Naths from Scratch for Biologists Alan J. Cann



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Maths from Scratch for Biologists

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Preface

This book arose from my own need for a text that I would be happy to recommend to my students. Although there is no particular shortage of volumes claiming to help biologists with mathematics, all those I am familiar with have one of two flaws. Either they are written by well-meaning mathematicians and pay scant attention to biology, or they are not appropriate for the level at which most of the problems lie – new college students who do not have much confidence in approaching mathematical problems, in spite of extensive prior exposure to mathematics in school.

I make no claim to be a mathematical genius. Indeed, I believe my struggle to explain the material in an easily accessible form is one of the strengths of this book, bringing me closer to the students I am trying to communicate with. I reject any charges of 'dumbing down' - anyone who has ever tried to help a panic-stricken student in the grip of maths phobia will know that a calming but not patronizing voice is an essential attribute in these circumstances. Throughout, my intention is to provide a highly accessible text for students who, with or without formal mathematics qualifications, are frightened by the perceived 'difficulty' of mathematics and unwilling, inept or inexperienced in applying mathematical skills. To accommodate these students, many of whom opt to undertake studies in biology in the belief (conscious or unconscious) that this is a way of pursuing a scientific career while avoiding mathematics, the ethos of the book is consciously informal and intended to be confidence-building.

The maths in this volume has been checked vigorously, but I cannot guarantee that the text is entirely free of numerical errors. In addition there may be some passages where the subject matter is not expressed as clearly as I would have hoped. I rely on readers to point these out to me – as I am sure they will.

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Maths in Biology

Mathematics, from the Greek, manthano, 'to learn'

Some people opt to undertake studies in biology in the belief (conscious or unconscious) that this is a way of pursuing a scientific career while avoiding maths. This book is designed to be accessible to students who, with or without formal mathematical qualifications, are frightened by the perceived 'difficulty' of maths and hence are unwilling to apply what mathematical skills they might have. Have you ever noticed when you have been taught how to solve a mathematical problem, that you still don't know why you need to do a particular step? This is the root of many problems with maths, so this book will try explain the *why* of addition to the *how*. Sometimes, these maths. in explanations may seem unnecessary, but I urge you not to skip them – understanding why you need to do something is the key to remembering how to do it. The intention is to be informal and confidence-building to ensure that all readers will gain a general appreciation of basic mathematical, statistical and data handling techniques appropriate to biology. I will try to explain the jargon which confuses the non-numerically minded.

In subsequent chapters, we will look at manipulating numbers, units and conversions, molarities and dilutions, areas and volumes, exponents and logs and statistics. However, the basic advice in this chapter is really the most important part of the book, so please keep reading.

1.1. What can go wrong?

It is easy to make mistakes with maths. One answer looks much like another, so how can you tell if it is right or not? Look at some examples of the sort of mistakes it is all too easy to make. Everyone knows that numbers are meaningless without the units which define what they mean (more of this in Chapter 3). Even if we avoid the elementary mistake of forgetting this and giving an answer of '33.6' (33.6 what? volts? metres? frogs?), things are not always simple. Consider the following questions:

An aquarium has internal dimensions of 100 * 45 * 45 cm. What is its volume in litres?

This is fairly simple. Calculate the volume in cubic centimetres then convert to litres. 1 litre = 1000 cm^3 so divide by 1000:

 $100 * 45 * 45 = 202500 \, \text{cm}^3 \div 1000 = 202.5$ litres

However, life is not always that simple. If the same calculation is given in a different way, it is not as easy to answer:

An aquarium has internal dimensions of 39 * 18 * 18 inches. What is its volume in litres?

This is harder because the units in which the data is given and those in which the answer is required are from different systems of measurement. In real life, this happens all too frequently.

WARNING!

Using mixed units is dangerous (see Chapter 3).

To avoid mistakes we need to convert the units so that they are consistent throughout. However, this means there are two ways to do the calculation:

1. Convert inches to centimetres (1 inch = 2.54 cm), then perform the calculation as above,

(39 * 2.54) * (18 * 2.54) * (18 * 2.54)

= 99.06 * 45.72 * 45.72

 $= 207\,066.94\,\text{cm}^3 \div 1000 = 207.067$ litres

2. Calculate the volume in cubic inches, then convert to litres (1 cubic inch = 0.0164 litres, so conversion factor = 0.0164):

 $39*18*18 = 12\,636*0.0164 = 207.23$ litres

In general, the best method is the one which requires fewer conversions and fewer steps (b). However, this depends on what conversion factors you have to hand – if you have to calculate a conversion factor from cubic inches to litres, it may be better to use (a). Note that the accuracy of conversions from one unit to another depends on the number of significant figures used. Significant figures are: 'the minimum number of digits needed to write a given value (in scientific notation) without loss of accuracy'. The **most** significant figure is the left-most digit, the digit which is known most precisely. The **least** significant figure is the right-most digit, the digit which is known least precisely.

Significant figures are important when reporting scientific data because they give the reader an idea of how accurately data has been measured. Here are the rules:

1. All **non-zero numbers** (1, 2, 3, 4, 5, 6, 7, 8, 9) are always significant, e.g. 12 345 has five significant figures; 1.2345 also has five significant figures.

2. All **zeroes between non-zero numbers** are always significant, e.g. 10 002 has five significant figures; 1.0002 also has five significant figures.

3. All zeroes which are to the right of the decimal point and at the end of the number are always

significant. This rule sometimes confuses people since they cannot understand why. The reason is because these zeros determine the accuracy to which the number has been calculated, e.g. 1.2001 has five significant figures; 12 000 has two significant figures; 1.0200 has five significant figures (here the 'placeholder' zero to the right of the decimal point is significant because it is between non-zero numbers).

4. All other zeroes are not significant numbers, e.g. 1 000 000 has one significant figure (the zeros are just 'placeholders'); 1 000 000.00 has three significant figures (the 1 and the two zeros at the end of the number); 0.0200 has three significant figures (the 'placeholder' zero to the right of the decimal point is not significant since it is not between non-zero numbers); 1 000 000.01 has nine significant figures (zeros between non-zero numbers).

Using the appropriate number of significant figures in calculations is important, since it prevents loss of accuracy. give However, computers and calculators frequently ridiculously large numbers of significant figures - way beyond the accuracy with which a measurement could be made. For this reason, and for ease of performing calculations (particularly when estimating, see below), it is often necessary to 'round off' the number of significant figures in a number. Note that this is 'rounding off', not 'rounding up', which leads to inaccuracy and errors. 'Rounding up' a digit which is followed by a 5 (e.g. 5.45) becomes 5.5) introduces errors in calculations because the digits one, two, three and four are 'rounded down' (four possibilities) but the digits five, six, seven, eight and nine are all 'rounded up' (five possibilities). 'Rounding off' avoids this error:

1. If the digit following the figure that is to be the last digit is **less than 5**, drop it and all the figures to the

right of it.

2. If the digit following the figure that is to be the last digit is **more than 5**, increase by 1 the digit to be rounded, i.e. the preceding figure.

3. If the digit following the figure that is to be the **last digit is 5**, round the preceding figure so that it is even.

Examples

Round 123.456789 to three significant figures = 123 (rule a: round the number off)

Round 123.456789 to five significant figures = 123.46 (rule b: round the last digit up)

Round 123.456789 to four significant figures = 123.4 (rule c: make the last digit even)

Round 123.356789 to four significant figures = 123.4 (rule c: make the last digit even)

Round 123.456799 to eight significant figures = 123.45680 (note that 9 rounds up to 10, not down to 0).

1.2. Estimating

Whenever you have calculated an answer, always make a rough estimate to see if your answer is sensible and to avoid mistakes.

Calculators and computers spit out numbers at the press of a key, but are the answers right? Estimating is a vital skill if you wish to become confident and proficient with numbers. However, estimating and calculating are **not** the same thing and it is important to understand the difference. Where calculation attempts to produce the most accurate answer possible (within limits of experimental error), estimation deliberately avoids accuracy in order to simplify working out the answer.

1. If the question is 6 * 5 and your calculated answer is 4, could this possibly be correct? Could the answer be *less* than the numbers multiplied together?

2. If you are asked to solve an equation for x (Chapter 2) and your answer is 7x, something is wrong.

3. When you calculate the answer to $6.42213 \div 2.36199$ to six significant figures (2.71895), make an estimate to one or two significant figures to check: $6 \div 2 = 3$, so 2.71895 looks right, whereas 27.1895 looks wrong.

If you have used a computer or calculator to calculate an answer, it is best to work out the estimate in your head or on a scrap of paper in order to check for any errors you may have introduced by using the machine. This is why estimation involves simplifying the calculation - an estimate is not meant to be accurate, but it should be easy to calculate and a reliable check. Aside from performing the calculation, estimating is the most important part of ensuring that answers to problems are correct. Some calculations in biology are complex and involve many steps (Chapter 5). Estimating is particularly important here to ensure the answer looks sensible. Manipulation of numbers and equations may not give a numerical answer but a mathematical term (e.g. 3y - 2). Here, the trick is to check your answer by substituting back into the original equation to see if it works (Chapter 2).

1.3. How to use this book

If you have been told to use this book as part of a particular course, you had better follow the instructions given by whoever is running the course. Other than that, you can use this book however you want. Some people may want to read though all (or most) of the chapters in order. Others may skip sections and dip into chapters that they feel they need. Either way is fine, as long as you can solve problems consistently and accurately and, most importantly, that you gain the knowledge and confidence to start to try to work out possible answers.

1.4. Mathematical conventions used in this book

To make them easier to read, numbers with more than four digits are split into groups of three digits separated by spaces (not commas), e.g. 9 999 999 is nine million, nine hundred and ninety nine thousand, nine hundred and ninety nine. I have also chosen to use the asterisk (*) as a multiplication sign rather than 'x' or a dot, since these are sometimes confusing when written.

Manipulating Numbers

Algebra (from the Arabic, al-jabr, 'the reduction') – a form of maths where symbols are used to represent numbers

LEARNING OBJECTIVES:

On completing this chapter, you should be able to:

- understand the basic rules of algebra;
- perform simple algebraic manipulations;
- identify and manipulate fractions.

Arithmetic is concerned with the effect of operations (e.g. addition, multiplication, etc.) on specified numbers. In algebra, operations are applied to variables rather than specific numbers. Why? Here is a classic example:

John is 10 years old. His father is 35 years old. After how many years will the father be twice as old as the son?

You could try to find the answer by experimenting with different numbers, but this is laborious. The better way is to treat this an algebra problem and write the problem as an equation which we can then solve.

Let the father be twice as old as the son in x years time. The son will then be (10 + x) years old and the father will be (35 + x) year old:

2(10+x) = 35+x

Therefore,

20 + 2x = 35 + x

Simplify this by subtracting x from each side to keep the equation balanced:

20 + x = 35

Simplify by subtracting 20 from each side to keep the equation balanced:

x = 15 years (son is 25 and father is 50)

2.1. Manipulating numbers

To manipulate numbers, you need to know the rules. In mathematics, this is known as the 'Order of Operations' – an internationally agreed set of arbitrary rules which allows mathematicians the world over to arrive at the same answers to problems:

BEDMAS	Order of operations – the order in which operations are performed:
	Brackets (work from the inside out)
	Exponents (see Chapter 6)
	Division
	Multiplication
	Addition (left to right)
	Subtraction (left to right)

In algebra, there are two sorts of statement which you need to be able to recognize:

1. A mathematical expression is a string of symbols which describes ('expresses') a (potential) calculation using operators (symbols indicating an operation to be performed, e.g. plus, minus, divide, etc.) and operands (symbols which the operators act on), e.g.

2x + y

Expressions do not contain an equal sign, but can often be simplified, that is converted to a simpler form containing fewer terms.

2. A mathematical equation contains an equal sign. The terms (groups of numbers or symbols) on both sides of the equal sign are equivalent, e.g.

2x = y

You can do anything you want to an equation, as long as you treat both sides equally. To solve an equation, you must find the values(s) of the variable(s) which make the equation true, that is both terms equal. A mathematical formula also represents a relationship between two or more variables (symbols or terms whose values may vary) and/or constants (numbers or terms whose value is fixed), e.g.

 $e = mc^2$

A formula is simply an equation which expresses a rule or principle as symbols, i.e. the recipe which allow you to calculate the value of the terms.

2.2. Solving equations

To 'solve' an equation, you must find the value(s) of the variable(s) which make the equation 'true', i.e. makes the terms on either side of the equal sign equal. There are seven steps to follow in order to solve an equation ('**BICORS**'):

1. **Brackets** – if an equation contains brackets ('**B**'; also known as parentheses, which group symbols together), solve these first. Multiply each item inside the bracket by the symbol just outside the bracket.

2. **Isolate** – move all the terms containing a variable to the same side of the equal sign ('isolate' the variable; '**I**').

3. **Combine** – combine like terms, that is if an equation contains more than one term containing the same variable (e.g. z), combine them ('**C**').

4. **Opposite** – for each operator in an equation, perform the opposite process ('**O**'), for example, if the equation contains a minus sign, add, or if it contains a multiplication sign, divide.

5. **Reduce** – reduce ('**R**') fractions to their lowest terms (e.g. 33/11 = 3/1 = 3).

6. **Substitute** – finally, *always* check your answer by putting this value back into the original equation ('substitute' for the variable; **'S**').

You will not always have to perform all of these steps, depending on the equation. For example, if an equation does not contain any brackets, just move on to the next step, but do go through all the steps in order. Solving equations often involves simplifying the expressions they contain, which means getting all similar terms (e.g. x) on the same side of the equal sign. All of this sounds more complicated than it actually is and is best illustrated by some examples.

Examples

Solve for x (i.e. find the value of x that makes the equation true):

4x = 2(6x) - 4

Expand *Brackets* (Bicors):

4x = 12x - 4

Simplify to *Isolate* (blcors) the variable:

4x - 12x = -4

Combine (**biCors**) like terms:

-8x = -4

Carry out the *Opposite* (bicOrs) process:

8x = 4

Divide by the coefficient of the variable (variable = x, coefficient = 8):

8x/8 = 4/8

Simplify the equation by *Reducing* (**bicoRs**) fractions to their lowest terms:

x = 1/2

Check the answer by **Substituting** (**bicorS**) it back into the original equation:

$$4(1/2) = 2[6(1/2)] - 4$$

$$2 = 2(3) - 4$$

$$2 = 6 - 4$$

$$2 = 2$$

Solve for *x* (find the value of *x*):

5(x-4) = 20
5x - 20 = 20
5x = 40
x = 40/5 = 8
5(8-4) = 20
5(4) = 20
20 = 20

Solve for *z* (find the value of *z*):

	z/4 + 4 = 16
(B, I, C)O (−4):	z/4 = 12
O(R) (*4):	z = 48
S:	48/4 + 4 = 16
	12 + 4 = 16
	16 = 16

Note that equations do not always have a numerical answer – sometimes the value of the variable can only be expressed in terms of its relationship with another variable:

Solve for *x* (find the true value of *x*):

	2x + 4 = 2y + 4
(B, I, C)O (−4):	2x = 2y + 4 - 4
R (/2):	2x=2y
	x = y
S:	2y + 4 = 2y + 4
	2y = 2y
	y = y

Solve for *t* (find the true value of *t*):

(B, I, C)O (-5): (R)S: t + 5 = x t = x - 5 x - 5 + 5 = xx = x

There are two main sorts of equation:

1. Linear equations – equations where the exponents of all the variables (powers of the variable, see Chapter 6) are equal to 1 and there is no multiplication between variables. Graphs of linear equations plot as straight lines, e.g. y = 2x + 3.

2. Non-linear equations – equations where the exponent (power, see Chapter 6) of one or more of the variables is not equal to 1 or there is any multiplication between variables. Graphs of non-linear equations plot as curves. This includes all polynomial functions [e.g. $f(x) = 4x^3 + 3x^2 + 2x + 1$], such as:

• quadratic equations, e.g. $x^2 + 5x + 6 = 0$;

• cubic equations, e.g. $x^3 + bx^2 + cx + d = 0$, etc.

Although non-linear equations are common in biology, this chapter is primarily concerned with linear equations. Many people find the idea of solving equations difficult. The answer to this is to practise. For this, you can use the problems at the end of this chapter. When you become more confident, you can move on to non-linear equations. Word problems are particularly useful to help you think through what you are being asked, but can be surprisingly difficult for some people. In real life, information is frequently presented in this form rather than as an equation. The trick is to start by converting words into numbers. Again, this is a skill that you can acquire by practice – use the problems at the end of this chapter.

2.3. Why do you need to know all this?

You need to know all this because you cannot go very far in biology without encountering topics like enzyme kinetics.

Example

In an enzyme-catalysed reaction, the reactant (S) combines reversibly with a catalyst (E) to form a complex (ES) with forward and reverse rate constants of k_1 and k_{-1} , respectively. The complex then dissociates into product (P) with a reaction rate constant of k_2 and the catalyst is regenerated:

 $E + S \xrightarrow[k_{-1}]{k_1} ES \xrightarrow{k_2} E + P$

From this can be derived the Michaelis-Menten equation:

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

where v = reaction rate (velocity), [S] = substrate concentration, $V_{\text{max}} =$ maximum rate, $K_{\text{m}} =$ Michaelis-Menten constant = substrate concentration at half the maximal velocity (V), i.e. $K_{\text{m}} = [S]$ when $V = V_{\text{max}}/2$.

 $K_{\rm m}$ measures enzyme/substrate affinity – a low $K_{\rm m}$ indicates a strong enzyme – substrate affinity and vice versa. However, $K_{\rm m}$ is not just a binding constant that measures the strength of binding between the enzyme and substrate. Its value includes the affinity of substrate for enzyme, but also the rate at which the substrate bound to the enzyme is converted to product (see Table 2.1).

For ribonuclease, if $[S] = K_m = 7.9 * 10^{-3}$ **M**, then substituting into the Michaelis-Menten equation:

$$v = \frac{V_{\max} * 7.9 * 10^{-3}}{7.9 * 10^{-3} + 7.9 * 10^{-3}}$$

Table 2.1 Km for various enzyme reactions

Enzyme	Reaction catalysed	$K_{\mathbf{m}}\left(\mathbf{M}\right)$
Chymotrypsin	$Ac-Phe-Ala + (H_2O) \rightarrow Ac-Phe + Ala$	$1.5 * 10^{-2}$
Carbonic anhydrase	$HCO_3^- + H^+ \rightarrow (H_2O) + CO_2$	$2.6 * 10^{-2}$
Ribonuclease	Cytidine 2',3' cyclic phosphate +	$7.9 * 10^{-3}$
	$(H_2O) \rightarrow cytidine 3'-phosphate$	
Pepsin	$Phe-Gly + (H_2O) \rightarrow Phe + Gly$	$3 * 10^{-4}$
Tyrosyl-tRNA synthetase	Tyrosine + tRNA→ tyrosyl-tRNA	$9 * 10^{-4}$
Fumarase	$Fumarate + (H_2O) \rightarrow malate$	$5 * 10^{-6}$

Simplifying this by dividing the top and bottom of this equation by $7.9 * 10^{-3}$,

 $K_{\rm m} = [S], \quad V = V_{\rm max}/2$

S0

 $v = \frac{V_{\max} * 1}{2}$

When $[S] = K_{m}$, $v = V_{max}/2$ and hence the Michaelis-Menten equation works.

2.4. Fractions

When you perform algebraic manipulations, you soon encounter fractions, which means parts of numbers. We all learned to manipulate fractions in school, but in these days of computers and calculators, many people have forgotten how to do this. Remembering how to multiply and divide fractions causes particular problems.

All fractions have three components – a numerator, a denominator and a division symbol:

Numerator

Denominator

The division symbol in a simple fraction indicates that the entire expression above the division symbol is the numerator and must be treated as if it were one number, and the entire expression below the division symbol is the denominator and must be treated as if it were one number. The same order of operations (BEDMAS) applies to fractions as to other mathematical terms. Brackets instruct you to simplify the expression within the bracket before doing anything else. The division symbol in a fraction has the same role as a bracket. It instructs you to treat the quantity above (the numerator) as if it were enclosed in a bracket, and to treat the quantity below (the denominator) as if it were enclosed in another bracket:

(Numerator)

In a simple fraction, the numerator and the denominator are both integers (whole numbers), e.g.

 $\frac{1}{2}$

A complex fraction is a fraction where the numerator, denominator or both contain a fraction, e.g.

 $\frac{1/2}{3}$

To manipulate (e.g. add, subtract, divide or multiply) complex fractions, you must first convert them to simple fractions.

A compound fraction, also called a mixed number, contains integers and fractions, e.g.

 $\frac{4-1/2}{3}$

As with complex fractions, to manipulate compound fractions, you must first convert them to simple fractions.

No fraction (simple, complex or compound) can have a denominator with an overall value of zero. This is because, if the denominator of a fraction is zero, the overall value of the fraction is not defined, since you cannot divide by zero. A numerator is allowed to take on the value of zero in a fraction, although any legitimate fraction (denominator not equal to zero) with a numerator equal to zero has an overall