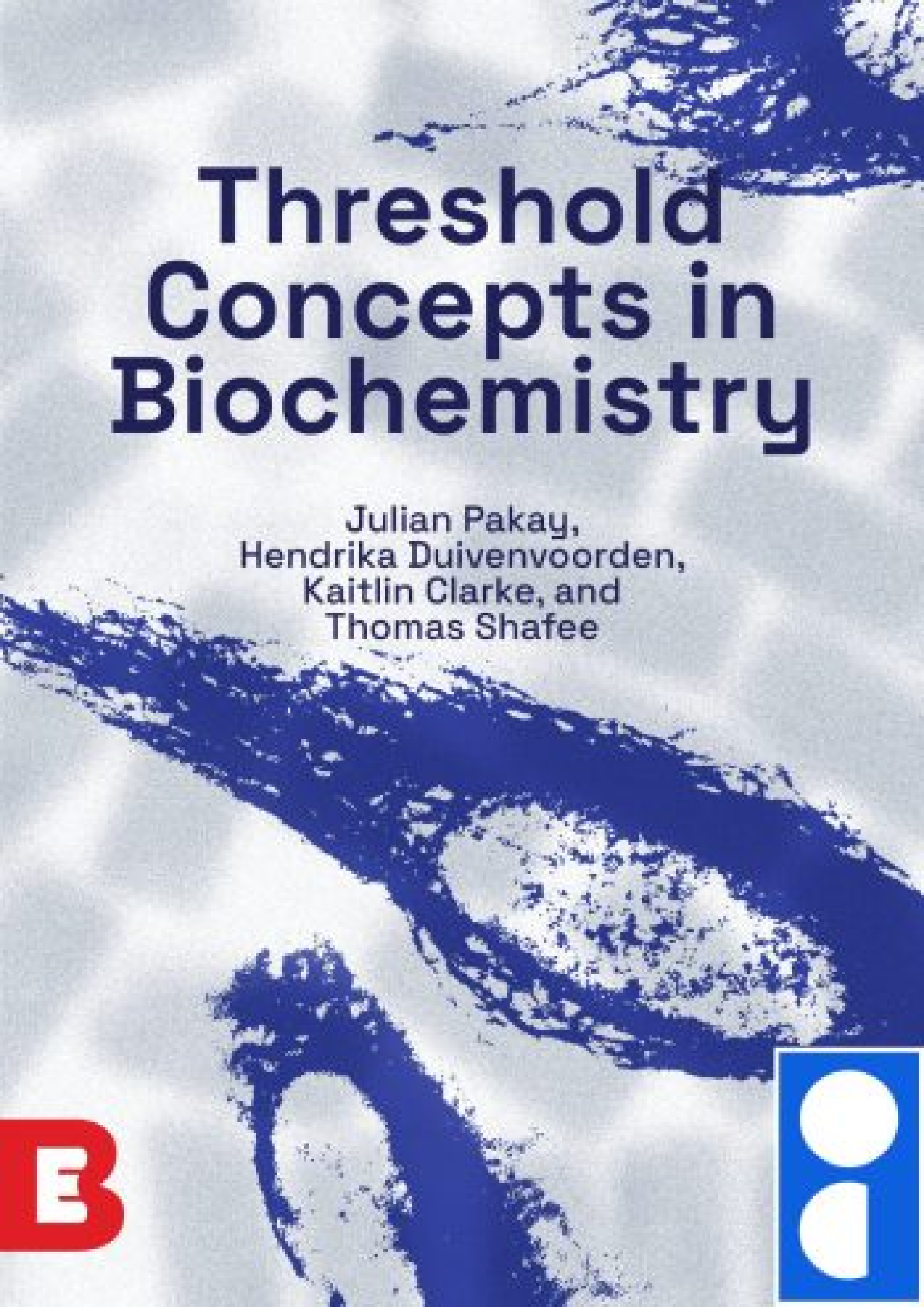
Threshold Concepts in Biochemistry

Julian Pakay,
Hendrika Duivenvoorden,
Kaitlin Clarke, and
Thomas Shafee



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Contents

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About the Authors

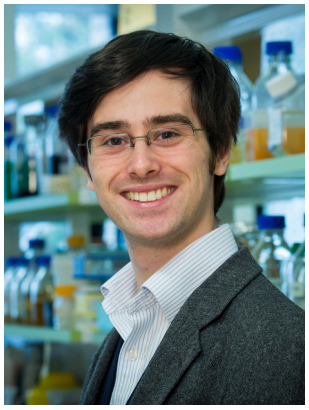
Dr Julian Pakay is a teaching-focused academic in the Department of Biochemistry and Chemistry at La Trobe University with over 12 years' experience teaching Biochemistry and Molecular Biology at all tertiary levels from 1st year through to Masters. He has completed a graduate certificate in higher education and is a fellow of the Higher Education Academy.

His teaching is informed by both experience and a scholarly approach to identify deficiencies in student understanding. His main research interests are to developing strategies to improve teaching of quantitative literacy[1] and to improve employability skills through authentic learning[2], [3] This work earned the education award at the 44th FEBS congress in Krakow, 2019.[4] His research has informed curriculum development and led to authoring an open education textbook on quantitative literacy in biomedical science, *Foundations of Biomedical Science* (in preparation). He has successfully authored numerous research articles, conference papers and education articles. In 2018, he was awarded the La Trobe Pro-Vice Chancellor's Teaching Award for redeveloping the Biochemistry capstone curriculum to support students by focusing on current concepts, functioning knowledge and employability skills.

Dr Hendrika Duivenvoorden is an education-focused lecturer and course coordinator of the Master of Genome Analytics within the School of Biological Sciences at Monash University. Over the past nine years she has taught at three independent universities, with experience teaching both undergraduate and master's year levels. Hendrika has completed a Graduate Certificate in Higher Education, is a Higher Education Academy Fellow and is the co-founder of the 'Biology Researchers in Greater Higher education and Training' (BRIGHT) group at Monash, to empower emerging education-focused academics to plan and publish their education research. Hendrika has published 12 research articles (three as first author) and was an invited speaker at the 2021 Monash University Learning and Teaching conference.

Hendrika's passion lies in transforming curricula and resources to be more engaging, authentic, and interactive for students, informed by her field and current research. She also has an interest in electronic teaching resources and assessments, on which she has presented at the Monash Science Faculty Annual Science Symposium in 2020. In 2021 Hendrika was awarded the Faculty of Science Dean's Citation for Outstanding Contributions to Student Learning.

1. Pakay, J., and D. Spencer. 2013. "Assessing competence in numeracy skills in molecular biology students." In Proceedings of The Australian Conference on Science and Mathematics Education (formerly UniServe Science Conference).
2. Pakay, J. 2017. 'Learning Artefacts: Building a Portfolio for Science Students', Australian Biochemist, 48: 11.
3. Silva, A. J. D., L. L. Alves, and J. Pakay. 2016. 'Green fluorescent protein purification through Immobilized Metal Affinity Chromatografy (IMAC) and its relevance for Biomedical Science students during Biochemistry practical classes at La Trobe University - Australia', Revista De Ensino De Bioquimica, 14: 34-45.
4. Pakay, J., J. Young, and F. Carroll. 2019. "Improving quantitative literacy in incoming biomedical science students." In 44th FEBS Congress. Krakow, Poland.



Dr Thomas Shafee is a data scientist and bioinformatician with experience in extracting actionable insights from large and complex datasets, and communicating complex concepts to a broad range of audiences. After completing a PhD in evolutionary biochemistry at University of Cambridge and Medimmune, he transitioned to postdoctoral work in bioinformatics and data science at Hexima and La Trobe University. There he developed a wide array of skills in data analysis, particularly network and multidimensional scaling analyses as well as a range of statistical techniques.

He also has a keen interest in visualising data in a human-intelligible way in order to make abstract information more intuitive. This links into his wide experience in science communication to a range of stakeholders (other academics, industry partners, students, clinicians, policymakers, and the broader public). As well as direct data analysis and visualisation, he is able to advise on research data management and ethics best practices – whether securely handing sensitive data or efficiently disseminating open data.

Having a versatile skillset has enabled him to provide advice and expertise to national and international organisations ranging from pharmacology (MIMS Australia) to psychology (H-GAPS), Antarctic research (SCAR), and knowledge dissemination initiatives (Wikimedia Foundation).

Kaitlin Clarke is a researcher and casual teaching academic, completing a PhD in the Department of Biochemistry and Chemistry at La Trobe University. Kaitlin holds a bachelor's and master's degree by Research in Biochemistry. Her high achievement throughout undergraduate studies were recognised by academic achievement awards including the La Trobe University Vice Chancellors Award and the ASM Nancy Millis Student Award in microbiology. She prepared and delivered a talk presenting her postgraduate research at the international FAOBMB conference in 2021. As a specialist subject support tutor and demonstrator, Kaitlin has been involved in curriculum development and extensive experience in guiding undergraduate students grappling with difficult concepts. Additionally, she has several years' experience in laboratory demonstration/tutoring including Anatomy at The University of Newcastle and Biochemistry at La Trobe University helping students to bridge the gap between theory and practical application. She brings this experience and importantly a "near-peer" sensibility to the project. Kaitlin is a capable author and recently submitted a 10,000-word review first author paper to *Frontiers in Immunology* which will be published this year.

Acknowledgements

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CAUL has been at the forefront of sector-wide initiatives that focus on developing the capacity and capability to publish open textbooks and other open educational resources in Australia and New Zealand.

Chapter 1: Studying biology at the molecular level

1.1 Introduction

This e-book is designed to be a relatively succinct resource for learning the key threshold concepts in biochemistry and molecular biology. Since these key concepts underpin everything in biology, this resource is designed for any students beginning a tertiary course related to biology, not just those who are focused on biochemistry or molecular biology. It is also useful for students who may be coming back to study after a hiatus and need to refresh their understanding of concepts or for anyone who wants a reasonably quick primer on biology at the molecular level. This e-book is not designed to be a replacement for traditional textbooks but rather this text focuses on the key threshold concepts agreed by experts in this discipline to be particularly important for establishing a solid foundation. These concepts are by their nature ones which many students tend to find initially difficult and problematic but, as the name 'threshold concepts' implies, once understood will provide a gateway for further understanding the discipline.

Overview of the contents

Chapter 2 makes a case for all biologists to have a fundamental literacy of life at the molecular level, and we provide some advice (based on hard-won experience!) on how to effectively study this discipline. We provide an overview of what biochemistry and molecular biology are and how they came to be. The story of their development provides a way to gain an overview of the discipline. The 'black boxes' in understanding of the early pioneers mirror the black boxes that all students must draw around unfamiliar concepts and their relationships as they learn them for the first time.

In Chapter 3, we define life itself at the molecular level, concentrating on what all life on Earth has in common, from the smallest microorganisms through to complex multicellular organisms like us.

Subsequently, each chapter tackles an overarching **threshold concept**. In turn we focus on:

Chapter 4: The flow of genetic information in living systems

Chapter 5: How matter and energy are transformed in living systems

Chapter 6: How cells control and regulate their internal environments

Chapter 7: How structure is related to function at the molecular level

Chapter 8: The importance of the theory of evolution to understanding biology at the molecular level

Navigating the material

The overarching threshold concepts are broken down into smaller threshold concepts. You will recognise these by the **doorway** icon alongside them. Learning these and replacing prior misconceptions will open the door to greater overall understanding.

Work through the material actively – take notes and check your understanding at every opportunity. Wherever you see the **knowledge check** icon there will be some limited choice or short-answer questions to test your vocabulary or fundamental understanding.

Wherever you see the **discussion question** icon, there will be some questions probing your deeper understanding of the topic. These will require more thought and ask you to apply your knowledge to a complex problem. These can make good questions to discuss collaboratively with peers, tutors, study groups and so on.

We hope that once you understand these threshold concepts in biochemistry and molecular biology you will be inspired to continue learning more!

Australia and New Zealand in focus

Wherever you see the **Australia and New Zealand in focus** icon we will highlight the contributions made to this discipline by researchers from Australia and New Zealand or how Australia and New Zealand contribute a unique perspective to the discipline.

You should not only feel proud and inspired by these historical contributions but also by the current research occurring in Australia and New Zealand. Our biochemistry and molecular biology communities rank amongst the world's best in terms of the number and quality of publications per head of population and our research facilities are world-class. We sincerely hope this specific focus allows you to recognise the opportunities this discipline can provide to you and the importance to our society as a whole.

1.2 Information for instructors

Biochemistry and molecular biology represent one of the fastest-growing fields of scientific research and technical innovation, and the resulting biotechnology is increasingly applied to other fields of study. So, an understanding of biochemistry and molecular biology (we use these terms largely interchangeably here) is critically important for students in all biological disciplines. However, at the same time, the content is inherently complex, highly abstract, and often deeply rooted in the pure sciences – mathematics, chemistry, and physics. This makes it difficult to learn and to teach.

Due to the rapid pace of change and accumulation of knowledge in biochemistry it is conceded that it is impossible to cover content exhaustively. Therefore, decisions must be made regarding which information is crucial to the study of biochemistry and which information can be omitted. In response to this, several studies have been undertaken to identify the key foundational concepts and skills required by majors in the discipline. Our experience in teaching biochemistry is consistent with others in that many students fail to grasp these concepts early. This presents a major barrier to learning, progressing in the discipline, and attaining the requisite skills. Almost always, the barriers to learning are misconceptions related to understanding key threshold concepts.

Threshold concepts have been identified in numerous disciplines and while often they are relatively few, mastering them causes a transformative shift in a student's understanding and appreciation of that field and empowers students to connect prior and new knowledge in more sophisticated ways. Threshold concepts are partly defined by their transformative nature but also by their 'troublesome' nature. In 2014, a study[1] funded by the American National Science Foundation identified the key threshold concepts critical for biochemistry in five major areas:

1. The central importance of the theory of evolution to all biological sciences
2. Matter and energy transformation
3. Homeostasis, control and regulation
4. Biological information
5. Macromolecular structure and function

A key barrier to understanding these concepts is their abstract nature. This resource attempts to lower this barrier through careful explanation of domain-specific language using vocabulary students already understand, by using visualisations and metaphors of complex concepts and by applying knowledge checks in which students can check their understanding. Students will also be able to apply their newly acquired conceptual understanding to novel problems with access to worked solutions.

This e-book is designed as a succinct and focused resource, specifically aimed at helping students grasp key threshold concepts in biochemistry – a cognitively demanding task. By focusing on the specific information required to understand the threshold concept and minimising extraneous detail, our intention is that cognitive load will be reduced. This will free students to focus on mastering the foundational concepts necessary in this discipline.

1. Loertscher, J., Green, D., Lewis, J., Lin, S., & Minderhout, V. (2014). Identification of threshold concepts for biochemistry. CBE Life Sciences Education, 13(3), 516–528.

1.3 Target audience

This resource is primarily aimed at novice students beginning their studies of biochemistry or molecular biology. However, given the fundamental importance of the threshold concepts covered to the mastery of the discipline and their inherently abstruse nature, this resource will be useful for reinforcement and remediation for students entering more advanced courses, where it will be assumed knowledge. This is particularly relevant for those students who failed to grasp these concepts early on or to help rebuild knowledge for those students who have misconceptions. Furthermore, it is worth noting that many science courses no longer require prerequisite knowledge in biology and this resource can help bridge the gap into tertiary study.

It will also be useful for students in other biological disciplines (e.g. genetics, microbiology or biomedical science) that are underpinned by basic biochemistry and molecular biology. In addition, it will make a useful primer for students engaged in other biological disciplines with a tangential biochemical/molecular focus (e.g. zoology or botany) where a basic literacy in the foundational knowledge of the threshold concepts of biochemistry or molecular biology is increasingly desired.

The open nature of this resource also allows it to be freely used by instructors in all of the disciplines above as directed reading or for the problems and case studies within, which can be selectively used to supplement other course materials.

We have included content that focuses on biochemistry and molecular biology through a prism of Australian and New Zealand research. The discipline in Australia and New Zealand is represented by outstanding Nobel laureates including Howard Florey (Australia), Maurice Wilkins (New Zealand), Peter Doherty (Australia) and Elizabeth Blackburn (Australia's first female Nobel laureate). We hope that students feel inspired by this and also by current research. This e-book promotes the discipline from a uniquely local perspective and allows students to recognise opportunities for themselves and the importance of the field to society. However, if you are instructing students from outside Australia or New Zealand, feel free to substitute our local content with something more relevant for your students.

1.4 Why study biology at the molecular level?

There is a molecular basis to life. That is, all biological function depends on events that occur at the molecular level. We now understand that these events are coordinated by (often) complex molecular machinery even if we do not fully understand every aspect of their function. These complex molecular machines are comprised of large molecules or clusters of molecules that include proteins, nucleic acids such as deoxyribonucleic acid (DNA), carbohydrates and lipids.

For example, we now understand the molecular basis of inheritance – that DNA, ribonucleic acid (RNA) and the genetic code transmit hereditary information from parents to offspring. We understand how functional gene products (e.g. proteins) work. That is, we are able to relate the complex and varied structure of proteins to their functional roles. We have developed techniques to map the interactions of these molecules, quantitate their abundance, determine their localisation within the cell and study the processes they mediate.

This **molecular revolution** began in earnest in the 1950s following key scientific breakthroughs that linked our understanding of inheritance to the internal molecular machinery of cells. It has transformed *every* aspect of biology. Ecologists can now track organisms using their DNA (see *Monitoring the platypus with environmental DNA*), evolutionary relationships can be accurately mapped using molecular data, taxonomy is resolved by molecular data, understanding the molecular basis of disease has revolutionised diagnosis and treatments, and molecular understanding has improved agriculture and land management.

If one visits most modern biology laboratories regardless of their discipline, whether it is biomedicine, agricultural biology, zoology, microbiology or botany, they tend to appear alike. This is because there is an incredible similarity and overlap in the technical approaches used, regardless of the biological system being studied. Any differences you do notice will likely be due to the underlying biological system under investigation. For example, a microbiology laboratory may use agar plates upon which to culture microorganisms or a plant biology laboratory may use a greenhouse to grow the plants under study. However, even laboratories that study disparate systems may use common approaches such as culturing vinegar flies (*Drosophila*) or zebra fish (both animals are common genetic models for various useful reasons). The actual molecular techniques used are likely to be very similar. It is not uncommon for researchers in biology who are working at the molecular level to never see the organism under investigation! All the experiments are undertaken using material extracted from the organism in question. It is also possible that a biologist working on a specific problem does not even see biological material at all! This is because due to the staggering amount of data available, some investigations can now even be undertaken solely *in silico*; that is, by analysing online databases.

You will find biochemists and molecular biologists working in all biological disciplines. Even if they describe themselves as a zoologist, botanist or ecologist, they will often have functional literacy, if not proficiency, in biochemical and molecular techniques.

Figure 1.1 A typical biology laboratory: Almost all modern biology laboratories look alike (at least at the cursory level) as much of the research is focused on understanding biology at the molecular level. The researcher here could be working on almost any aspect of biology from conservation ecology through to human disease. Image: 'Woman In White Long Sleeved Laboratory Gown Standing' by Polina Tankilevitch from Pexels used under Pexel license.

Monitoring the platypus with environmental DNA

All organisms shed DNA into the environment as they lose cells, hair, skin, scales, faeces etc. With recent improvements in technology, it is now possible to collect and sequence this DNA. These trace amounts of DNA, known as environmental DNA (eDNA), can be used to determine which species are present in a particular environment without having to directly observe or capture them. As every organism has a unique DNA sequence, their shed DNA provides a signature that can be used to trace them. For example, from a small sample of water it is possible to obtain a genetic profile of all the organisms present in a waterway.

Australia and New Zealand have been at the forefront in using eDNA to manage both endangered and also invasive species. The iconic Australian animal the platypus is at risk due to habitat loss and drought. eDNA is allowing this notoriously elusive species to be monitored. By understanding its range, environmental scientists are able to make better informed decisions regarding land and waterway management. Since the collection of eDNA is a simple task – a water sample is all that is required – monitoring can be assisted by members of the public. In Australia, one of the world's largest citizen science projects, *The Great Australian Platypus Search*, was launched in 2021, to map platypus populations across the state of Victoria.

Figure 1.2 A wild platypus from a river in Victoria, Australia: By using techniques to monitor environmental DNA (eDNA) it is possible determine the distribution of species like the platypus without having to directly observe or capture them. Image: 'Wild Platypus' by Klaus from Wikimedia Commons used under CC BY-SA 2.0.

What exactly is analysed in eDNA?

Typically, a gene that is highly conserved and found in all species is used for eDNA analysis. For example, for analysis of the microbiome (all the microbes in an environment) the 16S ribosomal RNA gene is used for identifying species present (all life has ribosomes – see Chapter 3.) For animals, the mitochondrial cytochrome c oxidase I (COI) gene is often used. This gene is useful as it is found in mitochondrial DNA, and mitochondria are found in all eukaryotes. Each cell has many copies of this DNA, so there are more copies of mitochondrial DNA than nuclear DNA. Importantly, there are regions in the sequence of this gene that show enough variability for it to provide a unique signature, allowing it to be used to distinguish individual species.

Chapter 2: How to study biology at the molecular level

2.1 What is molecular biology?

Biochemistry and molecular biology are used interchangeably in this book, and they are increasingly recognised as a unified discipline, rather than as two distinct disciplines or subdisciplines. Probably this is due to widespread adoption of the techniques of both disciplines by all biologists. However, historically molecular biology emerged from a convergence between biochemistry and genetics. **Biochemistry** is centred in chemistry and principally deals with understanding the function of proteins. **Genetics** is principally concerned with the function of genes and inheritance. **Molecular biology** emerged later, once the molecular mechanisms (biochemistry) of gene function were determined, and focuses on the relationship between genes and functional gene products (which are in most cases proteins). So molecular biology could be viewed as the nexus between biochemistry and genetics.

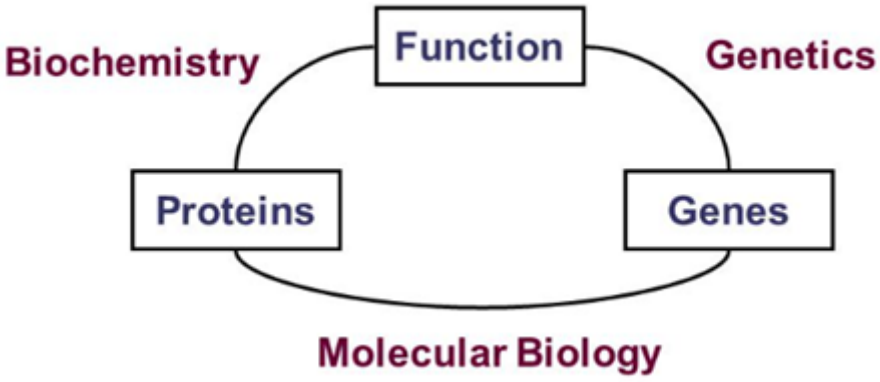

Figure 2.1 The relationship between biochemistry, genetics, and molecular biology: Molecular biology war born out of discoveries which linked genes and inheritance to with functional gene products (proteins).

2.2 What makes biochemistry and molecular biology so difficult?

Biochemistry and molecular biology have a reputation for being difficult to understand. This is not altogether undeserved! When you begin these disciplines, there is a lot of new information, many new terms to learn and some difficult concepts. One aspect that makes biochemistry and molecular biology difficult is that they draw on knowledge from other disciplines – most heavily from biology, which provides the relevance; but also chemistry, which provides the molecular understanding; and to a certain extent mathematics and physics (see Figure 2.2). As a student you will need to be prepared to integrate knowledge from these other disciplines. If you were to specialise in biochemistry or molecular biology, it is likely you would take classes at some point in all of these disciplines.

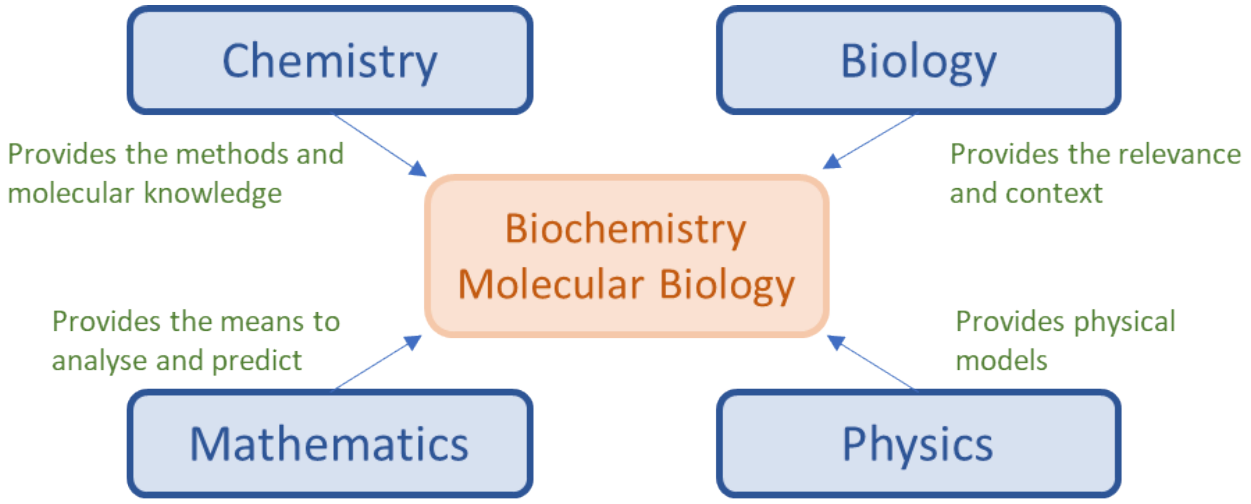

Figure 2.2: While biochemistry and molecular biology are disciplines themselves, the underlying concepts rely heavily on other disciplines.

2.3 How much chemistry will I need?

This is a very common question from students beginning a biological discipline. You *will* need to understand some chemistry! This text assumes some familiarity with basic concepts. For example, you should understand atomic structure, elements, periodicity and molecular structure. You will need to know about covalent and non-covalent bonding, polarity (electronegativity), ionisation, acids and bases, and pH. A knowledge of chemical reactions is important, so stoichiometry, oxidation-reduction chemistry and catalysis should be familiar concepts to you. A basic understanding of organic chemistry and the common functional groups is also very useful.

If these terms are unfamiliar, or you realise you need to refresh these concepts, it is worth spending some time reading an introductory chemistry text.

Knowledge check: How is your chemistry?

This short diagnostic will test your knowledge of chemistry and provides links to further resources to help you get up to speed if necessary.

An interactive H5P element has been excluded from this version of the text. You can view it online here:
https://oercollective.caul.edu.au/threshold-concepts-in-biochemistry/?p=141#h5p-7

Help – this is all too abstract!

Biology at the molecular level is complex. It involves multiple processes that interact and impinge on each other. Life represents an emergent property of these processes acting together (see Chapter 3). So by definition it is impossible to understand these processes fully by looking at them in isolation. Things only start to make sense after you learn how they work together.

This is a problem when you first begin learning and it is normal for things to initially seem a bit abstract! That is, it is normal to learn about a process but not be completely sure about how it fits into biology in general. For example, consider how information flows through a biological system (see Figure 4.6). Genetic information is stored as discrete hereditary units called genes in DNA (a nucleic acid) and the information is transcribed to RNA (also a nucleic acid) before being translated into protein. Proteins are the functional products of genes.

It might thus seem reasonable to start your learning with DNA, since it represents the start of that process. The problem with this approach is that it is impossible to really understand how this transfer of information works without understanding proteins (the functional products of genes) in the first place! It is the proteins that facilitate the whole process.

In Figure 2.3 the proteins that catalyse this transfer of information are written in pink. DNA polymerase, a protein, makes new copies of DNA during cell division, RNA polymerase, another protein, makes an RNA transcript using the DNA as a template and ribosomes (a molecular machine made from many proteins and also RNA molecules) translate the information in the RNA into proteins.

Okay, so since proteins are important, then the answer might be to start with understanding what proteins are and how they work. But the problem now is that proteins are encoded by genes and therefore understanding proteins fully requires understanding how DNA works!

Whatever you start with will require drawing a ‘black box’ around something else, and things will only start to make sense once you understand enough concepts (see Figure 2.3). This example of the interplay between DNA and protein, which plagues most beginner biology students, also mirrors the situation the pioneers of molecular biology faced. These researchers made significant inroads into understanding processes such as inheritance or biological catalysis often with very limited knowledge of the biological molecules responsible.

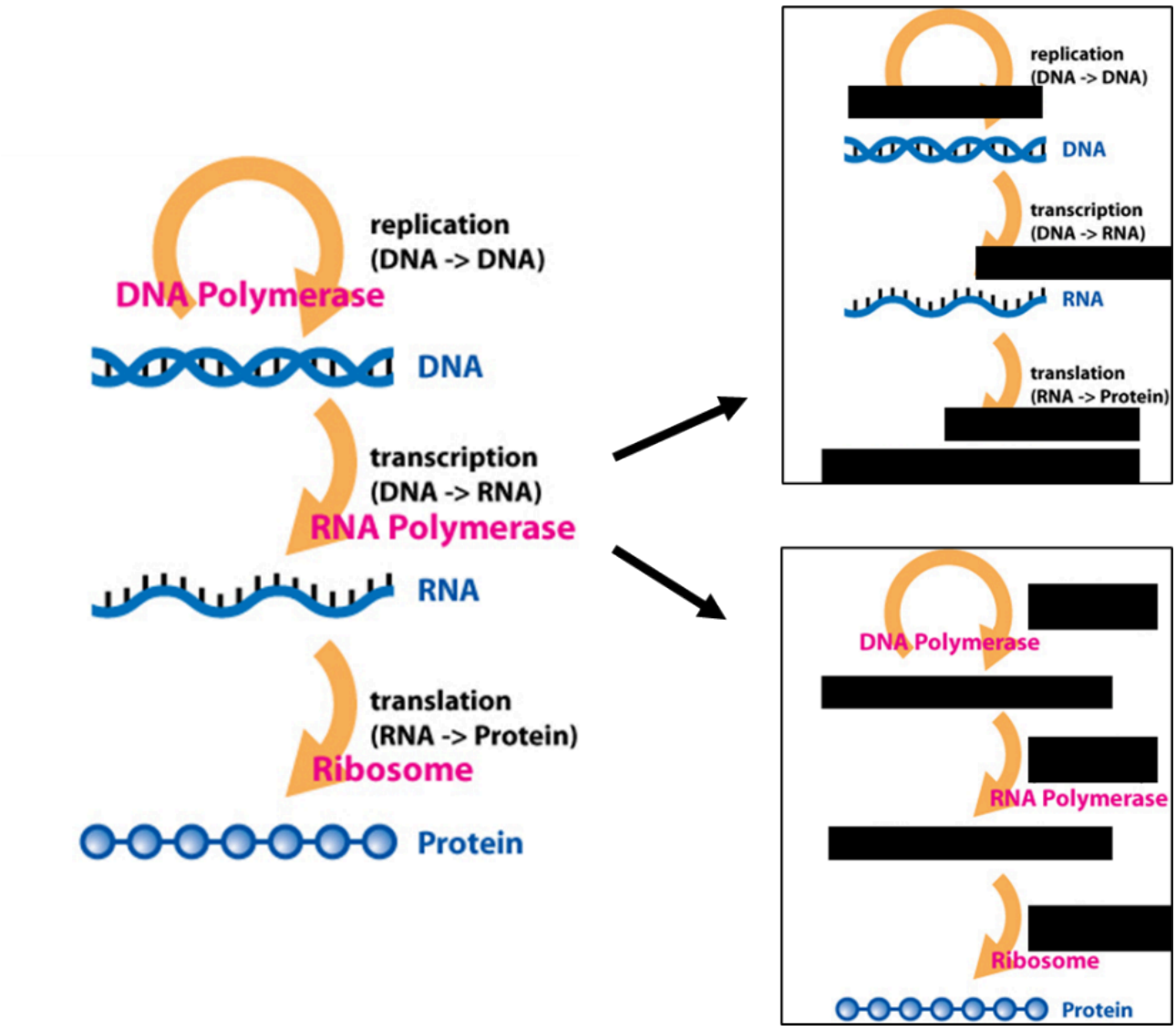

Figure 2.3: Understanding the flow of biological information, from DNA to RNA to protein, requires an understanding of both nucleic acids and proteins. Whichever you learn about first, requires drawing a "black box" around the other. It is only when you learn about both DNA and proteins does the process become clear.
Image: Adapted from Central Dogma of Molecular Biochemistry with Enzymes by Daniel Horspool from Wikimedia Commons used under CC BY-SA 3.0.

Can it be less abstract?

One way to make things less abstract is to try to get an overview first. This will initially seem overwhelming, and you have to accept that lots of detail will be missing, but once you have a sense of the bigger picture, then as you learn things in more detail, they will fit easier in place. A quick way to get an overview is to follow the timeline of the major discoveries in biology which led to our current understanding of molecular biology. The major concepts will be revealed to you sequentially, it will be easier to remember new terms if you know their origins, and you will learn about DNA and protein in terms of their function.

2.4 Advice for studying biology at the molecular level

Yes, biochemistry and molecular biology at times can be challenging, but it is not all bad news! There are a few things to note and a few approaches you can follow that should make things easier than they initially appear or pay dividends in the long run.

All extant life is related. This is a very good thing!

All extant life (living organisms which exist now on Earth) has a common ancestor. The evidence for this is presented in Chapter 3. This means that even with all of the amazing diversity of life around us, because all living things are related, they work in fundamentally the same way at the molecular level. For example, all life uses DNA to store genetic information and codes it essentially in the same way, and all life uses the same or similar basic molecular building blocks and organises them in the same way. This means that once you understand a few basic principles, you will be able to apply this knowledge to all living things. Imagine how difficult it would be if this were not the case, and we had to learn everything from scratch when we moved on to a new organism!

Finding the patterns

Biology (and in fact all science) is concerned with discovering relationships between variables. That is, it is about discovering trends and patterns. The most useful discoveries in biology are those that are explanations for general phenomena. Similarly, when you are learning a discipline, it is most useful to learn the principles that have the broadest applicability.

When you first learn biology at the molecular level it might seem that there is a bewildering amount of information to learn. There is a lot! But you will also realise that many processes work in a similar way or even use the same or very similar components.

In his essay ‘Evolution and Tinkering’, published in *Science* in 1977, the French biologist and Nobel laureate, François Jacob described evolution as a ‘dogged tinkerer’. What he meant by this is that evolution should not be compared to engineering, where a new function is designed and created from scratch. Rather, the process is similar, in Jacob’s words, to a ‘tinkerer [who] picks up an object which happens to be in his stock and gives it an unexpected function. Out of an old car wheel, he will make a fan; from a broken table, a parasol.’

We often mention **adaption** when discussing evolution. This is where changes to a population or species occur due to selective pressure of the environment (see **Growth, reproduction and evolution** in Chapter 3). However, there is another important process called **exaptation**. This is where a trait can shift in function during evolution. That is, like how the tinkerer works, the trait is given an unexpected new function.

This might be difficult to understand at this stage but will become clearer after you read chapters 3 and 4. At the moment just understand that because evolution will reuse and repurpose biological components for new functions, you will see that similar mechanisms occur in different cellular processes. The same molecule or mechanism will be seen in different pathways, and different complex signalling or biosynthetic pathways will contain the same modular components.

For example, the molecule adenosine is a component of DNA, RNA, adenosine triphosphate (ATP), coenzyme A, nicotinamide adenine dinucleotide (NAD), flavin adenine dinucleotide (FAD) and cyclic adenosine monophosphate (cAMP). These participate in many different cellular processes but once you first learn about adenosine you will much more easily see how it fits into all these different places.

Another example is G-protein coupled receptors, a large superfamily of cell surface receptors that have incredibly diverse functions (photoreception, taste, pain and smell; they also mediate cell recognition, metabolism and growth) despite having a very similar structure and common mechanism of action. All G-protein coupled receptors share two properties – they have seven transmembrane domains, and they interact with specialised proteins (called G proteins) to influence intracellular pathways after binding extracellular signals (see Figure 2.4).

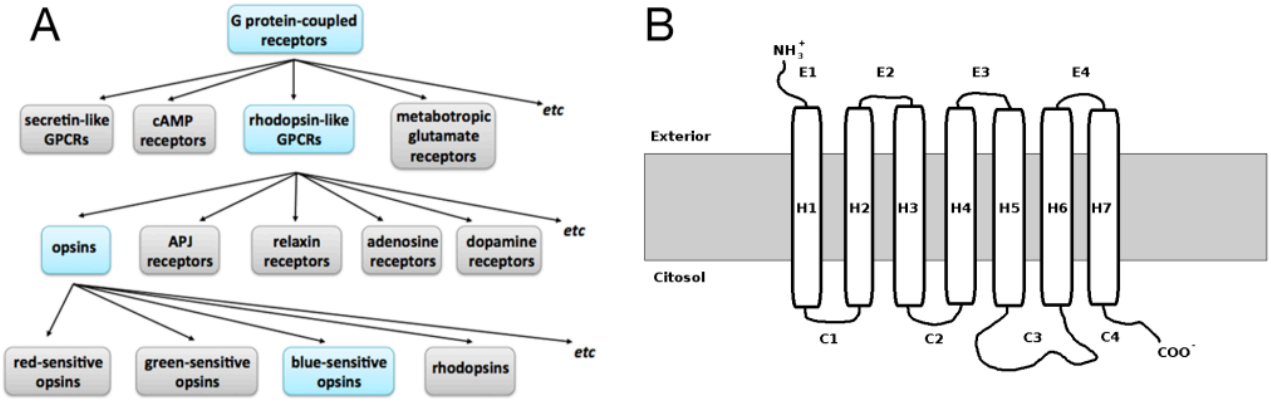

Figure 2.4 A: The G-protein coupled receptors are a diverse family of proteins which have myriad biological functions. To illustrate this the diversity of the opsin sub-family are shown with the short-wave light sensitive opsin proteins highlighted in blue. Image: 'Hierachical relationship of G-protien' from www.edi.ac.uk used under CC BY 4.0.
Figure 2.4 B: Despite the diversity of functions this entire family of proteins share a common canonical structure containing seven transmembrane domains and a common mode of action elicited through a coupled g-protein. Image: 'GPCR' by Retama from Wikimedia Commons used under CC BY-SA 3.0.

Getting to grips with the language

Part of the challenge you will face initially with biochemistry is learning new terms. The American author and educator Neil Postman said[1]:

Biology is not plants and animals. It is language about plants and animals …

This quote highlights the importance of language when learning about biology. It is not just about learning new words but also how to use words you already know in a biological or scientific context. Without understanding language and naming conventions to a level where you use them in your speech and writing, your learning will be limited. This is not trivial – in science classes the number of new terms can be comparable to foreign language classes!

In addition, there are two ways in which language is confusing in biochemistry:

1. Postman, N. (1980). Language Education in a Knowledge Context: A Review of General Semantics, 37(1), 25–37.

1. Words are often borrowed from everyday English and repurposed. This can make it difficult as you will need to re-learn a word you know but in its scientific context.

For example, when we speak about *tissues* in everyday language, the brand Kleenex may come to mind. However, in cell biology, *tissues* refer to a level of organisation in multicellular organisms consisting of a group of either functionally or structurally similar cells plus their surrounding intercellular material.

Similarly, words like *transcription* or *translation* have a meaning in everyday writtend and spoken language. However, in molecular biology they specifically refer to the transfer of genetic information in living organisms.

With this kind of terminology, the key is to ensure that you understand the *processes* they are associated with. Understanding them in context is the key to not confusing their counterpart meaning in everyday English.

2. Many words are long and complex and have origins from other languages, principally Greek and Latin. These, just because of their unfamiliarity and length, will be difficult to read and intimidating to say aloud.

Becoming fluent in the language of biology

When learning anything complex it is a good idea to break it down into smaller parts to make it more accessible.

Scientific words often have three parts – a prefix, a root and a suffix, as shown in the following table.

Prefix	Root	Suffix
Appears at the beginning of a word. Many are used frequently, so you will eventually learn their meaning.	The root of a word often has a standalone meaning. These often have a Greek or Latin origin.	Appears at the end of a word to provide additional meaning.
hypo – below *hyper* – above *cyclo* – ring *poly* – many *endo* – within *exo* – outside of	*iso* – equal *allo* – other *chloro* – green *cyte* – cell	*-phillic* – love, affection *-phobic* – hate, fear *-lysis* – breakdown *-some* – body *-oma* – abnormal, cancer

You will be surprised how often the same prefix, root or suffix will appear in different words. Once you learn a few, things will start to get easier. For example, the Greek word *therm* means 'heat'. You will find this word in a large family of scientific terms, including exothermic, thermogenesis, thermoregulation, isothermal, ectotherm, thermodynamics, hypothermia and many others.

Knowing the word origin (etymology) of a term can also help to identify its likely meaning and make it easier to understand in biochemistry.

For example, the word **eukaryote** is a noun describing a cell containing a nucleus. It is derived from the prefix **eu–** (from Greek, meaning good, well or true), the root **kary** (from the Greek word *karyon*, which means kernel or nut but now indicates the cell nucleus) and the suffix –**ote** (a singular form of the Greek-derived word *osis*, which means process or state).

Resources

There are many useful websites that can help you with understanding the etymology of words.

- **Online Etymology Dictionary**
- **The Free Dictionary** also contains a thesaurus, medical dictionary and many other features. You can listen to a pronunciation of almost all words in the dictionary.

When learning new words, writing them in a sentence of your own construction can help integrate them into your vocabulary faster. Also say them aloud. Try not to be intimidated by their length – most of the time they will be phonetic (sound the way they are spelled). So just break them down into their component parts and at first say them slowly until you get used to pronouncing them! When you can confidently say them in your head, reading will be much easier, and your learning will rapidly accelerate.

Concepts rule!

The reason for learning anything in the first place is to be able to apply that knowledge to novel situations. This means that it is always much more important to learn **concepts** rather than isolated facts. Biochemistry and molecular biology as disciplines are no different. This does not mean that facts are unimportant! It is just that understanding ideas and concepts will help you learn facts faster. **Learn to understand rather than just simply memorise.**

An excellent example of the importance of concepts versus facts is the development of the periodic table of the elements. The Russian chemist Dmitri Mendeleev set out to order the known chemical elements in the 1860s (at the time only 63 elements were known). He noticed that there was a correlation between atomic weight and the chemical properties of elements. This led to ordering elements by increasing atomic weight but also into horizontal rows called periods, where each period number

indicates the number of electron orbitals for the elements in that row. As elements were discovered they were added logically to the gaps in the table.

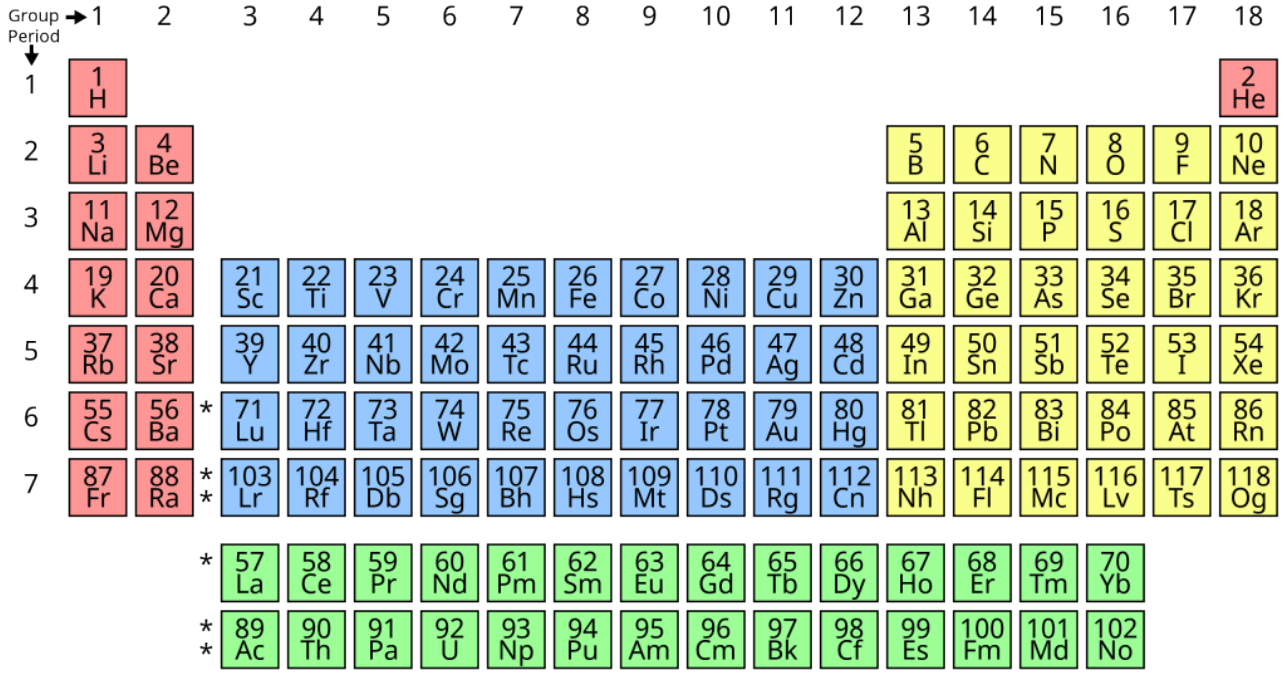

Figure 2.5 The periodic table of the elements represents the advantage of learning concepts over facts: By understanding the significance of the organisation of the rows (groups) and periods it is possible to predict the properties of an element from its position in the table. Image: 'Hierachical relationship of G-protien' by Offnfopt from Wikimedia Commons used under CC BY-SA 4.0.

For students of chemistry (and biochemistry!) where knowledge of the elements is important, it is far better to understand the main concepts underlying the periodic table than to memorise the chemical properties of individual elements.

Conceptual learning is important but there is a hierarchy of concepts too. Some are more important than others in the sense that by learning them they will allow you to connect many different concepts. We call these **threshold concepts**, and mastering them is the purpose of this e-book.

Mastering the threshold concepts

A threshold concept refers to one of the core concepts in a subject whose understanding is key to transforming the way you understand the subject as a whole. To understand what we mean by a threshold concept, consider this example from the unrelated discipline of history.

When you begin learning history you may focus on names and dates and accept an initial historical account you read to be accurate. However, as you study in more depth, you begin to understand that historical accounts can be biased, and there can in fact be different competing historical accounts. Often there is no clear definition of why something happened or even a definitive account of what actually happened! The **threshold concept** in this case is that there is an **interpretive** aspect to history. This is transformative as once you understand it, you will never read history in the same way again.

So, threshold concepts are **transformative** (create a significant shift in your understanding), proba-

bly **irreversible** (once learnt are difficult to unlearn), **integrative** (allow you to make links between different topics) and potentially **troublesome** (difficult to initially grasp and often counterintuitive).

The focus of this resource is to help you understand the key threshold concepts in biochemistry and molecular biology. These have been identified by research[2] funded by the American National Science Foundation. Key threshold concepts critical for biochemistry were identified in five major areas:

1. The central importance of the theory of evolution to all biological sciences
2. Matter and energy transformation
3. Homeostasis, control and regulation
4. Biological information
5. Macromolecular structure and function

Applying active learning

Despite the importance of concepts some things just need to be committed to memory. However, memorisation is far more effective if it is done by active learning rather than passive learning. If you simply read text or watch lectures, the information will wash over you. However, if you write things down (preferably by hand), create diagrams and flowcharts and constantly check your knowledge by answering questions, you will be far more likely to successfully commit important information to memory. Give yourself plenty of time to study, and leave enough time between knowledge checks to ensure you are not just testing your short-term memory.

2. Loertscher, J., Green, D., Lewis, J., Lin, S., & Minderhout, V. (2014). Identification of threshold concepts for biochemistry. CBE Life Sciences Education, 13(3), 516–528.

Chapter 3: The universality of life

3.1 How can we define life?

Previously, we defined biochemistry and molecular biology as the study of chemical processes within and relating to living organisms. But how do we define life itself? This might seem like a simple question, but there is no single, widely accepted definition of life. Even biologists (who study life) don't agree on what 'life' is! When we think about life, most often our definitions are operational. That is, they allow us to differentiate non-living matter from living matter but don't give a definition for life.

If you search for a succinct definition of life you might come across NASA's contribution:

Life is a self-sustaining chemical system capable of Darwinian evolution.

This compact definition was formulated for astrobiologists. These scientists are searching for extraterrestrial life and do not want to be restricted to a definition that applies only to the example of life on Earth. However, the NASA definition is controversial. It is broad enough to encompass viruses, which most biologists would not include as living organisms, and it may exclude organisms not capable of reproduction such as mules (which are sterile, even though we would agree that a mule is alive).

Given that life is so difficult to define, rather than attempting to provide a succinct yet all-encompassing answer, it is more useful to describe life or living things by their common characteristics. These include:

- Organisation
- Metabolism
- Homeostasis
- Growth, reproduction and evolution

Organisation

Living systems are organised, meaning simply that they are arranged in a particular manner. When we use the term **organised** in biology it includes two fundamental ideas. One is that in living systems, things are arranged in a hierarchical manner; the other idea is that living systems tend to be less random than their surrounding environment.

 All living systems exhibit a hierarchical level of organisation, have metabolic processes, maintain homeostasis and are capable of growth and reproduction as well as the capacity to evolve.

The hierarchy of organisation

Living systems exhibit a **hierarchical level of organisation** where each level of the hierarchy exhibits greater complexity then the previous level and is comprised of components from the previous level.

Understanding this hierarchy is the key to understanding how life works mechanistically; that is, how all the components fit together.

We will go into more depth with the common components of life, but it is worth getting an overview of them now. Figure 3.1 demonstrates this hierarchical organisation of life, starting with amino acids and proteins. We could certainly show a similar hierarchy using DNA, lipids (fats) or sugars as the example.

We can think of the hierarchy of organisation of life beginning with atoms forming molecules. The most common elements found in living organisms are carbon, hydrogen, oxygen and nitrogen (two other relatively common elements are phosphorous and sulphur). Atoms from these elements make up about 96% of any life form. For example, hydrogen and oxygen atoms combine to form water, which a major component of all living things.

Molecules can combine to form more complex molecules such as amino acids. Some of these molecules can combine further to form macromolecules such as proteins. These macromolecules can combine further to form complexes such as chromosomes, or large protein complexes which themselves provide the basic architecture of cells.

Cells are common to all living things and are considered the fundamental unit of life. That is, a cell is the smallest unit that we consider to be alive. A living organism can be a single cell, or it can be multicellular. In multicellular organisms, the organisation can be incredibly complex, with many different types of specialised cells. These cells can cluster to form tissues which in turn form organs and organ systems, which make up the organism. The hierarchy continues as communities of organisms interact with their physical environment to create ecosystems. All the ecosystems on Earth together form the biosphere.

Living systems exhibit a hierarchical level of organisation where each level exhibits greater complexity than the previous level and is comprised of components from the previous level.

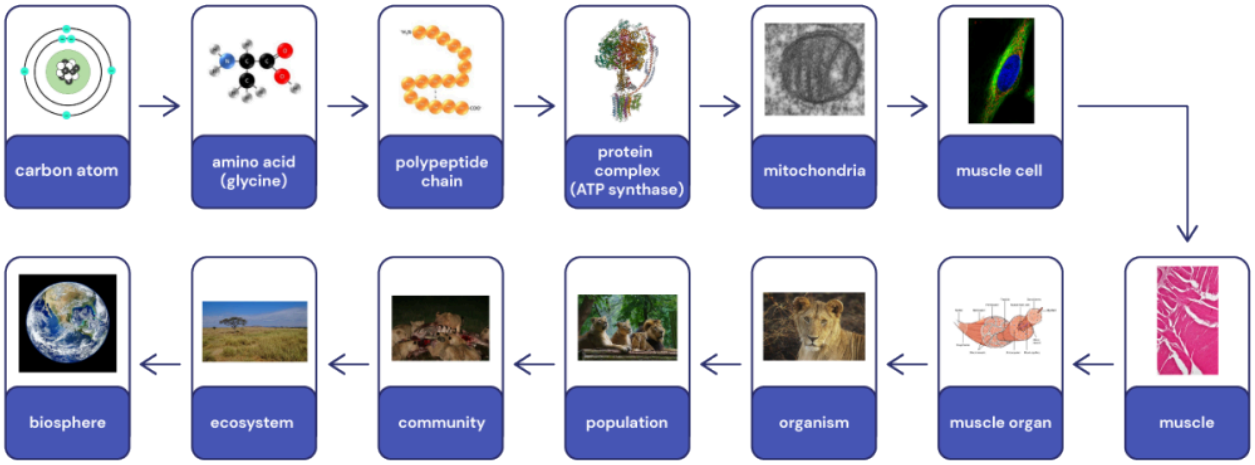

Figure 3.1 The hierarchical organisation of life: **The simplest component of living things is the atom. Atoms combine to form molecules. Molecules can combine to form macromolecules. Multiple macromolecules help form cells. Cells function together as tissues, and tissues can combine to form organs. Organs work together to form organ systems and organ systems combine to make a living organism. Groups of the same organism living together in an area is called a population, and interacting populations form a community. Communities interact not only with each other but also with the physical environment and are known as ecosystems. All the ecosystems together make up the biosphere, which is the full extent of life on Earth.**

How does this organisation come about?

How organisations arise is not a trivial question. By understanding it you will understand a key concept in biochemistry – that a constant input of energy is needed in order to maintain life.

The second law of thermodynamics states that:

> *the entropy of isolated systems left to spontaneous evolution cannot decrease as they always arrive at a state of thermodynamic equilibrium where the entropy is highest at the given internal energy.*

Okay, so what does this mean?

First, we need to define what is meant by **entropy**. Entropy is a measurable physical property that is associated with disorder, randomness and uncertainty. So the second law of thermodynamics is stating that isolated systems will tend to become more random and disordered over time.

A good analogy is a neatly stacked pile of bricks. Over time you might expect some bricks to fall and the stack to eventually collapse. Another good analogy might be your bedroom which, if like the authors', tends to become messy and disorganised over time! The reverse – reforming a neat stack of bricks or tidying your bedroom – won't happen spontaneously. You must put some energy (work) into the system.

Figure 3.2 A neatly stacked pile of bricks collapsing over time is another good analogy for the second law of thermodynamics: Over you time you would expect the pile of bricks to eventually collapse, that is move from order to disorder. That is, you would expect the entropy of this system to increase. The only way to decrease the entropy would be to re-stack the bricks, that is put energy into the system. Image: 'Fallen Bricks' by Tomas Castelazo from Wikimedia Commons used under CC BY-SA 4.0.

But living systems exhibit complex organisation, which represents a decrease in entropy. Does that mean that life violates the second law of thermodynamics?

The answer is no because living systems are not isolated. Energy enters the system (on Earth, primarily from the Sun) and is used to decrease entropy locally. This local decrease in entropy is compensated by an increase in entropy somewhere else. For our stack of bricks, if a worker were to restack a random (disordered) pile of bricks (decreasing local entropy), they would release heat from their muscles and small molecules such as carbon dioxide and water broken down from larger molecules in food by their metabolism (increasing the entropy of the universe).

The complex organisation that living systems exhibit means they are in a state of thermal disequi-