ABOUT LIFE

About Life

Concepts in Modern Biology

by

PAUL S. AGUTTER
Theoretical and Cell Biology Consultancy,
Glossop, Derbyshire, U.K.

and

DENYS N. WHEATLEY
BioMedES, Inverurie,
Aberdeenshire, U.K.

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TABLE OF CONTENTS

PREFACE

Thanks to the popular media, and to books by Dawkins, Fortey, Gould, Margulis and other writers, people are informed about many aspects of biology. Everyone seems to know a little about evolution, for example, and about DNA and the possibilities (good and bad) afforded by research in molecular genetics. Most people know some of the arguments for and against the likelihood of life on other planets. And so on. We are glad that these pieces of information have become so widely available. However, we do not assume any particular knowledge (other than the most basic) in this book. Our aim is to address *general* questions rather than specific issues. We want to enable our readers to join their disparate pieces of knowledge about biology together.

The most basic of these general questions – and perhaps the most difficult – can be expressed in beguilingly simple words: “What is life”? What does modern biology tell us about the essential differences between living organisms and the inanimate world? An attempt to answer this question takes us on a journey through almost the whole of contemporary cell and molecular biology, which occupies the first half of the book. The journey is worth the effort. The provisional answer we attain provides a coherent, unifying context in which we can discuss evolution, the origin of life, extraterrestrial life, the meaning of “intelligence”, the evolution of the human brain and the nature of mind. In other words, it enables us – as we said - to help our readers to join their disparate pieces of information together.

Although we assume virtually no knowledge of biology and use non-technical language as far as possible, we cannot avoid using some technical terms. These will be unfamiliar to many readers, so we have added a glossary and pronunciation guide after the final chapter.

We intend this book to be the first volume of a trilogy. In the second volume we plan to explore what science is, and why scientific thinking originated and flourished in western society. We want to investigate the ways in which biology resembles other sciences and the ways in which it differs from them. In the third book, we hope to explore the most controversial topics associated with biology today: patenting of human genes, cloning, genetic modification of crops, the obliteration of habitats, the extinction of species, and so on. This first volume is a prelude to these future projects.

We are grateful to many colleagues for discussions and advice during the several years of gestation of this book, and to the Carnegie Trust for a grant to support the project. All the illustrations were prepared by Dr Ruth Campbell, whose diligence in this work we gratefully acknowledge. Some of the illustrations are reproduced with permission from published sources: Fig. 2.1 from Goodsell (1991) "Inside the living cell," *Trends Biochem. Sci.* **16**, 206-210; Figs. 3.1(a) and 7.1 (b) from Mayer, Wheatley and Hoppert (2006) in *Water and the Cell*, chapter 12, Springer, Dordrecht; Figs. 5.3 and 13.5 from de Robertis and de Robertis (1980) *Cell and Molecular Biology*, 7th edition, Saunders, Philadelphia; Fig 6.5 from http://personalpages.umist.ac.uk/staff/goughlecture/the-cell/diffdev3/haemo.jpg; Fig. 8.3 from Wheatley (1982) *The Centriole: a Central Enigma of Cell Biology*, North Holland Biomedical Press; Fig. 10.2 from Hogben (1958) *Science and the Citizen*, George Allen and Unwin; Fig. 10.3 from <http://www.ug.edu.au/school> science lessons /3.0; and Fig. 12.2 from <http://steve:gb.com/images/science/hydrothermal.jpg>.

While we have done our best to distil the basic concepts that guide biology today, informed readers are likely to consider parts of the text to be in need of revision or correction. We shall be glad of critical feedback. Science is a collective activity, and we are part of the collective.

PSA
DNW

Chapter 1

INTRODUCTION

On a fine day in late spring or early summer, preferably around sunrise or sunset, go to a patch of uncultivated or wooded land as far as possible from people and traffic. Find a comfortable place where you can remain quiet and still for half an hour. Wait, watch and listen. For a while you hear only the sounds of insects, the alarm calls of small birds and the breeze among foliage; nothing moves except leaves and clouds. But after ten or fifteen minutes there is a transformation. Birds settle and feed. Shiny beetles sidle down tree trunks and over the ground. Furry bodies dart to and fro. The world around you has come alive.

Such experiences bring us into contact with other species and seem to satisfy a deep human hunger. "Communing with Nature" is sometimes said to refresh the spirit. The sights and sounds and smells of non-human life in its natural setting arouse our curiosity. They fascinate and enchant. They are the source of much poetry, music and visual art - and of science.

Science - in this case the science of life, biology – has its roots in curiosity. What we see raises questions. These might be simple questions, such as the names of the trees and the shiny beetles and the owners of the furry bodies. Or they might be more complicated ones, such as how birds and flowers are made, how they do the things they do, why they do them; and why they exist at all. *Science is a way of framing such questions and trying to answer them*. It is not the only way, but it is a very informative and productive one. It works by considering things in themselves, taking no account of whether they are beautiful or ugly or good or bad. The nature and origins of science and its effects on the world are topics for a different book. For present purposes a simple definition will suffice: *science is a way of satisfying our curiosity by formulating questions about what we observe and answering them dispassionately* – that is, without making value judgements.

You might ask how "communing with Nature" can still enchant a person - a scientist - who devotes his or her working life to dispassionate analytical inquiry. Surely, when curiosity is satisfied, wonder is lost? In fact, for most scientists, the opposite holds. Understanding the techniques of counterpoint and sonata form can enhance our appreciation of Bach fugues and Beethoven symphonies. Analysis of literary styles can help us to relish the subtle ways in which Henry James or Charles Dickens convey character and tension and a sense of place. In much the same way, the fruits of scientific inquiry increase both our understanding of the natural world and our wonder at its workings. Framing and answering questions does not destroy our pleasure in what we see around us; quite the contrary. Knowledge (especially the acquisition of knowledge) is pleasurable in itself, and it augments other pleasures.

However, research scientists ask different *kinds* of questions from other people. Two individuals who witness the same burgeoning of life during a spring sunrise might experience similar feelings of wonder and excitement. But if one of them is a practising biologist and the other is not, their curiosity will take different forms. The non-specialist might ask why certain insects visit primroses but not wood anemones, or how the shiny beetle manages to feed on the unappetising trunk of the oak tree; or how swallows, swooping from the bright sunlit air into the windowless barn, adapt so quickly to the sudden darkness that they unerringly find their nestlings and never collide with beams or walls. The specialist, the scientist, might be able to answer such questions; if not, then answers will surely be found among the wealth of available wildlife documentaries, books and magazine articles. But personally, he or she will be interested in different matters: the exact mechanism, say, whereby the primrose flower synthesises its chemoattractant, and why insects of one species but not others respond to it; or precisely what place the shiny beetle has in the ecology of mixed woodland. For both individuals, the pleasure of questioning and answering enhances the immediate sensory experience. But the biologist's pleasure in knowledge is difficult to share, except with those who have the same specialist background. There is a comprehension barrier, which we need to try to cross so that scientific knowledge becomes more generally accessible.

Popular science books, television and radio documentaries, science articles in newspapers – all these have gone a long way towards overcoming this barrier. Nevertheless scientists still tend to feel, and to be, misunderstood. This is apparent in their reactions to the most general, basic-seeming questions, the sorts of questions that a child might ask. Scientists tend to consider such questions unanswerable: too vague, too resistant to accepted technical vocabulary, too remote from the rigorous demands of ongoing research; in a word, too hard. For instance, when after a quarter of an hour's stillness in a chosen rural spot you have merged into the landscape and the world has "come alive" around you, what exactly does that phrase mean? Of course it "means" that local animal life has come out of hiding and revealed itself, but *what do the words "alive" and "life" really denote*? What fundamental properties do the primrose, the oak tree, the beetle, the swallow and the darting weasel have in common that distinguish them from the soil and rock beneath them, the air around them, the clouds above them, or the sunlight on which they all ultimately depend?

We can broaden this question. The bodies of the oak, the swallow and every other plant and animal are swarming with microscopic inhabitants such as bacteria. So is the soil itself. There are probably more bacteria in a handful of soil than there are leaves in the entire wood. What properties do these minute living things, scraps of matter that cannot be seen without a powerful microscope, share with the primrose and the beetle and the weasel but not with anything inanimate? *What is "life*"? Many have asked this question. It is the main topic of this book.

Thanks to a number of excellent popular scientific publications, most people nowadays might answer "What is life?" by saying "DNA". All living things contain DNA, but no inanimate ones do. DNA is the material of the coded instructions - the *genome* - for making and maintaining an organism. Cracking the code, unravelling the genome sequence, helps us to understand everything there is to know about that organism. The non-living world has no genome, no coded instructions. That is the difference between the living and the inanimate. For very good reasons, this answer has become deeply entrenched in modern thought: life is DNA. The double helix has become a major cultural icon. The complete sequencing of genomes (not least the human genome) has been hailed as one of the greatest achievements of human history.

However, without belittling this achievement or doubting that DNA is indeed basic to life on Earth, we can challenge the answer. Indeed, *is* it an answer? DNA itself is not living. Pure DNA in a test tube does not behave like anything alive; in fact, it does not behave at all. A freshly fallen leaf contains just the same DNA as it did before it fell, but it is no longer alive. Moreover, the fallen leaf still contains the materials – the proteins and their products - that the genome instructed it to make. So non-living things such as test tubes, and once-living things such as dead leaves, can contain DNA *and* the substances that DNA codes for. Yet they are not alive.

There are other objections, too. For instance, there might be entities on planets far across the galaxy that we would (if we ever saw them) describe as "living" because they shared certain characteristics with terrestrial organisms. Suppose we could analyse one of these hypothetical entities, and suppose we found that it contained no DNA. Would we then declare: "Our mistake. Despite appearances, these entities aren't living after all"? Surely not. So we are back where we started. We might accept that DNA is fundamental to life on Earth (whatever we mean by "fundamental" and "life"), but neither DNA nor the materials it encodes are sufficient to define the living state. The question “What is life?” remains open.

Many biologists are impatient with the question. They point to past attempts to distinguish the living from the non-living (traditionally, organisms are said to *eat, breathe, excrete, grow, move, respond to stimuli* and *reproduce*) and tell us, quite rightly, that all such attempts have proved inadequate. The reason why they have proved inadequate is simple. "Eating" involves wildly different processes in, say, oak trees and weasels. Weasels "move" in ways that oaks do not. And so on. Any definitions of "eating" and "moving" that are broad enough to encompass such a range of meanings would be useless. They would apply to many non-living things as well as living ones; and however broad we made our definitions, there would probably still be living things to which they would *not* apply. The quest for a clear distinction between living and non-living has always been vain, say the sceptics, so it is a waste of time to consider the question further.

This attitude is understandable but it unsatisfactory. If biology is the study of life and we cannot define life, then we cannot define what biology is about. This elementary logic ought to make the sceptics uncomfortable. Also, if we cannot define life, what do we mean by the "origin of life"? The origin of what? Similar problems abound. One more example: an established tenet of biology is that *the cell is the fundamental unit of life*; in other words, every organism comprises one or more cells. (We shall start to explore what we mean by a “cell” in the next chapter.) But if we cannot define life, of what is the cell the fundamental unit?

Other biologists take a different view, less sceptical but not very helpful. The living, they say, can be distinguished from the non-living by our detailed knowledge of the workings of organisms, knowledge that we have acquired through centuries of research world-wide. In principle, this view is unexceptionable. Any definition or characterisation of the living state *must* be based on what we have learned through the progress of science. But the amount of published biological data is colossal. Consider cell biology alone. The workings of some types of cell, such as the intestinal bacterium *Escherichia coli* or a rat liver cell, are known in mind-numbing - though not yet exhaustive - detail. The existing mass of information about such cells is far too unwieldy to provide a comprehensible distinction between the living and the non-living. And what essential facts might lurk among the details we have not yet discovered? Moreover, though all living cells share many features, each type of cell is also distinctive; and the common features might not suffice to identify an object as "living". So although a general account of the living state must be firmly based on what we know about particular living cells, this approach to answering "What is life?" is impractical if we take it literally.

In this book we shall construct a provisional, somewhat abstract answer to the question "What is life?" by generalising from these masses of information. We shall express this answer in non-technical terms as far as possible. We believe that our answer is interesting enough to publish, but it is not written on tablets of stone. It will probably be challenged by other biologists; indeed, we hope it will. Science - like the communication of science - progresses by trying out ideas, finding flaws in them, and trying again. If no ideas are put forward there is nothing in which to find flaws and therefore no progress. So although we are prepared to defend our provisional answer, we want it to be a target for rational criticism. Rational criticism will lead to better answers.

The words *alive* and *life* define the main theme of this book, but we shall also look at some related issues. Some of these issues, such as the origin of life and the existence of extraterrestrial life, have received much attention from other authors. Our contribution, a small one, is to reconsider them in the light of our general "definition" (or rather *characterisation*) of the living state. Inevitably we shall discuss evolution - it is impossible to write a book about biology without mentioning biology's central theory - but again we shall take advantage of the excellent popular treatments of this subject that are already in print.

One question recurrently asked about extraterrestrial life is whether it might be "intelligent" in the sense that our species is intelligent. To consider this question, we shall briefly discuss the nature and evolution of the organ of human intellect, the brain. Once more we shall take advantage of popular accounts, and of the revolutionary progress made in neurobiology during the last two decades of the twentieth century; but we shall suggest a new perspective on the topic.

To summarise: we begin the book by focusing on the "fundamental unit of life", the cell, and we spend the first few chapters developing our characterisation of the living state. In chapter 11 we turn to evolution, and in the remainder of the book we consider the origin of life, the evolution of "intelligence" and the question of extraterrestrial life.

Our aim is to share ideas equally with fellow-biologists and non-specialists. We invite all our readers to challenge the central idea in this book, the fundamental difference between the living and the non-living, and to improve on it. Any reasonable attempt to answer "What is life?" will help to develop more coherent views about the origin and evolution of life on Earth, the nature and evolution of intelligence, the possibilities for extraterrestrial life, and other big topics.

It is enjoyable to debate these topics, so this seems a worthwhile aim in itself. But there is another point: to have clear ideas about such broad issues enhances the wonder and pleasure that we gain from contemplating the world around us. In consequence, our thoughts and reflections when we "commune with Nature" at sunset will continue long after the stars come out.

Chapter 2

INGREDIENTS OF THE SIMPLEST CELLS

Prokaryotes and the sizes of their contents

Cells are small. To see them you need a microscope, and to see their contents in detail you need an electron microscope. Objects so minute that they cannot be seen with the naked eye are - by definition - remote from everyday experience. This makes it hard to grasp the *scale* of cells and their contents. And without a grasp of scale it is impossible to acquire a clear mental picture of a cell.

In this chapter and the following one we shall describe large-scale models of cells that can be made from ordinary household materials. These models use the familiar to represent the unfamiliar. We urge our readers to *make* them. They are very simple, and entertaining to build if two or three people work together on them. Seeing and touching the models will create more vivid and memorable pictures than simply reading our instructions and comments. Building them will not reveal how cells work; we shall explore that in later chapters. But it will familiarise you with the main components of cells, and it will illustrate the relationships among these components and indicate their relative sizes. The relative sizes will prove surprising.

Before we begin on the models we must introduce two technical terms that might not be familiar to everyone. Terrestrial organisms are of two kinds: *prokaryotes* and *eukaryotes*. Prokaryotes are tiny one-celled organisms such as bacteria that do not contain a separate nucleus. “Prokaryote” is derived from Greek roots meaning “before the kernel (nucleus)”. Eukaryotes are organisms consisting of one or more cells, each of which *does* have a separate nucleus containing the bulk of the DNA. “Eukaryote” comes from the Greek for “well-formed kernel (nucleus)”. Single-celled organisms such as yeasts and amoebae are eukaryotes. So are all multicellular organisms: all fungi, all plants from mosses and seaweeds to primroses and oak trees, and all animals from sponges and worms to beetles and swallows and humans. (Most scientific terms come from Greek and

Latin, or occasionally Arabic, roots. This is because, until the early 20th century, science was the pursuit of gentlemen who were educated in the Classics, and much of our knowledge has Classical and Arabic foundations. Words that are not in common use and are employed only for special technical purposes have a great advantage: their meanings remain stable and unambiguous. For science students, the drawback of such words is that they have to be learned.)

Despite appearances, which are misleading because we can only see multicellular organisms - and not even all of those - with our unaided eyes, the world's prokaryotes greatly outnumber the eukaryotes. Also, prokaryotes are far more venerable: the earliest prokaryotes lived on Earth twice or three times as long ago as the most ancient eukaryote. Bacteria have a bad press because, for historical reasons, we associate them with infectious diseases. However, very few bacteria cause disease. The overwhelming majority are not only harmless, but in some cases essential for other forms of life. For example, if it were not for the bacteria that make atmospheric nitrogen available to plants, plants would not exist – and as a result, neither would any animals, including ourselves.

Let us return to the matter of cell size. A metre ruler is divided into a thousand parts – millimetres. Everyone knows that; we can *see* a metre ruler and its millimetre divisions. But try to imagine a *millimetre* ruler divided into a thousand parts. Each part would be a thousandth of a millimetre; that is, a millionth of a metre, or *micrometre*. (“Millimetre” is abbreviated to “mm”. “Micrometre” is abbreviated to “µm”. The Greek letter *mu*, µ, is the usual way of indicating “a millionth of”.) This imaginary ruler is almost impossible to picture, but to measure cells we would need only a small portion of it. A typical prokaryote is just one or two micrometres long. Eukaryotic cells vary in size (for example, plant cells are usually bigger than animal cells), but a cell in your liver – to take an example at random – might be some fifteen or twenty micrometres across. A small eukaryotic cell is around ten times greater in linear dimensions (that is, ten times longer, wider and taller) than a prokaryotic cell. This means it is around a thousand times greater in volume. (Picture two cubes, one with one-centimetre edges and the other with ten-centimetre edges. The second cube has a thousand times greater volume than the first - one litre compared to one cubic centimetre – but the difference in linear dimensions is tenfold.) In other words, eukaryotic cells are much bigger than prokaryotic ones. They also have more complicated structures. Therefore, we are going to describe two different "household" models, one for each main type of cell. In this chapter we shall describe a matchbox-sized model for a prokaryote. In the next chapter we shall describe a cardboard carton-sized one for a eukaryotic cell.

A matchbox model of a prokaryote: the advantage of being small

An ordinary matchbox measures roughly 2 inches by 1 inch by 1 inch (5 cm x 2.5 cm x 2.5 cm). Prokaryotic cells are not exactly rectangular, as matchboxes usually are, but they have similar proportions. To make a matchbox model of a prokaryote, let one inch (2.5 centimetres) of matchbox represent one micrometre of cell. So the matchbox corresponds to a prokaryote of "typical" size, 2 μm x 1 μm x 1 μm.

We have magnified the cell to the size of a matchbox, so we must magnify its contents in proportion. First, we need to consider the DNA. Prokaryotic DNA is circular; we can represent it by cutting a piece of thread of suitable length and knotting the ends together. A real bacterial DNA is about one third to one half of a *millimetre* long (300-500 μm)[1], so the matchbox model will need to contain a thread that is between 25 and 42 *feet* (7.7 and 13 metres) long. When you cut a thread of this length and knot the ends together, the result is a tangled circle. When you push this circle into the matchbox it becomes even more tangled. Unless you have used very fine thread the circle will have overfilled the matchbox – a problem, since we have many more items to add to the model; DNA is only one of the cell's many constituents.

Although the model is far from complete it has already demonstrated some important points. First, it has shown that DNA is an extremely long molecule, hundreds of times longer than the cell that contains it. Second, DNA must also be a very thin molecule, or it would not fit into the cell however hard you pushed it. Third, when DNA is packed into a cell, it is twisted and folded into a shape undreamed of by the most mischievous kitten among knitting wool. Making the matchbox-and-thread model brings these points home convincingly.

Cell functions are not topics for this chapter, but most people know that DNA is the material of the genes. A gene is a segment of DNA. In the matchbox model, an average-sized gene is represented by about one centimetre of the 'DNA' thread. For the time being we shall assume that each gene codes for one cell protein. (This assumption is not exactly true but it will suffice until chapter 11.) To make the protein corresponding to one gene, i.e. the protein *encoded* in that gene, the cell needs the right equipment. This equipment includes various kinds of *RNA*; molecules

[1] Bacterial DNA is roughly one million bases long, a "base" being a single unit (letter) of the coded information that the molecule contains. In the commonest double-helical form of DNA, one base occupies a length of 0.34 nanometers, a nanometre being a thousand-millionth of a metre (i.e. a thousandth of a micrometre or a millionth of a millimetre). One million bases at 0.34 nanometres per base comes to 0.34 millimetres (340 micrometres) in total.

similar to DNA but much shorter and less stable. One sort of RNA, known as "messenger", is a copy or imprint of a gene or a small group of genes.

Think of the DNA as a library of master documents, none of which can be removed from the library but any of which can be photocopied. Each document is a gene, a coded instruction for making a particular protein. The messenger RNA molecules are the photocopies; they *can* be taken out of the library. Each messenger photocopy is fed into the *ribosomes*, remarkable machines that scan the photocopied document, translate its instructions and make the protein encoded in the gene. Thanks to this system, the instructions in a gene can be used for manufacturing thousands of copies of the same protein. Proteins are responsible for all the structures and activities of the cell: holding the cell together, sensing and responding to the environment, taking in nutrients and metabolising them, controlling the energy supply, manufacturing other cell constituents, copying DNA, making RNA, using ribosomes, and so on. The *proteins*, not the DNA that codes for them, are largely responsible for the "living state".

RNA molecules, ribosomes and proteins all need to be represented in the matchbox model. At any moment a prokaryote contains roughly as much RNA as it does DNA. So cut another ten metres or so of thread and put that into the matchbox. (For authenticity, you should snip this second piece of thread into 1-10 centimetre segments. This would represent the RNA molecules more realistically. However, repeated snipping is tedious and adds little to the point of the exercise.) A rounded teaspoonful of lentils represents the ribosomes. The cell's proteins can be represented by a rounded teaspoonful of sugar. If a prokaryote is magnified to the size of a matchbox, each protein molecule it contains is, on average, about the size of a sugar grain, and each ribosome is about the size of a lentil.

These proportions might seem hard to believe. Many biologists can remember feeling incredulous about them on first encounter. (One of the present authors recalls checking the calculations six times, sure there must be a mistake somewhere.) The circular 'DNA' thread in the matchbox model represents about 1000 genes, so the average gene corresponds to roughly one centimetre of thread. On the same scale, the protein encoded by the gene corresponds to a grain of sugar. Gene is to protein as a centimetre of thread is to a sugar grain. Yet that single grain of sugar, the protein molecule, is the whole *point* of the gene, because the proteins are responsible for virtually all the cell's structures and activities.

We have dealt now with most of the contents of a prokaryote: the huge circular DNA molecule, the many shorter RNA molecules copied from the DNA, the proteins that are necessary for the cell's structure and all its activities, and the ribosomes for making the proteins. There are tiny nutrient molecules as well, and the cell could not function without them, but *in toto* they occupy relatively little space. Some prokaryotes contain storage granules (food reserves), so add half a dozen dried peas to the matchbox to represent these. And of course there is water - about 20 ml in the matchbox model - but we would not recommend actually adding it; the results would be messy. Just imagine that the remaining space in the model is water not air, and ask yourself how the matchbox can accommodate 20 ml of it, considering the space occupied by the other contents.

Then close the box.

A question will strike you immediately. Why is everything packed so tightly? Why is the cell not bigger? If you have so much luggage to pack why not use a suitcase? The accepted answer is as follows. If you reproduce in the simplest possible way, that is, by duplicating all your contents and then splitting into two pieces so that one copy of everything goes into each half, it is an advantage to be small. The smaller you are, the less of you there is to duplicate, so the less time and energy it takes. Therefore, by being as small as an organism can be, prokaryotes maximise their reproductive rates. So their populations grow at the greatest possible speed - until they run out of nutrients.

Producing the maximum number of descendants is a basic biological "drive". The aim is the long-term survival of the genes. Explosive population growth helps to ensure this outcome. Because they are as small as possible and therefore reproduce as quickly as possible, bacteria can transmit their genes to large populations of descendants in the shortest possible time. At maximum growth rate, a bacterial cell may divide every twenty minutes. If there is one cell at time zero, there are two after twenty minutes, four after forty minutes, eight after an hour, sixty-four after two hours, and so on. Given an inexhaustible nutrient supply, there would be about 4,722,366,483,000,000,000,000 cells, 14,000 tonnes of solid bacteria, after a day's growth from a single cell. Of course the nutrient supply would run out long before that number was reached, but bacteria do proliferate very quickly under optimal conditions. It gives their genes the best long-term chance of survival.

The prokaryotic cell surface: the drawback of being small

The matchbox model has served its two main purposes: (1) to give a clear impression of the relative sizes of cell, DNA molecule, protein molecules and ribosomes, and (2) to show that a prokaryotic cell is about as small as it can possibly be - it is very tightly packed. The model has also led to a discussion of the relationship between cell size, population growth, and the biological imperative to transmit genes to future generations. (More about this "drive" later.) Like any model, however, it has limitations. We have mentioned two of these already: prokaryotes do not have sharp corners and edges like a matchbox; and the model is static - it does not represent any of the myriad activities, including reproduction, in which a cell engages. There is another limitation as well, rather an important one: the model misleads us about the nature of the cell surface.

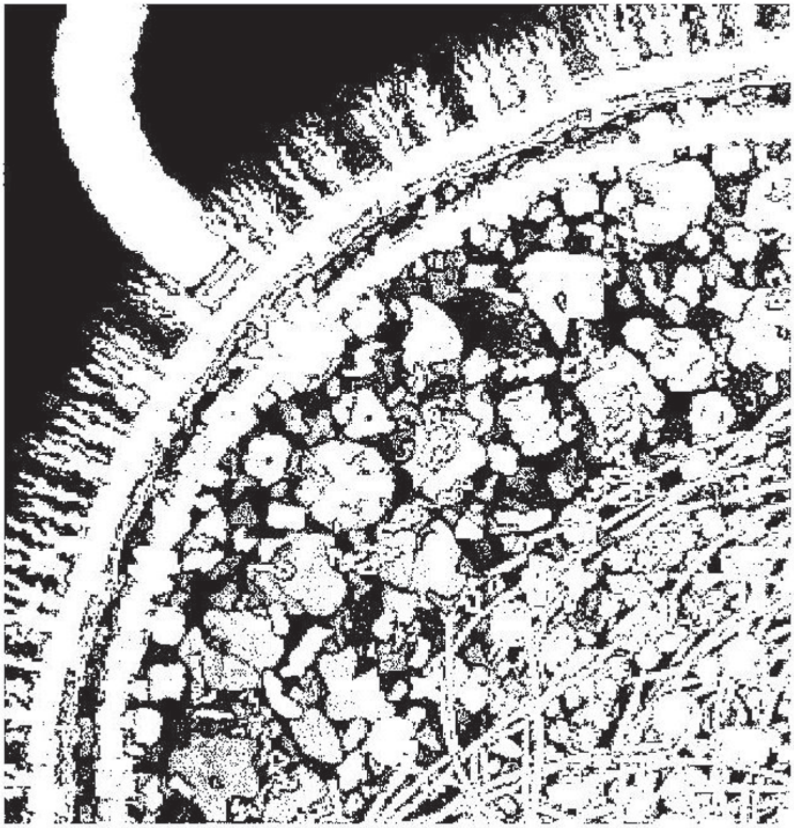

Fig. 2-1: A bacterial cell surface.

The cardboard of the box can be taken to represent the tough protective coat surrounding most prokaryotes, the *cell wall*. Inside the cell wall, however, there is a very thin continuous coat, the *cell membrane*[2], which in

[2] Some prokaryotes (Gram negative bacteria, for instance) have an extra membrane outside the cell wall, but we shall not develop this point here.

our matchbox model would have to be represented by an unbroken seal of polythene or cellophane about a quarter of a millimetre thick. Despite its unimpressive appearance, the membrane is one of the most active and versatile parts of the cell. It jobs include:-

- Separating the cell interior from the outside world, preventing inadvertent mixing.
- Controlling the flow of materials into and out of the cell.
- Enabling items of food in the outside world to be digested, and importing the products of digestion to the cell.
- Detecting stimuli (the whereabouts of food, the location of danger, etc) and initiating appropriate responses.
- Playing a central role in making energy available to the cell. In some prokaryotes, it traps energy from the outside world and changes this energy to a form that the cell can use. (Cyanobacteria, for example, trap the energy of sunlight.)
- Housing the equipment for manufacturing many of the cell's constituents, including the external wall.
- Initiating and controlling the duplication of the DNA - the essential step before cell division (reproduction).

The first two of these functions are clearly linked. The surface membrane must be a barrier but not an impermeable one; it has to be selective. It must enhance the entry of materials that the cell needs and the exit of waste products, but it must be a barrier to everything else. Designing a structure with such exacting properties would be an engineer's nightmare, particularly if the barrier had to be no more than ten nanometres (one hundred-millionth of a metre) thick, the usual thickness of biological membranes. Yet life on Earth produced this structure thousands of millions of years ago.

Because of the membrane's remarkable range of functions, being small is in some ways a *disadvantage* for prokaryotes. The smaller the cell, the smaller the area of the cell membrane. The smaller the membrane area, the less equipment can be fitted into it. The fewer the pieces of equipment, the more limited the range of membrane functions. Thus, the number of different materials that can be exchanged across the cell surface, the variety of cell components that can be manufactured, the range of stimuli to which the cell can respond, and so on, are all limited because prokaryotes are as small as they can be. In other words, being small restricts the adaptability[3] of a prokaryote to changing conditions. It cramps the cell's lifestyle.

[3] "Adaptability" is an ambiguous word. It is used in different senses in different biological contexts, particularly when evolution is being discussed. Here we use it to mean the ability to survive changes in environmental conditions.

Prokaryotes have evolved remarkable ways of circumventing these limitations. Some bacteria change when the going gets tough into a very durable quiescent form, an *endospore* - a sort of suspended animation. They come back to life when conditions improve. Some can swim away from danger to a more comfortable environment. Some have genes that switch on

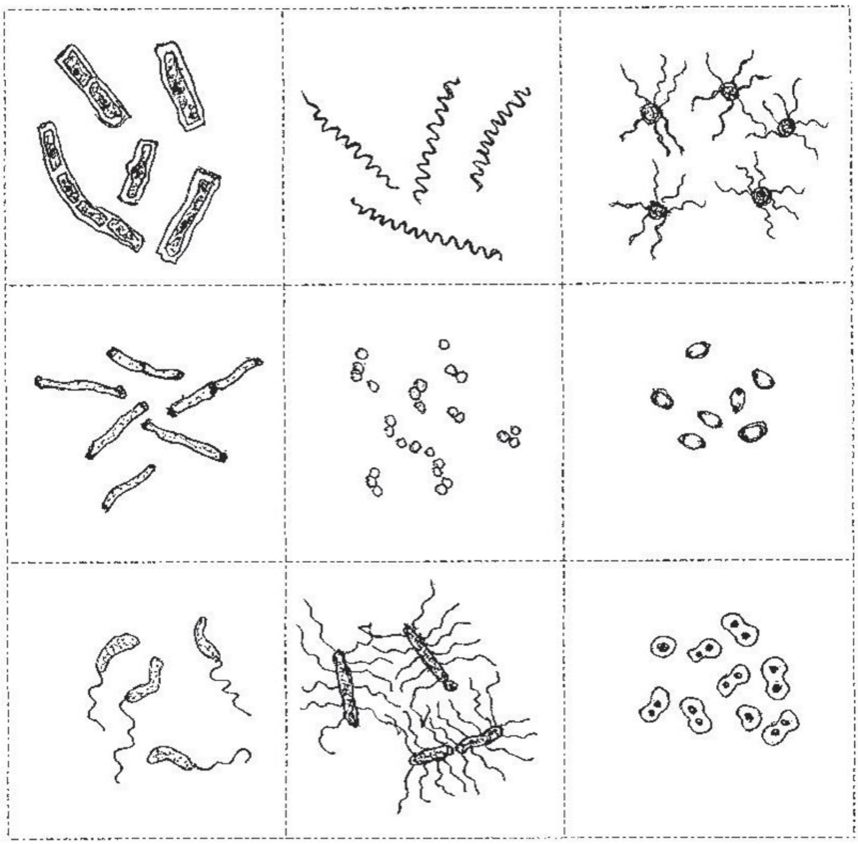

Fig. 2-2: Variety of shapes of cells belonging to just one group of bacteria (cocci).

and off in response to changing conditions, increasing adaptability. Many bacteria can exchange pieces of DNA with other kinds of bacteria, passing genes to quite different organisms. This is how antibiotic resistance has spread, creating a significant worry for the medical profession. Also, bacteria work in teams. In their natural habitats, different types of prokaryotes can assemble into mixed groups and pool their resources and capabilities for the advantage of all. These groups often have beautiful geometries.

To witness such devices is to realise that our wonder at Nature need not - indeed, should not – be restricted to the everyday macroscopic world of oaks, primroses and beetles. Nature under the microscope is wonderful and enchanting too. This is a case where the ability to explain what we observe is a major ingredient of our enchantment. Knowledge does not merely enhance pleasure; sometimes, as when we contemplate these startling assemblies of bacteria, it is essential for it.

Nevertheless, despite the remarkable devices by which bacteria cope with difficult circumstances, the limitation imposed by the small cell membrane area is intractable. Being small enables cells to reproduce at maximum speed. But it imposes severe restrictions on their individual ability to adapt.

Chapter 3

BIGGER CELLS

Eukaryotic cells and their contents

We promised not to consider evolutionary theory until later in the book, but we have already invoked it several times, mentioning biological "drive", transmission and survival of genes, adaptation, and so on. This shows how difficult it is to survey any part of modern biology without referring at least implicitly to biology's central theory. During the next few chapters, these implicit references will continue. However, we shall defer explicit discussion of the theory until chapter 11.

Our attention at present is on cell structure. So far, this seems to have brought us no closer to understanding what "life" is or why the cell should be considered the “fundamental unit of life”. We ask for your patience. The question we are addressing is complicated and we have to approach our answer to it in stages.

The stage we reach in this chapter concerns cells that have overcome the basic limitation of prokaryotes: restricted membrane area. Eukaryotic cells do not have such restricted membrane areas, so they have elaborated membrane functions to a high degree. As a result, they have versatile manufacturing capabilities, they can respond to an impressive variety of stimuli, and so forth. This is only partly because eukaryotic cells have bigger surface areas than prokaryotes. (A thousand-fold greater cell volume means a hundred-fold greater surface area, if the cells being compared have the same geometries.) A more important point is that only three of the functions of the prokaryotic cell membrane *have* to be associated with the cell surface:-

- Preventing accidental mixing of the cell contents with the environment - keeping the outside out and the inside in.
- Controlling the flow of materials into and out of the cell.
- Detecting stimuli from outside and initiating appropriate responses.

The surface membrane of a eukaryotic cell is almost exclusively devoted to these three functions. So it is not only much bigger than its prokaryotic counterpart, it is also more specialised and more sophisticated. The other jobs done by the prokaryotic membrane are delegated in eukaryotes to membrane structures inside the cell.

The total area of these internal membranes can be vast. If they were confined to the surface then the length and width of – say – a liver cell would be about a millimetre - impossibly big for an active animal cell. Membrane internalisation has prevented eukaryotic cell size from becoming unmanageable. Each internal membrane system has its own functional specialism, and they all have impressive names[4]. We would not expect readers to remember these names but we need to introduce them here; the model we are going to construct would make little sense if we could not name the parts and have some idea of the functions of each part. When we mention the names again later in the book we shall remind you what they mean.

Intracellular digestion is carried out by small membrane-bound spheres called *lysosomes*. When a tasty morsel touches the outside of the cell, part of the surface membrane pinches off to enclose the morsel, forming an *endocytic vesicle*. The endocytic vesicle fuses with a lysosome, the morsel is digested, and the digestion products pass through the lysosomal membrane into the body of the cell, where they are used.

When the cell's own proteins and nucleic acids wear out, they too are broken down (digested) so that their components can be recycled. This is usually accomplished not by lysosomes but by structures called *proteasomes*. In vertebrates, proteasomes can also break down foreign proteins. In this case, the resulting fragments can be presented to the animal's immune system. If the foreign protein reappears, an immune response results.

[4] For readers who are interested in etymologies, here are the roots of these names and their literal meanings. *Chloroplast* comes from the Greek words *chloros* (= pale green) and *plastos* (= moulded). *Cytoplasm* comes from the Greek *kytos* (= vessel or cell) and *plasma* (= form or body). *Lysosome* comes from the Greek *lysis* (= dissolution) and *soma* (= body). All these are directly descriptive of appearance or function. *Mitochondrion* comes from the Greek *mitos* (= thread) and *chondros* (= granule), "thread-granules" describing the appearance that mitochondria presented to the 19th century microscopists who first observed them. *Endoplasmic reticulum* combines the Greek for "inside the form (body)" (*endo* + *plasma*) with the Latin for "little net" (*rete* = net; "*reticulum*" is the diminutive form). *Endocytotic vesicle* combines the Greek for "inside the vessel (cell)" (*endo* + *kytos*) with the Latin *vesica* (= bladder or blister). *Nucleus* comes from the Latin *nux* (= nut or kernel). The *Golgi complex* is named after the cell biologist who first described the structure in the 1890s, Camillo Golgi (1843-1926).