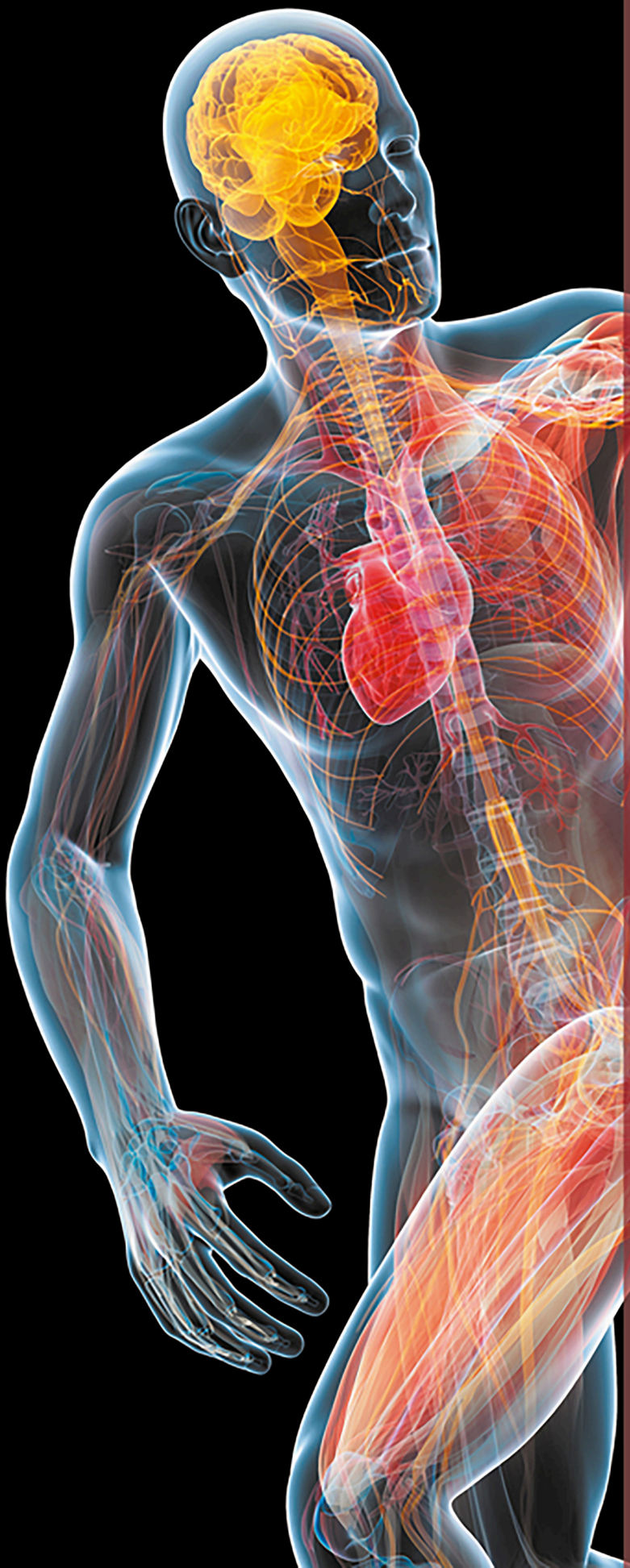

Physiology at a Glance

Fourth Edition

Jeremy P. T. Ward
Roger W. A. Linden

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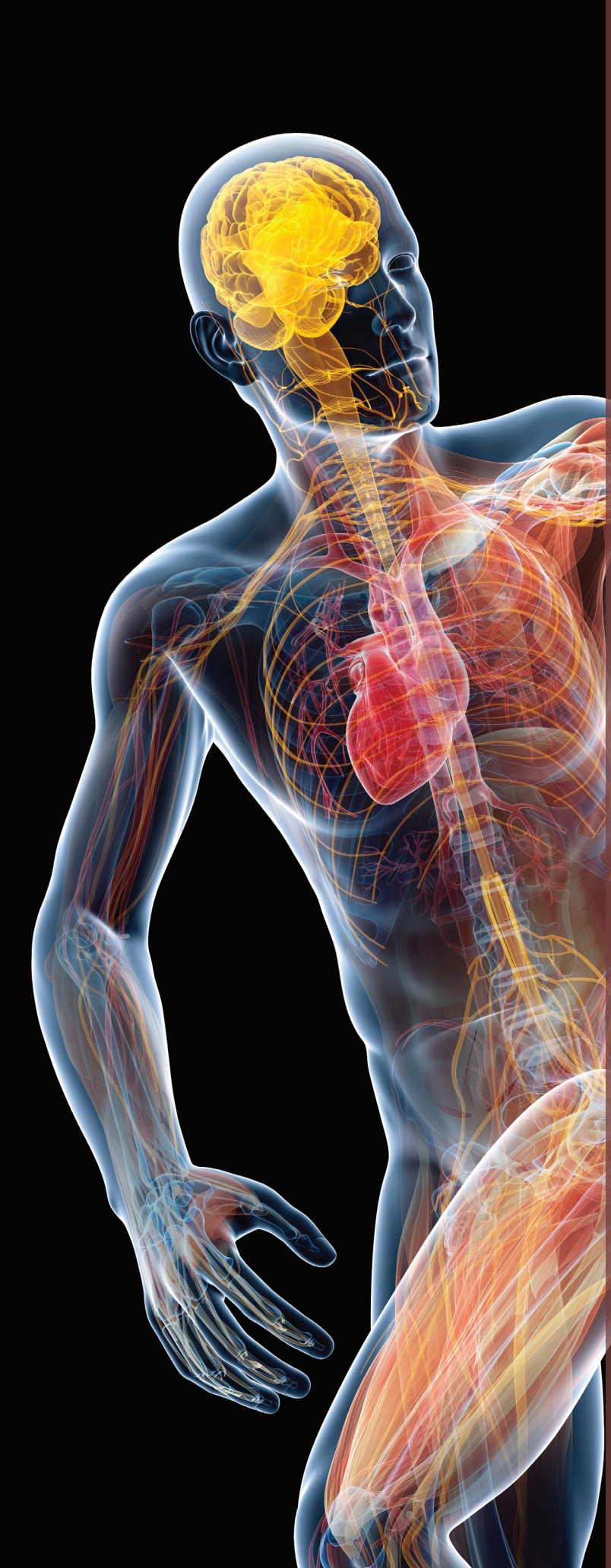

Physiology at a Glance

Fourth Edition

Jeremy P.T. Ward
PhD
Professor of Respiratory Cell Physiology
Emeritus Professor of Physiology
Faculty of Life Sciences & Medicine
King's College London
London, UK

Roger W.A. Linden
BDS PhD MFDS RCS
Emeritus Professor of Craniofacial Biology
Faculty of Life Sciences & Medicine
King's College London
London, UK

WILEY Blackwell

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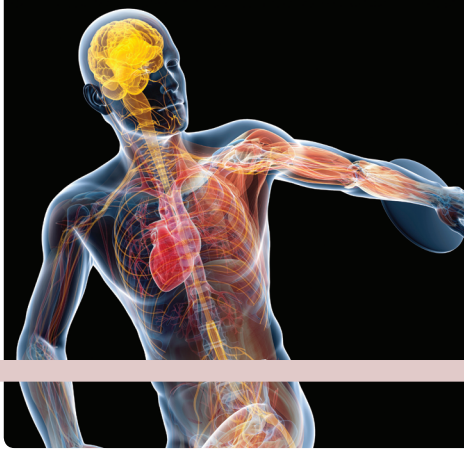
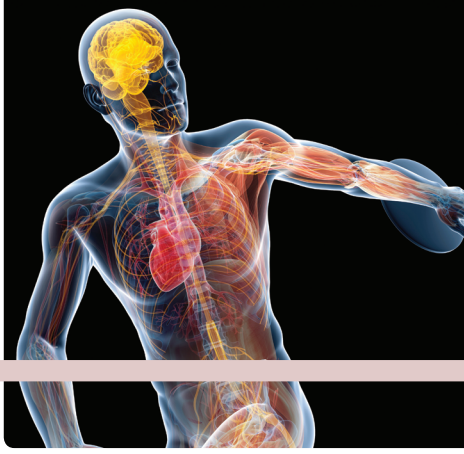
Contents



Preface



Physiology is defined as 'the scientific study of the bodily function of living organisms and their parts'. There is a natural symbiosis between function (physiology) and structure (anatomy) from which physiology emerged as a separate discipline in the late 19th century. A good understanding of anatomy and physiology is an essential prerequisite for understanding what happens when things go wrong – the structural abnormalities and pathophysiology of disease – and as such underpins all biomedical studies and medicine itself. Following a century of reductionism, where the focus of research has progressively narrowed down to the function of individual proteins and genes, there is now a resurgence in integrative physiology, as it has been realized that to make sense of developments such as the Human Genome Project we have to understand body function as an integrated whole. This is considerably more complex than just the sum of its parts because of the multiplicity of interactions involved. True understanding of the role of a single gene, for example, can only be gained when placed in the context of the whole animal, as reflected by the often unexpected effects of knock-out of single genes on the phenotype of mice.

This volume is designed as a concise guide and revision aid to core topics in physiology, and should be useful to all students following a first-year physiology course, whether they are studying single honours, biomedical sciences, nursing, medicine or dentistry. It should also be useful to those studying system-based curricula. The layout of *Physiology at a Glance* follows that of the other volumes in the *At a Glance series*, with a two-page spread for each topic (loosely corresponding to a lecture), comprising a large diagram on one page and concise explanatory text on the other. For this fourth edition we have extensively revised the text and figures, there are three completely new chapters, on Cell signalling, Thermoregulation, and Altitude and aerospace physiology, and we have added a Glossary.

Physiology is a large subject, and in a book this size we cannot hope to cover anything but the core and basics. *Physiology at a Glance* should therefore be used primarily to assist basic understanding of key concepts and as an assistance to revision. Deeper knowledge should be gained by reference to full physiology and system textbooks, and in third-year honours programmes to original peer-reviewed papers. Students may find one or two sections of this book difficult, such as that on the physics of flow and diffusion, and detailed elements of cell signalling. Though such material may not be included in some introductory physiology courses, an understanding of these concepts can assist in learning how body systems behave in the way they do, and in understanding primary research papers.

In revising this fourth edition we have been helped immensely by constructive criticism and suggestions from our colleagues and students, and junior and senior reviewers of the last edition. We thank all those who have given us such advice; any errors are ours and not theirs. We would also like to thank the team at Wiley-Blackwell who provided great encouragement and support throughout the project.

Jeremy Ward
Roger Linden

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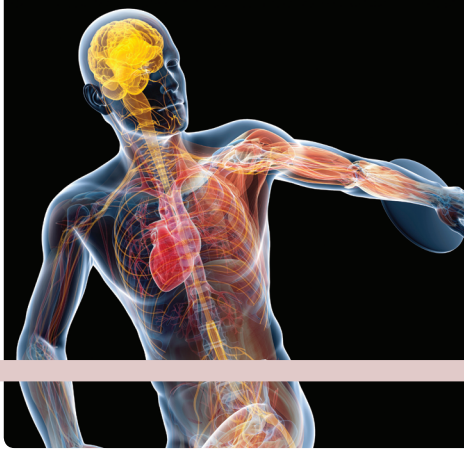
Mehta, A. and Hoffbrand, V. (2009) *Haematology at a Glance* (3rd edition). Wiley-Blackwell, Oxford.

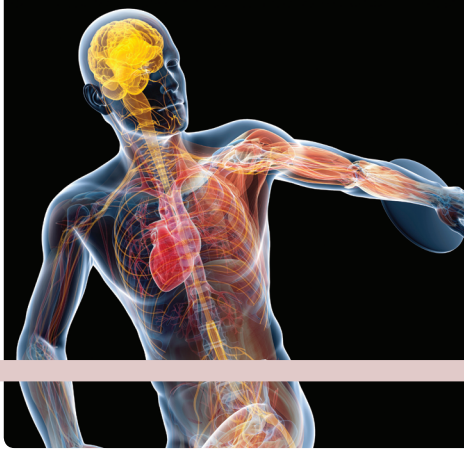
Abbreviations



1,25-$(OH)_2D$	1,25-dihydroxycholecalciferol
2,3-DPG	2,3-diphosphoglycerate
5-HT	5-hydroxytryptamine; serotonin
µG	micro-gravity (weightlessness)
ACE	angiotensin-converting enzyme
ACh	acetylcholine
ACTH	adrenocorticotrophic hormone
ADH	antidiuretic hormone (also called vasopressin)
ADP	adenosine diphosphate
AIDS	acquired immune deficiency syndrome
AMH	anti-Müllerian hormone
AMS	acute mountain sickness
ANP	atrial natriuretic peptide
ANS	autonomic nervous system
AP	action potential
APC	active protein C *or* antigen presenting cell
ATP	adenosine triphosphate
ATPase	enzyme that splits ATP
AV node	atrioventricular node (heart)
AVAs	arteriovenous anastomoses
BAT	brown adipose tissue
BSA	body surface area
BTPS	body temperature and pressure, saturated with water
CaM	calmodulin
CaM-kinase	calcium–calmodulin kinase
cAMP	cyclic adenosine monophosphate
CaSR	calcium-sensing receptor (protein)
CCK	cholecystokinin
CDI	central diabetes insipidus
cGMP	cyclic guanosine monophosphate
CICR	Ca^{2+}-induced Ca^{2+} release
CNS	central nervous system
CO	cardiac output
COMT	catechol-*O*-methyl transferase
COX	cyclooxygenase
CRH	corticotrophin-releasing hormone
CSF	cerebrospinal fluid
CVP	central venous pressure
Da	Dalton (unit for molecular weight)
DAG	diacylglycerol
DHEA	dehydroepiandrosterone
D_{LO_2}	O_2 diffusing capacity in lung; transfer factor
DNA	deoxyribonucleic acid
DOPA	dihydroxyphenylalanine
$E_{(ion)}$	equilibrium potential for ion (e.g. K^+, Na^+, Ca^{2+} or Cl^-)
ECF	extracellular fluid
ECG (EKG)	electrocardiogram (or graph)
EDP	end diastolic pressure
EDV	end diastolic volume
EGF	epidermal growth factor
E_m	membrane potential
EMG	electromyogram
EPO	erythropoietin
EPP	end plate potential
ERV	expiratory reserve volume
ESV	end systolic volume
ETC	electron transport chain
F_{ab}	hypervariable region of antibody molecule
F_c	constant region of antibody molecule
FEV_1	forced expiratory volume in 1 s
FFA	free fatty acids
FGF	fibroblast growth factor
F_{N_2} (F_{O_2})	fractional concentration of nitrogen (oxygen) in a gas mixture
FRC	functional residual capacity
FSH	follicle-stimulating hormone
FVC	forced vital capacity
G-LOC	G-forces induced loss of consciousness
G-protein	GTP-binding protein
GDP	guanosine diphosphate
GFR	glomerular filtration rate
GH	growth hormone
GHRH	growth hormone-releasing hormone
GI	gastrointestinal
GIP	gastric inhibitory peptide
GLP-1	glucagon-like peptide 1
GLUT-1, 2 or 4	glucose transporters
GnRH	gonadotrophin-releasing hormone
GPCR	G-protein-coupled receptor
GRP	gastrin-releasing peptide
GTP	guanosine triphosphate
GTPase	enzyme that splits GTP
HACE	high-altitude cerebral oedema
HAPE	high-altitude pulmonary oedema
[Hb]	haemoglobin concentration

HbA	adult haemoglobin
HbF	fetal haemoglobin
hCG	human chorionic gonadotrophin
HIV	human immunodeficiency virus
HMWK	high molecular weight kininogen
ICF	intracellular fluid
IgA, E, G, M	immunoglobulin A, E, G or M
IGF-1 or 2	insulin-like growth factor (1 or 2)
IL-1b or 6	interleukin-1β or 6
IP_3	inositol trisphosphate
IRS-1	insulin receptor substrate 1
IRV	inspiratory reserve volume
ISF	interstitial fluid
JAK	Janus kinase
JGA	juxtaglomerular apparatus
LH	luteinizing hormone
MAO	monoamine oxidase
MAP	mean arterial pressure
MAPK(K)	mitogen-activated protein kinase (kinase)
MEPP	miniature end plate potentials
MHC I, II	major histocompatibility complex I or II
MIH	melanotrophin-inhibiting hormone
MLC	myosin light chain
MLCK	myosin light chain kinase
MLCP	myosin light chain phosphatase
mRNA	messenger RNA
MSH	melanotrophin-stimulating hormone
Na^+ pump	Na^+-K^+ ATPase
NAD^+ or (NADH)	nicotinic adenine dinucleotide (oxidized and reduced forms)
NCX	Na^+-Ca^{2+} exchanger
NDI	nephrogenic diabetes insipidus
NGF	nerve growth factor
NK	natural killer (cells)
NMJ	neuromuscular junction
NO	nitric oxide
NOS	nitric oxide synthase
P2Y or P2X	purinergic receptor type 2Y or 2X
PAH	*para*-aminohippuric acid
PAMP	pathogen-associated molecular pattern
P_B	barometric pressure
PDGF	platelet-derived growth factor
PEFR	peak expiratory flow rate
PGE_2	prostaglandin E_2
PGI_2	prostacyclin (prostaglandin I_2)
PI-3 kinase	phosphatidylinositol-3 kinase
pK	negative log of dissociation constant (buffers)
PKA	protein kinase A
PKC	protein kinase C
PKG	protein kinase G
PLA_2	phospholipase A2
PLC	phospholipase C
PMCA	plasma membrane Ca^{2+} ATPase
Po_2	partial pressure of oxygen
PRR	pattern recognition receptor
PTH	parathyroid hormone
Ras, Rho	small monomeric GTPases
ROC	receptor-operated channels
ROMK	renal outer medullary potassium channel
RPF	renal plasma flow
RTK	receptor tyrosine kinase
RV	residual volume ***or*** right ventricle
SA node	sinoatrial node
SERCA	smooth endoplasmic reticulum Ca^{2+} ATPase
SH2	Src-homology 2
SMAD	intracellular protein associated with streptokinases
SOC	store-operated channels
SP	Substance P
SR	sarcoplasmic reticulum
Src	a non-receptor tyrosine kinase
SST	somatostatin
STAT	signal transduction and activation of transcription (protein)
STIM	stromal interaction molecule
STPD	standard temperature and pressure, dry gas
SV	stroke volume
SWVP	saturated water vapour pressure
$T_{1\ or\ 2}$	mono- or di-iodotyrosine
T_3	tri-iodothyronine
T_4	thyroxine
T_C	Core temperature
TF	tissue factor
TGFβ	transforming growth factor β
TH	thyroid hormone
TLC	total lung capacity
T_m	tubular transport maximum (kidney)
TNF	tumour necrosis factor
TNZ	thermoneutral zone
tPA	tissue plasminogen activator
TPR	total peripheral resistance
TRa	thyroid hormone receptor
TRE	thyroid response element
tRNA	transfer RNA
TSH	thyroid-stimulating hormone
TUC	time of useful consciousness
TV	tidal volume
TXA_2	thromboxane A_2
UCP-1, 2 or 3	uncoupling protein-1, 2 or 3
V_A/Q mismatch	ventilation–perfusion mismatch (lungs)
VC	vital capacity
VIP	vasoactive intestinal polypeptide
vWF	von Willebrand factor

About the companion website



This book is accompanied by a companion website:

www.ataglanceseries.com/physiology

The website features:

- Interactive multiple choice questions
- Revision notes
- Interactive self-test flashcards

Introduction

Part 1

Chapters

1 Homeostasis and the physiology of proteins

Figure 1.1 Elements of a negative feedback system

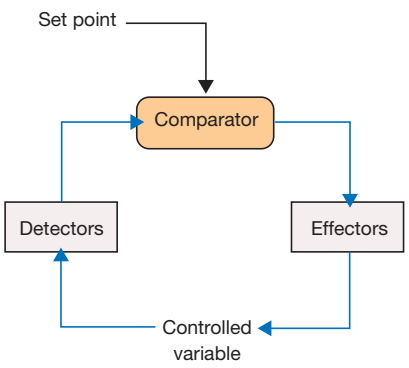


Figure 1.2 Operation of a negative feedback system

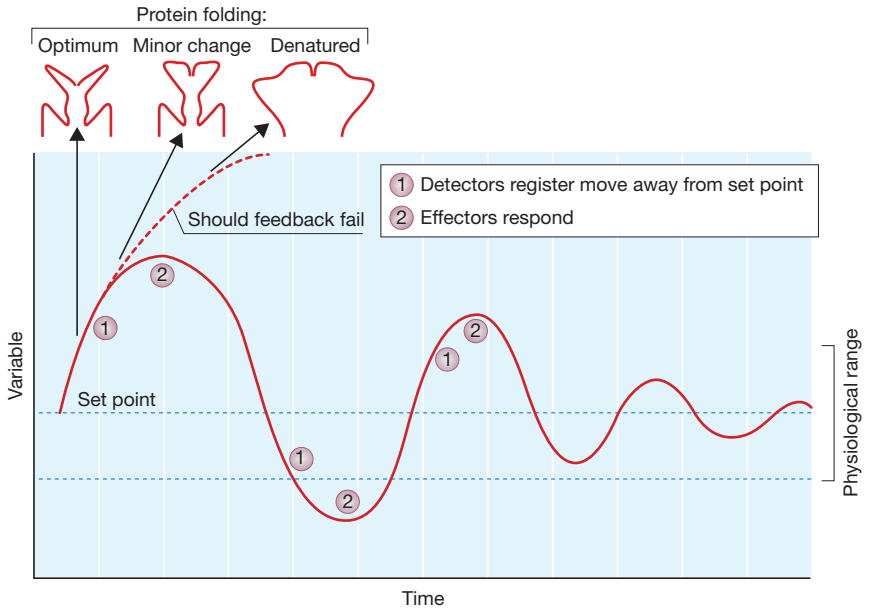


Figure 1.3 Primary protein structure (hypothetical)

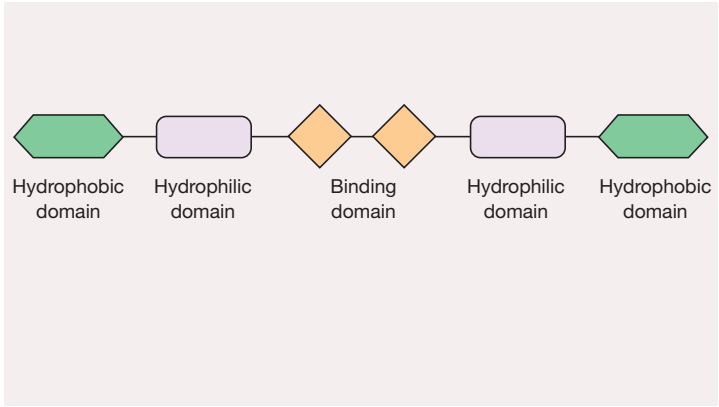
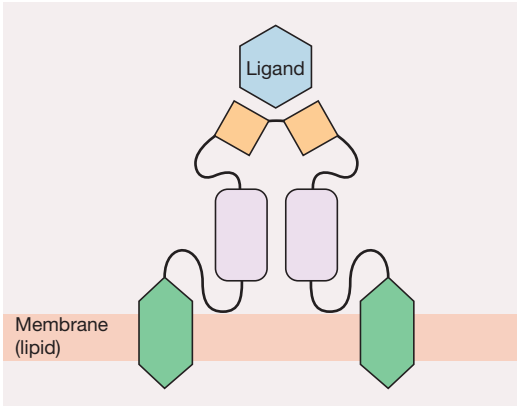


Figure 1.4 Folded (tertiary) structure



Claude Bernard (1813–1878) first described 'le mileau intérieur' and observed that the internal environment of the body remained remarkably constant (or in equilibrium) despite the ever changing external environment. The term **homeostasis** was not used until 1929 when **Walter Cannon** first used it to describe this ability of physiological systems to maintain conditions within the body in a relatively constant state of equilibrium. It is arguably the most important concept in physiology.

Homeostasis is Greek for 'staying the same'. However, this so-called **equilibrium** is not an unchanging state but is a dynamic state of equilibrium causing a **dynamic constancy** of the internal environment. This **dynamic constancy** arises from the variable responses caused by changes in the external environment. Homeostasis maintains most physiological systems and examples are seen throughout this book. The way in which the body maintains the H^+ ion concentration of body fluids within narrow limits, the control of blood glucose by the release of insulin, and the control of body temperature, heart rate and blood pressure are all examples of homeostasis. The human body has literally thousands of control systems. The most intricate are genetic control systems that operate in all cells to control intracellular function as well as all extracellular functions. Many others operate within organs to control their function; others operate throughout the body to control interaction between organs. As long as conditions are maintained within the normal physiological range within the internal environment, the cells of the body continue to live and function properly. Each cell benefits from homeostasis and in turn, each cell contributes its share towards the maintenance of homeostasis. This reciprocal

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interplay provides continuity of life until one or more functional systems lose their ability to contribute their share. Moderate dysfunction of homeostasis leads to sickness and disease, and extreme dysfunction of homeostasis leads to death.

Negative feedback control

Most physiological control mechanisms have a common basic structure. The factor that is being controlled is called the **variable.** Homeostatic mechanisms provide the tight regulation of *all* physiological variables and the most common type of regulation is by ***negative* feedback**. A negative feedback system (Figure 1.1) comprises: **detectors** (often neural **receptor cells**) to measure the variable in question; a **comparator** (usually a neural assembly in the central nervous system) to receive input from the detectors and compare the size of the signal against the desired level of the variable (the **set point**); and **effectors** (muscular and/or glandular tissue) that are activated by the comparator to restore the variable to its set point. The term 'negative feedback' comes from the fact that the effectors always act to move the variable in the opposite direction to the change that was originally detected. Thus, when the partial pressure of CO_2 in blood increases above 5.3 kPa (40 mmHg), brain stem mechanisms increase the rate of ventilation to clear the excess gas, and *vice versa* when CO_2 levels fall below 5.3 kPa (Chapter 32). The term 'set point' implies that there is a single optimum value for each physiological variable; however, there is some tolerance in all physiological systems and the set point is actually a narrow *range* of values within which physiological processes will work normally (Figure 1.2). Not only is the set point not a point, but it can be reset in some systems according to physiological requirements. For instance, at high altitude, the low partial pressure of O_2 in inspired air causes the ventilation rate to increase. Initially, this effect is limited due to the loss of CO_2, but, after 2–3 days, the brain stem lowers the set point for CO_2 and allows ventilation to increase further, a process known as **acclimatization** (Chapter 14).

A common operational feature of all negative feedback systems is that they induce oscillations in the variable that they control (Figure 1.2). The reason for this is that it takes time for a system to detect and respond to a change in a variable. This delay means that feedback control always causes the variable to overshoot the set point slightly, activating the opposite restorative mechanism to induce a smaller overshoot in that direction, until the oscillations fall within the range of values that are optimal for physiological function. Normally, such oscillations have little visible effect. However, if unusually long delays are introduced into a system, the oscillations can become extreme. Patients with congestive heart failure sometimes show a condition known as **Cheyne–Stokes' breathing**, in which the patient undergoes periods of deep breathing interspersed with periods of no breathing at all (**apnoea**). This is partly due to the slow flow of blood from the lungs to the brain, which causes a large delay in the detection of blood levels of CO_2.

Some physiological responses use ***positive* feedback**, causing rapid amplification. Examples include initiation of an action potential, where sodium entry causes depolarization which further increases sodium entry and thus more depolarization (Chapter 5), and certain hormonal changes, particularly in reproduction (Chapter 53). Positive feedback is inherently unstable, and requires some mechanism to break the feedback loop and stop the process (an off switch), such as time-dependent inactivation of sodium channels in the first example and the birth of the child in the second.

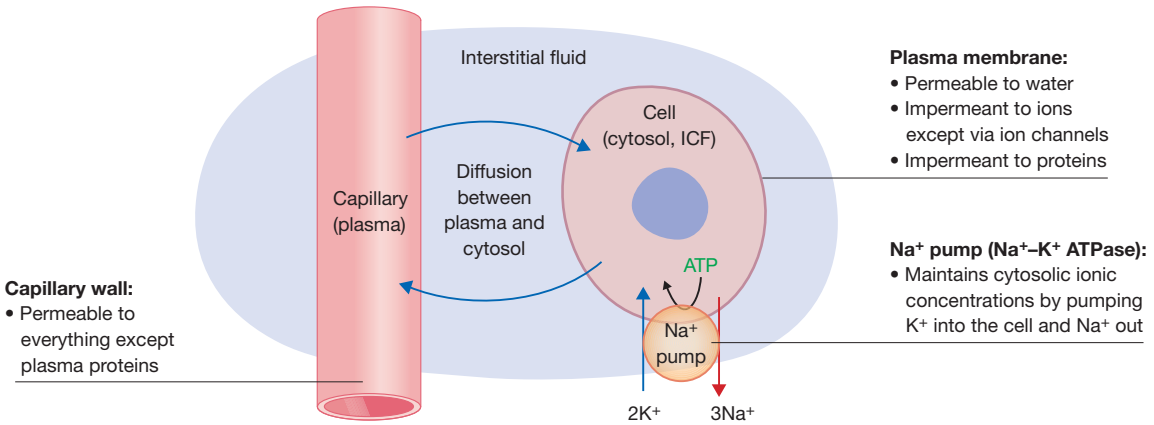
Protein form and function are protected by homeostatic mechanisms

The homeostatic mechanisms that are described in detail throughout this book have evolved to protect the integrity of the protein products of gene translation. Normal functioning of proteins is essential for life, and usually requires binding to other molecules, including other proteins. The specificity of this binding is determined by the three-dimensional shape of the protein. The **primary structure** of a protein is determined by the sequence of amino acids (Figure 1.3). Genetic mutations that alter this sequence can have profound effects on the functionality of the final molecule. Such gene **polymorphisms** are the basis of many genetically based disorders. The final shape of the molecule (the **tertiary structure**), however, results from a process of **folding** of the amino acid chain (Figure 1.4). Folding is a complex process by which a protein achieves its lowest energy conformation. It is determined by electrochemical interactions between amino acid side-chains (e.g. hydrogen bonds, van der Waals' forces), and is so vital that it is overseen by **molecular chaperones**, such as the **heat shock proteins**, which provide a quiet space within which the protein acquires its final shape. In healthy tissue, cells can detect and destroy misfolded proteins, the accumulation of which damages cells and is responsible for various pathological conditions, including **Alzheimer's disease** and **Creutzfeldt–Jakob disease**. Folding ensures that the functional sequences of amino acids (**domains**) that form, e.g. binding sites for other molecules or hydrophobic segments for insertion into a membrane, are properly orientated to allow the protein to serve its function.

The relatively weak nature of the forces that cause folding renders them sensitive to changes in the environment surrounding the protein. Thus, alterations in acidity, osmotic potential, concentrations of specific molecules/ions, temperature or even hydrostatic pressure can modify the tertiary shape of a protein and change its interactions with other molecules. These modifications are usually reversible and are exploited by some proteins to detect alterations in the internal or external environments. For instance, nerve cells that respond to changes in CO_2 (chemoreceptors; Chapter 32) possess **ion channel** proteins (Chapter 4) that open or close to generate electrical signals (Chapter 5) when the acidity of the medium surrounding the receptor (CO_2 forms an acid in solution) alters by more than a certain amount. However, there are limits to the degree of fluctuation in the internal environment that can be tolerated by proteins before their shape alters so much that they become non-functional or irreversibly damaged, a process known as **denaturation** (this is what happens to egg-white proteins in cooking). Homeostatic systems prevent such conditions from arising within the body, and thus preserve protein functionality.

2 Body water compartments and physiological fluids

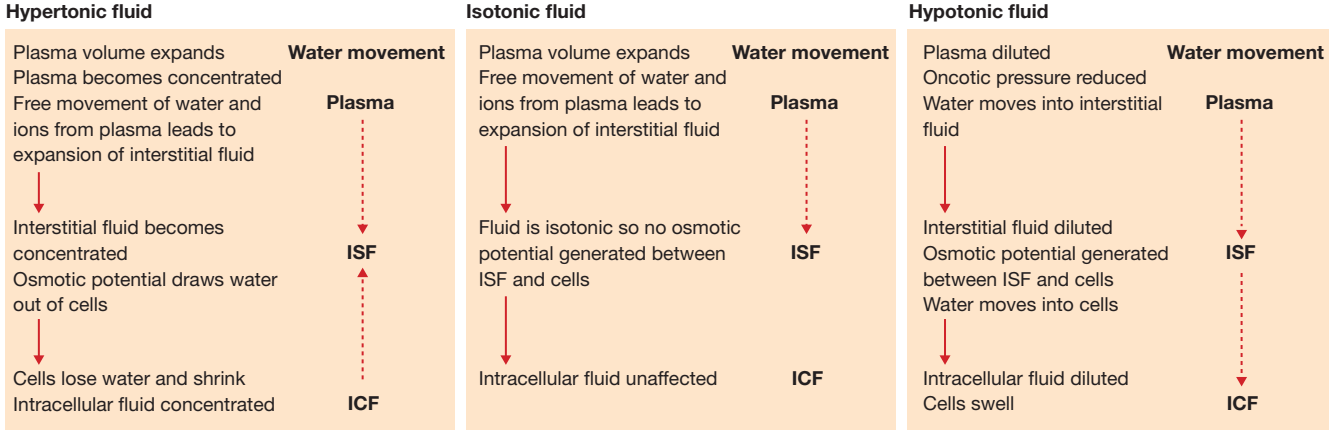
Figure 2.1 Physiological fluid compartments



Constituents of physiological fluids (approximate values, intracellular varies between tissues)					
		Plasma	**Interstitial**	**Intracellular**	**Unit**
Water:	% total body water	13%	22%	65%	%
	(volume in a **70 kg** person)	(3.5)	(9.5)	(27)	L
Osmolality		290	290	290	mosmol/kg H_2O
Cations:	Na^+	140	140	10	mmol/L
	K^+	4	4	140	mmol/L
	Ca^{2+} (free)	1	1	0.0001	mmol/L
Anions:	Cl^-	108	129	3–30	mmol/L
	HCO_3^-	26	26	9	mmol/L
	$Proteins^-$	10	1	50	mmol/L
	Other anions (mainly PO_4^{3-}, SO_4^{3-})	3	0	60–88	mmol/L

Notes: Ca^{2+} (and Mg^{2+}) tend to bind to plasma proteins, and their free concentrations are about 50% of the total. Ionic concentrations are sometimes given in mEq/L to reflect the amount of charge, where an equivalent (Eq) is 1 mole of charge. So 1 Eq of a monovalent ion such as Na^+ = 1 mole, but 1 Eq of Ca^{2+} = 0.5 mole

Figure 2.2 Effects of ingesting fluids of differing osmotic potential



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