# Physiology by Numbers

An Encouragement to Quantitative Thinking

SECOND EDITION

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PUBLISHED BY THE PRESS SYNDICATE OF THE UNIVERSITY OF CAMBRIDGE The Pitt Building, Trumpington Street, Cambridge, United Kingdom

CAMBRIDGE UNIVERSITY PRESS The Edinburgh Building, Cambridge, CB2 2RU, UK 40 West 20th Street, New York, NY 10011–4211, USA 10 Stamford Road, Oakleigh, Melbourne 3166, Australia Ruiz de Alarcón 13, 28014 Madrid, Spain

http://www.cup.cam.ac.uk http://www.cup.org

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First published 1994 Second edition published 2000

Printed in the United Kingdom at the University Press, Cambridge

Typeface Utopia 9.25/13.5 and Meta Plus. System Quark XPress® [SE]

A catalogue record for this book is available from the British Library

Library of Congress Cataloguing in Publication Data

Burton, R. F. (Richard F.)
Physiology by numbers: an encouragement to quantitative thinking / Richard F. Burton.
p. cm.
Includes bibliographical references and index.
ISBN 0 521 77200 1 (hb.). – ISBN 0 521 77703 8 (pbk.)
1. Human physiology – Mathematics Problems, exercises, etc.
I. Title.
QP40.B98 2000
612'.001'51-dc21 99-16237 CIP

ISBN 0 521 77200 1 hardback ISBN 0 521 77703 8 paperback

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# **1** Introduction to physiological calculation: approximation and units

One purpose of the many calculations in later chapters is to demonstrate, as 'an encouragement to quantitative thinking', that a little simple arithmetic can sometimes give useful insights into physiology. Encouragement in this chapter takes the form of suggestions for minimizing some of the common impediments to calculation. I have mainly in mind the kinds of arithmetical problem that can suggest themselves outside the contexts of pre-planned teaching or data analysis. Some of the ideas are elementary, but they are not all as well known as they should be. Much of the arithmetic in this book has deliberately been made easy enough to do in the head (and the calculations and answers are given at the back of the book anyway). However, it is useful to be able to cut corners in arithmetic when a calculator is not to hand and guidance is first given on how and when to do this. Much of this chapter is about physical units, for these have to be understood, and casual calculation is too easily frustrated when conversion factors are not immediately to hand. It is also true that proper attention to units may sometimes propel one's arithmetical thinking to its correct conclusion. Furthermore, analysis in terms of units can also help in the process of understanding the formulae and equations of physiology, and the need to illustrate this provides a pretext for introducing some of these. The chapter ends with a discussion of ways in which exponents and logarithms come into physiology, but even here there is some attention to the topics of units and of approximate calculation.

# 1.1 Arithmetic - speed, approximation and error

We are all well drilled in accurate calculation and there is no need to discuss that; what some people are resistant to is the notion that accuracy may sometimes take second place to speed or convenience. High accuracy in physiology is often unattainable anyway, through the inadequacies of data. These points do merit some discussion. Too much initial concern for accuracy and rigour should not be a deterrent to calculation, and those people who confuse the precision of their calculators with accuracy are urged to cultivate the skills of approximate ('back-of-envelope') arithmetic. Discussed here are these skills, the tolerances implicit in physiological variability, and at times the necessity of making simplifying assumptions.

On the matter of approximation, one example should suffice. Consider the following calculation:

 $311/330 \times 480 \times 6.3$ .

A rough answer is readily obtained as follows:

 $(nearly 1) \times (just under 500) \times (just over 6)$ = slightly under 3000.

The 480 has been rounded up and 6.3 rounded down in a way that should roughly cancel out the resulting errors. As it happens, the error in the whole calculation is only 5%.

When is such imprecision acceptable? Here is something more concrete to be calculated: *In a man of 70 kg a typical mass of muscle is 30 kg: what is that as a percentage*? An answer of 42.86% is arithmetically correct, but absurdly precise, for the mass of muscle is only 'typical', and it cannot easily be measured to that accuracy even with careful dissection. An answer of 43%, even 40%, would seem precise enough.

Note, in this example, that the two masses are given as round numbers, each one being subject both to variation from person to person and to error in measurement. This implies some freedom for one or other of the masses to be changed slightly and it so happens that a choice of 28 kg, instead of 30 kg, for the mass of muscle would make the calculation easier. Many of the calculations in this book have been eased for the reader in just this way.

Rough answers will often do, but major error will not. Often the easiest mistake to make is in the order of magnitude, i.e. the number of noughts or the position of the decimal point. Here again the above method of approximation is useful – as a check on order of magnitude when more accurate arithmetic is also required. Other ways of avoiding major error are discussed in Section 1.3.

Obviously, wrong answers can be obtained if the basis of a calculation is at fault. However, some degree of simplification is often sensible as a first step in the exploration of a problem. Many of the calculations in this book involve simplifying assumptions and the reader would be wise to reflect on their

appropriateness; there is sometimes a thin line between what is inaccurate, but helpful in the privacy of one's thoughts, and what is respectable in print. Gross simplification can indeed be helpful. Thus, the notion that the area of body surface available for heat loss is proportionately less in large than in small mammals is sometimes first approached, not without some validity, in terms of spherical, limbless bodies. The word 'model' can be useful in such contexts – as a respectable way of acknowledging or emphasizing departures from reality.

### 1.2 Units

Too often the simplest physiological calculations are hampered by the fact that the various quantities involved are expressed in different systems of units for which interconversion factors are not to hand. One source of information may give pressures in mmHg, and another in  $\rm cmH_2O$ , Pa (= N/m<sup>2</sup>) or dyne/cm<sup>2</sup> – and it may be that two or three such diverse figures need to be combined in the calculation. Spontaneity and enthusiasm suffer, and errors are more likely.

One might therefore advocate a uniform system both for physiology generally and for this book in particular – most obviously the metric *Système International d'Unité* or SI, with its coherent use of kilograms, metres and seconds. However, even if SI units are universally adopted, the older books and journals with non-SI units will remain as sources of quantitative information (and one medical journal, having tried the exclusive use of SI units, abandoned it). This book favours the units that seem most usual in current textbooks and in hospitals and, in any case, the reader is not required to struggle with conversion factors. Only occasionally is elegance lost, as when, in Section 5.10, the law of Laplace, so neat in SI units, is re-expressed in other terms.

Table 1.1 lists some useful conversion factors, even though they are not much needed for the calculations in the book. Rather, the table is for general reference and 'an encouragement to (other) quantitative thinking'. For the same reason, Appendix A supplies some additional physical, chemical and mathematical quantities that can be useful to physiologists. Few of us would wish to learn all of Table 1.1, but, for reasons explained below, readers with little physics should remember that  $1 N = 1 \text{ kg m/s}^2$ , that 1 J = 1 N m and that 1W = 1 J/s. The factor for converting between calories and joules may also be worth remembering, although '4.1855' could be regarded as over-precise for

<i>Time</i> 1 day (d)	86,400 s	1440 min
Distance		
1 metre (m)	39.4 inch	
1 foot	0.305 <b>m</b>	
1 km	0.621 mile	
1 Ångstrom unit	0.1 nanometre (nm)	
Volume		
1 litre (l)	$10^{-3}  m^3$	1 dm³
Velocity		
1 mph	0.447 m/s	1.609 km/h
Acceleration (gravitational)		
g	9.807 m/s <sup>2</sup>	32.17 ft/s <sup>2</sup>
Mass		
1 lb	0.4536 kg	16 oz (avoirdupois)
Force		
l newton (N)	1 kg m/s <sup>2</sup>	102 g-force
1 kg-force	9.807 N	1 kilopond
1 dyne	$10^{-5} \mathrm{N}$	1 g cm/s <sup>2</sup>
Energy		
1 joule (J)	1 N m	
1 erg	$10^{-7} \mathrm{N}\mathrm{m}$	1 dyne cm
1 calorie (cal)	4.1855 J	
1 m kg-force (1 kg m)	9.807 J	
Power		
1 watt (W)	1 J/s	860 cal/h
Pressure and stress		
1 N/m <sup>2</sup>	1 pascal (Pa)	
1 kg-force/m <sup>2</sup>	9.807 N/m <sup>2</sup>	1 mmH <sub>2</sub> O
1 torr	1 mmHg	13.6 mmH <sub>2</sub> O
1 mmHg	133.3 N/m <sup>2</sup>	0.1333 kPa
750 mmHg	100.0 kN/m <sup>2</sup>	
1 atmosphere	101.3 kN/m <sup>2</sup>	760 mmHg

Table 1.1. Conversion factors for units

*Note:* SI units, fundamental or derived, are in **bold** lettering.

#### Attention to units

most purposes. In a similar vein, the '9.807' can often be rounded to '10', but it is best written to at least two significant figures (9.8) since, especially without units, its identity is then more apparent than that of commonplace '10'. It helps to have a feeling for the force of 1 N in terms of weight; it is approximately that of a 100-g object – Newton's legendary apple perhaps. As for pressure, 1 kg-force/m<sup>2</sup> and 9.807 N/m<sup>2</sup> may be better appreciated as 1 mmH<sub>2</sub>O, which is perhaps more obviously small.

Units may be written, for example, in the form m/s<sup>2</sup> or m s<sup>-2</sup>. I have chosen what I believe to be the more familiar style. The solidus (/) may be read as 'divided by' or as 'per', and often these meanings are equivalent. However, there is the possibility of ambiguity when more than one solidus is used, and that practice is best avoided. We shortly meet (for solubility coefficients) a combination of units that can be written unambiguously as 'mmol/l per mmHg', 'mmol/l mmHg', 'mmol/(lmmHg)' and 'mmoll<sup>-1</sup> mmHg<sup>-1</sup>'. What is ambiguous is 'mmol/l/mmHg', for if each solidus is read as 'divided by' rather than as 'per', then the whole combination would be wrongly read as 'mmol mmHg/l'. In the course of calculations, e.g. involving the cancellation of units (see below), it can be helpful to make use of a horizontal line to indicate division, so that 'mmol/l per mmHg' becomes:

 $\frac{\text{mmol/l}}{\text{mmHg}} \text{ or } \frac{\text{mmol}}{\text{l mmHg}}.$ 

# **1.3** How attention to units can ease calculations, prevent mistakes and provide a check on formulae

Students often quote quantities without specifying units, thereby usually making the figures meaningless. All know that units and their interconversions have to be correct, but the benefits of keeping track of units when calculating are not always fully appreciated. Thus, their inclusion in all stages of a calculation can prevent mistakes of various kinds. Indeed, attention to units can sometimes lead to correct answers (e.g. when tiredness makes other reasoning falter), or help in checking the correctness of half-remembered formulae. Too many people flounder for lack of these simple notions. The illustrations that follow involve commonplace physiological formulae, but if some of them are unfamiliar that could even help here, by making the usefulness of the approach more apparent. The formulae are in a sense incidental, but, since they are useful in their own right, the associated topics are highlighted in bold type.

To illustrate the approach I start with an example so simple that the benefits of including units in the calculation may not be apparent. It concerns the excretion of urea. An individual is producing urine at an average rate of, say, 65 ml/h. The average concentration of urea in the urine is 0.23 mmol/ml. The rate of urea excretion may be calculated as the product of these quantities, namely  $65 \text{ ml/h} \times 0.23 \text{ mmol/ml}$ . The individual units (ml, mmol and min) are to be treated as algebraic quantities that can be multiplied, divided or cancelled as appropriate. Therefore, for clarity, the calculation may be written out thus:

$$65 \frac{\text{ml}}{\text{h}} \times 0.23 \frac{\text{mmol}}{\text{ml}} = 15 \frac{\text{mmol}}{\text{h}}$$
, i.e. 15 mmol/h.

With the units spelt out like that, it would immediately become apparent if, say, there were an inappropriate mixing of volume units, e.g. millilitres in 'ml/h' with litres in 'mmol/l'. (What would then need to be done is probably obvious, but there is one particular kind of procedure for introducing conversion factors – in this case the '1000' relating ml to l – that can be helpful when one is trying to calculate with units in an orderly fashion; see Notes and Answers, note 1.3A.) It would also be obvious if the mistake were made of dividing insteading of multiplying – since the 'ml' would not then cancel. If unsure whether to multiply the two quantities together, or to divide one by the other, one would only have to try out the three possible calculations to see which one yields a combination of units appropriate to excretion rate, i.e. mmol/h and not, say, ml²/(mmol h).

The calculation of **rates of substance flow** from products of concentration and fluid flow in that way is commonplace in physiology and the idea leads directly to the concept of **renal clearance**, and specifically to the use of inulin clearance as a measure of glomerular filtration rate (GFR). Often, when I have questioned students about inulin clearance, they have been quick to quote an appropriate formula, but have been unable to suggest appropriate units for what it yields. It is the analysis of the formula in terms of units that is my ultimate concern here, but a few lines on its background and derivation may be appropriate too. For the measurement of GFR, the plant polysaccharide inulin is infused into the body and measurements are later made of the concentrations in the blood plasma (P) and urine (U) and of the rate of urine flow (V). The method depends on two facts: first, that the concentration in the glomerular filtrate is essentially the same as the concentration in the plasma and, second, that the amount of inulin excreted is equal to the amount filtered. The rate of excretion is UV(as for urea) and the rate of filtration is GFR  $\times P($ again a flow times a concentration). Thus:

$$\operatorname{GFR} \times P = UV$$
,

so that:

$$GFR = \frac{UV}{P}.$$
(1.1)

Although the quantity calculated here is the GFR, it can also be thought of as the rate at which plasma would need to be completely cleared of inulin to explain the excretion rate (whereas in fact a larger volume is partially cleared). Hence the term 'renal plasma clearance'. The formula may be generalized to calculate clearances for other excreted substances:

renal plasma clearance = 
$$\frac{UV}{P}$$
. (1.2)

It may be obvious that GFR needs to be expressed in terms of a volume per unit time, but for the more abstruse concept of clearance the appropriate units are less apparent. This brings us to my main point, that appropriate units can be found by analysis of the formula.

If the concentrations are expressed as g/ml, and the urine flow rate is expressed as ml/min, then the equation can be written in terms of these units as follows:

units for clearance = 
$$\frac{g/ml \times ml/min}{g/ml}$$
.

Since 'g/ml' appears on the top and bottom lines, it can be cancelled, leaving the right-hand side of the equation as 'ml/min'. Such units (volume per unit time) are as appropriate to clearances in general as to GFR.

To reinforce points made earlier, suppose now that equation 1.1 is wrongly remembered, or that the concentrations of inulin in the two fluids are expressed differently, say one as g/l and one as g/ml. If the calculation is written out with units, as advocated, then error is averted.

It has been emphasized that rates of substance flow can be calculated as products of concentration and fluid flow. In another context, the rate of oxygen flow in blood may be calculated as the product of blood oxygen content and blood flow, and the rate of carbon dioxide loss from the body may be calculated as the product of the concentration (or percentage) of the gas in expired air and the respiratory minute volume. Such ideas lead straight to the **Fick Principle** as applied, for example, to the estimation of cardiac output from measurements of whole-body oxygen consumption and concentrations of oxygen in arterial and mixed-venous blood. The assumption is that the oxygen consumption is equal to the difference between the rates at which oxygen flows to, and away from, the tissues:

oxygen consumption

= cardiac output  $\times$  arterial [O<sub>2</sub>] - cardiac output  $\times$  mixed-venous [O<sub>2</sub>]

 $= cardiac \ output \times (arterial \ [O_2] - mixed \ venous \ [O_2]),$ 

where the square brackets indicate concentrations. From this is derived the Fick Principle formula:

cardiac output = 
$$\frac{\text{oxygen consumption}}{\text{arterial } [O_2] - \text{mixed-venous } [O_2]}$$
. (1.3)

Re-expressed in terms of units, this becomes:

cardiac output = 
$$\frac{\text{ml } O_2/\text{min}}{\text{ml } O_2/\text{l } \text{blood}} = \frac{\text{ml } O_2}{\text{min}} \times \frac{1 \text{ blood}}{\text{ml } O_2} = 1 \text{ blood/min.}$$

Note two points. First, mistakes may be avoided if the substances (oxygen and blood) are specified in association with the units ('ml  $O_2/l$  blood' rather than 'ml/l'). Second, the two items in the bottom line of equation 1.3 have the same units and are lumped together in the treatment of units. Actually, since one is subtracted from the other, it is a necessity that they share the same units. Indeed, if one finds oneself trying to add or subtract quantities with different units, then one should be forced to recognize that the calculation is going astray.

We turn now to the **mechanical work** that is done when an object is lifted and when blood is pumped. When a force acts over a distance, the mechanical work done is equal to the product of force and distance. Force may be expressed in newtons and distance in metres. Therefore, work may be expressed in N m, the product of the two, but also in joules, since 1 J = 1 N m(Table 1.1). Conversion to calories, etc. is also possible, but the main point here is something else. When an object is lifted, the work is done against gravity, the force being equal (and opposite) to the object's weight. Weights are commonly expressed as 'g' or 'kg', but these are actually measures of mass and not of force, whereas the word 'weight' should strictly be used for the downward force produced by gravity acting on mass. A mass of 1 kg may be

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more properly spoken of as having a weight of 1 kg-force. Weight depends on the strength of gravity, the latter being expressed in terms of *g*, the gravitational acceleration. This is less on the Moon than here, and it is variable on the Earth in the third significant figure, but for the purpose of defining 'kg-force' the value used is  $9.807 \text{ m/s}^2$ , with 1 kg-force being 9.807 N (Table 1.1). This distinction between mass and weight is essential to the procedures advocated here for analysing equations in terms of units and including units in calculations to avoid error.

In relation to the pumping of blood, the required relationship is not 'work equals force times distance', but 'work equals increase in pressure times volume pumped'. If unsure of the latter relationship, can one check that it makes sense in terms of units? The analysis needs to be in terms of SI units, not, say, calories, mmHg and litres. Areas are expressed as m<sup>2</sup>, and volumes as m<sup>3</sup>. Accordingly:

work (J) = pressure × volume = N/m<sup>2</sup> × m<sup>3</sup> = 
$$\frac{N}{m^2}$$
 × m<sup>3</sup> = N m = J.

Next we have a situation requiring the definition of the newton as  $1 \text{ kg m/s}^2$ . The **pressure due to a head of fluid**, e.g. in blood at the bottom of a vertical blood vessel, is calculated as  $\rho gh$ , where  $\rho$  is the density of the fluid, g is the gravitational acceleration (9.807 m/s<sup>2</sup>) and h is the height of fluid. To check that this expression really yields units of pressure (N/m<sup>2</sup>), we write:

$$\rho gh = \frac{kg}{m^3} \times \frac{m}{s^2} \times m = \frac{kg}{m s^2}$$

Recalling that  $1 \text{ N} = 1 \text{ kg m/s}^2$ , we now write:

pressure = 
$$\frac{N}{m^2} = \frac{kg m}{s^2} \times \frac{1}{m^2} = \frac{kg}{m s^2}$$
,

which is the same expression as before.

There are some quantities for which the units are not particularly memorable for most of us, including peripheral resistance and the solubility coefficients for gases in liquids. Appropriate units may be found by analysis of the equations in which they occur. Peripheral resistance is discussed in Section 4.3, while here we consider the case of gas **solubility coefficients**, and specifically the solubility coefficient of oxygen in body fluids such as blood plasma. The concentration of oxygen in simple solution,  $[O_2]$ , increases with the partial pressure,  $P_{O_2}$ , and with the solubility coefficient,  $S_{O_2}$ :

$$[O_2] = S_{O_2} P_{O_2}. \tag{1.4}$$

The concentration may be wanted in ml  $O_2/l$  fluid or in mmol/l, with the partial pressure being specified in mmHg, kPa or atmospheres, but let us choose mmol/l and mmHg. Rearranging equation 1.4 we see that  $S_{O_2}$  equals the ratio  $[O_2]/P_{O_2}$ , so that the compatible solubility coefficient is found by writing:

$$\frac{[O_2]}{P_{O_2}} = \frac{\text{mmol}}{\text{l}} \times \frac{1}{\text{mmHg}} = \frac{\text{mmol/l}}{\text{mmHg}} = \text{mmol/l per mmHg or mmol/l mmHg}.$$

To reinforce the theme of how to avoid errors, note what happens if an incompatible form of solubility coefficient is used in a calculation. In different reference works, solubility coefficients may be found in such forms as 'ml/lper atmosphere', 'mmol/(lPa)', etc., as well as mmol/lper mmHg. If the first of these versions were to be used in a calculation together with a gas pressure expressed in mmHg, then the units of concentration would work out as:

$$\frac{\text{ml }O_2/\text{l fluid}}{\text{atmosphere}} \times \text{mmHg} = \text{ml }O_2 \text{ mmHg}/(\text{l fluid atmosphere}).$$

The need to think again would at once be apparent.

The above illustrations have variously involved SI and non-SI units in accordance with need and convenience, but other methods of analysis are sometimes appropriate that are less specific about units, at least in the early stages. It is mainly to avoid complicating this chapter that a description of 'dimensional analysis' is consigned to Notes and Answers, note 1.3B, but it is also less generally useful than unit analysis. We look next at diffusion to illustrate a slightly different approach in which the choice of units is deferred.

Suppose that an (uncharged) substance S diffuses from region 1 to region 2 along a diffusion distance d and through a cross-sectional area a. The (uniform) concentrations of S in the two regions are respectively [S]<sub>1</sub> and [S]<sub>2</sub>. The **rate of diffusion** is given by the following equation:

$$rate = ([S]_1 - [S]_2) \times a/d \times D, \tag{1.5}$$

where *D* is the 'diffusion coefficient'. The appropriate units for *D* may be found by rearranging the equation and proceeding as follows:

$$D = \frac{\text{rate}}{[S]_1 - [S]_2} \times \frac{d}{a} = \frac{\text{rate}}{\text{concentrations}} \times \frac{\text{distance}}{\text{area}}$$

The rate of diffusion is the amount of S diffusing per unit of time and concentrations are amounts of S per unit of volume. Therefore:

 $D = \frac{\text{amount}}{\text{time}} \times \frac{\text{volume}}{\text{amount}} \times \frac{\text{distance}}{\text{area}}$ .

Following the practice adopted above, the various items in the right-hand expression could have been given in terms of kg, s,  $m^3$ ,  $m^2$  and m, and that approach would be valid. Diffusion coefficients are in fact commonly given as  $cm^2/s$ , so let us now specify distance, area and volume in terms of cm,  $cm^2$  and  $cm^3$ , and time in seconds. Then the expression becomes:

units for  $D = \frac{\text{amount}}{\text{s}} \times \frac{\text{cm}^3}{\text{amount}} \times \frac{\text{cm}}{\text{cm}^2} = \frac{\text{cm}^2}{\text{s}}$ .

Note that it is irrelevant here how the amount of substance is expressed, whether it be in g, mmol, etc. For another form of diffusion coefficient, relating to gas partial pressures, see Notes and Answers, note 1.3C.

It must be acknowledged finally that some equations are not sensibly analysed in terms of units. These are empirically derived formulae that have no established theoretical basis. For example, there are formulae that relate vital capacity, in litres, to age in years and body height in centimetres; there is no way of combining units of time and length to obtain units of volume. One must remember this general point to avoid being puzzled sometimes, but it is also true that the analysis of an empirical equation in terms of units or dimensions can sometimes lead to its refinement and to theoretical understanding.

# Conclusions

Although the main theme here is the avoidance of error by consideration of units, it has also provided a context in which to introduce various commonly used formulae. In case these have obscured the ideas pertinent to the main theme, it may be helpful to summarize those ideas here.

- 1. Units can be combined, manipulated and cancelled like algebraic symbols.
- 2. The two sides of an equation must balance in terms of units as well as numerically.
- 3. If a formula calls for quantities to be expressed in particular units, then mistakes in this regard are preventable by writing them out as part of the calculation.

## 12 Introduction to physiological calculation

- 4. When quantities of more than one substance are involved, it is usually advisable to specify these along with the units, writing, for example, 'ml  $O_2$ /ml blood' rather than simply 'ml/ml' (which cancels, unhelpfully, to 1).
- 5. Quantities expressed in differing units cannot be combined by addition or subtraction.
- 6. Attention to units may prevent quantities from being inappropriately combined in other ways too (multiplied instead of divided, for example). Indeed it may suggest the right way of calculating something when other forms of reasoning falter.
- 7. Analysis of units may provide a partial check on half-remembered formulae.
- 8. Appropriate units for unfamiliar quantities can be found by analysing the equations in which they occur.
- 9. Weight (force) must be distinguished from mass (quantity).
- 10. Analysis of units sometimes requires knowledge that  $1 \text{ N} = 1 \text{ kg m/s}^2$ .
- 11. Units on the two sides of an equation may not balance if the relationship is empirical and has no theoretical basis.

To these ideas may be added two others, relating to indices and logarithms, that emerge in the next Section.

- 12. Exponents (indices) must be dimensionless, i.e. they can have no units.
- 13. Strictly it is not possible to take the logarithm of a number that has dimensions or units, although there are situations in which it is acceptable to do so.

# Practice in unit analysis

Readers wishing to practise unit analysis might like to try the following exercises (some relating to physics rather than physiology). Help is given Notes and Answers.

 If SI units for viscosity are unfamiliar, find them by analysing Poiseuille's equation. This relates the rate of flow of fluid, i.e. volume per unit time, in a cylindrical tube (e.g. blood in a blood vessel) to viscosity, to the radius and length of the tube and to the difference in hydrostatic pressure between its two ends: flow rate  $\propto$  pressure difference  $\times \frac{\text{radius}^4}{\text{viscosity} \times \text{length}}$ . (1.6)

- 2. Einstein's ' $E = mc^2$ ' is well known. Treating energy, mass and velocity in terms of SI units, show that the two sides of the equation are compatible.
- 3. If  ${}^{\prime}RT/zF'$  is already familiar in relation to the Nernst equation, analyse it in terms of units. Its components are given in Appendix A, while the units for the whole expression are 'volts'. For this exercise, use the versions of *R* and *F* that involve calories. Appendix A also gives *F* in terms of coulombs; I have seen it given in physics textbooks as 'coulombs', 'coulombs/equivalent' and 'coulombs/volt equivalent', and this suggests another exercise. I give *F* as coulombs/volt equivalent, but is that correct? More specifically, do the relationships discussed in Section 7.6 then work out correctly in terms of units?
- 4. If the formula for calculating the period of a simple pendulum was once known, but is now forgotten, try reconstructing it by unit analysis, albeit partially, given only that the period increases with pendulum length and decreases with *g*.

# 1.4 Analysis of units in expressions involving exponents (indices)

Two main points are made here in relation to the unit analysis of equations containing exponents, one concerning the exponents themselves and the other having to do with other constants. At the same time, the opportunity is taken to say a little about exponential time courses and allometric relationships. The basic rules for working with exponents (indices) are given in Appendix B.

The first point is simply that exponents must be dimensionless quantities; they cannot have units. Thus, ' $3^2$  eggs' is meaningful, but ' $3^2$  eggs' is not. While the 2 in  $3^2$  eggs is a simple number, exponents can also be expressions containing two or more variables that do have units – such as  $3^{a/b}$ , for example. This is satisfactory provided that the units cancel out. Thus,  $3^{(4 \text{ eggs}/2 \text{ eggs})}$  equals  $3^2$ . As a more serious example, and one commonly encountered in physiology, the simplest kinds of exponential time course are described by equations of the form:

$$Y = Y_0 e^{kt}, \tag{1.7}$$

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where *Y* is the variable in question, *t* is time (in seconds, say), *Y*<sub>0</sub> is the the value of *Y*when *t* = 0 and *k* is a constant (the 'rate constant', often negative) with units of time<sup>-1</sup> (here s<sup>-1</sup> or 1/s). The *e* has its usual meaning, a number close to 2.718. Here the units in *kt* cancel out (i.e. s/s = 1). An alternative to  $e^{kt}$  in equation 1.7 is  $e^{t/\tau}$  where the commonly used symbol  $\tau$  (tau) is equal to 1/*k*, and is called the 'time constant'. This has the same units as *t*, so that  $t/\tau$ , like *kt*, is dimensionless.

The second point is one that could be harmlessly ignored (as it is by many physiologists) were it not that I have put so much emphasis on unit analysis. It concerns certain kinds of empirical relationship, as opposed to relationships founded in theory. Countless physiological and anatomical measurements have been made on mammals of different sizes, from shrews to whales, and the relationships between these and body mass have been explored. (In relation to purely human physiology, one may likewise explore relationships in individuals of differing size.) In very many cases the variable, *Y*, has been found to depend on body mass, *M*, in accordance with this equation:

$$Y = a M^b, \tag{1.8}$$

where *a* and *b* are constants. There is always some statistical scatter in these so-called 'allometric' relationships, with consequent uncertainty about the best values of the constants. To start with a case that gives no problem with unit analysis, it appears that heart mass is near-enough exactly proportional to *M* over seven orders of magnitude, such that  $Y = 0.006M^{1.0}$ , with both masses in kg. (This implies that the heart makes up about 0.6% of body mass over the full size range.) There is no difficulty with units here, the '0.006' having none. To see how problems can arise, consider next the case of skeletal mass.

As Galileo pointed out in 1637, relative skeletal mass should increase with body mass, at least in land mammals, if the largest are not to collapse under their own weight (or the smallest are not to be burdened with extra bone). Here is an equation that has been fitted to data on dry skeletal mass (Prange *et al.*, 1979):

skeletal mass (kg) = 
$$0.061 M^{1.09}$$
. (1.9)

Now there is a difficulty, for  $M^{1.09}$  has units of kg<sup>1.09</sup> and this suggests that the '0.061' has units of kg<sup>-0.09</sup> (with some uncertainty due to scatter in the data). This makes no obvious sense. A solution is to divide M by some reference mass, most conveniently 1 kg, so that the equation becomes, in the latter case:

#### Logarithms

skeletal mass (kg) = 0.061 
$$\left[\frac{M}{1 \text{ kg}}\right]^{1.09}$$
. (1.10)

Unlike *M*, the ratio M/(1 kg) is dimensionless. On this basis, the '0.061' is in kg, like skeletal mass. Put more generally, the constant *a* in equation 1.8 comes to have the same units as *Y*. Usually this rather pedantic procedure is not explicitly followed and no harm results. There is more on allometric relationships in Sections 1.5, 3.10, 3.12 and 6.16.

#### 1.5 Logarithms

Physiologists use logarithms in a variety of contexts, notably in relation to membrane potentials (Nernst equation), acid–base balance (pH, Henderson–Hasselbalch equation), sensory physiology (Weber–Fechner 'law') and graphical analysis (of exponential time courses, allometry, dose-response curves). Since logarithms now play a much smaller part in school mathematics than formerly, they are explained in Appendix B. The main purpose of this Section is to say a little more about their use in the contexts just mentioned, but it concludes by returning briefly to the topic of rough calculation. Given the emphasis I have placed on unit analysis earlier in the chapter, I must first make a comment relating to that.

On the matter of units, it should be noted that strictly one can only take logarithms of dimensionless numbers, i.e. quantities that lack units. I say 'strictly' because people do commonly flout this rule, and do so without consequent difficulties or opprobrium. Thus, the elementary, and oldest, definition of pH is that it equals  $-\log_{10}[H^+]$ , where  $[H^+]$  is the concentration of hydrogen ions in mol/l, the units being simply ignored in the calculation. The definition is in fact an oversimplification (Section 8.1), but we can move just one step towards a better definition by dividing [H+] by a standard concentration,  $[H^+]_s$ , of 1 mol/l{so that pH is defined as  $-\log_{10}([H^+]/[H^+]_s)$ }. The units of concentration are thus removed, while the number is unaffected (see the treatment of indices in Section 1.4). This exemplifies a general solution to the problem of taking logarithms of a quantity that has units: instead of ignoring them, one divides the quantity by some reference value, usually with a numerical value of 1. The next paragraph refers to logarithms of certain quantities *Y* and *M*; for propriety, these may be regarded as each divided by a reference quantity of one unit.

One use for logarithms is in the graphical analysis of exponential and allometric relationships (equations 1.7 and 1.8). In the case of equation 1.7, a graph of ln Y (=log<sub>e</sub>Y) against t yields a straight line of gradient k. Alternatively, a graph of log<sub>10</sub>Y against t gives a straight line of gradient klog<sub>10</sub>e. An example is shown in Figure 5.4. In the case of equation 1.8, a graph of log Y against log M yields a straight line of gradient b.

Actually, there is sometimes another reason for plotting logarithms in these contexts. This is notably true in relation to the allometry of mammals of widely varying size for, on a linear scale, it is simply too hard to show comfortably the masses of shrews, whales, and all mammals in between. To cope with that great range of masses, one may plot log M (ignoring the mass units to do so), or else show actual values of M, using a logarithmic scale (e.g. showing, say, 0.1 kg, 1 kg, 10 kg, etc. at equally spaced intervals). Logarithmic scales are often used, at least partly for the same reason, for displaying drug concentrations (for dose-response curves).

Returning to the subject of hydrogen ion concentrations, these too vary over a huge range of magnitudes, and this is one reason why people prefer to work with pH. Thus,  $10^{-4}$  and  $10^{-8}$  mol/l water translate to pH 4 and pH 8 respectively. Sound intensities likewise vary enormously, making the logarithmic decibel scale convenient for the same reason. The decibel scale ties in with the Weber–Fechner law, the tendency for sensation to vary (not always exactly) with the logarithm of stimulus intensity.

In line with the logarithmic nature of pH, the Henderson–Hasselbalch equation, relating pH to  $P_{CO_2}$  and bicarbonate concentration, is usually formulated in logarithmic terms (see Notes and Answers):

$$pH = pK_1' + \log \frac{[HCO_3]}{[CO_2]},$$
(1.11)

where  $pK_1$ ' is a dissociation constant. (It will be apparent soon why the equation is expressed this way, rather than more usefully as in equation 8.1, where  $SP_{CO_2}$  replaces [CO<sub>2</sub>].)

The pH meter responds linearly to log  $[H^+]$  (as if it were a sense organ obeying the Weber–Fechner law). This is because the electrical potential across the glass membrane of the electrode,  $E_{\rm H}$ , depends, at equilibrium, on the hydrogen concentrations (or rather activities) on its two sides in accordance with the Nernst equation:

$$E_{\rm H} = \frac{RT}{zF} \ln \frac{[{\rm H}^+]_1}{[{\rm H}^+]_2}.$$
 (1.12)

(*R*, *T* and *F* are often described simply as 'having their usual values'; they are given in Appendix A. *z* is the valency of the hydrogen ion, i.e. 1.) The sub-

#### Logarithms

scripts 1 and 2 denote the two sides of the membrane. The pH on the inside of the glass electrode is constant. This description of the pH electrode is incidental, but the Nernst equation is essential to the understanding of cell membrane potentials and ion transport, and it is in these contexts that the equation is more often encountered. Here it is reformulated for the equilibrium potential of potassium (at 37 °C):

$$E_{\rm K} \,({\rm mV}) = 61.5 \log \frac{[{\rm K}^+]_1}{[{\rm K}^+]_2}.$$
 (1.13)

Note that we have here the logarithm of a ratio, the ratio of two quantities expressed in identical units, i.e.  $[K^+]_1$  and  $[K^+]_2$ . The same is true of equations 1.11 and 1.12. Such ratios are dimensionless, so that there is no problem here of taking the logarithms of quantities that have units. However, a further point can be made in this connection. Note that the expression log  $([K^+]_1/[K^+]_2)$  is equal to  $(\log [K^+]_1 - \log [K^+]_2)$ ; if the first is valid, so too is the latter. Where there is a difference between two logarithms like that, the impropriety of one is cancelled out by the impropriety of the other.

Finally, we return to the subject of approximate arithmetic. In Appendix B there is a brief comment on the effects on calculations of inaccuracies occurring in logarithmic terms. (Question: how wrong might [H<sup>+</sup>] be if pH is only accurate to two decimal places?) Appendix B also emphasizes the usefulness of remembering that  $log_{10}$  2 is close to 0.30. Let us explore an example. Equations 1.11, 1.12 and 1.13 each include the logarithm of a concentration ratio. If this ratio starts with a value *A*, and then doubles to 2*A*, then the logarithm of the ratio increases by 0.30 (because log 2A = log 2 + log A). Likewise, halving the ratio decreases its logarithm by 0.30. With the Henderson–Hasselbalch equation in mind, we can therefore see, without further calculation, that doubling of  $[HCO_3^-]$  or halving of  $[CO_2]$  should raise the pH by 0.30. Let us put this into the context of an approximate calculation that does not even require the back of an envelope:

Question: At constant  $P_{CO_2}$ , could a rise in bicarbonate concentration from 20 mM to 30 mM explain a rise in pH from 7.10 to 7.43?

Answer: No – even a doubling of concentration only leads to a rise of 0.3 unit.