Biomedical Calculations

Principles and Practice

Richard F. Burton Institute of Biomedical and Life Sciences University of Glasgow, UK



Biomedical Calculations

Biomedical Calculations

Principles and Practice

Richard F. Burton Institute of Biomedical and Life Sciences University of Glasgow, UK



Copyright © 2008

John Wiley & Sons Ltd, The Atrium, Southern Gate, Chichester, West Sussex PO19 8SQ, England

Telephone (+44) 1243 779777

Email (for orders and customer service enquiries): cs-books@wiley.co.uk Visit our Home Page on www.wileyeurope.com or www.wiley.com

All Rights Reserved. No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means, electronic, mechanical, photocopying, recording, scanning or otherwise, except under the terms of the Copyright, Designs and Patents Act 1988 or under the terms of a licence issued by the Copyright Licensing Agency Ltd, 90 Tottenham Court Road, London W1T 4LP, UK, without the permission in writing of the Publisher. Requests to the Publisher should be addressed to the Permissions Department, John Wiley & Sons Ltd, The Atrium, Southern Gate, Chichester, West Sussex PO19 8SQ, England, or emailed to permreq@wiley.co.uk, or faxed to (+44) 1243 770620.

Designations used by companies to distinguish their products are often claimed as trademarks. All brand names and product names used in this book are trade names, service marks, trademarks or registered trademarks of their respective owners. The Publisher is not associated with any product or vendor mentioned in this book.

This publication is designed to provide accurate and authoritative information in regard to the subject matter covered. It is sold on the understanding that the Publisher is not engaged in rendering professional services. If professional advice or other expert assistance is required, the services of a competent professional should be sought.

Other Wiley Editorial Offices

John Wiley & Sons Inc., 111 River Street, Hoboken, NJ 07030, USA

Jossey-Bass, 989 Market Street, San Francisco, CA 94103-1741, USA

Wiley-VCH Verlag GmbH, Boschstr. 12, D-69469 Weinheim, Germany

John Wiley & Sons Australia Ltd, 33 Park Road, Milton, Queensland 4064, Australia

John Wiley & Sons (Asia) Pte Ltd, 2 Clementi Loop #02-01, Jin Xing Distripark, Singapore 129809

John Wiley & Sons Canada Ltd, 6045 Freemont Blvd, Mississauga, Ontario, L5R 4J3

Wiley also publishes its books in a variety of electronic formats. Some content that appears in print may not be available in electronic books.

Library of Congress Cataloging-in-Publication Data

Burton, R. F. (Richard F.)
Biomedical calculations : principles and practice / Richard F. Burton.
p. cm.
Includes bibliographical references and index.
ISBN 978-0-470-51910-3 (cloth) – ISBN 978-0-470-51911-0 (pbk.)
1. Medical sciences–Mathematics. I. Title.
R853.M3B875 2008
610.1'53–dc22

2008016830

British Library Cataloguing in Publication Data

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

ISBN 978-0-470-51910-3 (HB) 978-0-470-51911-0 (PB)

Typeset in 10.5/13pt Minion by Aptara Inc., New Delhi, India Printed and bound by Markono Pte. Ltd., Singapore This book is printed on acid-free paper.

Contents

Preface		xi	
This	s boo	k, and how to use it	xv
Part	t I		1
1	Uni	t analysis: the neglected key to confidence	3
	1.1	Calculating with units	3
	1.2	Ways of writing composite units	5
	1.3	How unit analysis can guide thinking and help solve problems	5
	1.4	When to specify substances along with units	6
	1.5	The need to use appropriate and compatible units in formulae	7
	1.6	Checking and deriving formulae	8
	1.7	When unit analysis raises questions about formulae	10
	1.8	Dimensional analysis	10

Part II

13

2	Uni	ts: length, area, volume, mass, moles and equivalents	15
	2.1	The Système International and unit prefixes	15
	2.2	Length and distance	16
	2.3	Area	17
	2.4	Volume	17
	2.5	Mass	17
	2.6	Moles	18
	2.7	Equivalents	19
	2.8	Conversion between units	20
		Problems	22

COI	NTE	NTS
-----	-----	-----

3	Perc	centages	23
	3.1	When percentages mislead: human body fat and fat in milk	24
	3.2	Heat loss from the body: further questionable percentages	27
		Problems	28
4	Con	iposite units I – density	29
	4.1	Specific gravity	30
	4.2	Specific volume	30
	4.3	Two definitions of body density	31
	4.4	Thinking about a formula	33
		Problems	33
5	Con	iposite units II – concentration	35
	5.1	Concentrations: kilograms of water vs litres of solution	36
	5.2	Simple protein-free salt solutions	37
	5.3	Millimolar and millimolal concentrations in blood plasma	38
	5.4	Some quite different uses for Eq. (5.1)	39
		Problems	39
6	Asp	ects of problem solving	41
	6.1	Letting unit analysis solve the problem	41
	6.2	'Let x be the unknown'	44
		Problems	49
7	Mak	ring up and diluting solutions	51
	7.1	Preparing 250 mL of 150 mM NaCl from the dry salt	51
	7.2	Preparing dilutions from stock solutions	53
		Problems	56
8	Calo	culating drug doses	57
		Problems	59
9	Mor	e about solutions – electroneutrality, osmotic pressure	
		activity	61
	9.1	The principle of electroneutrality	61
	9.2	But what about membrane potentials and short-circuit currents?	64
	9.3	Anion gap	64
	9.4	Osmoles and osmolality	66
	9.5	Osmolar gap	68
	9.6	Osmosity	70
	9.7	Cell contents	70
	9.8	Effective osmolality, effective osmotic pressure	72
	9.9	Osmotic shifts of water between cells and extracellular fluid	73
	9.10	Free and bound concentrations, activities	76

vi

C0	N	ГE	N٦	٢S

Part III

1 2

10	Grap	hs, straight lines and equations	81
	10.1	Graphs: some terminology	81
	10.2	Advice on drawing graphs	81
	10.3	The equation of a straight line	82
	10.4	Finding the equation of a line that passes through two specified points	83
	10.5	Drawing a line that is defined by a specified equation	85
	10.6	Finding the equation of a line from its gradient and the coordinates	
		of a single point on it	86
	10.7	Finding the line that best fits a number of points when these lie	
		only roughly in a straight line	86
	10.8	'Proportional' and 'inversely proportional'	87
	10.9	Gradients of curves	87
		A note on units	87
	10.11	On the different kinds of formulae and equations	88
		Problems	90
11	On sl	hapes and sizes	93
	11.1	Areas and volumes of simple shapes	93
	11.2	Erythrocytes, cylinders and spheres	94
	11.3	The swelling of erythrocytes in hypo-osmotic solutions	96
	11.4	Distortion of erythrocytes in passing along narrow blood vessels	97
	11.5	An exercise in rearranging equations to eliminate an unwanted term	98
	11.6	Easy and general ways to check algebraic working	100
	11.7	Solving the equation by trial and error in a spreadsheet	101
	11.8	Why do we not have naturally spherical erythrocytes?	101
	11.9	General properties of simple geometrical shapes	102
	11.10	Replacing volumes with masses in these equations	105
		A digression on graphs	105
	11.12	Calculating surface area from volume and height: another exercise in	
		re-arranging equations and eliminating unwanted terms	106
		Another digression to check algebraic working	107
		Generalizing the formula to include the human body	108
		Surface/volume and surface/mass ratios	110
		The surface area of the human body	112
		Standard formulae for body surface area	113
	11.18	An exercise in comparing formulae containing exponents	116
		Problems	118
12	Body	size, body build, fatness and muscularity:	
	unit	analysis as an aid to discovery	121
	12.1	Variations in fat-free mass with height and age	122
	12.2	The Rohrer index, or 'height-weight index of build'	125
	12.3	The body mass index; estimating body fat from body mass and height	126

CONTENTS

12.4	Upper arm muscle: how its cross-sectional area varies with body height	131
12.5	Weightlifting – and the cross-sectional area of muscle	133
12.6	Estimating body fat from skinfold thickness measurements	136
12.7	Postscript	138
	Problems	139

Part IV

13

141

Intro	Introducing time	
13.1	Frequency	143
13.2	Speed and velocity	144
13.3	Acceleration	145
13.4	Rates of flow of substances carried in fluids	145
13.5	Thinking about a formula	146
13.6	The concept of renal clearance	151
13.7	Relating the clearance formula for renal plasma flow to the	
	Fick Principle	154
13.8	Creatinine clearance as a measure of GFR, and a convenient formula	
	for estimating it	154
	Problems	156

Part V

159

14	Force	e, pressure, energy, work and power	161
	14.1	Force and weight	161
	14.2	Pressure	163
	14.3	Columns of water, columns of blood	164
	14.4	Osmotic pressure and colloid osmotic pressure (oncotic pressure)	165
	14.5	Energy and work	167
	14.6	Power	169
	14.7	An overview of units – from mass to pressure and power	170
		Problems	171
15	Less	ons from another formula	173
	15.1	Poiseuille's equation and viscosity	173
	15.2	Peripheral resistance	175
		Problems	176
16	Heat	and temperature	177
	16.1	Temperature scales	177
	16.2	The temperature coefficient, Q_{10}	179
	16.3	Heat capacity and specific heat	179
		Problems	180

17		s: dry and wet gas mixtures, partial pressures, gases	
	in so	lution	181
	17.1	A reminder of units	182
	17.2		182
	17.3	The gas laws	182
	17.4	A closer look at Eq. (17.1) and the universal gas constant, with attention to units	100
	17.5	Treatment of gas mixtures – percentages	183 185
	17.5	Treatment of gas mixtures – percentages Treatment of gas mixtures – partial pressures, tensions	185
	17.0	Water vapour pressure	180
	17.8	'Standard temperature and pressure, dry'	187
	17.9	Dissolved O_2 and O_2 in blood plasma and other fluids	189
	17.05	Problems	189
Devel	VT		102
Part	: VI		193
18	Intro	duction to logarithms	195
	18.1	Definitions	196
	18.2	Rules for working with logarithms	196
		The usefulness of remembering log ₁₀ 2	196
	18.4	Logarithmic scales on graphs	197
	18.5		201
	18.6	Natural logarithms Problems	201 202
19	Expo	nential time courses	203
	19.1	Use of semi-logarithmic plots	205
	19.2	Common complications	206
		Problems	207
20	Nern	st equations in physiology and biochemistry:	
	logar	ithms and ' <i>RT/zF'</i>	209
	20.1	More on RT/zF	210
		Problems	212
21	pH –	two definitions and a possible dilemma	
	for te	eachers	213
	21.1	pH as -log[H ⁺]	214
	21.2	The true definition of pH: pH as a number on a	614
		conventional scale	215
	21.3	The meaning of 10 ^{-pH}	216
	21.4	Final comments	217
		Problems	217

C0	NT	ΈN	ΤS

22 Equilibrium constants, the Henderson–Hasselbalch			
	equa	tion, dose–response curves	219
	22.1	Equilibrium constants	219
	22.2	Concentrations or activities?	222
	22.3	The Henderson-Hasselbalch equation	222
	22.4	Application of the Henderson-Hasselbalch equation to drugs	223
	22.5	The dependence of $[AB]$ on $[A]$ when $([B] + [AB])$ is constant	224
	22.6	Concentration-response curves and dose-response curves	227
		Problems	229
23	Buff	ering and acid-base balance	231
	23.1	Non-bicarbonate buffering	232
	23.2	A link with dose-response curves	235
	23.3	Bicarbonate buffering	236
	23.4	CO_2/HCO_3^- and non-bicarbonate buffers together	239
	23.5	The whole body: diet and the titratable acidity of urine	241
	23.6	Other aspects of acid-base balance	242
		Problems	243
Appendix A. Basic mathematics and mathematical language			245
Appendix B. Some non-metric units			253
Appendix C. Notes			255
Appendix D. Solutions to problems			265
References			287
Index			291

х

Preface

This is a guide to quantitative thinking in the biomedical sciences for students and professionals. Many students are unsure about such basic concepts as 10^{-3} , $x^{1/2}$, log *x*, reciprocal, percentage, microlitre, millimoles per litre, order of magnitude and calories. Other people who understand these well may yet falter in applying them – whether to straightforward situations like preparing drug solutions or to more interesting quantitative problems. The book is intended to help all such people. Its backbone is one simple, but neglected idea that can transform one's abilities. However, because no such idea can suffice if one lacks basic concepts like those I have just listed, I try to provide these in a way that will not alienate those who already have them. The biomedical examples may prove interesting in themselves, for some are not to be found in other textbooks.

I do not write books without some personal inner drive. (Moreover, echoing Spike Milligan, 'I vowed never to write another [science] book – and this is it'.) I am not innately clever at solving quantitative problems myself, but a few years ago I came upon the simple key, or guiding principle, to what I like to call 'calculating science'. I do not recall when the penny dropped, but there is nothing like revelations late in life for creating zealots! What I realized was that, if I paid more attention to the units involved (e.g. grams per litre, kg m s^{-2} etc.), answers to calculations could sometimes emerge automatically with little need for further reasoning - and my mistakes were fewer. The benefits were most obvious when a weary brain was applied to unfamiliar aspects of biology. Some readers will think I discovered the obvious. Indeed page four of the physics textbook I used at school implies in one paragraph much of what struck me only later as a revelation. However, that otherwise excellent book gave the matter too little emphasis and did not include units in the working of its subsequent calculations. Many recent physics textbooks also fail to do so. So what is really an ancient principle is too often neglected. Regardless of what schoolbooks may say about it and teachers teach, there are certainly many university students, and indeed professional scientists, who have not acquired this key to confident quantitative thinking.

A good name for this idea is 'unit analysis'. I spell it out in Chapter 1 and hope that its full nature and power will be further revealed throughout the book. So far I am emphasizing the value of unit analysis in calculations, but it may also be applied in contexts where no numbers are involved, as when one is trying to make sense of formulae and equations. In that context, readers familiar with 'dimensional analysis' will see that the two ideas are closely related. Dimensional analysis, which is outlined in Chapter 1, can be more elegant, but is often less helpful in biological contexts. For consistency it is just unit analysis that I use here.

My first proper research, which was about the shapes of leaves and long ago, would have proceeded faster if I had understood dimensional or unit analysis. Now the challenge of writing this book has led me into a sideline of research (anthropometry) that I had no reason to contemplate otherwise. Either technique of analysis can prove invaluable as one tries to understand relationships amongst biological variables, and anthropometry has given me some useful illustrations of this.

Unit analysis calls for an understanding of units and, following a unit theme, I look successively at length, area, volume, mass, moles and equivalents, combining some of these as units for density and concentration. Time is added later, allowing treatment of speed, acceleration and rates of flow. Subsequent chapters add force and pressure, and then energy, work, power and temperature. Other topics are integrated into this progression according to the following guiding principles.

- The mathematics should be simple, involving nothing more advanced than exponents, logarithms and very basic algebra, and help is offered even with these. Topics requiring logarithms are confined to the final chapters.
- Formulae are not just to be applied, but, where possible, to be understood.
- Plotting and interpreting graphs are necessary skills.
- There are topics of enough general importance that they need to be included, such as dosage calculation, renal clearance, gas mixtures, buffering and acid-base balance. Not every reader will require these, but I try to make more general points in dealing with them. As I like to illustrate, a particular quantitative approach a way of thinking or form of calculation may apply in varied contexts.

- Not all the biological topics need to be as exhaustively treated here as they are in standard courses and textbooks so long as sufficient background is provided.
- Desirable as it may be to work with a consistent set of units (e.g. SI), one should be able to cope happily with the variety of units that are inevitably encountered in the real world. Consistency is therefore unhelpful in this book.
- The reader should be offered problems for practice, preferably problems having useful or informative answers.

There is no one ideal way of selecting and ordering my topics and of balancing levels of difficulty for a diverse readership, but I trust that my choices prove helpful and interesting.

Acknowledgements

I thank Dr Dorothy Aidulis for her comments and Dr Francis Burton for reading much of the manuscript and helping in the preparation of figures.

Richard F. Burton