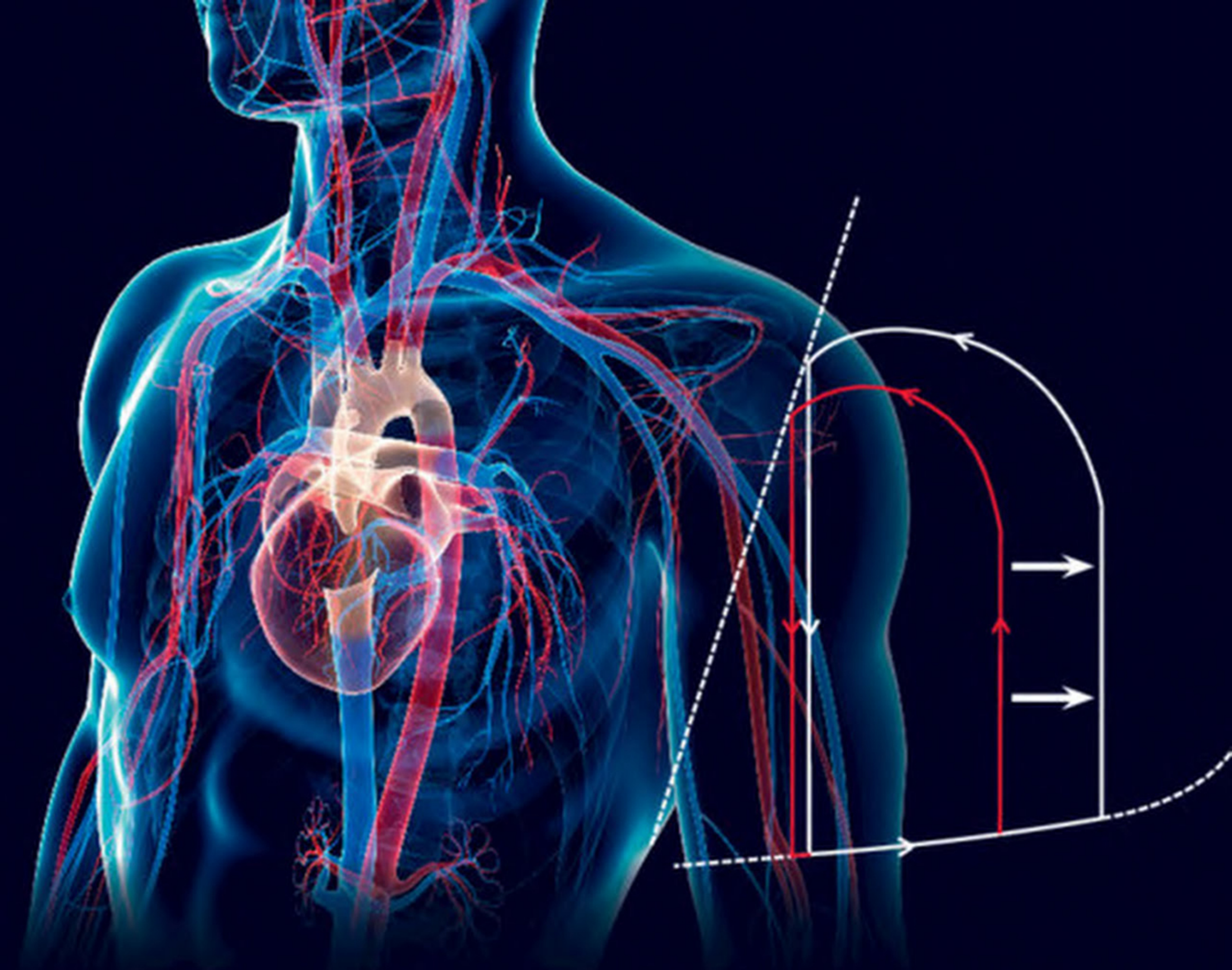

Basic Physiology for Anaesthetists

David Chambers, Christopher Huang
and Gareth Matthews

SECOND EDITION

CAMBRIDGE Medicine

Basic Physiology for Anaesthetists

Second Edition

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DC:
To Sally, for not vetoing this second edition.

CH:
To friends and teachers: Charles Michel, Morrin Acheson, Richard Adrian, Sir David Weatherall and John Ledingham. *In memoriam absentium, in salutem praesentium.*

GM:
To my wife, Claire, and our beautiful baby daughter, Eleanor. I also remain indebted to Professor Christopher Huang for fostering my original interest in physiology, as well as supporting me throughout my career.

Contents

Foreword

This second edition of *Basic Physiology for Anaesthetists* has carried forward the style, depth and content that made the first edition such a great success. It covers all aspects of human physiology that are essential for the art and science that is modern anaesthesia. Patients need to be reassured that their anaesthetists are well informed of the workings of the human body in health as well as disease.

The authors are both expert physiology scientists and clinicians – this combination is clearly seen in the book's structure. Each chapter explains the physiology and is followed by the clinical applications relevant to the speciality. The illustrations are simple line drawings that are easy to follow and, importantly for trainee anaesthetists, easy to recall or even reproduce in the exam setting. Not only should this book be essential reading for those new to the speciality or those preparing for exams, but established specialists and consultants should have access to a copy to give structure to their teaching, as well as to rekindle fading knowledge. Those sitting anaesthesia exams can be confident that many of those responsible for testing their knowledge will themselves have consulted this book!

Dr Russell Perkins FRCA
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Preface to the Second Edition

'Why are you writing a second edition? Surely nothing in classical physiology ever changes?' One of us (DC) has been asked these questions several times. It is true that many of the fundamental physiological concepts described in this second edition of *Basic Physiology for Anaesthetists* remain the same. What does change, however, is how we apply that physiological knowledge clinically. In the four years since we wrote the first edition of this book, high-flow nasal oxygen therapy has revolutionised airway management, cancer surgery has become the predominant indication for total intravenous anaesthesia and new classes of oral anticoagulants have emerged, to name but a few developments. All of these changes in daily anaesthetic practice are underpinned by a thorough understanding of basic physiology.

To that end, in addition to thoroughly revising and updating each chapter, we have added six new chapters, including those on the physiology of the eye and upper airway and on exercise testing. We have also sought to include more pathophysiology, such as cardiac ischaemia and physiological changes in obesity. We have tried to remain true to the principles with which we wrote the first edition, keeping the concepts as simple as possible whilst remaining truthful and illustrating each chapter with points of clinical relevance and easily reproducible line diagrams. In response to positive feedback, the question-and-answer style remains to best help readers prepare for postgraduate oral examinations.

Preface to the First Edition

An academically sound knowledge of both normal and abnormal physiology is essential for day-to-day anaesthetic practice, and consequently for postgraduate specialist examinations.

This project was initiated by one of us (DC) following his recent experience of the United Kingdom Fellowship of the Royal College of Anaesthetists examinations. He experienced difficulty locating textbooks that would build upon a basic undergraduate understanding of physiology. Many of the anaesthesia-related physiology books he encountered assumed too much prior knowledge and seemed unrelated to everyday anaesthetic practice.

He was joined by a Professor in Physiology (CH) and a Translational Medicine and Therapeutics Research Fellow (GM) at Cambridge University, both actively engaged in teaching undergraduate and postgraduate physiology and in physiological research.

This book has been written primarily for anaesthetists in the early years of their training, and specifically for those facing postgraduate examinations. In addition, the account should provide a useful summary of physiology for critical care trainees, senior anaesthetists engaged in education and training, physician assistants in anaesthesia, operating department practitioners and anaesthetic nurses.

We believe the strength of this book lies in our mixed clinical and scientific backgrounds, through which we have produced a readable and up-to-date account of basic physiology and provided links to anaesthetic and critical care practice. We hope to bridge the gap between the elementary physiology learnt at medical school and advanced anaesthesia-related texts. By presenting the material in a question-and-answer format, we have aimed to emphasize strategic points and give the reader a glimpse of how each topic might be assessed in an oral postgraduate examination. Our numerous illustrations seek to simplify and clearly demonstrate key points in a manner that is easy to replicate in an examination setting.

Abbreviations

ACA anterior cerebral artery
ACE angiotensin-converting enzyme
ACh acetylcholine
AChE acetylcholinesterase
ACI anterior circulation infarct
AChR acetylcholine receptor
ACom anterior communicating artery
ADH antidiuretic hormone
ADP adenosine diphosphate
AF atrial fibrillation
AGE alveolar gas equation
AMP adenosine monophosphate
ANP atrial natriuretic peptide
ANS autonomic nervous system
APTT activated partial thromboplastin time
ARDS acute respiratory distress syndrome
ARP absolute refractory period
ATP adenosine triphosphate
AV atrioventricular
BBB blood–brain barrier
BMR basal metabolic rate
BNP brain natriuretic peptide
BSA body surface area
CA carbonic anhydrase
C_aO_2 arterial oxygen content
CBF cerebral blood flow
CC closing capacity
CCK cholecystokinin
CI cardiac index
CMR cerebral metabolic rate
CNS central nervous system
CO cardiac output
CoA coenzyme A
COHb carboxyhaemoglobin
COPD chronic obstructive pulmonary disease
CPET cardiopulmonary exercise test
CPP cerebral perfusion pressure
CRPS complex regional pain syndrome
CSF cerebrospinal fluid
C_vO_2 venous oxygen content
CVP central venous pressure
CVR cerebral vascular resistance
DASI Duke activity status index
DBP diastolic blood pressure
DCML dorsal column-medial lemniscal
DCT distal convoluted tubule
DHPR dihydropyridine receptor
DNA deoxyribonucleic acid
DOAC direct-acting oral anticoagulant
DRG Dorsal respiratory group
ECF extracellular fluid
ECG electrocardiogram
EDPVR end-diastolic pressure-volume relationship
EDV end-diastolic volume
EEG electroencephalogram
EF ejection fraction
EPO erythropoietin
ER endoplasmic reticulum
ESPVR end-systolic pressure-volume relationship
ESV end-systolic volume
ETT endotracheal tube
FAD flavin adenine dinucleotide
FEV_1 forced expiratory volume in 1 s
F_iO_2 fraction of inspired oxygen
FRC functional residual capacity
FTc flow time corrected
FVC forced vital capacity
GABA γ-amino butyric acid
GBS Guillain–Barré syndrome
GCS Glasgow coma scale
GFR glomerular filtration rate
GI gastrointestinal
Hb haemoglobin
HbA adult haemoglobin
HbF foetal haemoglobin
HCN hyperpolarisation-activated cyclic nucleotide gated
HFNO High-flow nasal oxygen
HPV hypoxic pulmonary vasoconstriction
HR heart rate
ICA internal carotid artery
ICF intracellular fluid
ICP intracranial pressure
IRI ischaemic reperfusion injury
IVC inferior vena cava
LA left atrium
LBBB left bundle branch block
LMA laryngeal mask airway
LOH loop of Henle
LOS lower oesophageal sphincter
LV left ventricle
LVEDP left ventricular end-diastolic pressure
LVEDV left ventricular end-diastolic volume
LVESV left ventricular end-systolic volume

LVF left ventricular failure
MAC minimum alveolar concentration
MAO monoamine oxidase
MAP mean arterial pressure
MCA middle cerebral artery
MET metabolic equivalent of a task
MetHb methaemoglobin
MG myasthenia gravis
MI myocardial infarction
MPAP mean pulmonary artery pressure
MW molecular weight
N_2O nitrous oxide
NSTEMI non-ST elevation myocardial infarction
NAD^+ nicotinamide adenine dinucleotide
NMDA *N*-methyl-D-aspartate
NMJ neuromuscular junction
OER oxygen extraction ratio
OSA obstructive sleep apnoea
PAC pulmonary artery catheter
P_aCO_2 arterial tension of carbon dioxide
P_aO_2 arterial tension of oxygen
P_B barometric pressure
PCI percutaneous coronary intervention
PCT proximal convoluted tubule
PCA posterior cerebral artery
PCom posterior communicating artery
PCWP pulmonary capillary wedge pressure
PE pulmonary embolism
PEEP positive end-expiratory pressure
$PEEP_e$ extrinsic positive end-expiratory pressure
$PEEP_i$ intrinsic positive end-expiratory pressure
PEFR peak expiratory flow rate
PNS peripheral nervous system
PPP pentose phosphate pathway
PRV polycythaemia rubra vera
PV peak velocity
PVA pressure-volume area
PT prothrombin time
PTH parathyroid hormone
PVR pulmonary vascular resistance
RA right atrium
RAA renin–angiotensin–aldosterone
RAP right atrial pressure
RBC red blood cell
RBF renal blood flow
RMP resting membrane potential
RNA ribonucleic acid
ROS reactive oxygen species
RR respiratory rate
RRP relative refractory period
RSI rapid sequence induction
RV right ventricle
RVEDV right ventricular end-diastolic volume
RVF right ventricular failure
RyR ryanodine receptor
SA sinoatrial
S_aO_2 arterial haemoglobin oxygen saturation
SBP systolic blood pressure
SD stroke distance
SR sarcoplasmic reticulum
SSEP somatosensory evoked potential
STEMI ST elevation myocardial infarction
SV stroke volume
SVC superior vena cava
SVI stroke volume index
SVR systemic vascular resistance
SVT supraventricular tachycardia
SVV stroke volume variation
TF tissue factor
TIMI thrombolysis in myocardial infarction
TLC total lung capacity
TOE trans-oesophageal echocardiography
$\dot{V}/\dot{Q}$ ventilation–perfusion
$\dot{V}_A$ alveolar ventilation
V_A alveolar volume
VC vital capacity
V_D dead space volume
$\dot{V}_E$ minute ventilation
V_T tidal volume
VF ventricular fibrillation
VRG ventral respiratory group
VT ventricular tachycardia
VTI velocity-time integral
vWF von Willebrand factor

Chapter 1

General Organisation of the Body

Physiology is the study of the functions of the body, its organs and the cells of which they are composed. It is often said that physiology concerns itself with maintaining the status quo or 'homeostasis' of bodily processes. However, even normal physiology is not constant, changing with development (childhood, pregnancy and ageing) and environmental stresses (altitude, diving and exercise). Physiology might be better described as maintaining an 'optimal' internal environment; many diseases are associated with the disturbance of this optimal environment.

Anaesthetists are required to adeptly manipulate this complex physiology to facilitate surgical and critical care management. Therefore, before getting started on the areas of physiology that are perhaps of greater interest, it is worth revising some of the basics – this chapter and the following four chapters have been whittled down to the absolute essentials.

How do the body's organs develop?

The body is composed of some 100 trillion cells. All life begins from a single totipotent embryonic cell, which is capable of differentiating into any cell type. This embryonic cell divides many times and, by the end of the second week, gives rise to the three germ cell layers:

- **Ectoderm**, from which the nervous system and epidermis develop.
- **Mesoderm**, which gives rise to connective tissue, blood cells, bone and marrow, cartilage, fat and muscle.
- **Endoderm**, which gives rise to the liver, pancreas and bladder, as well as the epithelial lining of the lungs and gastrointestinal (GI) tract.

Each organ is composed of many different tissues, all working together to perform a particular function. For example, the heart is composed of cardiac muscle, conducting tissue, including Purkinje fibres, and blood vessels, all working together to propel blood through the vasculature.

How do organs differ from body systems?

The organs of the body are functionally organised into 11 physiological 'systems':

- **Respiratory system**, comprising the lungs and airways.
- **Cardiovascular system**, comprising the heart and the blood vessels. The blood vessels are subclassified into arteries, arterioles, capillaries, venules and veins. The circulatory system is partitioned into systemic and pulmonary circuits.
- **Nervous system**, which comprises both neurons (cells that electrically signal) and glial cells (supporting cells). It can be further subclassified in several ways:
  - Anatomically, the nervous system is divided into the *central nervous system* (CNS), consisting of the brain and spinal cord, and the *peripheral nervous system* (PNS), consisting of peripheral nerves, ganglia and sensory receptors, which connect the limbs and organs to the brain.
  - The PNS is functionally classified into an *afferent limb*, conveying sensory impulses to the brain, and an *efferent limb*, conveying motor impulses from the brain.
  - *The somatic nervous system* refers to the components of the nervous system under conscious control.
  - *The autonomic nervous system* (ANS) regulates the functions of the viscera. It is divided into *sympathetic and parasympathetic nervous systems.*
  - *The enteric nervous system* is a semiautonomous system of nerves that control the digestive system.
- **Muscular system**, comprising the three different types of muscle: skeletal, cardiac and smooth muscle.

- **Skeletal system**, the framework of the body, comprising bone, ligaments and cartilage.
- **Integumentary system**, which is essentially the skin and its appendages: hairs, nails, sebaceous glands and sweat glands. Skin is an important barrier preventing invasion by microorganisms and loss of water (H_2O) from the body. It is also involved in thermoregulation and sensation.
- **Digestive system**, including the whole of the GI tract from mouth to anus and a number of accessory organs: salivary glands, liver, pancreas and gallbladder.
- **Urinary system**, which comprises the organs involved in the production and excretion of urine: kidneys, ureters, bladder and urethra.
- **Reproductive system**, by which new life is produced and nurtured. Many different organs are involved, including the ovaries, testes, uterus and mammary glands.
- **Endocrine system**, whose function is to produce hormones. Hormones are chemical signalling molecules carried in the blood that regulate the function of other, often distant cells.
- **Immune system**, which is involved in tissue repair and the protection of the body from microorganism invasion and cancer. The immune system is composed of the lymphoid organs (bone marrow, spleen, lymph nodes and thymus), as well as discrete collections of lymphoid tissue within other organs (for example, Peyer's patches are collections of lymphoid tissue within the small intestine). The immune system is commonly subclassified into:
  - *The innate immune system*, which produces a rapid but non-specific response to microorganism invasion.
  - *The adaptive immune system*, which produces a slower but highly specific response to microorganism invasion.

The body systems do not act in isolation; for example, arterial blood pressure is the end result of interactions between the cardiovascular, urinary, nervous and endocrine systems.

What is homeostasis?

Single-celled organisms (for example, an amoeba) are entirely dependent on the external environment for their survival. An amoeba gains its nutrients directly from and eliminates its waste products directly into the external environment. The external environment also influences the cell's temperature and pH, along with its osmotic and ionic gradients. Small fluctuations in the external environment may alter intracellular processes sufficiently to cause cell death.

Humans are multicellular organisms – the vast majority of our cells do not have any contact with the external environment. Instead, the body bathes its cells in extracellular fluid (ECF). The composition of ECF bears a striking resemblance to seawater, where distant evolutionary ancestors of humans would have lived. Homeostasis is the regulation of the internal environment of the body to maintain a stable, relatively constant and optimised environment for its component cells:

- **Nutrients** – cells need a constant supply of nutrients and oxygen (O_2) to generate energy for metabolic processes. In particular, plasma glucose concentration is tightly controlled, and many physiological mechanisms are involved in maintaining an adequate and stable partial pressure of tissue O_2.
- **Carbon dioxide (CO_2) and waste products** – as cells produce energy in the form of adenosine triphosphate (ATP), they generate waste products (for example, H^+ and urea) and CO_2. Accumulation of these waste products may hinder cellular processes; they must be transported away.
- **pH** – all proteins, including enzymes and ion channels, work efficiently only within a narrow range of pH. Extremes of pH result in denaturation, disrupting the tertiary or quaternary structure of proteins or nucleic acids.
- **Electrolytes and water** – the intracellular water volume is tightly controlled; cells do not function correctly when they are swollen or shrunken. As sodium (Na^+) is a major cell membrane impermeant and therefore an osmotically active ion, the movement of Na^+ strongly influences the movement of water. The extracellular Na^+ concentration is accordingly tightly controlled. The extracellular concentrations of other electrolytes (for example, the ions of potassium (K^+), calcium (Ca^{2+}) and magnesium (Mg^{2+})) have other major physiological functions and are also tightly regulated.

- **Temperature** – the kinetics of enzymes and ion channels have narrow optimal temperature ranges, and the properties of other biological structures, such as the fluidity of the cell membrane, are also affected by temperature. Thermoregulation is therefore essential.

Homeostasis is a dynamic phenomenon: usually, physiological mechanisms continually make minor adjustments to the ECF environment. Following a major disturbance, large physiological changes are sometimes required.

How does the body exert control over its physiological systems?

Homeostatic control mechanisms may be intrinsic (local) or extrinsic (systemic) to the organ:

- **Intrinsic homeostatic mechanisms** occur within the organ itself through autocrine (in which a cell secretes a chemical messenger that acts on that same cell) or paracrine (in which the chemical messenger acts on neighbouring cells) signalling. For example, exercising muscle rapidly consumes O_2, causing the O_2 tension within the muscle to fall. The waste products of this metabolism (K^+, adenosine monophosphate (AMP) and H^+) cause vasodilatation of the blood vessels supplying the muscle, increasing blood flow and therefore O_2 delivery.
- **Extrinsic homeostatic mechanisms** occur at a distant site, involving one of the two major regulatory systems: the nervous system or the endocrine system. The advantage of extrinsic homeostasis is that it allows the coordinated regulation of many organs and feedforward control.

The vast majority of homeostatic mechanisms employed by both the nervous and endocrine systems rely on negative feedback loops (Figure 1.1). Negative feedback involves the measurement of a physiological variable that is then compared with a 'set point', and if the two are different, adjustments are made to correct the variable. Negative feedback loops require:

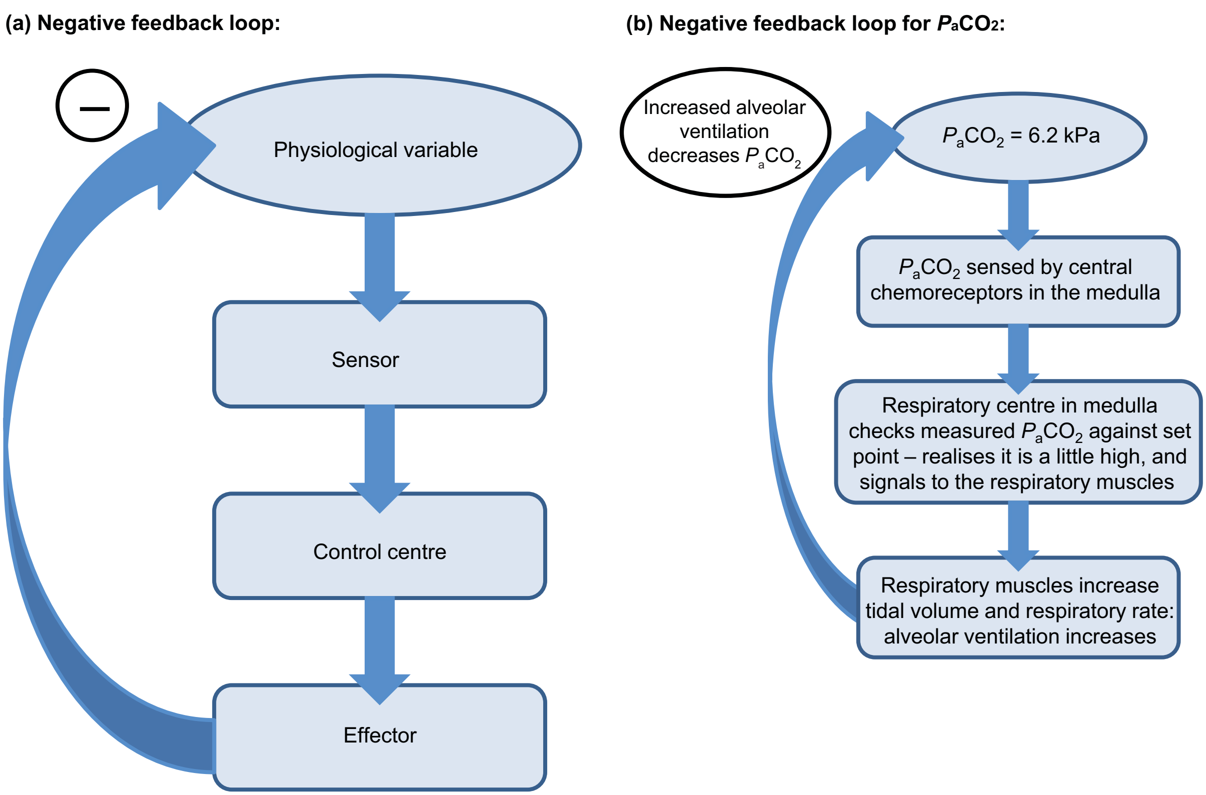

Figure 1.1 (a) Generic negative feedback loop and (b) negative feedback loop for arterial partial pressure of CO_2 (P_aCO_2).

- **Sensors**, which detect a change in the variable. For example, an increase in the arterial partial pressure of CO_2 (P_aCO_2) is sensed by the central chemoreceptors in the medulla oblongata.
- **A control centre**, which receives signals from the sensors, integrates them and issues a response to the effectors. In the case of CO_2, the control centre is the respiratory centre in the medulla oblongata.
- **Effectors**. A physiological system (or systems) is activated to bring the physiological variable back to the set point. In the case of CO_2, the effectors are the muscles of respiration: by increasing alveolar ventilation, P_aCO_2 returns to the 'set point'.

What is positive feedback?

In physiological terms, positive feedback is a means of amplifying a signal: a small increase in a physiological variable triggers a greater and greater increase in that variable (Figure 1.2). Because the body is primarily concerned with homeostasis, negative feedback loops are encountered much more frequently than positive feedback loops, but there are some important physiological examples of positive feedback:

- **Haemostasis**. Following damage to a blood vessel, exposure of a small amount of subendothelium triggers a cascade of events, resulting in the mass production of thrombin.
- **Uterine contractions in labour**. The hormone oxytocin causes uterine contractions during labour. As a result of the contractions, the baby's head descends, stretching the cervix. Cervical stretching triggers the release of more oxytocin, which further augments uterine contractions (Figure 1.2). This cycle continues until the baby is born and the cervix is no longer stretched.
- **Protein digestion in the stomach**. Small amounts of the enzyme pepsin are initially activated by decreased gastric pH. Pepsin then activates more pepsin by proteolytically cleaving its inactive precursor, pepsinogen.
- **Depolarisation phase of the action potential**. Voltage-gated Na^+ channels are opened by depolarisation, which permits Na^+ to enter the cell, which in turn causes depolarisation, opening more channels. This results in rapid membrane depolarisation.
- **Excitation–contraction coupling in the heart**. During systole, the intracellular movement of Ca^{2+} triggers the mass release of Ca^{2+} from the

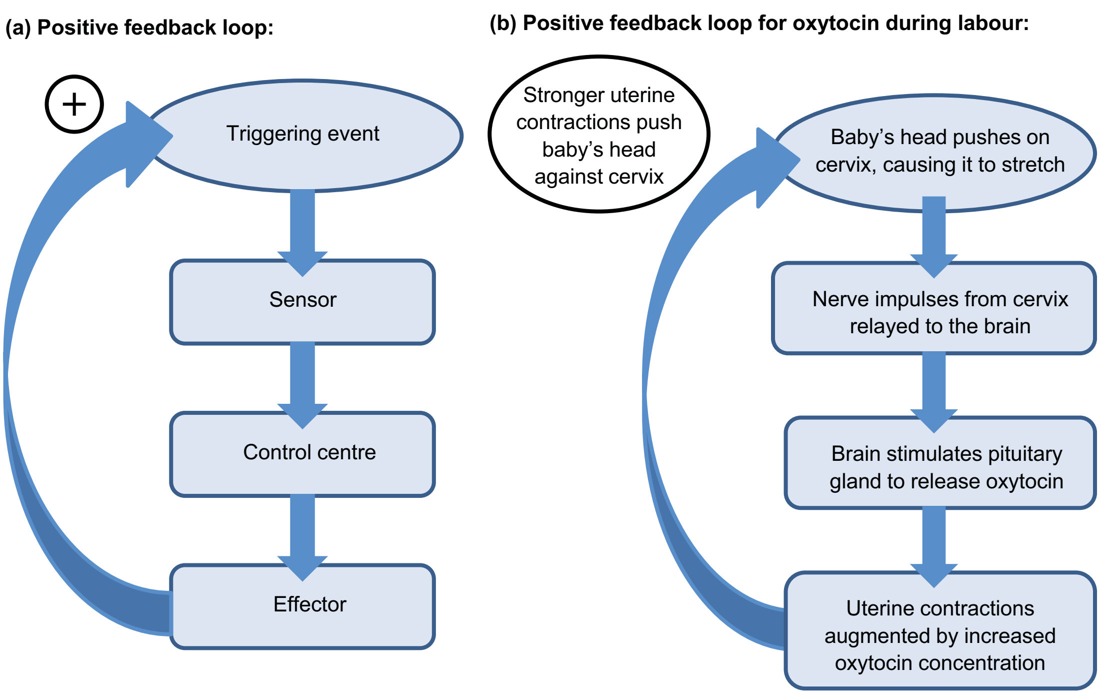

Figure 1.2 (a) Generic positive feedback loop and (b) positive feedback loop for oxytocin during labour.

sarcoplasmic reticulum (an intracellular Ca^{2+} store). This rapidly increases the intracellular Ca^{2+} concentration, facilitating the binding of myosin to actin filaments.

Where positive feedback cycles do exist in physiology, they are usually tightly regulated by a coexisting negative feedback control. For example, in the action potential, voltage-gated Na^+ channels inactivate after a short period of time, which prevents persistent uncontrolled depolarisation. Under certain pathological situations, positive feedback may appear as an uncontrolled phenomenon. A classic example is the control of blood pressure in decompensated haemorrhage: a fall in arterial blood pressure reduces organ blood flow, resulting in tissue hypoxia. In response, vascular beds vasodilate, resulting in a further reduction in blood pressure. The resulting vicious cycle is potentially fatal.

Further reading

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Chapter 2

Cell Components and Function

Describe the basic layout of a cell

Whilst each cell has specialist functions, there are many structural features common to all (Figure 2.1). Each cell has three main parts:

- **The cell surface membrane**, a thin barrier that separates the interior of the cell from the extracellular fluid (ECF). Structurally, the cell membrane is a phospholipid bilayer into which are inserted glycoproteins akin to icebergs floating in the sea. The lipid tails form a hydrophobic barrier that prevents the passage of hydrophilic substances. The charged phosphate-containing heads of the lipids are hydrophilic and thereby form a stable lipid–water interface. The most important function of the cell membrane is to mediate and regulate the passage of substances between the ECF and the intracellular fluid (ICF). Small, gaseous and lipophilic substances may pass through the lipid component of the cell membrane unregulated (see Chapter 4). The transfer of large molecules or charged entities often involves the action of the glycoproteins, either as channels or carriers.
- **The nucleus**, which is the site of the cell's genetic material, made up of deoxyribonucleic acid

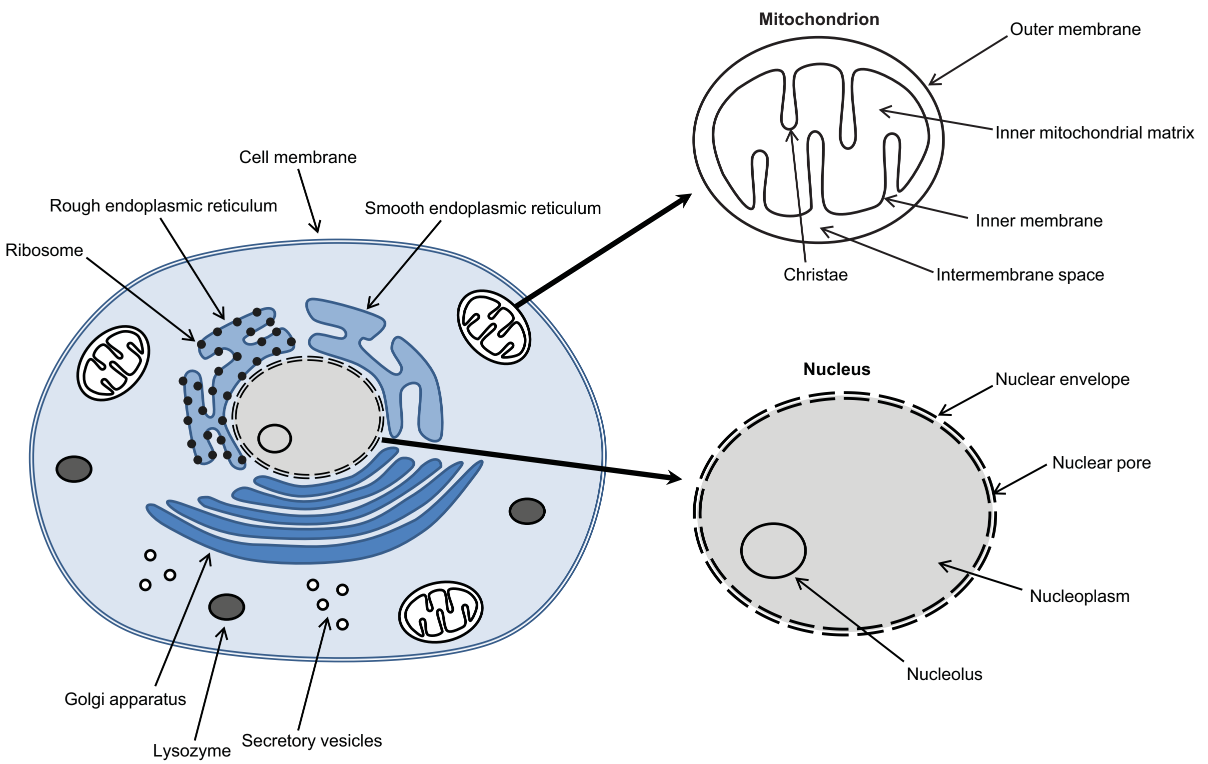

Figure 2.1 Layout of a typical cell.

(DNA). The nucleus is the site of messenger ribonucleic acid (mRNA) synthesis by transcription of DNA and thus coordinates the activities of the cell (see Chapter 3).
- **The cytoplasm**, the portion of the cell interior that is not occupied by the nucleus. The cytoplasm contains the cytosol (a gel-like substance), the cytoskeleton (a protein scaffold that gives the cell shape and support) and a number of organelles (small, discrete structures that each carry out a specific function).

Describe the composition of the cell nucleus

The cell nucleus contains the majority of the cell's genetic material in the form of DNA. The nucleus is the control centre of the cell, regulating the functions of the organelles through gene – and therefore protein – expression. Almost all of the body's cells contain a single nucleus. The exceptions are mature red blood cells (RBCs; which are anuclear), skeletal muscle cells (which are multinuclear) and fused macrophages (which form multinucleated giant cells).

The cell nucleus is usually a spherical structure situated in the middle of the cytoplasm. It comprises:

- **The nuclear envelope**, a double-layered membrane that separates the nucleus from the cytoplasm. The membrane contains holes called 'nuclear pores' that allow the regulated passage of selected molecules from the cytoplasm to the nucleoplasm, as occurs at the cell surface membrane.
- **The nucleoplasm**, a gel-like substance (the nuclear equivalent of the cytoplasm) that surrounds the DNA.
- **The nucleolus**, a densely staining area of the nucleus in which RNA is synthesised. Nucleoli are more plentiful in cells that synthesise large amounts of protein.

The DNA contained within each nucleus contains the individual's 'genetic code', the blueprint from which all body proteins are synthesised (see Chapter 3).

What are the organelles? Describe the major ones

Organelles (literally 'little organs') are permanent, specialised components of the cell, usually enclosed within their own phospholipid bilayer membranes. An organelle is to a cell what an organ is to the body – that is, a functional unit within a cell. Organelles found in the majority of cells are:

- **Mitochondria**, sometimes referred to as the 'cellular power plants', as they generate energy in the form of ATP through aerobic metabolism. Mitochondria are ellipsoid in shape and are larger and more numerous in highly metabolically active cells, such as red skeletal muscle. Unusually, mitochondria contain both an outer and an inner membrane, which creates two compartments, each with a specific function:
  - *Outer mitochondrial membrane*. This is a phospholipid bilayer that encloses the mitochondria, separating it from the cytoplasm. It contains porins, which are transmembrane proteins containing a pore through which solute molecules less than 5 kDa (such as pyruvate, amino acids, short-chain fatty acids) can freely diffuse. Longer-chain fatty acids require the carnitine shuttle (see Chapter 77) to cross the membrane.
  - *Intermembrane space*, between the outer membrane and the inner membrane. As part of aerobic metabolism (see Chapter 77), H^+ ions are pumped into the intermembrane space by the protein complexes of the electron transport chain. The resulting electrochemical gradient is used to synthesise ATP.
  - *Inner mitochondrial membrane*, the site of the electron transport chain. Membrane-bound proteins participate in redox reactions, resulting in the synthesis of ATP.
  - *Inner mitochondrial matrix*, the area bounded by the inner mitochondrial membrane. The matrix contains a large range of enzymes. Many important metabolic processes take place within the matrix, such as the citric acid cycle, fatty acid metabolism and the urea cycle.

  As all cells need to generate ATP to survive, mitochondria are found in all cells of the body (with the exception of RBCs, which gain their ATP from glycolysis alone). Mitochondria also contain a small amount of DNA, suggesting that the mitochondrion may have been a microorganism in its own right prior to its evolutionary incorporation into larger cells. The cytoplasm and hence mitochondria are exclusively

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