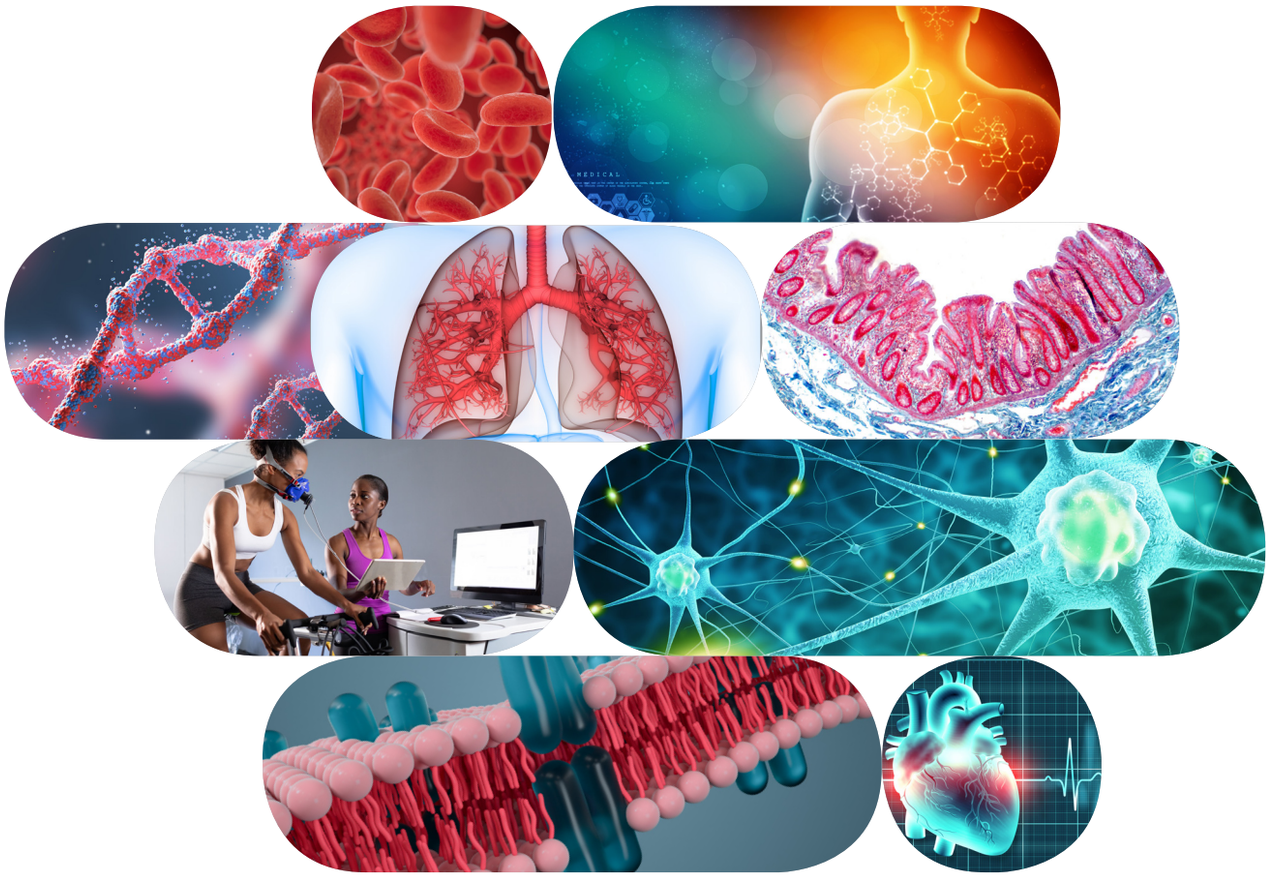
PHYSIOLOGY
CORE CONCEPTS
FOR AUSTRALIAN HIGHER EDUCATION



Contents

2023 edition

Professor Kathy Tangalakis
Victoria University
Task Force Leader

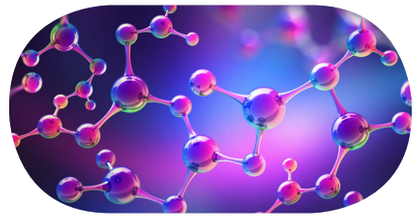
Foreward

I would like to acknowledge the passionate physiology educators across Australia who contributed to this important project. In particular the Task Force members, from 25 Australian universities across every State and the Australian Capital Territory, who gave generously of their time and extensive expertise over a 3 year period, and worked collegially and collaboratively on developing, unpacking and validating the core concepts and their constituent themes. Collectively we believe that embedding a set of core concepts developed by Australian physiology educators for the Australian Higher Education context, into physiology curricula across our universities, will provide consistency, improve assessment and teaching and learning, make benchmarking possible and provide better employability outcomes for our graduates. We call on all physiology educators to use the core concepts
and their icons in whatever context they choose. We are grateful to The Physiological Society UK for their funding support and thank the Australian Physiological Society for their support.

"Education is not the learning of facts, but the training of the mind to think."

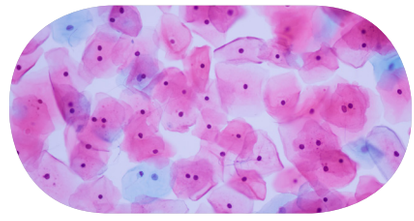
Albert Einstein

What are physiology core concepts



There are numerous ways in which to define a core concept and one accepted approach is to refer to a core concept as a “big idea” that is central to a discipline (Michael et al., 2017).

A focus on teaching core concepts is beneficial, as they provide a framework for teaching and learning, are applicable to many areas of a discipline, and can consolidate the content that students need to learn to have proficient knowledge in a discipline (Michael et al., 2017).



Nationwide consensus was reached on seven core concepts of physiology in the Australian context: Cell-Cell Communication; Cell Membrane; Movement of Substances; Homeostasis; Structure and Function; Integration; Physiological Adaptation. Each core concept has a descriptor and been unpacked into themes and subthemes.

How the physiology core concepts were developed

Tangalakis and colleagues found that a set of 15 core concepts of physiology, developed by U.S.-based educators, were not well represented in the learning outcomes across Australian university curricula (Tangalakis, Julien, et al., 2023).

A follow-up study was conducted aiming to establish consensus for the core concepts of physiology in the Australian higher education context. Using a Delphi consensus building technique, a Task Force of 25 physiology educators from 25 separate Australian universities, reached agreement on seven core concepts of physiology (Tangalakis, Lexis, et al., 2023).

Each core concept was endorsed by the physiology educator community across Australia, and the newly established core concepts were unpacked into themes and subthemes (Beckett et al., 2023*; Brown et al., 2023*; Chopin et al., 2023*; Estaphan et al., 2023*; Etherington et al., 2023*; Moro et al., 2023*; Perry et al., 2023*). The goal is for the core concepts to be embedded in Australian university physiology curricula, and to ultimately improve learning and teaching in the field.

Michael, J., Cliff, W., McFarland, J., Modell, H., & Wright, A. (2017). What are the core concepts of physiology? In The core concepts of physiology (pp. 27-36). Springer.

Tangalakis, K., Julien, B. L., Lexis, L., Hryciw, D. H., Thomas, C. J., Husaric, M., Towstoless, M., Mackinnon, P. J., Miao, Y., & Hayes, A. (2023). Mapping the core concepts of physiology across Australian university curricula. Advances in Physiology Education, 47(3), 411-418. https://doi.org/10.1152/advan.00139.2022

Tangalakis, K., Lexis, L., Hryciw, D. H., Towstoless, M., Bakker, A. J., Beckett, E., Brown, D., Cameron, M., Choate, J., & Chopin, L. (2023). Establishing consensus for the core concepts of physiology in the Australian higher education context using the Delphi method. Advances in Physiology Education, 47(3), 419-426. https://doi.org/10.1152/advan.00140.2022

* See full citations on the end page.

Physiology Core Concepts

01. **Cell-Cell Communication**

The function of the organism requires that cells pass information to one another to coordinate their activities.

02. **Cell Membrane**

Cellular membranes determine which substances enter or leave the cell or its compartments. They are essential for cell signalling, transport, and function.

03. **Movement of Substances**

The movement of substances (ions or molecules) is a fundamental process that occurs at all levels of organisation in the organism.

04. **Homeostasis**

The internal environment of the organism is actively regulated by the responses of cells, tissues and organs through feedback systems.

05. **Stucture and Function**

Structure and function are intrinsically related at all levels of the organism.

06. **Integration**

Cells, tissues, organs, and organ systems interact to create and sustain life.

07. **Physiological Adaptation**

Organisms adjust and adapt to acute and chronic changes in the internal and external environments across the lifespan.

Cell-Cell Communication

The function of the organism requires that cells pass information to one another to coordinate their activities.

01. Cell-to-cell communication occurs through electrochemical and chemical signalling and can be local or long distance.

1.1 Local communication occurs through electrochemical and chemical signalling.

- 1.1.1 Gap junctions allow direct electrochemical communication between adjacent cells.
- 1.1.2 Gap junctions allow movement of molecules between adjacent cells.
- 1.1.3 Autocrine signalling occurs when a chemical messenger acts on the cell that releases the messenger.
- 1.1.4 Paracrine signalling occurs where a chemical messenger diffuses to the site to act on adjacent cells.
- 1.1.5 Signalling through extracellular vesicles (including exosomes) allows local cell-to cell communication, and transport messengers including proteins, noncoding RNAs, DNA and lipid signals.
- 1.1.6 Local communication can be contact dependent. Cell surface cell adhesion molecules (CAMs) allow bidirectional signalling across the cell membrane of two cells when in direct contact.

1.2 Long-distance signalling occurs through chemical signalling in the nervous system and through chemical signalling (hormones) in the endocrine system.

- 1.2.1 The endocrine system secretes hormones (chemical messengers) into the bloodstream, which can exert long-lasting effects.
- 1.2.2 The nervous system releases chemical signals as neurotransmitters and neuromodulators at the synapse.
- 1.2.3 Exosomes are released from most cell types and transport messengers (including RNA, DNA, protein, and metabolites) over long distances.

02. A cell synthesises and releases a chemical messenger.

2.1 Messenger molecules can be proteins (or peptides), steroids, lipids, amines, amino acids, DNA, RNA or gases.

2.2 A cell synthesises a messenger molecule and either stores the messenger in vesicles or it escapes by diffusion.

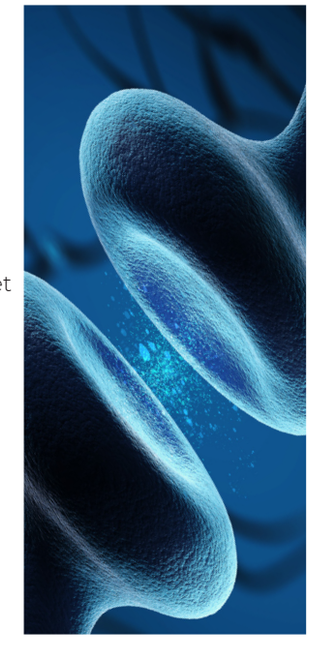
- 2.2.1 Peptides/proteins are synthesised in the cell and stored in secretory vesicles prior to release.
- 2.2.2 Steroid hormones are synthesised as required and diffuse from the cell.
- 2.2.3 Catecholamines are synthesised and stored in secretory vesicles.
- 2.2.4 Some hormones are produced and stored in an inactive form and cleavage leads to the active product (e.g., thyroid hormones and proinsulin/insulin).
- 2.2.5 Gases and eicosanoids are synthesised as required and diffuse across the cell membrane.

2.3 The rate of release of a chemical messenger from a cell is determined by the “sum” of the stimuli promoting and inhibiting that release.

2.4 Chemical signalling molecules can have biological effects even at low extracellular concentrations.

2.5 Chemical messengers that are stored prior to release can be secreted from the cell via exocytosis, or through the release of vesicles such as exosomes.

2.6 Cells that release messengers can be anywhere in the body.



03. The (solubility) hydrophilic/hydrophobic nature of the messenger can determine how the messenger molecule is transported.

3.1 The solubility of the molecule can influence how it is transported to its target cells.

- 3.1.1 Hydrophobic chemical messengers must travel with other carrier molecules i.e., binding proteins or plasma proteins.
- 3.1.2 Hydrophilic chemical messengers can travel dissolved in aqueous solution, attached to a binding protein, or transported within an exosome.

3.2 Only the messenger in solution that is free to diffuse is biologically active.

- 3.2.1 A chemical messenger bound to a binding protein in solution is biologically unavailable.

3.3 The extracellular fluid concentration of a messenger molecule depends on the balance between the production, release, and elimination of messenger molecules.

Cell-Cell Communication continued

04. The messenger must bind to a receptor protein in or on its target cell to produce a response.

4.1 Each messenger molecule binds with a certain affinity to a specific receptor molecule

- 4.1.1 Binding of a messenger to its receptor is a probabilistic event.

4.2. A cell can only respond to a messenger for which it has receptors.

4.3. The solubility/hydrophobicity of the messenger can influence the location of its receptor protein in/on the target cell.

- 4.3.1. Water-soluble (hydrophilic) primary messengers cannot pass through the cell membrane.
- 4.3.2. Water-soluble (hydrophilic) primary messengers signal through receptors on the target cell membrane (extracellular receptors).
- 4.3.3. Lipid-soluble (hydrophobic) messengers can pass through the cell membrane.
- 4.3.4. Lipid-soluble (hydrophobic) messengers can signal through either intracellular (cytoplasmic or nuclear) or extracellular receptors.
- 4.3.5. Lipid-soluble messengers that bind with intracellular receptors can interact with DNA to mediate genomic effects.
- 4.3.6. Lipid-soluble messengers that bind with extracellular receptors can mediate nongenomic effects.

4.4. The number of receptors for a particular messenger is variable.

4.5. There can be more than one type of receptor for the same messenger on different target cells, including different isoforms of the same receptor.

4.6. It is the receptor that determines the cellular response.

- 4.6.1. The same chemical signalling molecule can elicit a range of cellular responses based on the receptor subtypes it binds.
- 4.6.2. Cells have a large variety of different receptors, thus enabling them to respond to a large number of different messengers.

05. Binding of the messenger molecule to its receptor gives rise to signal transduction.

5.1. A single messenger molecule bound to its receptor can lead to the activation of signalling cascades to amplify the signal.

- 5.1.1. Because the target cell response is a multistep process and amplification occurs at each step, a single molecule can activate or alter many more molecules; the more steps in the intracellular signalling process, the greater the amplification can be.
- 5.1.2. Because the target cell response is a multistep process, there are many points at which different inputs (other messengers) can modify the response. This is referred to as integration.

5.2. There are a number of basic mechanisms for signal transduction.

- 5.2.1. Binding of a messenger molecule to an extracellular receptor can lead to signalling through a range of processes including the activation of enzymes, G proteins, or opening of ion channels.
- 5.2.2. Ion flux can activate signal transduction pathways and alter excitability.
- 5.2.3. Binding of a messenger molecule to a receptor can regulate gene expression.
- 5.2.4. The speed of the response to signalling pathways varies according to the signalling pathway.
  - 5.2.4.1. Ion channels are the fastest response mechanism.
  - 5.2.4.2. The signalling responses for extracellular receptors and second messenger systems are rapid, as second messenger molecules are already present in the cell and can be rapidly inactivated.
  - 5.2.4.3. The genomic signalling effects are slower, as transcription and translation of new molecules is required.

06. Messenger signal termination requires a combination of processes that effectively prevents the signalling molecule from binding to the receptor. This can include removal of the signalling molecule from the extracellular space or rendering the receptor unavailable.

6.1. Messenger release must be ceased.

6.2. The messenger signal can be terminated when the molecule is removed, either through diffusion (concentration becomes too low) or via chemical breakdown by enzymes or via specific transport or uptake into compartments away from the receptor.

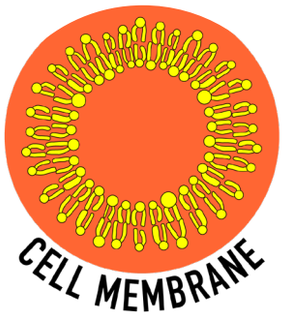
6.3. The messenger molecule must dissociate from the receptor or the receptor-messenger complex, can be internalised by endocytosis and digested in the cell, and the complex will cease to generate a signal.

6.4. Receptors can be made unavailable through internalisation, downregulation, or through pharmacological antagonism.

07. Some cells can communicate with neighbouring cells electrically; they are electrically coupled via gap junctions.

7.1. When electrically excited, current (ions) can flow from the excited cell to neighbouring cells via the gap junctions.

7.2. These currents then electrically excite the second cell synchronising depolarisation across a whole tissue.



Cell Membrane

Cellular membranes determine which substances enter or leave the cell or its compartments. They are essential for cell signalling, transport, and function.

01. Cellular membranes act as semi-permeable barriers around organelles and cells.

1.1 The plasma or cell membrane separates the fluid within the cell (intracellular fluid) from the extracellular fluids.

1.2 The structure of the cell membrane makes it semi-permeable, enabling certain substances to pass across the membrane while excluding others.

1.3 The intracellular fluid is comprised of physiological solutes (largely K^+, Cl^-) which the cell membrane helps to keep relatively constant.

1.4 Intracellular membranes enable organelles to maintain different intracellular compositions and specialised sub-cellular functions.

1.5 The structure and function of the cell membrane may vary between different regions of the same cell.

02. The cell membrane is composed of a phospholipid bilayer with associated proteins and carbohydrates.

2.1 The bilayer consists of two layers of phospholipid molecules, each with a polar (hydrophilic) head and two nonpolar (hydrophobic) tails.

- 2.1.1 Other lipids e.g., cholesterol embed in the phospholipid bilayer.
- 2.1.2 Carbohydrates can attach to phospholipid bilayers or membrane proteins.

2.2 Membrane proteins comprise integral proteins and peripheral proteins.

- 2.2.1 Integral proteins are embedded in the phospholipid bilayer and can span the membrane.
- 2.2.2 Peripheral membrane proteins attach to phospholipid bilayers or integral membrane proteins.

2.3 The cell membrane is dynamic, with moment-to-moment movement of proteins and lipids within the cell membrane.

2.4 Within a membrane there can be specialised regions with a different repertoire of proteins, carbohydrates and lipids, which enable different functions.

2.5 The membrane proteins and carbohydrates mediate functions including cell-cell adhesion, cell recognition, cell-cell communication and the transport of substances across cell membranes.

03. Transport of molecules across the cell membrane is a key aspect of cell function and follows physical and chemical principles.

3.1 Membrane transport can be passive or active.

- 3.1.1 Passive transport moves substances down an energy gradient following the principles of diffusion.
  - 3.1.1.1 Lipid soluble substances can move through the phospholipid bilayer down an energy gradient (simple diffusion).
  - 3.1.1.2 Water soluble substances (solutes) move through integral transport proteins down an energy gradient (facilitated diffusion).
  - 3.1.1.3 Facilitated diffusion uses integral transport proteins that can be channels or carriers.
    - 3.1.1.3.1 Channels are proteins with aqueous pores that solutes move through.
    - 3.1.1.3.2 Carriers transport solutes across the membrane by changing conformation (shape) in response to binding of the transported solute(s).
  - 3.1.1.4 Facilitated transport proteins show different degrees of selectivity, saturation and competition for transported solutes.
- 3.1.2 Active transport uses energy to move solutes against an energy gradient using integral transport proteins.
  - 3.1.2.1 Primary active transport uses energy directly.
    - 3.1.2.1.1 Active transport can pump ions across cell membranes using energy from ATP hydrolysis.
    - 3.1.2.1.2 Active transport (e.g., the sodium potassium ATPase) can generate and maintain gradients across the cell membrane that drive secondary active transport of other solutes.
  - 3.1.2.2 Secondary active transport uses the energy from existing electrochemical gradients to move other substances against their own electrochemical gradient.
    - 3.1.2.2.1 Secondary active transport can move different solutes in the same (co-transport) or opposite (counter-transport) directions.

3.2 Substances can cross cellular membranes via vesicular transport (e.g. exocytosis and endocytosis).

3.3 Water diffuses across the cell membrane to areas of higher solute concentration, facilitated by water channels called aquaporins.

04. Differences in ion concentrations across the cell membrane establish the membrane potential (a difference in electrical potential between the inside and outside of the cell membrane).

4.1 Most cells have a resting membrane potential that stays relatively constant.

4.2 Excitable cells rapidly change their membrane potential through opening and closing (gating) of ion channels, changing ion flow down electrical and/or chemical gradients.

05. Ion channels can be gated by ligand binding, mechanical or thermal stimulation, or a change in membrane potential.

Movement of Substances

The movement of substances (ions or molecules) is a fundamental process that occurs at all levels of organisation in the organism.

01. **Substances can be in gas, liquid (dissolved or colloid), or solid form.**

02. **The movement of substances within the body involves physical principles.**

03. **Substances move through the body, either within the same compartment, or between different compartments.**

3.1 Compartments can be extracellular or intracellular.

3.1.1 Movement between the intracellular and extracellular environment is referred to as Transmembrane movement.

3.1.2 Movement between extracellular compartments, which involves transmembrane movement, is referred to as Transcellular movement.

3.1.3 Movement between extracellular compartments, which does not involve transmembrane movement, is referred to as Paracellular movement.

3.1.4 Movement within a compartment is referred to as Luminal movement.

3.2 Compartments vary in shape and size.

3.3 Compartments can be fluid or gas filled.

04. **The movement of substances can be an active or a passive process.**

4.1 Passive movement involves substances moving down a concentration or pressure gradient, governed by the physical principles driving equilibrium.

4.2 Active movement requires energy to move substances up a concentration or pressure gradient, or against a resistance.

4.3 For electrically charged substances, the electrical gradient must also be considered, with similar charges repelling, and opposite charges attracting.

05. **Multiple gradients can act on a substance simultaneously. The sum of the gradients is the net force driving movement of the substance.**

06. **To move within or between compartments, substances must move against various levels of physical or electrical resistance.**

6.1 Charged or polar substances cannot easily move through nonpolar membranes, which act as a barrier.

6.2 Other characteristics, such as size of the substance, and temperature of the environment also affect its movement.

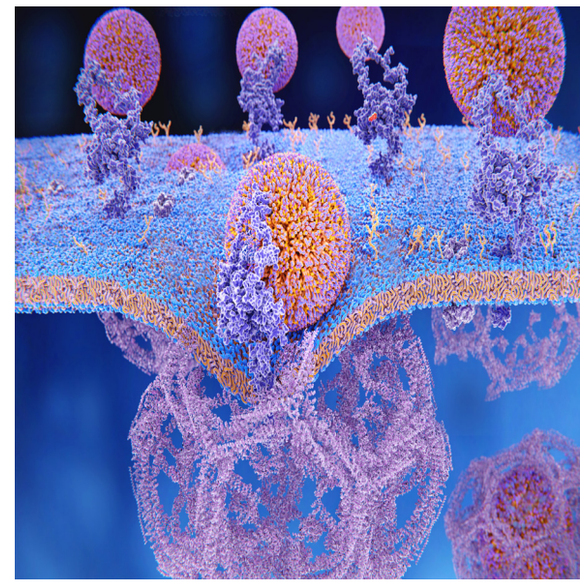
6.3 Permeability is a measure of how easily a substance moves through a barrier. Barrier permeability affects the rate of movement.

6.4 Substances moving within a fluid experience physical resistance.

6.5 Fluid moving through a compartment experiences physical resistance.

07. **Transmembrane or luminal transport of substances is also influenced by proteins (e.g., enzymes/protein carriers within blood).**

08. **Substance movement in the body can involve complex physiological transport processes such as endocytosis, exocytosis, receptor-substrate movement, phagocytosis, peristalsis, ventilation, cilia or flagella movement, etc..), which cannot be easily understood based on physical principles alone.**



Homeostasis

The internal environment of the organism is actively regulated by the responses of cells, tissues and organs through feedback systems.

01. The organism has regulatory mechanisms to maintain a relatively stable internal environment, a process known as homeostasis.

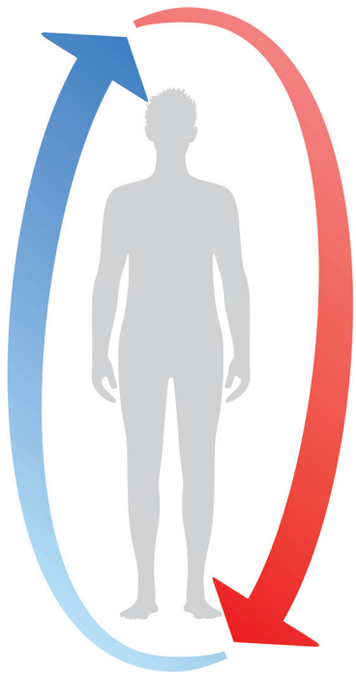
1.1. Key variables of the internal environment are kept stable by homeostatic mechanisms to sustain cell, tissue and organ function, these are known as regulated variables. If the regulated variables change too much, cells cannot function normally.

1.2. The regulated variable may be kept within a very narrow range or within a much wider range, despite changes in the external environment. The maintained range is referred to as a set-point.

1.3. To be classified as a homeostatic mechanism, 3 critical components are required: a sensor, a control centre and an effector. Note that these components may be physically far from or near to each other in the body and can even exist in the same cell.

1.4. Homeostatic regulatory mechanisms operate all the time to monitor and control the value of the regulated variable (they do not turn “on” or “off”; they are not like a “light switch,” they are like a “volume control”).

1.5. Some variables remain within a normal range but do not have the critical components of a homeostatic mechanism (e.g., heart rate).



02. Homeostatic mechanisms require internal sensors.

2.1 Homeostatic mechanisms employ a variety of types of sensors such as chemoreceptors, mechanoreceptors and thermoreceptors.

2.2 Regulated variables are constantly monitored by sensors.

2.3 Sensors detect the magnitude of the regulated variable and generate an output signal that is proportional to the magnitude of the stimulus input to the sensor.

2.4 The output signal from the sensor is relayed to the control centre.

03. Homeostatic mechanisms require a control centre.

3.1 The control centre is part of the endocrine and/or the nervous system. More than one homeostatic mechanism can contribute to the regulation of a particular variable.

3.2 The control centre (often called an integrator) receives signals from the sensors and determines the difference between the sensor input and the set range.

3.3 If the integrated input signal deviates from the set-point the control centre will send output signals to effectors, increasing or decreasing activity.

3.4 It is possible, in some circumstances, for the set-point to change (for example, body temperature in case of a fever).

3.5 Homeostatic mechanisms can be overridden by the sympathetic nervous system.

04. Homeostatic mechanisms require targets called effectors.

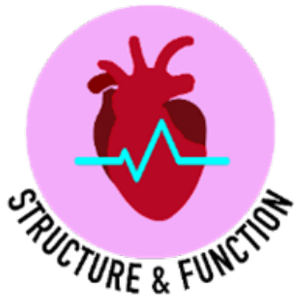
4.1 Effectors are cells, tissues, or organs that receive the control centre output.

4.2 Effectors adjust non-regulated variables (e.g., stroke volume) via physical or chemical responses (e.g., contraction of heart muscle) to adjust the regulated variable (e.g., blood pressure). Note that non-regulated variables are not directly sensed (i.e., there is no sensor for heart rate or stroke volume).

05. All homeostatic mechanisms utilise negative feedback.

5.1 Negative feedback is a control mechanism that limits the response brought about by the effector once the regulated variable is within the set-point range.

5.2 Not all negative feedback systems are homeostatic (e.g., negative feedback control of appetite).



Structure and Function

Structure and function are intrinsically related at all levels of the organism.

At the time of preparing this booklet, the renal system has been unpacked into themes and sub-themes. In the near future, we aim to complete our work on the Structure and Function core concept by unpacking the remaining physiological systems into themes and sub-themes.

The Renal System

01. **Comprises kidneys, ureters, a urinary bladder and a urethra.**

1.1 The kidney is structurally and functionally divided into a cortex and a medulla.

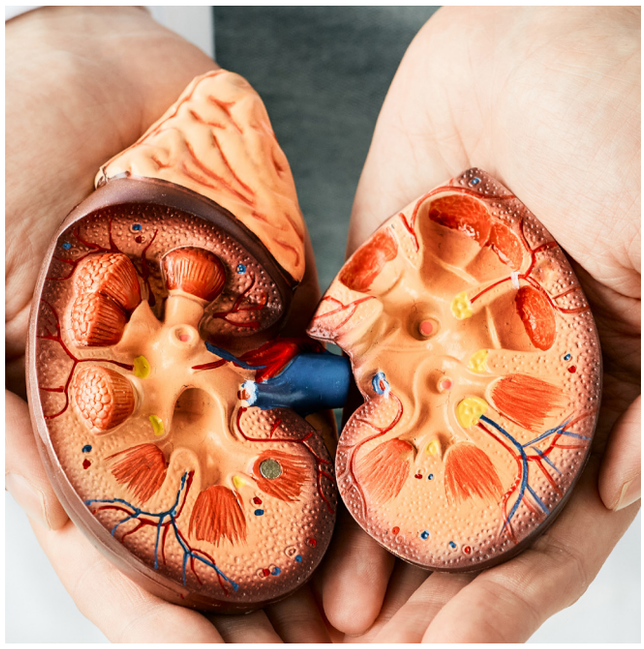
1.2 Nephrons are the functional units of the kidney and each kidney comprises approximately 1 million nephrons.

1.3 Nephrons are categorised according to their positioning and structure as cortical or Juxta medullary.

1.4 Each nephron consists of a renal corpuscle comprising a glomerulus and a glomerular capsule followed by a renal tubule that is continuous with the glomerular capsule.

1.5 The renal tubule from the glomerular capsule extends to the proximal convoluted tubule, the loop of Henle, distal convoluted tubule, and the collecting duct.

1.6 The collecting ducts collectively form renal pyramids and urine flows from here into the renal pelvis, ureter and on into the urinary bladder where it is held until micturition.



02. **Extracellular composition, volume and pH is maintained by the kidneys through physiological processes of glomerular filtration, tubular reabsorption and tubular secretion.**

2.1 The kidneys receive about 20% of cardiac output and are supplied by the renal arteries.

2.2 Renal arteries successively divide eventually forming afferent arterioles.

2.3 The afferent arteriole delivers blood to the glomerulus where small particles are filtered under pressure through filtration slits comprising fenestrations with overlying podocytes.

2.4 Filtration pressure is determined by the sum of systemic hydrostatic pressure, opposing capsular hydrostatic pressure and the oncotic pressure of the glomerulus.

2.5 The efferent arteriole that leaves the glomerulus then forms low pressure capillary beds that entwine and are closely associated with, the renal tubule of each nephron known as peritubular capillaries.

2.6 The vasa recta in the medulla, also formed from efferent arterioles, are closely associated with the juxta medullary nephrons and play an important role in the in establishing a medullary osmotic gradient.

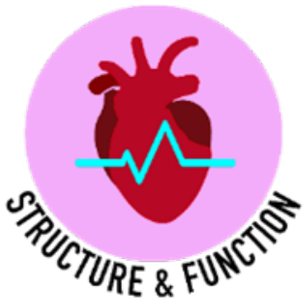
2.7 Filtrate moves from the glomerular capsule into the renal tubule where the filtrate composition is refined, and volume modified via tubular reabsorption and tubular secretion.

2.8 Tubular reabsorption (from tubule to blood) and tubular secretion (from blood to tubule) involves passive and active transport mechanisms and the exchange of water and solute particles between tubular cells and surrounding capillaries.

2.9 Balance of tubular transport in proximal tubule (bulk transport), Loop of Henle (counter-current exchange), distal tubule and collecting duct (fine tuning) determine the excretion of substances.

2.10 Reabsorption of sodium and water in the collecting duct is under the influence of the hormones Aldosterone and Antidiuretic hormone, respectively.

2.11 Urine in the collecting ducts flows into the renal pelvis (from the renal pyramids) and then through the ureters into the urinary bladder.



Structure and Function continued

03. **Micturition is the term used to describe the emptying of the bladder.**

3.1 Stretching of the bladder wall, as urine accumulates, initiates the micturition reflex and its emptying.

3.2 Emptying of the bladder involves contraction of the detrusor muscle and relaxation of the internal sphincter.

3.3 Micturition can be delayed through voluntary control of the external sphincter.

04. **Between the afferent arteriole and the distal convoluted tubule lies the Juxta glomerular apparatus (JGA) which plays a critical role in regulating renal blood flow, glomerular filtration and systemic blood pressure.**

4.1The JGA comprises the macula densa, extra glomerular mesangial cells and glandular cells.

4.2 Glandular cells are specialised smooth muscle cells mainly in the walls of the afferent arterioles that synthesise, store, and secrete the enzyme renin, and is involved in the regulation of systemic blood pressure via the renin-angiotensin-aldosterone mechanism.

4.3 Intrinsic and extrinsic mechanisms provide regulation of Glomerular Filtration Rate (GFR).

4.4 Autoregulation (intrinsic) involving tubule glomerular feedback and myogenic reflexes enables constant renal blood flow and GFR.

4.5 Extrinsic hormonal and neural input to the kidney maintains GFR.

05. **The kidney is critically important in red blood production in the adult.**

5.1 The kidney responds to chronic low levels of circulating blood oxygen by secreting Erythropoietin (EPO).

5.2 EPO is produced primarily by interstitial fibroblasts in the kidney in the adult and to a lesser extent hepatocytes. The liver in the main site of EPO production in the foetal and perinatal periods.

5.3 EPO is secreted into the blood circulatory system and targets erythroid progenitor cells in the bone marrow to stimulate red blood cell production (erythropoiesis) and acts to protect circulating red blood cells from destruction.

Integration

Cells, tissues, organs, and organ systems interact to create and sustain life.

01. **The body is organised within a hierarchy of structures, from atoms to molecules, cells, tissues, organs, and organ systems.**

1.1 The body differentiates into cells, tissues, organs, and organ systems from embryonic tissues and stem cells.

1.2 Individual cell functions can impact whole tissues, organs, organ systems and the organism due to integration within and between structural levels.

02. **The function of tissues, organs, organ systems, and the organism involves integration and coordination of processes occurring at the various levels of structural organisation.**

2.1 Communication between systems is performed through various signalling pathways (e.g., chemical, electrical) to achieve integration.

2.2 Coordination between systems is important, and may be facilitated, for example, through autonomic and somatic responses.

03. **The integration and coordination of processes occurring in response to external and internal stimuli are necessary for survival.**

3.1 Some stimuli require a rapid response with multiple mechanisms working together (i.e., reflexes, polysynaptic and diverging signals) to bring about an integrated response.

3.2 Effective homeostasis requires integrations between multiple organ system responses (e.g., thermoregulation, blood pressure).

3.3 The body must defend against infections and respond to immune threats through its structural organisation and coordination of cellular mechanisms.

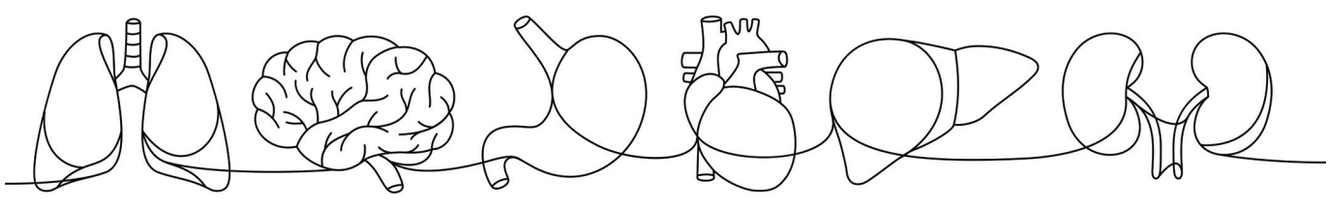
04. **Normal integrative processes can be impacted by an imbalance at any level of the system and have widespread effects.**

4.1 Medications and pharmaceuticals can imbalance, or assist to balance, the overall system's function.

4.2 Diseases (e.g., diabetes, hypertension, cancer) can impact multiple organ systems and integrated functions.

4.3 The actions of the individual can impact the internal environment, resulting in a failure to coordinate (e.g., stress, malnutrition, sedentary lifestyle).

05. **Growth must be regulated and coordinated at a systemic level (e.g., puberty, aging).**



Physiological Adaptation

Organisms adjust and adapt to acute and chronic changes in the internal and external environments across the lifespan.

01. **Changes in the internal or external environment of an organism can disturb homeostasis and disturbed homeostasis can lead to acute and/or chronic adjustments at the molecular, cellular, tissue, organ, organ system, and/or organism level.**

1.1 Disturbances in homeostasis induce a state of stress and the nature of the stressor(s) (e.g., type, intensity, onset, duration, and frequency of exposure) determines the type and extent of the physiological adjustment.

1.2 Several simultaneous stressors may interact and influence the overall physiological adjustment.

1.3 Adjustments at the molecular, cellular, tissue, organ, organ system, and/or organism level can lead to adaptation that may improve the organisms' suitability to their environment.

1.4 Adaptation persists beyond the exposure to the stressor.

1.5 Adaptation may or may not be reversible.

02. **For a given stressor, the capacity for physiological adaptation can differ between individuals and across the life span.**

03. **The capacity for physiological adaptation is on a continuum and can be trained through repeated or chronic exposure.**

04. **The integration and coordination of processes occurring in response to external and internal stimuli are necessary for survival.**

4.1 The mechanisms that lead to adaptation may initially be beneficial for a specific body function but may negatively impact other physiological processes/functions.

4.2 Failure to initiate adaptation or adequately adapt may lead to damage or disease.

4.3 The detrimental outcome may or may not be reversible and could result in death.

4.4 The repair and/or regeneration capacity of the organism at the molecular, cellular, tissue, organ, and/or organ system level determines the degree of reversibility of detrimental outcomes arising from failure to adapt.

Using the physiology core concepts

There is no single or correct way to embed the core concepts in physiology curricula. It is suggested that it should be possible to cover all core concepts in one subject, or alternatively, scaffold them across some or all year levels of a degree.

Case study 1: Introductory physiology subject

This case study illustrates how six of the seven core concepts could be included in a skeletal muscle topic that is part of a 1st year physiology subject that introduces students to all body systems. The homeostasis core concept is not included, but would most likely be covered elsewhere in the subject, demonstrating that not all core concepts have to be taught in every topic.

	CORE CONCEPT	EXAMPLES FROM SKELETAL MUSCLE TOPIC
	**Cell-Cell Communication**	Skeletal muscle contraction Neurotransmitter (acetylcholine) is released from the motor neuron axon terminal and binds to receptors on the motor end plate, resulting in depolarisation.
	**Cell Membrane**	The sarcolemma has t-tubules, which are projections of the sarcolemma forming narrow tubules into the interior of the cell, which allows the spread of action potentials deep into the skeletal muscle cell.
	**Movement of Substances**	Skeletal muscle contraction and relaxation · Release of neurotransmitter (acetylcholine) from the motor neuron axon terminal via exocytosis, and diffusion of acetylcholine across the synapse to acetylcholine receptors on the motor end plate (contraction) · Diffusion of calcium from the sarcoplasmic reticulum to the sarcoplasm (contraction) · Active uptake of calcium from the sarcoplasm to the sarcoplasmic reticulum (relaxation).
	**Structure and Function**	Skeletal muscle cells are long multinucleated cells at maturity (up to 30 cm in length); the protein architecture of muscle fibres facilitates contraction. Fibres also contain reserves of molecules important for rapid generation of ATP for muscle fibre contractions.
	**Integration**	Skeletal muscle contraction relies on signalling from the somatic nervous system · Action potentials travel along a motor neuron, triggering release of neurotransmitter (acetylcholine) from the axon terminal · Acetylcholine diffuses across the synapse and binds to receptors on the motor end plate, resulting in depolarisation and action potentials in skeletal muscle, leading to contraction
	**Physiological Adaptation**	Hypertrophy: enlargement of muscle due to increased muscle activity Atrophy: loss of muscle mass due to a lack of activity Regular endurance training promotes structural and biochemical changes in skeletal muscle: · Increased growth of capillaries serving skeletal muscle cells, and increased number of mitochondria · These adaptations improve blood delivery to muscle during exercise and increase the cell's ability to produce ATP aerobically.

Case study 2: Advanced physiology subject

Core concepts of physiology can be expanded upon in a 2nd year physiology subject that increases coverage of integration and adaptation.

	CORE CONCEPT	EXAMPLES FROM CARDIORESPIRATORY AND RENAL TOPIC
	**Cell-Cell Communication**	Cardiac muscle cells are connected electrically. Carotid bodies detect dissolved oxygen, sending nerve signals to the medulla. Anti-diuretic hormone (ADH) is released by the hypothalamus and acts on the collecting duct to stimulate water reabsorption.
	**Cell Membrane**	Nodal cells are spontaneously permeable to sodium and calcium, which can be influenced to control heart rate. Oxygen and carbon dioxide are lipid soluble molecule that diffuse the phospholipid bilayer. Reabsorption in the proximal tubule uses primary-active transport, secondary active co- and counter-transport, facilitated diffusion, simple diffusion, paracellular transport and osmosis to influence tubular fluid composition.
	**Movement of Substances**	Blood flows down a gradient generated by contraction of the heart. Ventilation occurs at the rate and depth to replace consumed oxygen and remove carbon dioxide. Urine composition is a balance of filtration, reabsorption and secretion processes – with potassium involved in all three.
	**Homeostasis**	The transient fall in mean arterial pressure when you stand up is detected and activates the sympathetic nervous system to restore (and even slightly increase) it. Breathholding elicits a transient increase in alveolar ventilation to return arterial oxygen and carbon dioxide partial pressures back to normal. Single nephron higher GFR leading to increase in fluid delivery to the macula densa cells causes a vasoconstriction in the afferent arteriole, reducing the hydrostatic pressure driving filtration, reducing GFR.
	**Structure and Function**	Elastic arteries help to convert intermittent pumping by the heart into constant blood flow at the tissue level. Repeated branching from a single trachea into millions of alveoli ensure oxygen diffusion equilibrium, the rate of which is determined by Ficks Law. The Loops of Henle absorb water in the descending limb and ions in the ascending limb to create the gradient that the collecting duct uses to influence urine composition.
	**Integration**	Control of blood flow is commonly a balance of metabolic vasodilatory signals coming from organs and sympathetic nervous system activation causing vasoconstriction of arterioles. Ventilation and perfusion in the lungs are matched to promote oxygen diffusion, which becomes bound to haemoglobin to be delivered by the blood stream to exercising muscles. Carbon dioxide is carried in the blood primarily as bicarbonate, important for maintaining acid-base balance. Osmoreceptors and baroreceptors monitor ECF osmolarity and volume, respectively, causing the release of hormones such as aldosterone and ADH to influence water and electrolyte balance by the kidney.
	**Physiological Adaptation**	Left ventricular hypertrophy can be detected as a left axis shift measured by an ECG. Exercise promotes greater SV, lower resting HR and increased capillarisation of skeletal muscles. Loss of elastic recoil as occurs with obstructive diseases such as emphysema alters the balance of forces acting on the lung to increase functional residual capacity, leading to inflated lungs. Living at high altitude decreases the response of the carotid bodies, minimising the usual increased ventilatory response to low oxygen, thus preventing respiratory alkalosis.

Physiology core concepts publications

Hayes, A., & Tangalakis, K. (2023). Australian core concepts to align learning outcomes, curriculum design, and assessment. Advances in Physiology Education, 47(3), 582-583. https://doi.org/10.1152/advan.00213.2022

Tangalakis, K., Julien, B. L., Lexis, L., Hryciw, D. H., Thomas, C. J., Husaric, M., Towstoless, M., Mackinnon, P. J., Miao, Y., & Hayes, A. (2023). Mapping the core concepts of physiology across Australian university curricula. Advances in Physiology Education, 47(3), 411-418. https://doi.org/10.1152/advan.00139.2022

Tangalakis, K., Lexis, L., Hryciw, D. H., Towstoless, M., Bakker, A. J., Beckett, E., Brown, D., Cameron, M., Choate, J., & Chopin, L. (2023). Establishing consensus for the core concepts of physiology in the Australian higher education context using the Delphi method. Advances in Physiology Education, 47(3), 419-426. https://doi.org/10.1152/advan.00140.2022

Chopin, L. K., Choate, J., Rathner, J. A., Towstoless, M., Hayes, A., Hryciw, D. H., Lexis, L., Tangalakis, K., & Force, T. (2023). Unpacking and validating the "cell-cell communication" core concept of physiology by an Australian team. Advances in Physiology Education, 47(3), 443-452. https://doi.org/10.1152/advan.00143.2022

Etherington, S. J., Moorhouse, A. J., Paravicini, T. M., Towstoless, M., Hayes, A., Hryciw, D. H., Lexis, L., Tangalakis, K., & Force, T. (2023). Unpacking and validating the "cell membrane" core concept of physiology by an Australian team. Advances in Physiology Education, 47(3), 575-581. https://doi.org/10.1152/advan.00143.2022

Brown, D., Uebergang, T., Masters, N., Towstoless, M., Hayes, A., Hryciw, D. H., Lexis, L., Tangalakis, K., & Force, T. (2023). Unpacking the "movement of substances" core concept of physiology by an Australian team. Advances in Physiology Education, 47(3), 514-520. https://doi.org/10.1152/advan.00149.2022

Beckett, E. A., Gaganis, V., Bakker, A. J., Towstoless, M., Hayes, A., Hryciw, D. H., Lexis, L., Tangalakis, K., & Force, T. (2023). Unpacking the homeostasis core concept in physiology: an Australian perspective. Advances in Physiology Education, 47(3), 427-435. https://doi. org/10.1152/advan.00141.2022

Perry, B. D., Cameron, M. S., Cooke, M. B., Towstoless, M., Hryciw, D. H., Hayes, A., Lexis, L., Tangalakis, K., & Force, T. (2023). Unpacking the renal system component of the "structure and function" core concept of physiology by an Australian team. Advances in Physiology Education, 47(3), 453-460. https://doi.org/10.1152/advan.00150.2022

Moro, C., Douglas, T., Phillips, R., Towstoless, M., Hayes, A., Hryciw, D. H., Lexis, L., Tangalakis, K., & Force, T. (2023). Unpacking and validating the "integration" core concept of physiology by an Australian team. Advances in Physiology Education, 47(3), 436-442. https://doi.org/10.1152/advan.00144.2022

Estaphan, S., Wadley, G. D., Todd, G., Towstoless, M., Hryciw, D. H., Lexis, L., Hayes, A., Tangalakis, K., & Force, T. (2023). Unpacking and Validating the'Physiological Adaptation'Core Concept of Physiology. Advances in Physiology Education, 47(4), 673-888. https://doi. org/10.1152/advan.00083.2023

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Executive Team

Kathy Tangalakis (lead, *Victoria University*), Alan Hayes (co-lead, *Victoria University)*, Michelle Towstoless (project officer, *Victoria University*), Louise Lexis, (*La Trobe University*) and Deanne Hryciw (*Griffith University*).

Task Force Members

Louise Lexis (*La Trobe University*), Deanne H. Hryciw (*Griffith University*), Anthony J. Bakker (*University of Western Australia*), Elizabeth Beckett (*University of Adelaide*), Daniel Brown (*Curtin University*), Melissa Cameron (*University of Sydney*), Julia Choate (*Monash University*), Lisa Chopin (*Queensland University of Technology*), Matthew B. Cooke (*Swinburne University*), Tracy Douglas (*University of Tasmania*), Suzanne Estaphan (*Australian National University*), Sarah Etherington (*Murdoch University*), Voula Gaganis (*Flinders University*), Andrew Moorhouse (*University of New South Wales*), Christian Moro (*Bond University*), Tamara Paravicini (*RMIT University*), Ben Perry (*Western Sydney University*), Ruben Phillips (*Edith Cowen University),* Christopher Scott (*Charles Sturt University*), Gabrielle Todd (*University of South Australia*), Tanya Uebergang (*Australian Catholic University*), Glenn Wadley (*Deakin University*), Matthew Watt/Yossi Rathner (*University of Melbourne*), Nicole Masters (*University of Sunshine Coast*), Alan Hayes (*Victoria University*).

Correspondence

Professor Kathy Tangalakis
Email: kathy.tangalakis@vu.edu.au
Tel: +61 3 9919 2618

Professor Alan Hayes
Email: alan.hayes@vu.edu.au
Tel: +61 3 9919 4658; +61 3 83958227

VICTORIA UNIVERSITY
MELBOURNE AUSTRALIA