but must not be a constant. What is what, must be stated or in scientific equations is often obvious. To introduce new mathematical ideas, we usually make use of commonly used letters such as x, y to denote variables, f to denote a function. However, for applications of mathematical formula in the biosciences, we may prefer other conventions. For example in the following (biochemical) expression

Vocabulary

$$v = \frac{V_{\max} \cdot [S]}{K_m + [S]} ,$$

the letter v denotes a variable ('velocity'), $V_{\max}$ and K_m denote constants and $[S]$ is another variable ('substrate concentration', where the square brackets are used to denote concentrations). This may initially be confusing but you will hopefully find that notation is as useful as it is a nuisance. The equation above will be discussed in greater detail in Section 17

Generalisation through variables is an extremely important concept. In science, a measured set of experimental data is the evidence we use to establish or validate a *principle* (or 'natural law'). The data are only one particular example from which we try to generalise. This usually leads to an equation (or set of equations), consisting of variables and constants as the one shown above. This representation of an observed phenomena is called a (mathematical) **model**. If we are fortunate and clever, the model will be a reasonable approximation to the natural system under consideration. If this is the case, we can make simulations and predictions.

Biological systems are much more complex than what engineers, physicists and applied mathematicians can successfully deal with in their field and therefore interdisciplinary collaborations have become very important in the life sciences.

> **Remark:** The most famous equation of all is Albert Einstein's $E = m \cdot c^2$ by which he showed that energy (E) is equivalent to mass (m). In the equation, E and m are variables and c is a constant: the speed of light which in a vacuum is the enormous (and yet finite..) $299\,792\,456.2 \pm 1.1\ \frac{\mathrm{m}}{\mathrm{s}}$. Einstein's life, the revolutions in physics that took place during his time, how the equation $E = m \cdot c^2$ came about and how on earth they measured the speed of light, is a fascinating story. If you want to know more, a readable book on the story of $E = m \cdot c^2$ is [2].

8 Algebraic Expressions and Equations

Algebra is a branch of elementary mathematics that generalises arithmetic by using variables to range over numbers. The following vocabulary is in use. **Terms** are constants or variable expression. Arbitrary examples are: 3a; $-5c^4d4$; $25mp^3$; 7 are all terms. Algebraic **expressions** are terms that are connected by either addition or substraction. For example, $2s + 4a^2 - 6$ is an algebraic expression with three terms. Algebraic **equations** are statements of equality between at least two terms. Examples: $4z = 28$ and $3(a - 4) + 6a = 10 - a$. As can be seen from the examples, in algebraic expressions we use letters or symbols to represent a quantity. Take for instance the demonstration of the *commutative law of addition*:

$$a + b = b + a \ ,$$

or the *law of association*:

$$\begin{aligned} 5b + a - b &= 5b - b + a \\ &= 4b + a \ . \end{aligned}$$

Short forms and brackets

In the equation above, we simplified $5 \cdot b$ to $5b$. If not stated otherwise, one uses only single letters and xy denotes the product $x \cdot y$. This should only be done if no confusion is possible. To make associations clear we often will use brackets in forming expressions. Although this is done to make things clearer, brackets are also a source for errors when manipulating equations. Make sure that whatever quantity or symbol is found adjacent to the left-hand side of the brackets must multiply the contents of the brackets, including the addition and substraction sign. Take for example the expression

$$a - (b + c) = a - b - c \ . \tag{8.1}$$

Note that the sign in front of c has changed with the removal of the brackets. On the other hand

$$(a-b)+c=a-b+c$$

Browse back through the notes and remind yourself of the rules in Section 5!

PRACTICE. *Try these examples, **NOW**. Simplify the following expression where possible:*

1. $a-(2a+c)$
2. $a+p-c$
3. $xy+2x-y+4yx$
4. $-2(3-y)$

Priority rules

For evaluation, rearrangement and simplification of expressions it is important to take care of the order in which operations are performed. Thus, for example, $5\cdot 3+2\cdot 4-3$ is 20, not 25 or 65 because multiplication must be done before addition or substraction. Have a look at the following priority rules:

Evaluate expressions within brackets first	$2\cdot(5+3)=2\cdot 8=16$	not $10+3=13$
Evaluate 'inner' brackets before 'outer'	$5\cdot(6+3\cdot(3+4))$ $=5\cdot(6+3\cdot 7)$ $=5\cdot(6+21)$ $=5\cdot 21=135$	not $5\cdot 9\cdot 7=315$
Take powers before multiplying or dividing	$5\cdot 3^2=5\cdot 9=45$	not $8^2=64$
With powers within powers work down from the top	x^{-2y^2} means $x^{(-2y^2)}$	not $(x^{-2y})^2$
Multiply and divide before adding and subtracting	$3\cdot 4+8/2=12+4$ $=16$	not $3\cdot 12/2=18$

Multiplication and division are done in the order in which they are found going left to right; that is, if division comes first going from left to right then it is done first. Similarly, addition and subtraction are done in the order in which they are found going left to right; that is, if subtraction comes first, going left to right, then it is done first. Note that the order or priority rules apply algebraic expression with variables and constant as well as for expression with numbers only.

Substitution

If in doubt with the result of a manipulation, use **substitution**, i.e., replacing symbols with numerical values. For example, considering equation (8.1) from above, let $a=6$, $b=3$ and $c=2$:

$$a-(b+c)=a-b-c$$
$$6-(3+2)\stackrel{?}{=}6-3-2$$
$$6-5\stackrel{!}{=}1$$

which shows that both sides of the equation are balanced. Now try the same equation but with $a = 6$, $b = 3$ and $c = 5$:

$$a \;-\; (b \;+\; c) \;=\; a \;-\; b \;-\; c$$
$$\stackrel{?}{=}$$
$$\stackrel{!}{=}$$

Another example of expanding brackets is the following:

Expansion:

$$\boxed{\begin{array}{c}(a+b)(c+d) = \\ ac+ad+bc+bd\end{array}}$$

$$3(x-2y) = 3x + 3 \cdot (-2y) = 3x - 6y$$

or

$$(x+1)(x-2y) = x^2 - 2xy + x - 2y$$

Try this one:

$$(2x-y)(x+y)y =$$

In **factorisation** we express a number or expression in terms of a product. For example, the number 16 can be expressed in terms of its factor four ($16 = 4 \cdot 4$). Many of us use factorisation in mental multiplication. For example, to solve $34 \cdot 7$, we could do the following:

Factorisation:

$$\boxed{ab + ac = a(b+c)}$$

$$\begin{aligned} 34 \cdot 7 &= (30+4) \cdot 7 \\ &= 30 \cdot 7 + 4 \cdot 7 \\ &= 210 + 28 \\ &= 238 \ . \end{aligned}$$

We can apply the same idea to algebraic expressions. Consider the following expression and factorise it in x:

$$2x - 2xy + 3zx + x = x(2 - 2y + 3z + 1) = x(3 - 2y - 3z)$$

Factorisation often allows the cancellation of common factors and thereby simplifies an expression:

$$\begin{aligned} &\frac{x}{xy - 3x} && \text{factorise } xy - 3x, \\ &\qquad = \frac{x}{x(y-3)} && \text{cancel common factors,} \\ &\qquad = \frac{1}{y-3} \ . \end{aligned}$$

PRACTICE. *Try simplifying the following expressions.*

1. $a \cdot b + a \cdot c =$

2. $a^2 \cdot b + a \cdot c =$

Use an extra sheet of paper for more space: Keep track of all steps.

3. $\frac{ac}{b} + \frac{a^3d}{a^2} =$

4. $\frac{2ab}{ab + 3ab} =$

5. $\frac{2}{a + b} - \frac{6}{b} =$

Rearranging equations

Factorisation and expansion are two concepts frequently used to rearrange equations. In rearranging an equation we need to remember that we have to maintain the 'balance' on both sides, i.e., we must preserve the equality of both sides. If you subtract, add, multiply and divide one side, the same has to happen to the other. Look at the following example, in which we try to isolate a to the left-hand side of the equation:

$$\begin{aligned} a \cdot b + c \cdot d &= 1 && \text{subtract } (c \cdot d) \text{ from both sides,} \\ a \cdot b \cancel{+cd} \cancel{-cd} &= 1 - c \cdot d \\ a \cdot b &= 1 - c \cdot d && \text{divide both sides by } b, \\ \frac{a \cdot \cancel{b}}{\cancel{b}} &= \frac{1 - c \cdot d}{b} \\ a &= \frac{1 - c \cdot d}{b} \ . \end{aligned}$$

Normally you would not write the terms that cancel out and the second step in this example would therefore usually not be written out but is here included for completeness. In the example, I also wrote $a \cdot b$ which, here, is equivalent to ab. We could also have written $(a \cdot b) + (c \cdot d)$ but this is not necessary because of the order in which operations are performed: multiplication first, addition afterwards.

I said above that an equation is a statement that two quantities are equal, for instance 1 metre = 1000 mm. More often an equation contains an unknown quantity which we desire to find. In the equation $5x - 7 = 23$, x is the unknown quantity. There is only one value of x such that the left hand side (LHS) of the equation is equal to the right hand side (RHS). This value is $x = 6$. When we have calculated this value of x we have solved the equation and the value of x obtained is called the solution to the equation. In this example, the solution is $x = 6$. In the process of solving an equation the appearance of the equation may be considerably altered but the values on both sides must remain the same. A common problem is to isolate the variable. For example, to express x in terms of y and z:

$$\begin{aligned} xy - 2x &= 3zx - 1 && \text{isolate all terms in } x \text{ on one side,} \\ xy - 2x - 3zx &= -1 && \text{factorise, in terms of } x, \\ x(y - 2 - 3z) &= -1 && \text{divide both sides by } (y - 2 - 3z) \\ x &= -\frac{1}{y - 2 - 3z} \end{aligned}$$

Try solving the following equation:

$$9x + 3 = 7x + 21$$

Solution: $x = 9$

It is important to **check** your result by inserting the solution into the original equation and checking the balance: when $x = 9$, LHS $= 9 \cdot 9 + 3 = 84$. RHS $= 7 \cdot 9 + 21 = 84$. Correct. When an equation contains brackets, remember to remove them first and then solve:

$$5(2x + 6) = 10$$

Solution: $x = -2$

Check: when $x = -2$, LHS $= 5 \cdot (2 \cdot x - 2 + 6) = 5 \cdot 2 = 10 =$ RHS. Hence the solution is correct. When an equation contains fractions, multiply each term by the Lowest Common Multiple (LCM) of the denominators. The LCM of a set of numbers is the smallest number into which each of the given numbers will divide exactly (See Section 3). For example, solve

$$\frac{x}{4} + \frac{3}{5} = 3 \cdot \frac{x}{2} - 2$$

Solution: $x = \frac{52}{25} = 2.08$

Check:

Solve

$$\frac{x - 4}{3} - \frac{2x - 1}{2} = 4$$

Solution: $x = -\dfrac{29}{4} = -7.25$

Check:

PRACTICE. *Rearrange the following equations.*

1. *Express b in terms of a, c and d (isolate b to the left-hand side):* $bc + ad = d^2 - ad$

2. *Express a in terms of c, b and d:* $ad^2 - ba = ca^2$

3. *Express c in terms of a and b:* $\dfrac{b-1}{c+1} = a + b$

4. *Express y in terms of x:* $y^2 + 2y + 1 = x$

An important task in solving practical problems is to be able to translate information into symbols and thereby making up an algebraic expression. For example, find an expression which will give the total mass of a box containing x articles if the box has a mass of 8kg and each article has a mass of 400g. Produce a table in which you caculate for $0, 1, 2, \ldots$ articles the total mass of the box. Then translate the table into a graph:

> **Remark:** This process of building (hypothesizing) an equation, producing a table and a graph is central to mathematical modelling in the biosciences. We return to this issue in Section 12. The equatioin you derived here will re-appear in a general form in Section 13.

If the price of an article is reduced from x pence to y pence, make an expression giving the number of extra articles that can be bought for £1:

If x sweets can be bought for 60 pence, what is the cost of y sweets?

To summarise this section,

1. To solve an equation the same operation must be performed on both sides. Thus the same amount can be added or subtracted from each side, or both sides can be multiplied or divided by the same amount.

2. After an equation has been solved the solution should be checked by substituting the result into the original equation. If each side of the equation has the same value, the solution is correct.

3. To construct a simple equation the quantity to be found is represented by a symbol. Then using the given information the equation is formed. Note that both sides of the equation must be in the same units.

Remark: The word 'algebra' comes from a ninth century book by Al-Khwarizmi (an Arab mathematician) called 'Hisab al-jabr w'al-muqabala' meaning 'Calculation by Restoration and Reduction'. Algebra is a highly compact and efficient set of tools for solving practical and theoretical problems.

9 Measurement and Units

The basic idea of measurement is to compare and order. In Section 5 we used the number line to identify the order of real numbers and found that for any two numbers, the one on the right is greater than the other. An important concept for ordering is *transitivity*. This says that if I know that b is greater than a, and c is greater than b, then c must also be greater than a. To allow the comparison of attributes we require measurement or *ratio scales* such as length, area, volume, mass, weight, time interval, angle and many others. Official standards are in metric or SI (Systéme Internationale d'Unités) units: SI units

Attribute	SI unit	Abbreviation
length	metre	m
mass	kilogram	kg
time	second	s
temperature	kelvin	K
amount of substance	mole	mol

Derived or *compound units* are

Quantity	Unit	Symbol	Definition
Energy	joule	J	$\text{m}^2\text{kg s}^{-2}$
Force	newton	N	m kg s^{-2}
Pressure	pascal	Pa	$\text{m}^{-1}\text{kg s}^{-2} = N\text{m}^{-2}$
Area	square metres	m^2	
Volume	cubic metres	m^3	
Capacity	litre	L	

Note that the definitions become clearer when written as fractions. For example, the pressure is defined as the force per square meter: $1\text{Pa} = \frac{1\text{N}}{1\text{m}^2}$. A great advantage of the SI system is that it uses a base 10 system, with standard prefixes to indicate the size of units:

giga	G	10^9	deci	d	10^{-1}	micro	μ	10^{-6}
mega	M	10^6	centi	c	10^{-2}	nano	n	10^{-9}
kilo	k	10^3	milli	m	10^{-3}	pico	p	10^{-12}

The system makes it easy to change from one size to another. So to express 2.11m in centimeters, it is only necessary to multiply by 100, so 2.11m = 211cm because 1m = 10^2cm = 100cm. Obviously there are again some rules to follow with units:

1. If you are dealing with measurements, never forget to write down the units and 'carry' them through your calculations.

2. Only quantities which have the same units can be added or subtracted.

3. In ratios units can cancel. For example:

$$\frac{6\text{ m}}{12\text{ m}} = 0.5 \qquad \text{but} \qquad \frac{6\text{ m kg s}^{-2}}{12\text{ kg}} = 0.5\text{ m s}^{-2}$$

A typical lab experiment (and exam question) involves conversions. For example, convert 55 millilitres to litres:

$$\begin{array}{lll} \text{Since} & 1000 \text{ millilitres} & = 1 \text{ Litre} \\ \text{then} & 1 \text{ millilitre} & = \frac{1}{1000} \text{ Litre} \\ \text{and} & 55 \text{ millilitres} & = 55 \cdot \frac{1}{1000} \text{ Litres} \\ & & = \frac{55}{1000} = \frac{11}{200} \text{ Litre} \end{array}$$

Converting 2.11m into cm, we can use the knowledge that 1m = 100cm and therefore only need to multiply by 100: $2.11 \cdot 100 = 211.0$ or 2.11m = 211cm. Notice that to multiply by one hundred we move the decimal point two places to the right:

Changing prefixes = moving the decimal point.

$$2\,.\,1\,1 \cdot 1\,0\,0 = 2\,1\,1\,.\,0$$

Similar, to convert 2.11m into mm, we know that 1cm = 10mm and 1m = 100cm = 1000mm. Multiplying by 1000 we move the decimal point three places to the right:

2.11m = mm

PRACTICE. *Try the following and observe the movement of the decimal point:*

$2.11m =$ km

$23mL =$ L

$23mL =$ μL

$0.054g =$ kg

$0.054g =$ μg

$0.054g =$ mg

The conversion of units and rewriting of numbers with different prefixes is a common source of errors. I would recommend you "explain" the following interconversions of non-SI and SI units of volume, by using the concept of powers with base ten, introduced in Section 2. Make a drawing to illustrate how the decimal point moves as you make the conversion!

Skip back to Section 2!

1 litre (L)	10^3mL	= 1 dm^3	= $10^{-3}m^3$
1 millilitre (mL)	1mL	= 1 cm^3	= $10^{-6}m^3$
1 microlitre (μL)	10^{-3}mL	= 1 mm^3	= $10^{-9}m^3$
1 nanolitre (nL)	10^{-6}mL	= 1 nm^3	= $10^{-12}m^3$

The following table summarises the conversion between few common units to their SI quivalents:

Unit	Symbol	SI-equivalent
Ångstrøm	Å	10^{-10}m
Inch	in.	0.0254m
Ounce	oz	28.3g
Pound	lb	0.4536kg
Centigrade degree	°C	(t°C + 273)K
		[(5/9)(°F-32)]°C
millimeters mercury	mmHG	133.322Pa
Atmosphere	atm	101325Pa
Calorie	cal	4.186J

PRACTICE. *Try these questions without a calculator.*

1. *The height of the author of these notes is 2.11m. Given that 1 feet (ft) is 0.3048m, what is his height in feet?*

2. *Travelling to other countries you may find this useful: A gallon of fuel costs £2.55. (A gallon is approximately 4.5 litres). What is the price per litre?*

3. *Convert 4570 milligrams to grams.*

> **Remark:** We used $\div b$ to make clear that we divide by b, e.g., a/b or we used $\times$ to describe the task of multiplication, e.g. $a \times a$ to denote the process of multiplying $a \cdot a$. Most symbols, like for example % are recognised regardless of nationality, culture and have not changed over time. However, communicating your experimental results with colleagues in Germany and France you should note the following differences. While in Britain we write 0.4 (nought point four) there it is written as $0,4$. Thousands are also the other ways round: in Britain we write $1,000$ while for example in Germany one thousand is written 1.000. Of course measurement units are another example where some countries adopt different conventions. The emphasis is on convention – there is no true or correct standard and the next time you drive with a German to a pub (on what for him is the wrong side of the road) remember that "miles" and "pints" aren't *natural* to him or her.

10 Concentrations

In the following two sections we deal with two common tasks in laboratory work: calculating concentrations and giving approximate results.

$$\text{concentration} = \frac{\text{quantity}}{\text{volume}}$$

In your laboratory work, a *solution* is defined in terms of the amount of *solute* (material) and the amount of *solvent* (liquid). Concentrations are expressed most commonly in terms of weight by volume (w/v) in which a given amount of solid is dissolved in a solvent to a fixed total volume, including the solute. Less frequently solutions are expressed as weight/weight (w/w), in which case a fixed mass of solvent is added to dissolve the solute. In summary, the following cases can be distinguished [10]:

1. **Percentage weight/volume:** % (w/v) = weight in grams of solute per 100mL of solution. Example: 1g $(100\text{mL})^{-1}$ = 1% (w/v) solution. In some textbooks or journal papers you may see concentration measured in milligrams per cent (mg%). This is defined as the weight of solute in milligrams per 100mL of solution.

2. **Percentage volume/volume:** % (v/v) = volume in millilitres of solute per 100mL of solution. Example: 1mL methanol plus 99mL water = 1% (v/v) solution.

3. **Percentage weight/weight:** % (w/w) = the weight in grams of solute per 100g of solution. Example: 15g of salt plus 85g of water = 15% (w/w) solution.

If the concentration is very low it is common for either parts per million (p.p.m.) or parts per billion (p.p.b.) to be used, the assumption being made that the density of water approximates to 1g cm^{-3}. Gas mixture concentrations are expressed as p.p.m or p.p.b on a volume/total volume basis.

Molarity, Mole

Molarity (M) is another very common expression of concentration. It expresses the number of moles of a substance that are present in a given volume of solution. A **mole** of a substance in grams (the *gram mole*) is numerically equal to its molecular mass. For example, for sodium chloride, which has a molecular mass of 58.5 daltons (from atomic weights:

Na=23 daltons, Cl=35.5 daltons) one mole is 58.5g. A 1M solution of a substance contains one mole of the substance in 1 litre of solution.

Various units of concentration are therefore possible and the conversion rules for units, introduced in the previous section, are important. Familiarise yourself with the following interconversions of mol, mmol and μmol in different volumes to give different concentrations:

Skip back to page 4 and 10!

M	mM	μM
1 mol dm^{-3}	1 mmol dm^{-3}	1 μmol dm^{-3}
1 mmol cm^{-3}	1 μmol cm^{-3}	1 nmol cm^{-3}
1 μmol mm^{-3}	1 nmol mm^{-3}	1 pmol mm^{-3}

PRACTICE. *Try the following questions.*

1. *Assuming that in* 100*mL of water are* 3*g of salt. How much is in* 20*mL?*

2. 100*mL of a* 10*% (w/v) solution is prepared. Assume that the salt is evenly distributed throughout the solution.* 50*mL of the solution is removed.*

   (a) What is the amount of salt present, in grams?

   (b) What is the concentration of the 50*mL sample that is removed?*

3. *What are the following concentrations in % (w/v)?*

   (a) 5*g of glucose in a final volume of* 50*mL.*

   (b) 7.5*g of glucose in a final volume of* 75*mL.*

11 Accuracy

Significant figures

In Section 2 the scientific or standard notation was introduced as a way to present very large and very small numbers. Handling experimental data it is often necessary to decide what level of accuracy is required. The required accuracy is expressed by the number of **significant figures**.

To express 349 to two significant figures, only the first two digits are displayed while the remaining digits are set to zero. Since the third digit is larger than 5, the result is 350. In general, if the last significant figure is smaller than five you round down, while for the last digit being greater than five you round up. The purpose of this is to minimise the error in rounding. For example, expressing 19 732 to three significant figures, we notice that position four is less than 5 and hence we leave the last significant figure as it is. The answer is therefore 19 700.

The even/odd rule

So far we have not mentioned what to do if the last significant figures is equal to 5. To minimise the error it is better to use the rule that if the last significant figure is odd, i.e., $\{1, 3, 5, 7, 9\}$, then it should be rounded up, but if the last figure is even it should be rounded down. For example, 365 to two significant figures: The number in position three is 5 and hence the rule is applied. Since the last significant figure, 6 is even, we round down. The answer is 360.

Decimal places

Our previous examples only considered integer values. To express 2.342 to two decimal places, we notice that the third digit after the decimal point is the value 2, which is less than five and hence the answer is 2.34. To compare both, significant figures and decimal places, consider the number 0.0457 and express it first to two significant figures: We count only non-zero values, so the first figure considered is 4. The value at position three is greater than 5; hence the answer is 0.046. To express 0.0457 to two decimal places, we notice that the value at position three is 5, so we round up and 0.0457 becomes 0.05 to two decimal places.

PRACTICE. *Try the following questions.*

1. *Express* 7849 *and* 375 *to two significant figures. Describe the error for rounding up and down.*

2. *Represent the following to three decimal places: (i)* 45.09653 *(ii)* 0.464782 *(iii)* 0.00089 *(iv)* 1289.632

3. *Represent the following to three significant figures: (i)* 23.347893 *(ii)* 128904 *(iii)* 0.003429 *(iv) 267491.954*

12 Relations and Functions

A **set** X is a collection of arbitrary objects (e.g. points in the plane, real numbers or symbols), called the *elements* of X. If x is an element of X, we write $x \in X$. Curly brackets are used to write a set as a list of elements, $X = \{x\}$. A **relation** is a set of ordered pairs; the set of first elements in each ordered pair is called the *domain*, and the set of second elements is called the *range*. A **function** is a relation for which each value in the domain corresponds to a unique value in the range. A function is also referred to as a **mapping** or map for short (See Figure 12.1). The term mapping suggests some form of 'rule' that describes how elements in the domain are related to the elements in Y. For example, in Section 6, we discussed logarithms: assuming a base b, and given a number x, the logarithm determines the exponent $y = \log_b(x)$ such that $b^y = x$. With base 10 and $x = 1000$ the logarithm is 3 since $10^3 = 1000$. While we keep the base fixed, there is no reason why we shouldn't explore what happens for other numbers. In Section 6, we produced a table for some obvious candidates. Assuming a fixed base b, and replacing a particular number by the symbol x, we treat x and its logarithm y as variables. In the equation $y = \log_b(x)$ the brackets are used to emphasise the dependency of y on x. y is then also called the *dependent* variable while x the *independent* variable. With this generalisation we obtain a *logarithmic function*.

Relations are multi-valued while functions assign unique elements

Skip back to Section 6!

Independent and dependent variables.

In another example, let the domain, denoted X, be a subset of all genes in a genome and let the range, Y, denote all known 'functional classes'[1]. The relationship between genes and gene products is a relation not a function because more than one gene can code for the same product.

[1]Most areas of research have evolved their individual way of communicating and representing knowledge. The mathematician's and the life scientist's vocabulary overlap occasionally. The term 'function' is an example. In mathematics the definition of a function is unambiguous and we are going to use the alternative term 'mapping' if there is a risk of confusion.

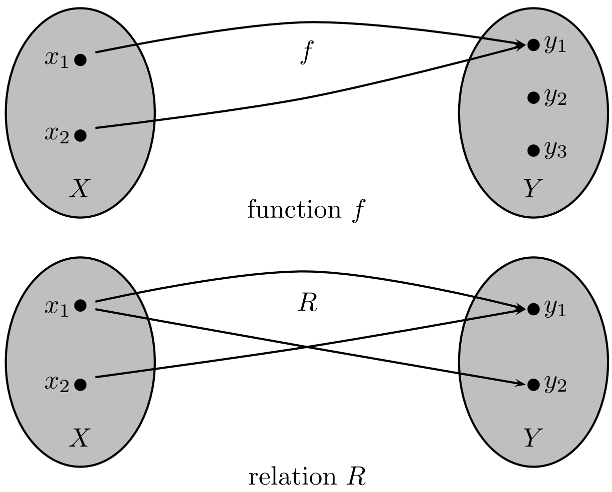


Figure 12.1: Examples of a relation (bottom) and a function (top). While a relation is multi-valued, one element in domain X can be related with more than one element in the range Y.

The concept of mathematical relations is frequently used by computer scientists (think of relational databases). However, the definition of a function, which is stricter than that of a relation, provides the basis for very powerful methodologies developed within the areas of applied mathematics, physics and engineering.

Cartesian coordinates

There are several ways of representing functions but a plot in the Cartesian plane remains the most revealing form of presentation. In 1637, the French philosopher and mathematician Descartes published a book entitled *La Géométrie* which set out a new way of linking algebra and geometry. The system, which grew out of his work describes a point with reference to two perpendicular lines or axes. Figure 12.2 illustrates a relation in the Cartesian space, denoted $X \times Y$ and formed by all points in the plane (ordered pairs (x, y)). For a function, the set of ordered pairs $\{(x, y)\}$ is called its **graph**.

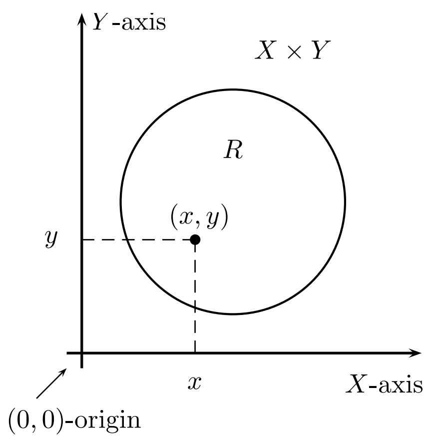


Figure 12.2: A relation R defined in the Cartesian plane $X \times Y$ is a subset of $X \times Y$, i.e., a set of ordered pairs $\{(x, y)\}$.

Let us consider a somewhat idealised situation in which you conducted an experiment in which you studied the growth of bacteria. Starting off with one cell at an arbitrary time 0, you make four consecutive measurements after equal time intervals. Let us assume you obtained the following data:

time	0	1	2	3	4
count	1	2	4	8	16

Visualised with their Cartesian coordinates, in Figure 12.3 (on the left), the experimental data suggest that we may be able to *model* the data and then simulate the experiment with a function (why not a relation?). In Figure 12.3 on the right we see the plot of the function $y = 2^x$ which shows a good approximation to the experimental data and if it is reasonable representation of the biology would allow us to make *predictions*.

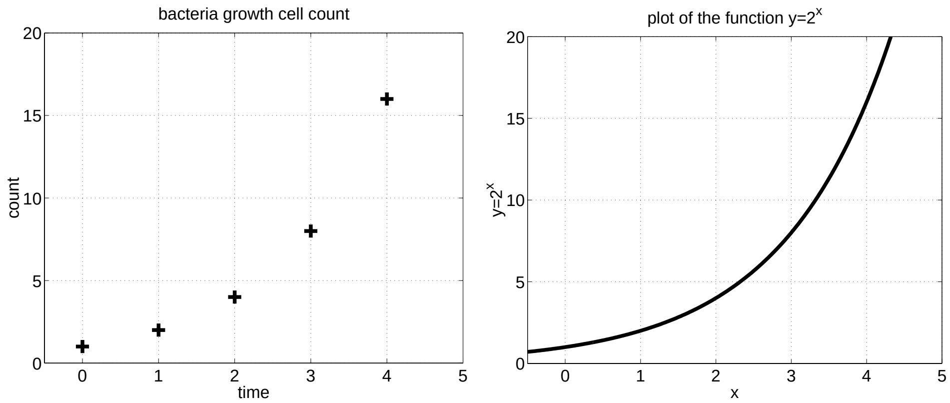


Figure 12.3: Experimental data on the left and plot of exponential function $y = 2^x$ on the right. The function (model) allows us to make predictions.

The purpose of mathematical modelling

The principal purpose of experimentation is to generalise from the special case obtained in our experiment to what one would expect to observe if the experiment is repeated and measurement errors are minimal. In other words, we try to recognise a pattern in the data. Ultimatively, we like to postulate some principle by which the natural system under consideration operates. The process of mathematical modelling is illustrated in Figure 12.4.

Despite the enormous advances in applied mathematics and the very successful representation of natural systems in physics, the complexity of biological systems has meant that we often face a dilemma, Albert Einstein summarised as follows:

> So far as the laws of mathematics refer to reality, they are not certain. And so far as they are certain, they do not refer to reality.

Despite the difficulties in building accurate mathematical models of genetic systems, mathematics and statistics play a major role in state-of-the-art molecular biology, biochemistry and bioinformatics. The discovery of structure in data, the formulation of causal entailment in genetic systems will always be the natural scientist's job; mathematical modelling is a way of thinking that helps you in the discovery! The need for theory and mathematical modelling was nicely summarised by Henri

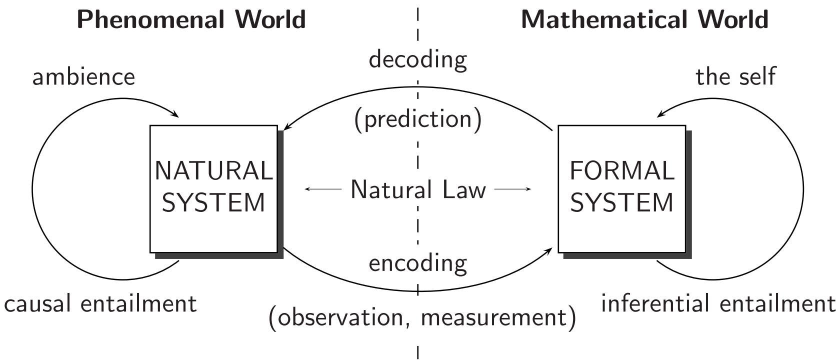
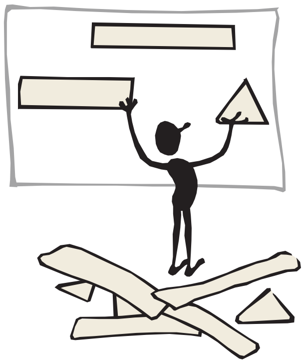


Figure 12.4: The modelling relation between a natural system $\mathfrak{S}$ and a formal or mathematical system $\mathfrak{M}$. If the modelling relation brings both systems into congruence by suitable modes of encoding and decoding, it describes a *Natural Law*. In this case $\mathfrak{M}$ is a *model* of $\mathfrak{S}$, that is, $\mathfrak{S}$ is a realisation of $\mathfrak{M}$.



Poincaré: 'Science is built up of facts, as a house is with stones. But a collection of facts is no more a science than a heap of stones is a house.'

Figure 12.3 shows how we can generalise from our experimental data. Given $y = 2^x$ we can calculate the value y for any time in the future or in between the instances at which we made our measurements. For example, at $x = 2.5$, using the model $y = 2^x$, we find $y = 2^{2.5} = 5.66$. Despite the apparent success of our modelling approach there is scope for questions. The mathematical function $y = 2^x$ grows to infinity as x increases but if we had continued our measurements, would the number of cells increase indefinitely? With your cultures growing on a plate of limited size, this is unlikely. Also, how do we get any function $y = f(x)$ from any set of training data? Admittedly, the data were deliberately chosen to fit to the exponential function and with more general situations and measurement errors we enter the area of statistics which is not part of this course. In statistics, specifically *regression analysis*, a number of very powerful methods are available to fit functions to experimental data. Most software packages, which handle data, have such functions built-in.

Statistics, regression analysis

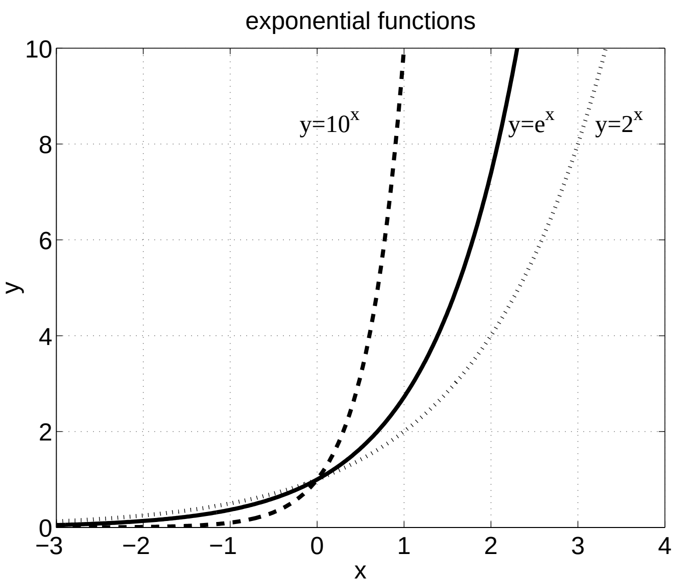


Figure 12.5: A selection of exponential functions.

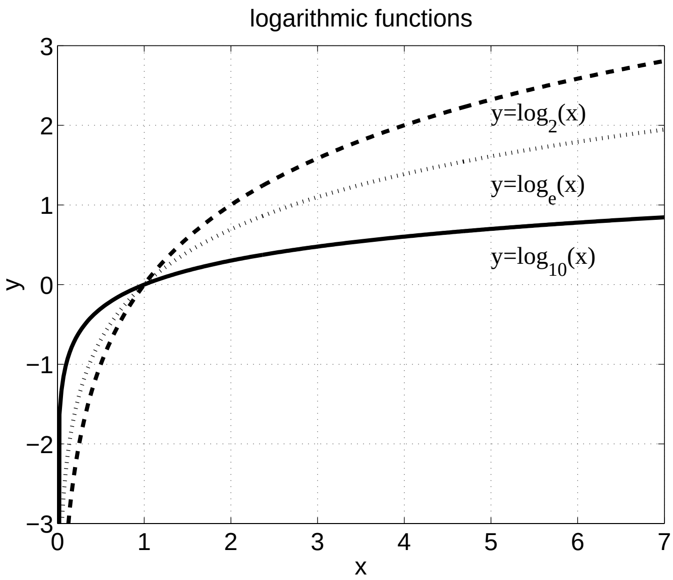


Figure 12.6: A selection of logarithmic functions.

The irrational, if not bizarre, number e and its functions such as $\log_e(x)$ and e^x play an important role in applied mathematics[2]. Examples are:

1. In a system at thermal equilibrium at an absolute temperature T, the numbers n_1 and n_2 of molecules in two states with energies E_1 and E_2 respectively are related according to the equation

$$\frac{n_1}{n_2} = e^{\frac{E_2 - E_1}{kT}}$$

in which k is the Boltzmann constant ($= 1.38 \times 10^{-23}\text{JK}^{-1} = R/N$, where $R = 8.31\text{JK}^{-1}\text{mol}^{-1}$ is the gas constant and $N = 6.02 \times 10^{23}\text{mol}^{-1}$ is the Avogadro constant). If we take the natural logarithms on both sides, we can express the difference between the energies as

$$E_2 - E_1 = kT \log_e \left(\frac{n_1}{n_2} \right)$$

2. In a first-order reaction with rate constant k, the extent of reaction after time t is proportional to $1 - e^{-kt}$. See Figure 12.7. More on this later!

3. The decay of a radio-isotope to a non-radioactive form can be described in the form 'the instantaneous change in a quantity with time is equal to a constant times the current value'. Translated into a mathematical expression, we get the following differential equation

$$\frac{\mathrm{d}}{\mathrm{d}t} m(t) = k \cdot m(t) \qquad (12.1)$$

[2] An important property of the function $y = e^{kx}$ is that it is the only function which is equal to its own derivative, i.e., if $y = e^{kx}$, $\mathrm{d}y/\mathrm{d}x = e^{kx}$.

In other words, the rate of decay of a radioactive substance – and the amount of radiation it emits – is at every moment proportional to its mass m. The solution of this differential equation is

$$m(t) = m_0 \cdot e^{kt} \tag{12.2}$$

where $m(t)$ is the number of radioactive particles in the sample at time t, and m_0 is the amount in the starting material (the mass at $t = 0$) and k is the decay constant and is unique to each isotope. From the equation above, which is plotted in Figure 12.7, we can see that m will gradually approach 0 but never reach it. This explains why, years after disposal, radioactive waste can still be a hazard. The value of k determines the rate of decay of the substance and is usually measured by the *half-life* time, the time it takes a radioactive substance to decay to one-half of its initial mass. Different substances have vastly different half-life times. For example, the common isotope of uranium[3], U^{238}, has a half-life of about five billion years, ordinary radium, Ra^{226}, about sixteen hundred years, while Ra^{220} has a half-life of only twenty-three milliseconds. I am going to explain differentials and differential equations in Section 15; don't worry if you are unfamiliar with them!

4. If money is compounded *continuously* (that is, every instant) at an annual interest rate k, the balance grows exponentially in time.

5. When sound waves travel through air (or any other medium) their intensity is governed by a first-order differential equation where y denotes the intensity and x the distance travelled. A similar law, known as Lambert's law, holds for the absorption of light in a transparent medium.

Note that with numerous elements, such as fractions, in the exponent, it is sometimes typographically inconvenient to write function e^x and instead we may write $\exp(x)$ which is identical.

$\exp(x) \equiv e^x$

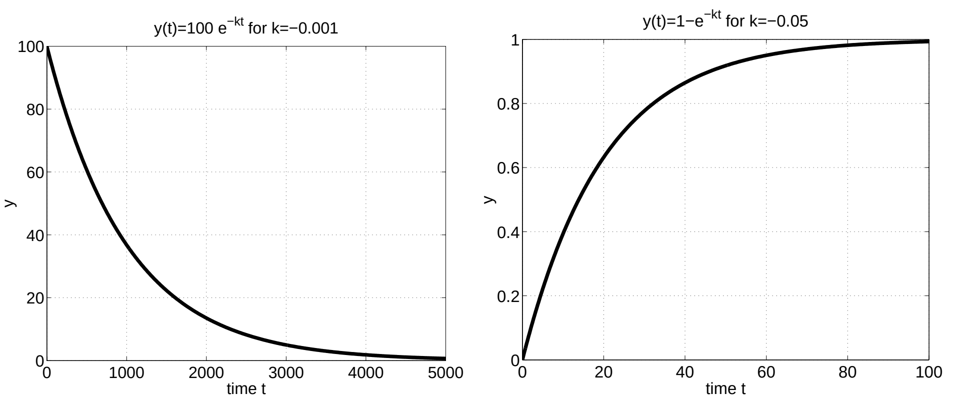


Figure 12.7: Radioactive decay example (left) and example of first-order reaction (right).

[3]The expression U^{238} is a notation used in chemistry and is not the power of a number U!

Equation (12.2), describing the exponential decay of radioactive material, is interesting because there are a number of natural processes that can be modelled by this equation. We are going to see it again in Section 15 and Section 16 where we discuss a population model and rate equations, respectively. Another example that has led to its fame is **radiocarbon dating**. The method can be explained with the following example. If a fossilised bone contains 25% of the original amount of radioactive carbon C_6^{14}, what is its age? The idea to answer this question was honored with the Nobel Prize in chemistry for W. Libby in 1960. He concluded that in the atmosphere, the ratio of radioactive carbon C_6^{14} and ordinary carbon C_6^{12} is constant, and that the same holds for *living* organisms. When an organism dies, the absorption of C_6^{14} by breathing and eating terminates. Hence one can estimate the age of a fossil by comparing the carbon ratio in the fossil with that in the atmosphere. The half-life of C_6^{14} is 5730 years. A result is obtained from the solution (12.2) to differential equation (12.1):

Radiocarbon dating

More about the "half-life" on page 51

$$m(t) = m_0 \cdot e^{kt}$$

Here, m_0 is the initial amount of C_6^{14}. By definition, the half-life (5730 years) is the time after which the amount of radioactive substance, C_6^{14}, has decreased to half of its original value. Thus,

$$m_0 \cdot e^{k \cdot 5730} = \frac{1}{2} m_0, \quad e^{5730 \cdot k} = \frac{1}{2}, \quad k = \frac{\log_e 0.5}{5730} = -0.000121 \ .$$

The time after which 25% of the original amount of C_6^{14} is still present can now be calculated from

$$m_0 \cdot e^{-0.000121 \cdot t} = \frac{1}{4} m_0, \quad t = \frac{\log_e 1/4}{-0.000121} = 11460 \text{ years} \ .$$

Hence the mathematical answer is that the bone has an age of 11460 years. Actually, the experimental determination of the half-life of C_6^{14} involves an error of about 40 years. Also a comparison with other methods shows that radiocarbon dating tends to give values that are too small, hence, 12000 or 13000 is probably a more realistic answer to our present problem.

In Section 6, I mentioned that scientific data are often plotted using a logarithmic scale in graphical representations of the data. Considering the exponential function $y = 2^x$, Figure 12.8 illustrates why it makes sense to visualise data in this way. Without a logarithmic scale, the y values increase exponentially and become very large, very quickly. Plotted on a log-scale, we obtain a simple straight line and it then becomes easier to read off values for a larger range of x. In Section 16, (see Figure 16.3) we are going to encounter a useful example for log-scales.

Log-scale plots

Before we conclude this section, we have a look at two more curious functions: the logarithmic spiral and the 'hanging chain'. Suspending a chain between two poles, its shape is closely modelled by the equation

$$y = \frac{a}{2} \left(e^{-\frac{x}{a}} + e^{-\frac{x}{a}} \right) \ .$$

Probably one of the most famous equations which has inspired mathematicians, biologists and artists alike is the logarithmic spiral:

$$r = a \cdot e^{b\Theta}$$

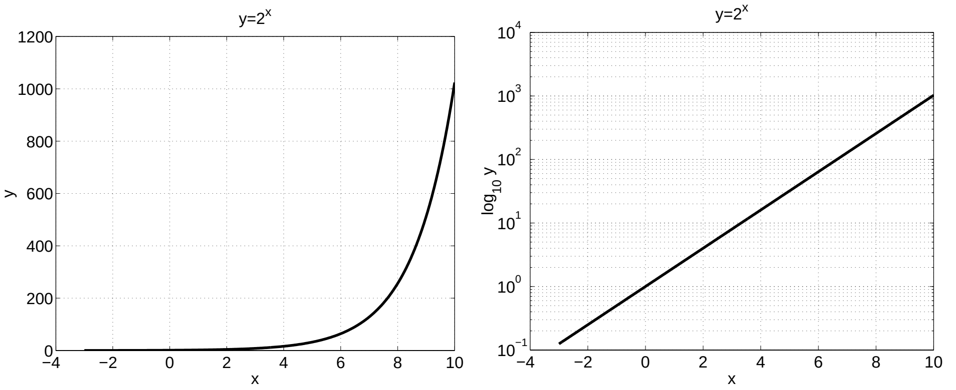


Figure 12.8: Representing data with log-scales. For both plots the same values of the function $y = 2^x$ are calculated. What is different, is the way the information is visualised.

where r is radius of a line with angle Θ to the abscissa. The shape of the logarithmic spiral resembles the cross-section of nautilus shell but many other examples, which show this pattern have been found in the natural world. See the books [11, 12, 8] and in particular [1], which has many beautiful illustrations. Many other books on 'chaos theory' and 'fractals', are filled with examples with astonishingly good matches between mathematics and nature. Does this suggest that nature and natural laws are mathematical? Is π in the sky? Do mathematicians *discover* mathematics or is it an *invention* that fits the world around us only so well because it is the creation of the human mind, which is part of the natural world? The book by Evelyn-Fox Keller [6] provides a fascinating discussion of the use of models in physics and the difference between the physical and biological sciences.

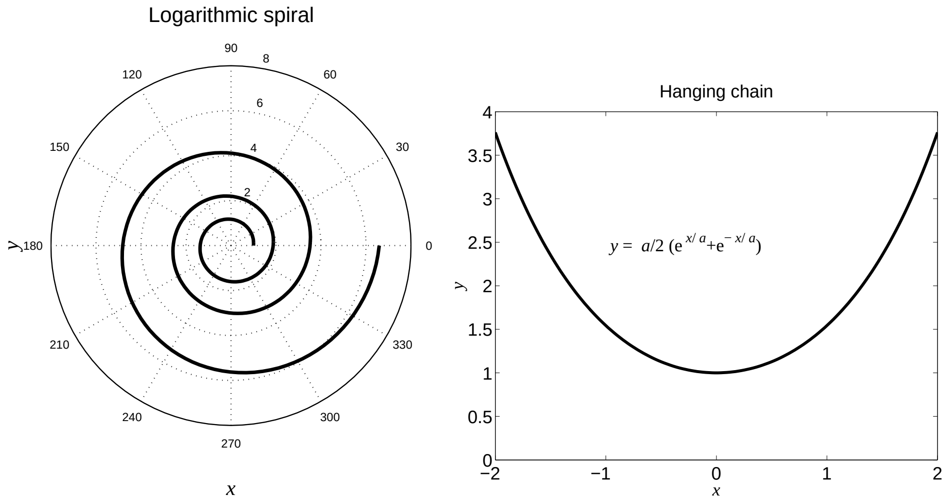


Figure 12.9: Logarithmic spiral (left), $a = 1$, $b = 0.1$ and $0 \leq \Theta \leq 6\pi$. The 'hanging chain', $a = 1$ (right).

Conclusions

A conclusion from this and the following sections should be that plots of functions are a powerful tool to analyse real-world problems and to visualise results. Central to all this is the concept of a mapping or function. For example, a mapping which we use when travelling by train is that between a set of names of stations and a set of times of day:

Manchester	→ 10.00
Stockport	→ 10.09
Wilmslow	→ 10.17
Watford Station	→ 12.24
Euston	→ 12.44

As so often in mathematical modelling, this timetable makes a somewhat idealistic assumption – that the train from Manchester to London is fast and reliable... . Here is a mapping which might be of interest to parachutists. It gives the total distance fallen for various times after they jump, before the parachute opens, and neglecting air resistance:

Time in seconds:		Distance in metres:
0	→	0
1	→	4.9
2	→	19.6
3	→	44.1
4	→	78.4
5	→	122.5

A function was defined as any rule or method whereby, for any and every object in the original set, we can find a (unique) corresponding element in its range. Different ways of symbolising the same function helps us to understand, or to centre our attention on, different aspects of it. We used words to describe functions;, Venn diagrams with arrows as in Figure 12.1; algebraic equations; tables or sets of ordered pairs and graphs. The graph of a function is particularly useful and we will use this frequently in subsequent sections. You should not hesitate to make drawings, sketches to illustrate written ideas, tables and equations!

PRACTICE. *Try the following questions.*

1. *If a bacterial culture contains $N(t)$ bacteria at time t, then the growth of the population can be modelled by the equation:*

$$N(t) = N_0 \cdot 2^n$$

where N_0 is the number of bacteria at the start and n is the number of generation times that have occurred. For example [10], a Bacillus subtilis bacterium divides approximately every 40min and a culture was found to contain 103 bacterial cells. How many cells are present after 10h?

2. *For the decay of a radio-isotope as described above, the half-life for an isotope is the time taken for the amount of material to decrease by 50%. For ^{32}P, the half-time $t_{1/2}$ is 14.3 days. What is the value of the decay constant k?*

3. *A population increases at an annual rate of 4% to 360 000 over a period of ten years. Assuming exponential growth, what was the original size of the population?*

Remark: The irrational number $e = 2.718\ldots$ is indeed strange, and fascinating. The number e and exponential function $e(\cdot)$ are hugely important in science and engineering. Most of us get used to using e, directly or indirectly, without ever questioning it. If you are baffled by this number you are in good company. Most of your lecturers will not be able to tell you what e really is, what it means and why it appears in so many areas and disciplines. If you want to know more, I recommend the books by Maor [8] and Lakoff [7].

13 More on Functions

In the previous section, we pointed out that the aim of most scientific experiments is to try to identify relationship from data. In the Cartesian plane this means that we wish to quantify the relationship between variables x and y. We referred to y as the dependent variable, and the function f is to describe the process by which a value x is transformed to the 'output' y. In mathematical notation, the statement "function f is a mapping from domain X to range Y" is written as

$$f : X \to Y$$

and the statement "function f maps an argument x into the value y" is written as

$$x \mapsto y \qquad \text{where } y = f(x) \ .$$

In this representation of a function, f is deliberately not specified and we have numerous possibilities to consider. In previous sections we considered for example:

$$x \mapsto y = \log_b(x) \ , \qquad x \mapsto y = 2^x \ , \qquad x \mapsto y = e^x \ .$$

One of the simplest (hence useful and important) functions is that of a straight line. Figure 13.1 shows the plot of the general straight line for which the equation is

Straight line equation:

$\boxed{y = a + b\,x}$

$$y = a + b\,x \ . \tag{13.1}$$

In this equation, b and a are a coefficient and constant respectively.

The straight line cuts the y-axis (or *ordinate*) at a distance a from the origin. Because of this relationship, a is known as the **intercept** on the y-axis. The intercept on the x-axis is found by putting $y = 0$, which gives $a + bx = 0$, and so $x = -b/a$. The meaning of b follows from consideration of how y changes when x changes. Suppose that y changes from y_1 to y_2 as x changes from x_1 to x_2. Then

Intercept a

$$y_1 = a + bx_1 \ , \qquad y_2 = a + bx_2$$

If the first equation is subtracted from the second, the constant a disappears:

$$y_2 - y_1 = a + bx_2 - a - bx_1 = bx_2 - bx_1 = b(x_2 - x_1)$$

and if we divide both sides of the equation by $(x_2 - x_1)$ and interchange the left- and right-hand sides we obtain the expression for b:

Gradient b

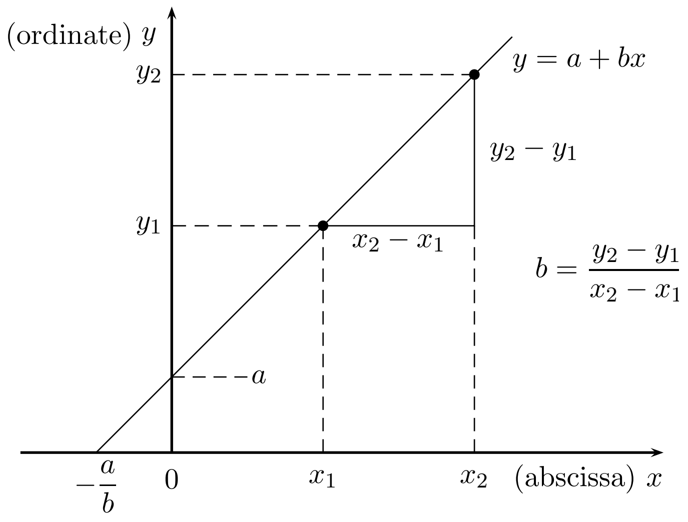


Figure 13.1: Plot of the general straight line $y = a + b\,x$.

$$b = \frac{y_2 - y_1}{x_2 - x_1} \tag{13.2}$$

The coefficient b has a meaning very similar to that of the *slope* or **gradient** of a hill: the steeper the hill, the greater the gradient. It describes a **rate of change**: if we change x by one unit, y changes by b units.

"Rate of change"

Suppose you need to find the equation of the line given only two points in the plane through which the line passes: $(0, 3)$ and $(3, 9)$. The gradient is given by:

Determining the equation of a straight line

$$\begin{aligned} b &= \frac{y_2 - y_1}{x_2 - x_1} \\ &= \frac{9 - 3}{3 - 0} \\ &= \frac{6}{3} \\ &= 2. \end{aligned}$$

The equation of a straight line is $y = a + bx$, so if we substitute for x, y and b the given values and the gradient from above:

$$\begin{aligned} 9 &= a + (2 \cdot 3) \\ a &= 9 - 6 \\ &= 3\ . \end{aligned}$$

The equation of the line is therefore given as $y = 3 + 2x$.

PRACTICE. *Rearrange the following equations into 'straight line' form. What are the gradients (slopes) and intercepts (on the x-axis)?*

1. $y - 3x = 1$

2. $2y - 3x - 1 = x$

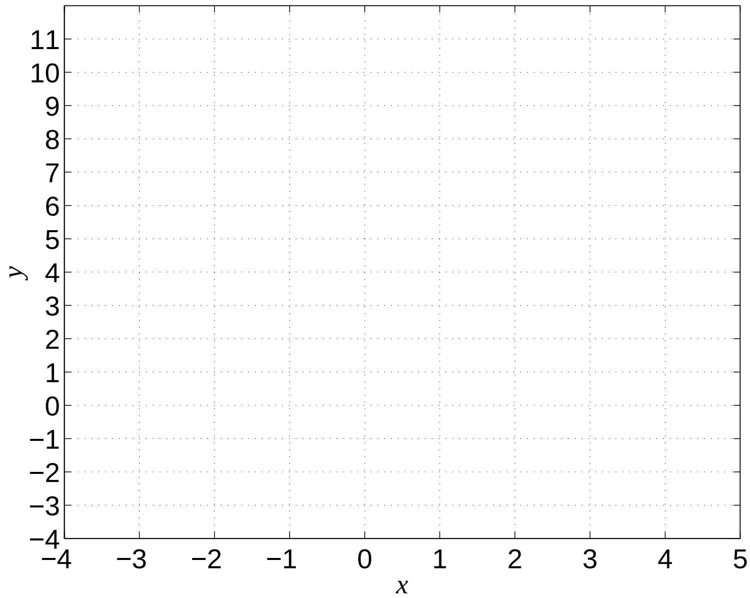
3. $0 = 4y + 5(2x - 3 + 10)$

4. *Assuming two variables x and y are linked by a linear relationship, find the equation of the line from the following data: $(0, 2)$ and $(2, 5)$ fall on the line.*

5. *The straight line has a y intercept 3 and includes the ordered pair $(4, 4)$, what is the equation of the linear relationship?*

6. *Given the point $(7, 3)$ lies on the line and that $b = 4$ find the equation for the straight line.*

7. *Sketch the following functions: $y = 2x + 3$, and $-1 = y - x$*



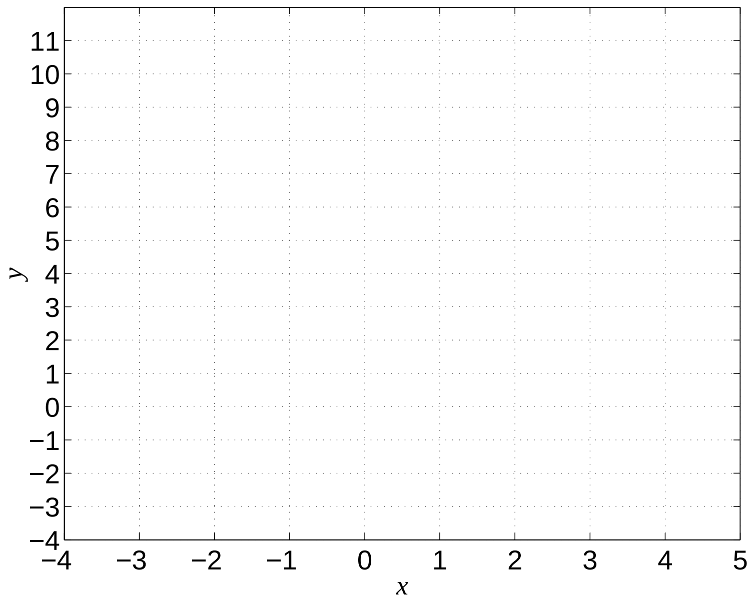


Figure 13.2: Plain grids for the exercise. Notice the aspect-ratio of the y and x axis. This is the usual representation from computer programmes - why?

14 Proportionality

In this section we briefly look at a simple special case of the linear equation (13.1):

$$y = a + b\,x\ .$$

Consider the example

$$y = 3x\ ,$$

where each time there is a change in x, there is a change in y which is two-fold greater than that of x. The equation can be rearranged so that x and y are represented as a **proportion**:

$$y/x = 2$$

Any two quantities that can be represented as a proportion such that

Proportion:

$A \propto B$ implies $A = kB$

$$y/x = \text{ a constant}$$

are said to be proportional. The symbol for proportionality is '$\propto$' and indicates that both sides of the equation are not equal but that they are related and can be represented as a proportion. In general, we can write

$$A \propto B \quad \text{implies} \quad A = kB$$

where k is a constant terms the **constant of proportionality**. The example $y = 3x$ is a special of equation (13.1):

$$y = bx$$

which shows that if two variables, here x and y, are related by this special linear equation, the constant of proportionality is equal to the gradient ($y/x = 3$) (Figure 14.1).

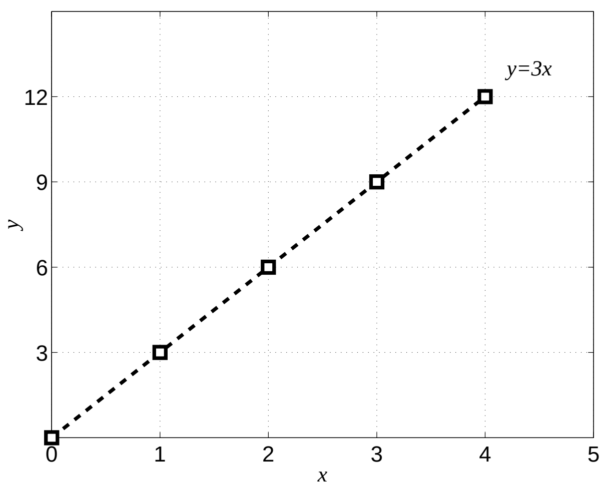


Figure 14.1: Plot of x and y such that $y = 3x$.

15 Differential Equations

In Section 13, we introduced the concept of a function f:

Skip back to page 39 if the notation appears unfamiliar.

$$\begin{aligned} f\colon\ X &\to Y \\ x &\mapsto y = f(x)\ . \end{aligned}$$

In the equation $y = f(x)$, the variable y is referred to as the *dependent variable* while x is called the *independent variable*. We call this a *general* equation because function f is not explicitly specified. A particular example for the general case $y = f(x)$ is the exponential equation we encountered previously:

Equation $y = f(x)$:
Dependent variable y.
Independent variable x.
Function f.

$$y(t) = y_0 \cdot e^{kt}\ .$$

In this equation y_0 and k are coefficients, i.e., some fixed numbers, while t is used to replace x. The letter t is most commonly used to describe time. Therefore in case the equation above is intended to model some natural phenomena, time t is the independent variable and to emphasise the dependence of y on t we write $y(t)$.

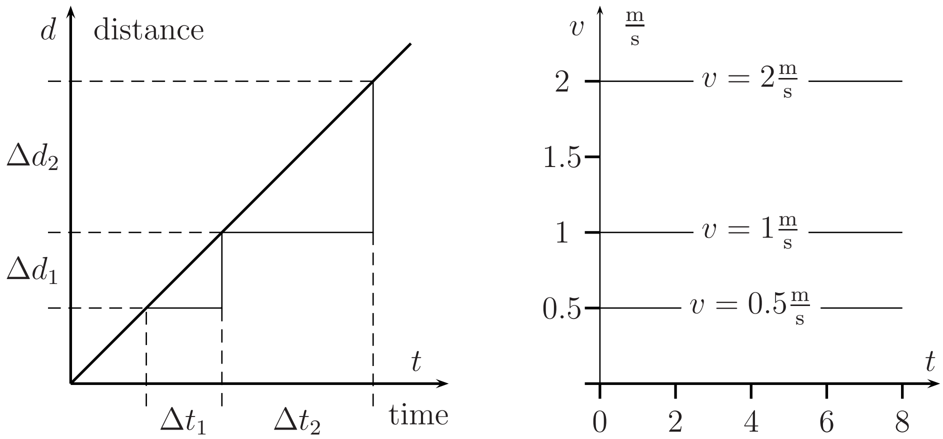


Figure 15.1: Translation (horizontal movement) of a mass with constant velocity.

For many practical situations, the equation $y = f(x)$ is unknown. However, through observation and experimentation we can often assess rates of changes of variable y. For example, watching a moving car, we observe its velocity as the rate of change of position[1]. As illustrated in Figure 15.1, we find that for a car with constant velocity,

Cf. page 40!

$$v = \frac{\Delta d_1}{\Delta t_1} = \frac{\Delta d_2}{\Delta t_2} = \frac{\Delta d_3}{\Delta t_3} = \cdots$$

and therefore for constant velocity, the quotient of the travelled distance and the time required are independent of the length and position of the time interval considered.

The **derivative** of a function $y = f(x)$ is the *rate* at which the quantity $y = f(x)$ is changing with respect to the independent variable x. We denote the derivative as $\frac{\mathrm{d}y}{\mathrm{d}x}$ and translating the previous sentence into mathematical jargon, we obtain the definition

Derivative $\dfrac{\mathrm{d}}{\mathrm{d}x}$ of function $y = f(x)$.

[1]Speed is a measure of the distance travelled during a given time period, whereas velocity is a measure of the change in position during a given period of time.

$$\frac{\mathrm{d}y}{\mathrm{d}x} = \lim_{\Delta x \to 0} \frac{f(x+\Delta x) - f(x)}{\Delta x} \tag{15.1}$$

The derivative is therefore defined as the *limit* of the change in which we imagine the increment Δx tends to 0. If y is dependent on only one variable, the derivative is equivalent to the *gradient*, introduced in Section 13 and illustrated in Figure 13.1. See Figure 15.2 for an illustration of the derivative of a general function. In Figure 15.2, we can see how the derivative is related to the limit of the gradient of the chord joining the points $(x, f(x))$ and $(x+\Delta x, y+\Delta y)$.

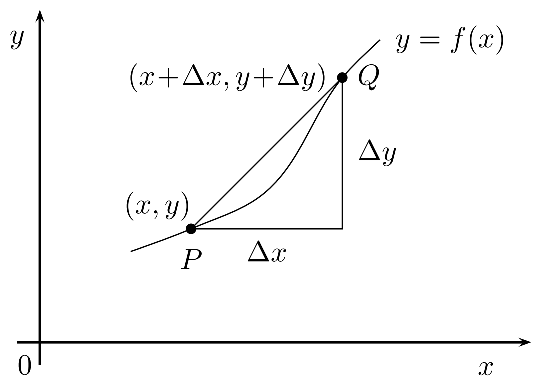


Figure 15.2: Derivative of function $f(x)$ at the argument x. $\mathrm{d}y/\mathrm{d}x$ is the limit of $\Delta y/\Delta x$ as Q approaches P.

Differential equations

An equation relating an unknown function and one or more of its derivatives is called a **differential equation**. Because a rate of change is about the difference between some quantity now and its value an instant into the future, equations of this kind are called differential equations. We find that many *natural laws* (principles by which nature appears to operate) are formulated as equations that relate not the bio-physical quantities of primary interest but the rates at which those quantities change with time, or the rates at which those rates change with time. In fact most molecular, genetic or natural processes are in fact *dynamic processes*. Although we ought to describe most processes by differential equations, this is often only feasible for simple systems. In this case one can often make assumptions which turn differential equations into simpler linear equations.

Population modelling

Let us consider an example which was already briefly mentioned in Section 13. We denote the size of a population with the letter P and in order to emphasise the dependency on time we write $P(t)$. The *time rate of change* of a population $P(t)$ with constant birth and death rates is, in many simple cases, proportional to the size of the population. That is, a possible mathematical model is the differential equation

$$\frac{\mathrm{d}P}{\mathrm{d}t} = k \cdot P \ , \tag{15.2}$$

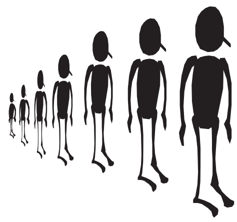
where k is the constant of proportionality. Even if the value of the constant k is known, the differential equation $\mathrm{d}P/\mathrm{d}t = kP$ has *infinitely many* different solutions. The solutions are all of form

$$P(t) = C \cdot e^{kt} \ , \tag{15.3}$$

where any constant C defines one possible solution. To verify this assertion, we take the derivative of $P(t)$:

$$\frac{\mathrm{d}P(t)}{\mathrm{d}t} = Cke^{kt} = k(Ce^{kt}) = kP(t) \qquad \text{for all numbers } t.$$

Once more the number e and the exponential function appear and the reason is that it is the only function that is equal to its derivative. (See also page 34). Suppose that $P(t) = Ce^{kt}$ is the population of bacteria at time t, that the population at time $t = 0$ (hours, h) was 1000, and that the population doubled after 1 h. This additional information about $P(t)$ yields the following equations:



$$1000 = P(0) = Ce^0 = C$$
$$2000 = P(1) = Ce^k \ .$$

It follows that $C = 1000$ and that $e^k = 2$, so $k = \log_e 2 \approx 0.693147$. With this value of k the differential equation in (15.2) is

$$\frac{\mathrm{d}P}{\mathrm{d}t} = (\log_e 2)P \approx 0.693147 \cdot P \ .$$

Substitution of $k = \log_e 2$ and $C = 1000$ in equation (15.3) yields the particular solution

$$P(t) = 1000e^{(\log_e 2)t} = 1000 \cdot \left(e^{\log_e 2}\right)^t = 1000 \cdot 2^t \qquad (\text{because } e^{\log_e 2} = 2)$$

that satisfies the given conditions. The "power" of mathematical modelling lies in the fact that we can use this particular solution to predict future populations of the bacteria colony. For instance, the predicted number of bacteria in the population after one and a half hours (when $t = 1.5$) is

$$P(1.5) = 1000 \cdot 2^{3/2} \approx 2828 \ .$$

Initial condition

The condition $P(0) = 1000$ in this example is called an **initial condition** because we frequently write differential equations for which $t = 0$ is the "starting time".

The population growth example illustrates the process of mathematical modelling (Figure 15.4):

1. Formulate your problem related to a biological system in mathematical terms, that is, construct the mathematical model.

2. Analyse, solve and/or simulate the mathematical model.

3. Interpret mathematical results in the context of the real process, try to answer the question you are investigating.

4. Validate the mathematical model with experimental data.

Mathematical modelling

In the population example, the problem we investigate is to determine the population at some future time. The mathematical model consists of a set of variables, (P and t), coefficients, (k), together with one or more equations relating the variables, ($\mathrm{d}P/\mathrm{d}t = kP$, $P(0) = P_0$), that are

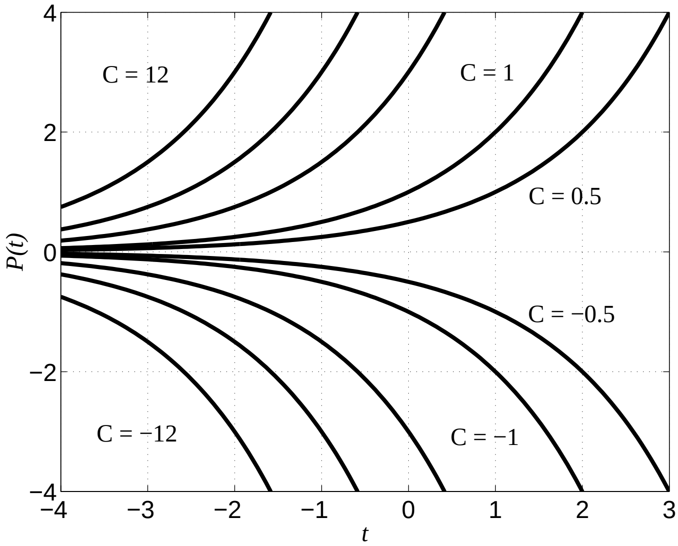


Figure 15.3: Graphs of $P(t) = Ce^{kt}$ with $k = \log_e 2$ and $C = -12, -6, -3, -2, -0.5, 0.5, 1, 3, 6, 12$.

known or assumed to hold. The mathematical analysis consists of solving these equations, (here, for P as a function of t). Mathematical results, predictions or simulations have to be interpreted with observations made for the real system. The best way to validate a model is to compare simulation results with experimental data. This leads us into the domain of statistical techniques which are also used to identify *parameters* (here k) from data.

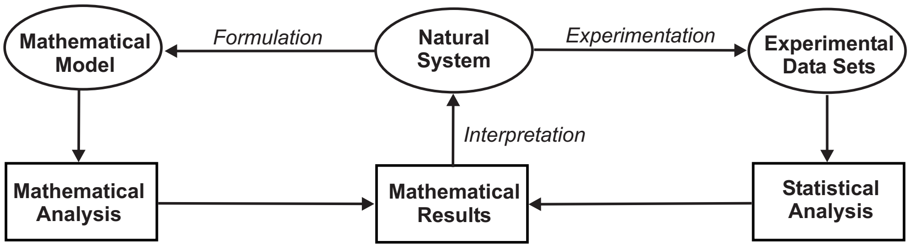


Figure 15.4: The process of mathematical modelling.

It is important to realise that the process of mathematical modelling makes assumptions and that it is quite possible that no one solution of the differential equation exists. The population model $P(t) = Ce^{kt}$ does only approximately describe a bacteria colony growing on an agar plate with limited space. Our population function $P(t)$ was also a *continuous* approximation to the actual population, which of course grows by integral increments. Mathematical modelling requires therefore a tradeoff between what is biologically, physically or chemically realistic and what is mathematically possible.

Remark: For some reason, unknown to mathematicians, differential equations are perceived as difficult by most who have no degree in mathematics. These difficulties are quite reasonable because mathematicians would have to admit that some of the implicit assumptions of the definition $\mathrm{d}y/\mathrm{d}x$ are 'suspicious' to say the least. In order to handle questions about rates of changes in physics, Isaac Newton and Gottfried Leibniz invented in the eighteenth century a new branch of mathematics, called *calculus*. At the root of calculus is the metaphor that 'instantaneous change is average change over an infinitely small interval'. Thus, for a function $f(x)$ and an interval of length Δx, instantaneous change is formulated as $\frac{f(x+\Delta x)-f(x)}{\Delta x}$. The instantaneous change in $f(x)$ at x is arrived at when Δx is "infinitely small". The limit metaphor we used in (15.1) states that Δx approaches zero, without reaching it. Baffled? There is no doubt that Newton's calculus and its applications to physics led to a revolution in physics and changed our view of the world. However, despite the apparent rigour of mathematics, many of the greatest ideas in math rely on 'tricks'. After all, if $\mathrm{d}x$ describes an infinitely small quantity, so does $\mathrm{d}y$ and $\mathrm{d}y/\mathrm{d}x$ appear to be a meaningless fraction 0/0. The full explanation is far from being trivial and for us and in our context, it is sufficient to view $\frac{\mathrm{d}}{\mathrm{d}x}$ as an *operator* which describes a rate of changes.
For a short but very good introduction to mathematical modelling and calculus I strongly recommend the small book 'Nature's Numbers' by Ian Stewart [11]. Another book, ideally suited for those who thought they would hate maths, is the beautiful book by Philip Ball on pattern formation in nature [1].

16 Rate Equations

In this section we summarise some of the insights gained and techniques learned in this course. You will find that virtually all ideas we have discussed so far, come together in the discussion of rate-equations as a model of kinetic processes.

Throughout biomolecular sciences we meet many processes which exhibit growth or decay, and may be described by rate equations. Several general examples were already listed in Section 12 (see page 34) and Section 15 (the population model). Others are enzyme properties such as activation, activity, proteolysis as well as cellular properties such as the growth considered previously. The common element in all these, is that the *rate* of the process is proportional to the amount of the substrate itself. Take for example a protease E, which cleaves a specific peptide bond in a substrate protein S, and thereby activating it to yield the modified cleaved form S'. The **rate** of cleavage (proteolysis) is **proportional** to the amount of inactive substrate S. We can write this as

Rates? See page 11
Proportionality? See page 43

$$\text{rate of proteolysis} = -k_p \cdot \text{ amount of } S$$

where k_p is a constant, referred to as the **rate constant** for this process. We write $-k_p$ because the process reduces the amount of S with increasing time. What I called "amounts", is more commonly written as *concentrations*. For concentrations, biochemists prefer to use following

Concentrations? See page 28

notational form[1] $[S]$. The rate of proteolysis is therefore the change in substrate concentration over time:

$$\frac{\mathrm{d}[S]}{\mathrm{d}t} = -k_p \cdot [S] \tag{16.1}$$

Where the notation $\mathrm{d}/\mathrm{d}t$ represented an instantaneous rate of change in time and is called a derivative (See page 45).

Notation: concentrations in square brackets.

Let us consider an example of such a process with k_p equal to 0.1 per second, and an initial concentration of 20mg of substrate. We have to give our rate constant units which relate how much is changed in a given unit of time. At time zero, $t = 0$, we have 20mg of substrate, and after one second, approximately $0.1\text{mg} \cdot 20$ are converted to the active form, giving 2mg. This leaves approximately $20 - 2 = 18$mg still uncleaved (and inactive). After another second, $0.1\text{mg}\cdot 18$ equal 1.8mg are converted, leaving $18 - 1.8 = 16.2$mg, and so on. These calculations are only approximate since the differential equation assumes *infinitesimally* small intervals of time rather than our chosen one second. Nevertheless, consider the table of eight data points, along with the corresponding value for S'.

Remember: "per second" is written $/s$ or s^{-1}

t	0	1	2	3	4	5	6	7	8
S	20	18	16.2	14.58	13.12	11.81	10.63	9.57	8.61
S'	0	2	3.8	5.42	6.88	8.19	9.37	10.43	11.39

The graphs of the data are plotted in Figure 16.1. Do you recognise the shape of the plots? Where have you seen them before?

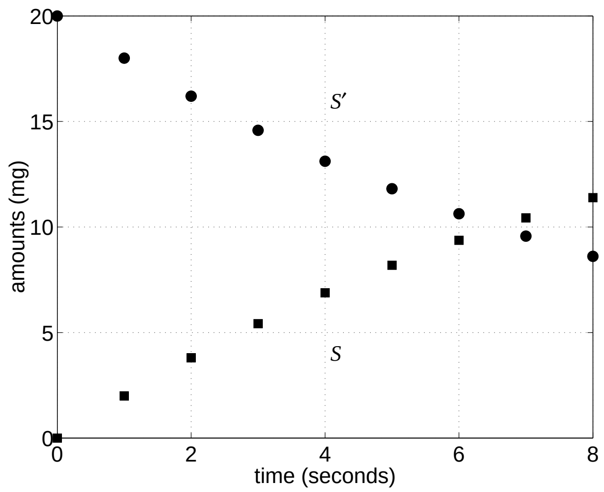


Figure 16.1: Graphs of the amounts for inactive protein S and the modified cleaved form S'.

In fact, the data show an exponential relationship and are suitably modelled by the function $y = e^{-x}$. Indeed, as we discussed in Section 15 on differential equations, the solution to our differential equation (16.1) is (See also Figure 15.3)

Remember: $\exp(x) \equiv e^x$

$$[S] = [S]_0 \cdot e^{-k_p \cdot t}$$

[1]Biochemical processes take place in a defined space (e.g. cell compartments). Assuming a compartment of known size, $[A]$ for some metabolite A is equivalent to the number of molecules of A. We could then use refer to the concentration or the number of molecules interchangeably.

At $t = 0$, we have $e^0 = 1$ and therefore $[S] = [S]_0$, where $[S]_0$ is the *initial value*, that is, the initial concentration or amount of the substrate protein. Let us rename S' as product P, then given that $[P] = [S]_0 - [S]$ we can substitute the equation for $[S]$ to obtain an equation of P:

Initial value.

$$\begin{aligned}[P] &= [S]_0 - [S] \\ &= [S]_0 - \left([S]_0 \cdot e^{-k_p \cdot t}\right) \\ &= [S]_0 \cdot \left(1 - e^{-k_p \cdot t}\right)\end{aligned}$$

Figure 16.2 shows the plot of the two mathematical equations for S and P.

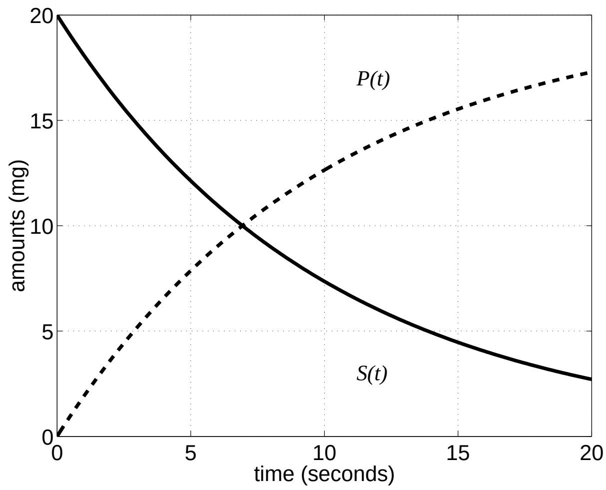


Figure 16.2: Graphs of the rate equations for $S = S_0 \cdot e^{-k_p t}$ and $P = S_0 \cdot (1 - e^{-k_p t})$, $S_0 = 20\text{mg}$, $k_p = 0.1\text{s}^{-1}$.

These are all **first-order kinetic processes**, which are very useful to describe a number of different systems. Very often, the amount of protein present is proportional to the activity of the protein, or some secondary measurement we can make regarding an enzyme or its properties. Typically, the rate-equations are used to represent irreversible processes, where "A" is "converted" or changed in some way to "B". This leads to the general equation

First-order kinetic processes

$$A = A_0 \cdot e^{-kt} \ .$$

If we can express our measured quantity as a fractional measure of the initial amount or activity, this can help us obtain a value for k. Rewriting the equation above, we obtain

$$\frac{A}{A_0} = e^{-kt}$$

Like substraction is the complementary or inverse operation to addition, or multiplication to division, so is the logarithm related to the exponential. Taking the natural logarithm, $\log_e \equiv \ln$, on both sides of the equation:

Logarithms? See page 16

$$\log_e \left(\frac{A}{A_0}\right) = -kt \ .$$

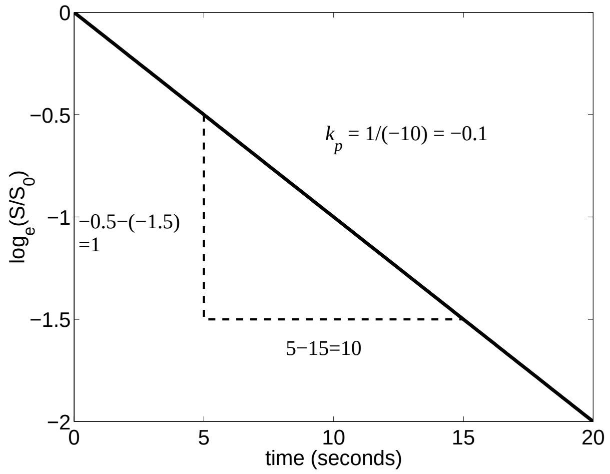


Figure 16.3: A value for the rate constant k_p can be obtained from the gradient of $\log_e(S/S_0)(t)$.

We can now obtain a value for k by plotting $\log_e(A/A_0)$ versus t and determining the gradient of the straight line. For our previous example, this is illustrated in Figure 16.3.

Half-life of a process

Another useful parameter we can discuss in the given context is that of the **half-life** of a process. This describes the time it takes for half of the initial quantity A to be converted into B. It does not matter how much A is there initially, the half-life, denoted $t_{1/2}$ is still the same. Consider the general rate equation for first-order kinetics:

$$A = A_0 \cdot e^{-kt}$$

At the half-life, $t_{1/2}$, $A = A_0/2 = B$, therefore,

$$\frac{A_0}{2} = A_0 \cdot e^{-kt_{1/2}}$$

Rearranging gives

$$\frac{1}{2} = e^{-kt_{1/2}} \qquad \text{or} \qquad \log_e\left(\frac{1}{2}\right) = -k \cdot t_{1/2}$$

Therefore

$$t_{1/2} = \frac{\log_e 2}{k} \; .$$

17 Michaelis-Menten Modelling

In Section 15 we introduced differential equations and as demonstrated in Section 16, we often observe rates of changes, $\mathrm{d}y/\mathrm{d}x$ of functions, y, rather than the functions y themselves. In this Section we continue the theme, highlight problems with differential equations and introduce an important formula.

Consider the reaction between two molecules A and B. Biochemists represent such an reaction using the following symbols and notation[1]:

$$A + B \;\rightarrow\; P$$

[1]Who thought that only mathematicians are fond of symbols and notation?

As we have seen before, the rate of reaction can often be modelled as being proportional both to the concentration of A and to the concentration of B, i.e.,

$$\frac{\mathrm{d}[P]}{\mathrm{d}t} = k[A][B] \tag{17.1}$$

where $[A]$, $[B]$, and $[P]$ are the concentrations of A, B and P, respectively, at time t and k is a constant. This equation is not very useful as it stands; it would not tell us how much product has been formed after a given amount of time. We have to rearrange the equation, simplify it and then solve it to obtain an equation with only $[P]$ and t in it.

The equation (17.1) reminds us of equation (15.2), the population model on page 45:

$$\frac{\mathrm{d}P(t)}{\mathrm{d}t} = k \cdot P(t) \qquad \text{(population model)},$$

where k is the constant of proportionality and $P(t)$ denotes the size of the population at time t. They are however not the same as there are four variables $([A], [B], [P])$, and t instead of only two, (P, t), in the population model. Taking account of the fact that every molecule of P that appears is the result of the disappearance of one molecule of A and one molecule of B; it follows that $([A]+[P])$ and $([B]+[P])$ are constants. Define $[A]_0$ and $[B]_0$ as the initial values of $[A]$ and $[B]$ at time $t = 0$ and when $[P] = 0$. We can then replace $[A]$ and $[B]$ in equation (17.1) with $([A]_0 - [P])$ and $([B]_0 - [P])$, respectively:

$$\frac{\mathrm{d}[P]}{\mathrm{d}t} = k([A]_0 - [P])([B]_0 - [P]) \; . \tag{17.2}$$

This is then a 'proper' differential equation with only one variable, $[P]$, depending on time t. Finding a solution to this differential equation is far more complicated than for the very similar population model. And yet the biochemical model is quite simple as it only models basic irreversible reactions. For a matter of completeness, and ignoring various steps of restructuring equation (17.2), we would obtain the following solution:

$$\frac{[A]_0([B]_0 - [P])}{[B]_0([A]_0 - [P])} = e^{([A]_0 - [B]_0)kt}$$

With this equation, given a time t and initial values for $[A], [B], [P]$ at $t = 0$, we could calculate a concentration $[P]$.

The moral of the story is that although we could, "in theory", find a solution for the model above, even simple kinetic models can lead to intractable mathematics. For example, the simplest model commonly discussed in enzyme catalysis is the Michaelis-Menten mechanism which leads to the following pair of simultaneous differential equations:

$$\begin{aligned}
\frac{\mathrm{d}[Y]}{\mathrm{d}t} &= k_1\Big([E]_0 - [Y]\Big)\Big([A]_0 - [Y] - [P]\Big) \\
&\quad - k_{-1}y - k_2 y + k_{-2}\Big([E]_0 - [Y]\Big)[P] \\
\frac{\mathrm{d}[P]}{\mathrm{d}t} &= k_2[Y] - k_{-2}\Big([E]_0 - [X]\Big)[P] \; .
\end{aligned}$$

Do not worry about the meaning of these equations, they serve to illustrate the complexity and what we can do about it. It is possible to remove $[Y]$ from these equations: first, using the second equation to express $[Y]$ in terms of $[P]$, and differentiating this gives an expression for $\frac{\mathrm{d}[Y]}{\mathrm{d}t}$ in terms of $[P]$ and its derivatives. These two can then be substituted into the first equation to give a single differential equation containing only two variables $[P]$ and t. However, this is as far as we can go, because the resulting differential equation has no known analytical solution. (We can solve and numerically simulate the equation for a specific set of initial conditions. Mathematicians would however prefer to study properties of general solutions - on paper.).

Steady-state kinetics

A common way out of this problem is to make assumptions that simplify the equations. For the example above, one can for instance assume (or adjust experimental condition such) that $[A]_0$ is much larger than $[E]_0$ and to consider only the time scale in which $\mathrm{d}[Y]/\mathrm{d}t$ can be regarded as negligible. This basic restriction leads to what is known as **steady-state kinetics**.

A simple enyzme-catalysed reaction which converts substrate S to product P is represented by biochemist as:

$$S + E \rightleftharpoons ES \rightarrow P$$

where E represents the enzyme and ES the enzyme-substrate complex. The rate of reaction can be measured as the change in product concentration with time. We can define this as the *velocity*, v, of the reaction:

$$v = \frac{\mathrm{d}[P]}{\mathrm{d}t}$$

where $[P]$ is the concentration of product P. This rate of reaction is a change of product concentration over time and hence its unit is specified as $\mathrm{mol} \cdot \mathrm{L}^{-1} \cdot \mathrm{min}^{-1}$. The rate of reaction as a function of the substrate concentration leads to what is known as the **Michaelis-Menten equation**:

Michaelis-Menten equation

$$v = \frac{V_{\max} \cdot [S]}{K_m + [S]} \tag{17.3}$$

in which $[S]$ is the concentrations of the substrate, respectively, at time t. $V_{\max}$ is often called *maximum velocity* or *limiting rate* because v cannot exceed it under steady-state conditions. K_m is called the *Michaelis constant* with unit $\mathrm{mol} \cdot \mathrm{L}^{-1}$. Since it is like v a velocity, it has the same units as v. The substrate concentration $[S]$ is measured in 'moles' per litre, $\mathrm{mol} \cdot \mathrm{L}^{-1}$. In Figure 17.1, the rate of reaction is plotted against substrate concentration. This plot is called the Michaelis-Menten plot.

Michaelis-Menten plot

The Michalis-Menten plot in Figure 17.1 shows that it is difficult to estimate $V_{\max}$ since the curve tends to $V_{\max}$ but will never reach it under experimental conditions. To estimate $V_{\max}$ it is therefore necessary to transform the curve defined by equation (17.3) into a straight-line equation of the form (13.1). A way to do this was developed by Lineweaver

Lineweaver-Burk plot

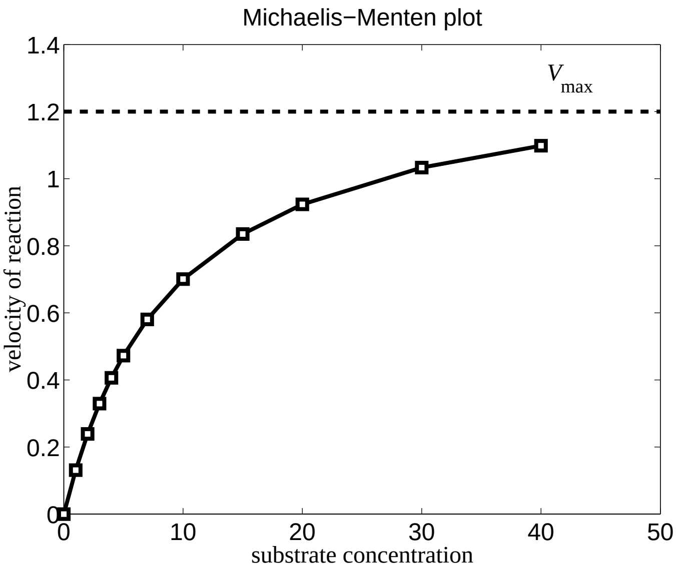


Figure 17.1: Michaelis-Menten plot.

and Burk:

$$v = \frac{V_{\max} \cdot [S]}{K_m + [S]} \qquad \text{invert, ...}$$

$$\frac{1}{v} = \frac{K_m + [S]}{V_{\max} \cdot [S]} \qquad \text{separate } K_m \text{ and } [S], \text{ ...}$$

$$= \frac{K_m}{V_{\max} \cdot [S]} + \frac{[S]}{V_{\max} \cdot [S]}$$

that is,

$$\frac{1}{v} = \frac{K_m}{V_{\max}} \cdot \frac{1}{[S]} + \frac{1}{V_{\max}}$$

This equation is now in the straight-line form $y = a + bx$, where

$$y = \frac{1}{v}; \quad x = \frac{1}{[S]}; \quad b = \frac{K_m}{V_{\max}}; \quad a = \frac{1}{V_{\max}}$$

The graph of $1/v$ against $1/[S]$ will therefore produce a straight line and the y intercept is equal to $1/V_{\max}$ so $V_{\max}$ can be found. The gradient is $K_m/V_{\max}$ and hence if $V_{\max}$ is known, we can determine K_m as shown in Figure 17.2.

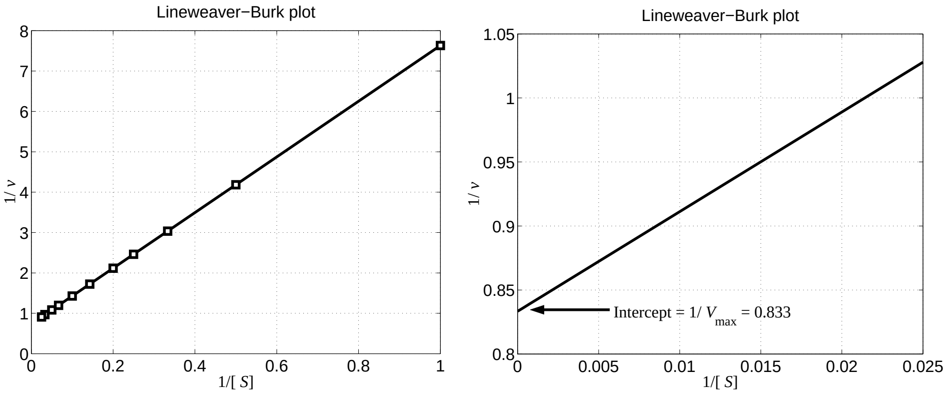


Figure 17.2: Lineweaver-Burk plot as a way to estimate the limiting rate $V_{\max}$.

Remark: Please note that this section does not provide a full introduction to modelling enzyme kinetic reactions. The material of this Section demonstrated how the previously introduced basic mathematical concepts come together when we try to devise mathematical models of cellular processes. There are numerous (interesting) issues associated with the assumptions and applications to cellular dynamics (e.g. pathway modelling). For example, one might argue that if we have to make so many assumptions and simplifications to establish a mathematical model, how can the model then be useful? I would argue that the purpose of mathematical modelling is not only to provide accurate, quantitative predictions but the modelling process itself helps the life scientist to design experiments, generate and test hypotheses. If you don't believe me, Sir Paul Nurse, winner of The 2001 Nobel Prize in Physiology or Medicine wrote a year before his award in the journal *Cell*: "Dealing with these system properties, which ultimately must underlie our understanding of all cellular behavior, will require more abstract conceptualizations than biologists have been used to in the past. We might need to move into a strange more abstract world, more readily analyzable in terms of mathematics than our present imaginings of cells operating as a microcosm of our everyday world.". What he refers to is a change of thinking, away from molecular characterizations of the nuts and bolts in cell systems to an understanding of functional activity. Technological developments in the post-genome era make it increasingly difficult to make sense of experimental data without mathematical modelling and data analysis.

18 Supplementary Material

The following books can be recommended for additional exercises and further reading (prices are estimated):

[10] Introductory mathematics for the life sciences.
229 pages. ISBN 0 7484 0428 7. £16

[4] Basic mathematics for biochemists.
221 pages. ISBN 9 780198 502166. £14

[3] GCSE math designed for post-16 students.
586 pages. ISBN 0 7487 5510 1. £16

There are a number of excellent software packages for mathematics and data analysis. The packages are well established and for which numerous introductory books have been published. For some of these programmes student and campus licenses are available.

- Matlab from MathWorks.
- Mathematica from Wolfram Research.
- Mathcad
- Maple [5]

The Internet provides of course a vast source of information, including a lot of material on mathematics. The following general reference may be useful. For example try searching the following sites for the keyword 'logarithm' !

- Google search engine: `http://www.google.com`
- Brittanica encyclopedia: `http://www.britannica.com/`
- Encarta from Microsoft: `http://encarta.msn.com/`

Other web-sites of interest are:

Mathematics WWW Virtual Library: `http://euclid.math.fsu.edu/Science/math.html`

Eric Weisstein's World of Mathematics: `http://mathworld.wolfram.com/`

19 More Exercises

Fractions

Try to simply the following fractions.

1. $\frac{12}{5} + \frac{3}{4} =$

2. $\frac{2}{5} \cdot \left(\frac{1}{3} + \frac{2}{5}\right) =$

3. $\frac{x}{y} + \frac{2x}{3y} =$

4. $\left(\frac{5}{6} \div \frac{1}{2}\right) \cdot \frac{3}{2} =$

5. $\frac{a}{b} - \left(\frac{2}{c} \cdot \frac{d}{3}\right) =$

6. $\frac{a^3 - b}{b - c} \div \frac{a}{c - b} =$

7. $\frac{d^2}{c} - \frac{d^2}{c^2} =$

8. $\frac{\frac{4x}{5y}}{10y^2} =$

Algebraic Expressions and Equations

Simplify the following expressions by finding common factors.

1. $a \cdot b + a \cdot c =$

2. $a^2 \cdot b + a \cdot c =$

3. $\dfrac{a^2 c}{b} + \dfrac{a^3 d}{a^2}$

Rearrange the following equations.

1. Express b in terms of a, c and d, i.e., determine $b =$?):
$b \cdot c + a \cdot d = d^2 - a \cdot d$

2. Express a in terms of c, b and d: $a \cdot d^2 - b \cdot a = c \cdot a^2$

3. Express c in terms of a and b for the following expression:
$\dfrac{b-1}{c+1} = a + b$

Variables and Constants

In the following problems, rearrange the equations to give y in terms of x and any constants. Remember that in these examples, x and y are the only *variables* and that all other terms are *constants* or *coefficients*. For each example, also work out whether y increases or decreases when x increases.

1. $A \cdot y + C \cdot x = 12$

2. $c \cdot y^2 - 17 = 18x$

3. $\dfrac{C}{1+y} = Z \cdot x$

Powers

1. Show that $\dfrac{10^m}{10^n} = 10^{m-n}$

2. Show that $10^{(a-b)}10^{(b-a)} = 1$

3. Simplify $10^a 10^a 10^a 10^a 10^a =?$

4. Simplify $(10^a)^3(10^a)^{-4} =?$

5. Simplify $\dfrac{1}{a^2}(3a - 4a^3b) =?$

Using your knowledge of powers, especially with base 10, evaluate the following (*without using your calculator*). Show your working. You can check your final answers with your calculator if you wish.

1. $\dfrac{0.00006}{2000} =$

2. $\dfrac{0.05 \cdot 200}{0.002} =$

3. $\dfrac{0.0009}{7000}\dfrac{1}{30}\dfrac{4.9 \cdot 10^5}{0.1} =$

4. $(0.0005)^2 =$

Simplify each of the following:

1. $2^5 \cdot 2^6$

2. $3^4 \cdot 3^7$

3. $5^3 \cdot 5^4 \cdot 5^6$

4. $3 \cdot 3^2 \cdot 3^5$

5. $\dfrac{7^5}{7^2}$

6. $\dfrac{3^{12}}{3^4}$

7. $\dfrac{2^8}{2^4}$

8. $\dfrac{10^5 \cdot 10^3}{10^4}$

9. $\dfrac{3^7 \cdot 3^6}{3^5}$

10. $\dfrac{2^5 \cdot 2^6}{2^2 \cdot 2^7}$

11. $\left(5^3\right)^4$

12. $\left(3 \cdot 5^4\right)^2$

13. $\left(10^3\right)^4$

14. $\left(2 \cdot 3^2 \cdot 5^3\right)^4$

15. $\left(\dfrac{3}{4}\right)^3$

16. $\left(\dfrac{5^2}{7^3}\right)^4$

SI Prefixes and Units

Work out the following in the correct SI units and using standard SI prefixes.

1. $\dfrac{3 \cdot 10^5 \mathrm{m}^2}{3 \cdot 10^2 \mathrm{m}} =$

2. $\dfrac{5 \cdot 10^3 \mathrm{ms}^{-2}}{5 \cdot 10^{-2} \mathrm{s}^{-2}} =$

3. $\dfrac{8 \cdot 10^3 \mathrm{ms}^{-2}}{2 \cdot 10^3 \mathrm{s}^{-1}} =$

4. $\dfrac{8 \cdot 10^2 \mathrm{mol} \cdot s^{-1}}{2 \cdot 10^8 \mathrm{s}^{-1}} =$

5. $5\dfrac{0.01 \mathrm{mol}^2}{1000 \mathrm{mol}} =$

Logarithms

Use the rules for manipulating logarithms to simplify the following expressions.

1. $\log(ab^2) - 2\log b =$

2. $\log\left(\frac{a^2}{b^2}\right) + 2\log b =$

3. $\log\left(3^2\right) - \log 3 - \log 18 =$

4. Express x in terms of y. All other terms are constants.
$y = (1 + y^2)e^x$

5. Express x in terms of y. All other terms are constants.
$y = -AB\ln x$

Functions

Rearrange the following into straight line form. What are the gradients (slopes) and intercepts (on the y-axis) of these straight lines? Remember that gradients have signs. You don't need to plot these functions to obtain these values.

1. $y - 3x = 1$

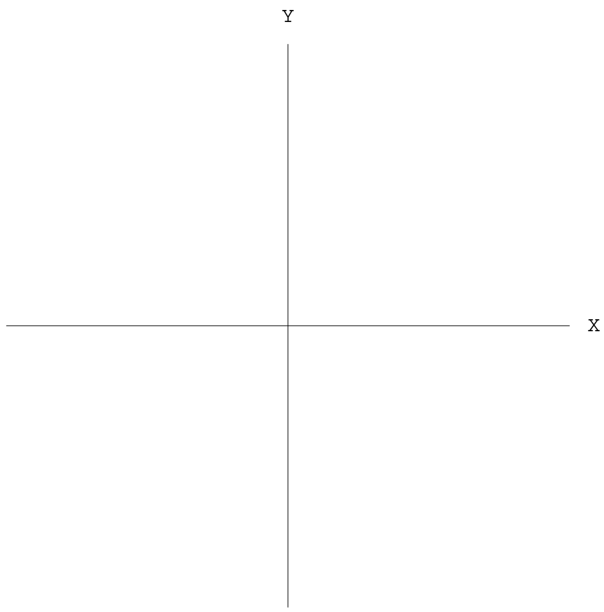
2. $2y - 3x - 1 = x$

3. $0 = 4y + 5(2x - 3) + 10$

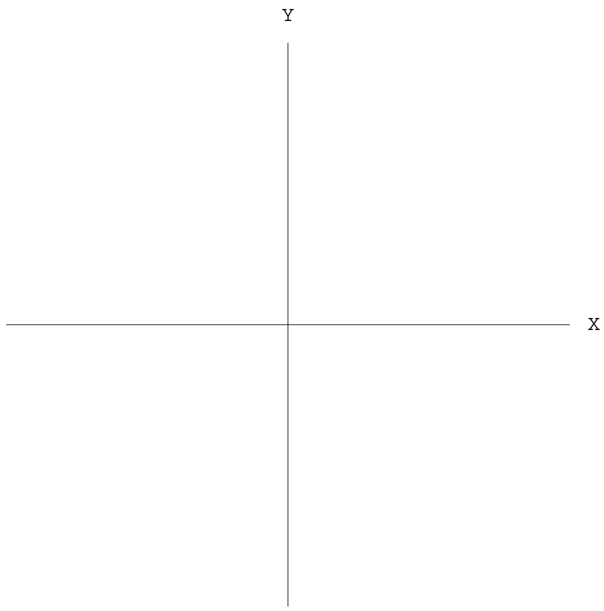
Graphs

Sketch graphs of the following functions. The scales have been deliberately omitted from the axes. This has been done to make you think about the scales yourself. You should work out a few points by substituting values into the equations before plotting them. It is not critically important that your plots should be perfectly proportioned, but they should have the right shape. For each plot, try and say something about the way the gradient changes, if at all. Does y increase when x increase? Is the gradient always the same sign (positive or negative)?

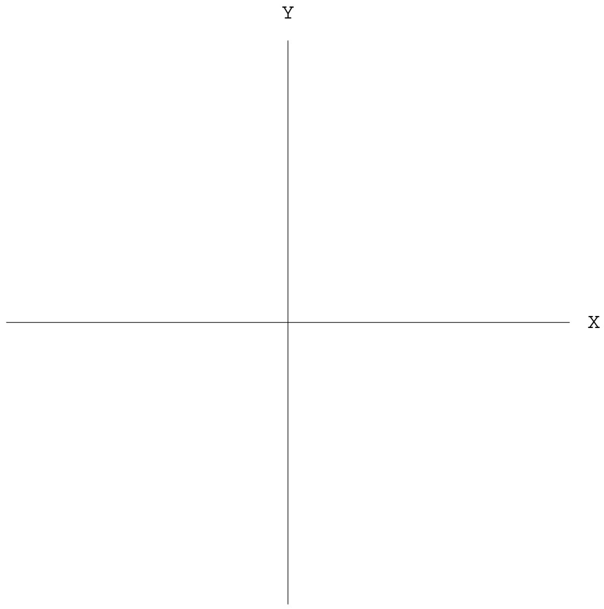
1. $y = x^2 - 6x + 2$



2. $y = \frac{5}{x} + 7$

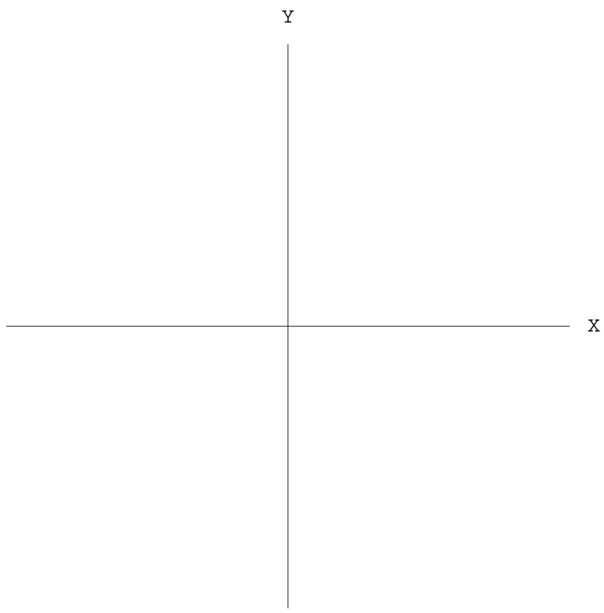


3. $y = \frac{20x}{x+5}$. How does y vary with x? What is the maximum value y can take?



4. Plot these two functions on the axes below. You will certainly need your calculator in order to do this. Make sure you are using the natural logarithm function and not $\log_{10}$

$$y = \ln x \text{ and } y = 2.718^x$$



What do you notice about these plots? Is there any relationship between them? From your graph, estimate the gradient at $x = 1$ for the function $y = 2.718^x$. What do you notice about this value? (Hint: For the first function, use values of x from 0.1 to 1.5, and for the second function use values of x from -1.0 to 1.0).

20 More Exercises: Solutions

Fractions

Try to simply the following fractions.

1. $\frac{12}{5} + \frac{3}{4} = \frac{48}{20} + \frac{15}{20} = 3\frac{3}{20}$

2. (Do the bracket first)
$\frac{2}{5} \cdot (\frac{1}{3} + \frac{2}{5}) = \frac{2}{5} \cdot (\frac{5}{15} + \frac{6}{15}) = \frac{2}{5} \cdot \frac{11}{15} = \frac{22}{75}$

3. $\frac{x}{y} + \frac{2x}{3y} = \frac{3x}{3y} + \frac{2x}{3y} = \frac{5x}{3y}$

4. $(\frac{5}{6} \div \frac{1}{2}) \cdot \frac{3}{2} = (\frac{5}{6} \div \frac{2}{1}) \cdot \frac{3}{2} = \frac{10}{6} \cdot \frac{3}{2} = \frac{5}{2}$

5. $\frac{a}{b} - (\frac{2}{c} \cdot \frac{d}{3}) = \frac{a}{b} - (\frac{2d}{3c}) = \frac{3ac}{3bc} - \frac{2bd}{3bc} = \frac{3ac-2bd}{3bc}$

6. Note: $(b - c) = -1 \cdot (c - b) = -(c - b)$ then you can cancel these terms out and simplify:
$\frac{a^3-b}{b-c} \div \frac{a}{c-b} = \frac{a^3-b}{b-c} \cdot \frac{c-b}{a} = \frac{a^3-b}{b-c} \cdot \frac{-(b-c)}{a} = \frac{b-a^3}{a}$

7. $\frac{d^2}{c} - \frac{d^2}{c^2} = \frac{cd^2}{c} - \frac{d^2}{c^2} = \frac{cd^2-d^2}{c^2} = \frac{d^2(c-1)}{c^2}$

8. $\frac{\frac{4x}{5y}}{10y^2} = \frac{4x}{5y} \div 10y^2 = \frac{4x}{5y} \cdot \frac{1}{10y^2} = \frac{4x}{50y^3} = \frac{2x}{25y^3}$

Algebraic Expressions and Equations

Simplify the following expressions by finding common factors.

1. $a \cdot b + a \cdot c = a(b + c)$

2. $a^2 \cdot b + a \cdot c = a(ab + c)$

3. $\frac{a^2c}{b} + \frac{a^3d}{a^2} = a^2(\frac{c}{b} + \frac{ad}{a^2}) = a^2(\frac{c}{b} + \frac{d}{a})$

Rearrange the following equations.

1. Express b in terms of c, b and d, i.e.,determine $b =$?
The simplest way to solve this one is to isolate the term in b on the left hand side by subtracting ad from both sides. Then you can factorise in a on the right hand side, before finally dividing both sides by c.
$bc + ad = d^2 - ad$
$bc = d^2 - ad - ad = d^2 - 2ad = d(d - 2a)$
$b = \frac{d(d-2a)}{c}$ or $\frac{d^2-2ad}{c}$

2. Express a in terms of c, b and d.
Factorise in a on the left hand side, and then divide both sides of the equation by a. You could also do this second step first if you wish (but be careful).
$a \cdot d^2 - b \cdot a = c \cdot a^2 \;\Rightarrow\; a(d^2 - b) = ca^2$
$\frac{a(d^2-b)}{a} = \frac{ca^2}{a} = d^2 - b = ca$
$a = \frac{d^2-b}{c}$

3. Express c in terms of a and b for the following expression.
(Treat the $a+b$ term as a single term, and then you can divide both sides of the equation by $(a+b)$. Similarly, you can then multiply both sides of the equation by $(c+1)$. Then it is simply a matter of subtracting 1 from both sides.)
$\frac{b-1}{c+1} = a+b$
$c+1 = \frac{b-1}{a+b}$
$c = \frac{b-1}{a+b} - 1$

Variables and Constants

In the following problems, rearrange the equations to give y in terms of x and any constants. Remember that in these examples, x and y are the only *variables* and that all other terms are *constants* or *coefficients*. For each example, also work out whether y increases or decreases when x increases.

1. $A \cdot y + C \cdot x = 12$. Take Cx from both sides. Then divide both sides by A.
$Ay = 12 + Cx$
$y = \frac{12-Cx}{A} \quad y \downarrow$ as $x \uparrow$

2. $c \cdot y^2 - 17 = 18x$ Add 17 to both sides. Divide both sides by c. Then take square roots. y increases if we only take the positive root.
$cy^2 - 17 = 18x$
$cy^2 = 18x + 17$
$y^2 = \frac{18x+17}{c}$
$y = \sqrt{\frac{18x+17}{c}} \quad y \uparrow$ as $x \uparrow$

3. $\frac{C}{1+y} = Z \cdot x$. This is just like the earlier rearrangement. You can treat the $(1+y)$ as a single term, and multiply both sides of the equation by $(1+y)$ and divide both sides by Zx. Then subtract 1 from both sides.
$1 + y = \frac{C}{Zx}$
$y = \frac{C}{Zx} - 1 \quad y \downarrow$ as $x \uparrow$

Simple Powers

1. Show that $\frac{10^m}{10^n} = 10^{m-n}$

$10^m \cdot \frac{1}{10^n} = 10^m 10^{-n} = 10^{m-n}$

2. Show that $10^{(a-b)}10^{(b-a)} = 1$

$10^{(a-b)}10^{(b-a)} = 10^{(a-b)+(b-a)} = 10^{a-a+-b} = 10^0 = 1$
or
$10^{(a-b)}10^{(b-a)} = \frac{10^{(a-b)}}{10^{-(b-a)}} = \frac{10^{(a-b)}}{10^{(a-b)}} = 1$

3. Simplify $10^a 10^a 10^a 10^a 10^a =?$

$= 10^{a+a+a+a+a} = 10^{5a}$

4. Simplify $(10^a)^3(10^a)^{-4} = ?$

$= \frac{(10^a)^3}{(10^a)^4} = \frac{1}{10^a} = 10^{-a}$

5. Simplify $\frac{1}{a^2}(3a - 4a^3b) = ?$

$\frac{3a}{a^2} - \frac{4a^3b}{a^2} = \frac{3}{a} - 4ab$ or $\frac{3-4a^2b}{a}$

Using your knowledge of simple powers, especially with base 10, evaluate the following (*without using your calculator*). Show your working. You can check your final answers with your calculator if you wish.

1. $\frac{0.00006}{2000} = \frac{6 \cdot 10^{-5}}{2 \cdot 10^3} = \frac{6}{2} \cdot 10^{-8} = 3 \cdot 10^{-8}$

2. $\frac{0.05 \cdot 200}{0.002} = \frac{5 \cdot 10^{-2} \cdot 2 \cdot 10^2}{2 \cdot 10^{-3}} = \frac{2 \cdot 5 \cdot 10^0}{2 \cdot 10^{-3}} = 5 \cdot 10^3 = 5000$

3. $\frac{0.0009}{7000} \frac{1}{30} \frac{4.9 \cdot 10^5}{0.1} = \frac{9 \cdot 10^{-4} \cdot 49 \cdot 10^4}{7 \cdot 10^3 \cdot 3 \cdot 10^1 \cdot 10^{-1}} = \frac{3 \cdot 10^{-4} \cdot 7 \cdot 10^4}{10^3} = 21 \cdot 10^{-3} = 2.1 \cdot 10^{-2} = 0.021$

4. $(0.0005)^2 = (5 \cdot 10^{-4})^2 = 25 \cdot 10^{-8} = 2.5 \cdot 10^{-7}$

Simplify each of the following:

1. $2^5 \cdot 2^6 = 2^{11}$

2. $3^4 \cdot 3^7 = 3^{11}$

3. $5^3 \cdot 5^4 \cdot 5^6 = 5^{13}$

4. $3 \cdot 3^2 \cdot 3^5 = 3^8$

5. $\frac{7^5}{7^2} = 7^3$

6. $\frac{3^{12}}{3^4} = 3^8$

7. $\frac{2^8}{2^4} = 2^4$

8. $\frac{10^5 \cdot 10^3}{10^4} = 10^4$

9. $\frac{3^7 \cdot 3^6}{3^5} = 3^8$

10. $\frac{2^5 \cdot 2^6}{2^2 \cdot 2^7} = 2^2$

11. $(5^3)^4 = 5^{12}$

12. $(3 \cdot 5^4)^2 = 3^2 \cdot 5^8$

13. $\left(10^3\right)^4 = 10^{12}$

14. $(2 \cdot 3^2 \cdot 5^3)^4 = 2^4 \cdot 3^8 \cdot 5^{12}$

15. $\left(\frac{3}{4}\right)^3 = \frac{3^3}{4^3}$

16. $\left(\frac{5^2}{7^3}\right)^4 = \frac{5^8}{7^{12}}$

SI Prefixes and Units

Work out the following in the correct SI units and using standard SI prefixes.

1. Keep the values and units separate. Do values first, units last (or the other way around) but not together. Treat the units like other index values.

$\frac{3\cdot10^5\text{m}^2}{3\cdot10^2\text{m}} = 10^3 \cdot \text{m}^2\text{m}^{-1} = 10^3\text{m} = 1000\text{m}$

2. $\frac{5\cdot10^3\text{ms}^{-2}}{5\cdot10^{-2}\text{s}^{-2}} = \frac{10^3\text{ms}^{-2}}{10^{-2}\text{s}^{-2}} = 10^{3+2}\text{m} = 10^5\text{m}$

3. Keep the 8 divided by 2 separate too. Treat the powers of 10 together. Calculate the correct units independently. Rearrange (if necessary) as the final step.

$\frac{8\cdot10^3\text{ms}^{-2}}{2\cdot10^3\text{s}^{-1}} = 4 \cdot 10^0\text{ms}^{-1} = 4\text{ms}^{-1}$

4. $\frac{8\cdot10^2\text{mol}\cdot\text{s}^{-1}}{2\cdot10^8\text{s}^{-1}} = 4 \cdot 10^{2-8}\text{mol} \cdot \text{s}^{-1}\text{s} = 4 \cdot 10^{-6}\text{mol}$

5. $\frac{0.01\text{mol}^2}{1000\text{mol}} = \frac{1\cdot10^{-2}}{1\cdot10^3}\text{mol} = 10^{-5}\text{mol}$

Logarithms

Use the rules for manipulating logs to simplify the following expressions.

1. Treat the $\log(ab^2)$ term as $\log(ac)$ where $c = b^2$. Then $\log(ac) = \log a + \log c$ (but $c = b^2$) so... Write it now as $= \log a + \log b^2$. Use $2\log b = \log b^2$ to finish it off.

$\log(ab^2) - 2\log b = \log a + \log b^2 - \log b^2 = \log a$

2. $\log(\frac{a^2}{b^2}) + 2\log b = \log a^2 - \log b^2 + logb^2 = \log a^2 = 2\log a$

3. $\log(3^2) - \log 3 - \log 18 = 2\log 3 - \log 3 - \log(6 \cdot 3) = \log 3 - \log 6 - \log 3 = -\log 6$

4. Express x in terms of y. All other terms are constants.
Rearrange equation to isolate x term. Take natural logs of both sides. Rearrange the left-hand-side.

$y = (1 + y^2)e^x$ leading to $e^x = \frac{y}{1+y^2}$ leading to $x = \ln(\frac{y}{1+y^2})$

5. Express x in terms of y. All other terms are constants.
Don't confuse exponentials and logarithms. Remember how to resolve $y = e^x$. Do not forget $\ln e = 1$.

$y = -AB\ln x$ leading to $\ln x = -\frac{y}{AB}$ leading to $x = e^{-\frac{y}{Ab}}$

Functions

Rearrange the following into straight line form. What are the gradients (slopes) and intercepts (on the y-axis) of these straight lines? Remember that gradients have signs. You do not need to plot these functions to obtain these values.

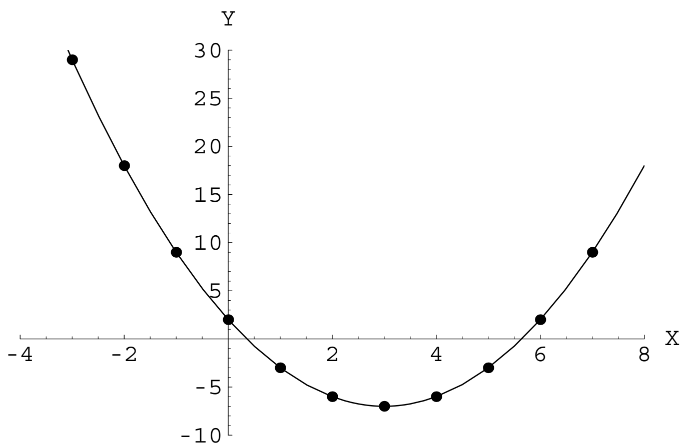
1. $y - 3x = 1 \Rightarrow y = 3x + 1$
$m = 3,\ c = 1$

2. $2y - 3x - 1 = x \Rightarrow 2y = x + 3x + 1 \Rightarrow 2y = 4x + 1 \Rightarrow y = 2x + 1/2$
$m = 2,\ c = 0.5$

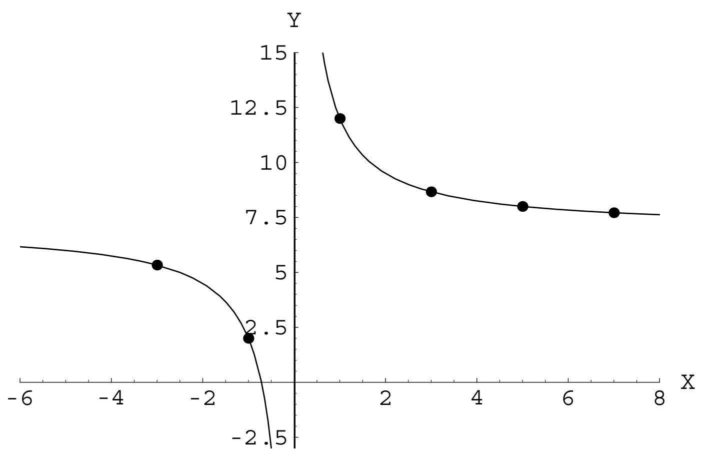
3. $0 = 4y + 5(2x - 3) + 10 \Rightarrow 4y + 10x - 15 + 10 = 0 \Rightarrow 4y = -10x + 5 \Rightarrow$
$y = -\frac{10}{4}x + \frac{5}{4} = -2.5x + 1.25$
$m = -2.5,\ c = 1.25$

Graphs

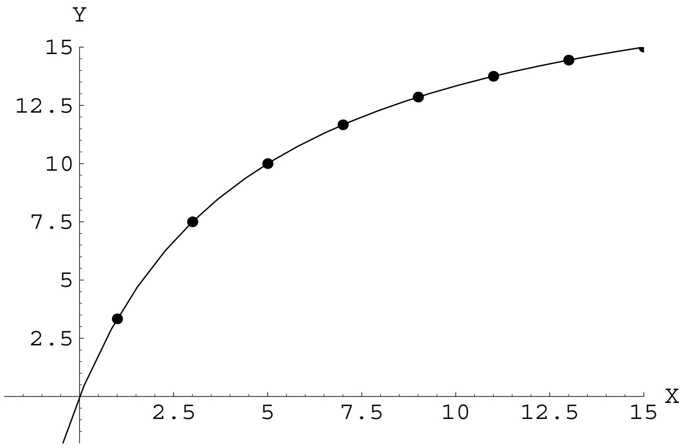
1. $y = x^2 - 6x + 2$. The gradient starts out negative and becomes positive with a point of inflection at $x = 3$.



2. $y = \frac{5}{x} + 7$. The function decreases as x increases, but is not determined at $x = 0$. It converges to $y = 7$ at very low and very high x.



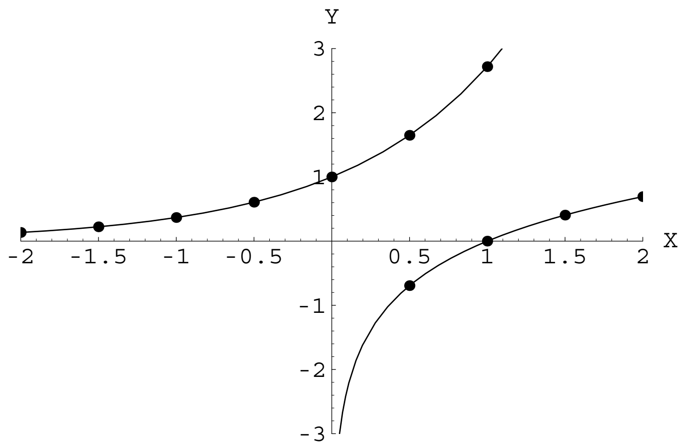
3. $y = \frac{20x}{x+5}$. The function increases with x, is not determined at $x = -5$, and slowly increases until a maximum value of 20.



4. Plot these two functions on the axes below.

$$y = \ln x \text{ and } y = 2.718^x$$

They are inverse functions. $e = 2.718$, so gradient at $x = 1$ is e. This holds true at every point, so that the gradient of e^x always equals e^x.



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