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Mike Boyle & Kathryn Senior

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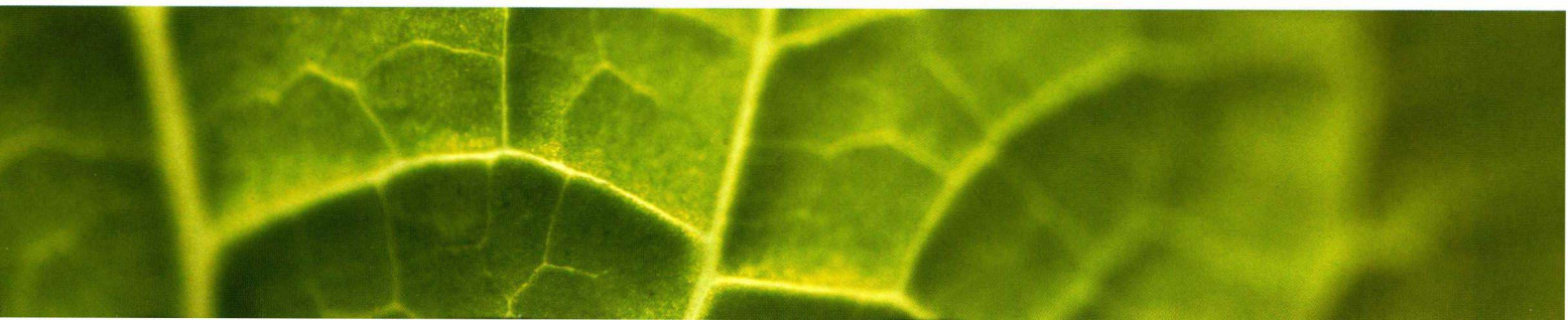
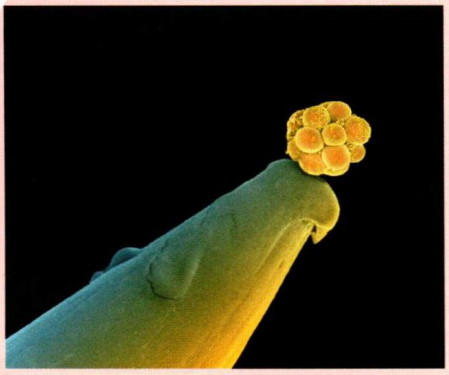


1

What's in a cell?

1 WHAT'S IN A CELL?

SCIENCE IN CONTEXT



SEM of an embryo on a pin point

You started life as a stem cell

The photo shows an embryo on the point of a pin. You were once that small, about nine months before you were born.

This embryo consists of just eight very special cells. They may not look like much, but they are stem cells – they have the potential to develop into any of the different cells that make up your body. Given time, these cells will divide and then differentiate into particular cell types, such as nerve, muscle, bone or blood.

Just how these cells divide and grow into a complete, healthy organism is the central puzzle of biology. We know that the key lies in the genes – tiny sections of DNA that code for making proteins – but we are still a long way from understanding how genes interact to control the growth and development and repair throughout an organism's life.

When we do unravel these mysteries, the potential benefits are enormous. Although there is a lot of research still to do, stem cells could be used to regenerate tissue that normally can't regenerate itself after injury or damage. Stem cells could be used to bridge spinal cord injuries to bring feeling and function back into limbs, or they could be used to regenerate heart muscle after a heart attack. There have already been some successful attempts to restore sight in people with damaged retinas. Transplanting stem cells in sheets over the damaged part of the retina can allow the eye to reclaim some of its function.

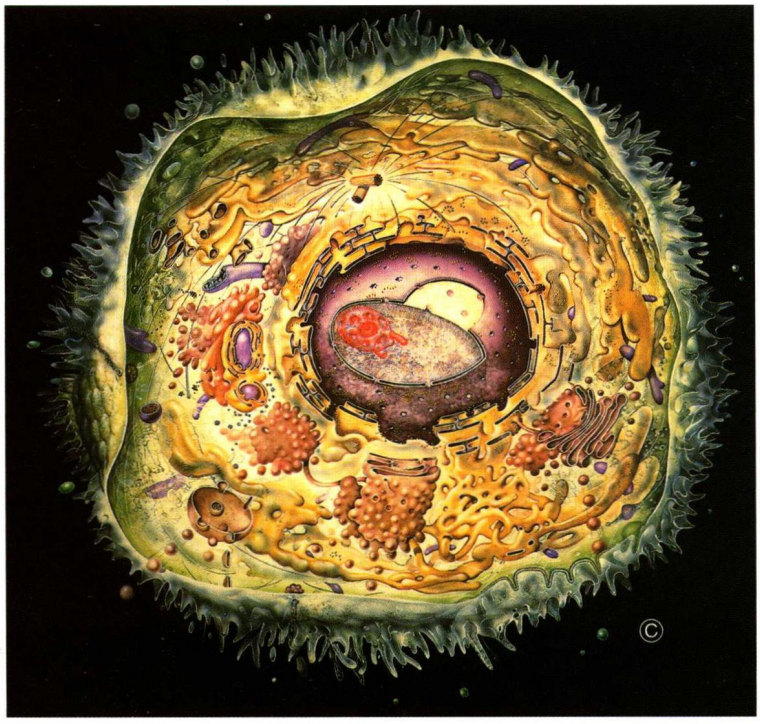


Fig 1.1 This painting illustrates something of the complexity of an animal cell. It was commissioned by the Science Museum on behalf of the Biochemical Society to provide the centrepiece of a permanent exhibition opened in 1987

1 THE COMPLEXITY OF CELLS

The artist who drew the cell in Fig 1.1 attempted to show something of the detailed structure of a human cell. This contrasts sharply with the images of animal cells that you will have seen with a light microscope (Fig 1.2). The first time you saw these little bags with dots you were probably disappointed and it is difficult to believe that something that looks like this can be so complex.

But all of your body cells are complex and you have about 50 million million (or 50 trillion) of them. Many are actively dividing. Cells from the lining of the digestive system, the blood and the skin are dying constantly and need to be replaced. In this chapter, you start to look at the complex internal structure of basic cell types. You will also investigate the techniques that have helped us learn more about the relationship between the structure of cells and their function.

2 THE CELL THEORY

Following the invention and refinement of the microscope came the **cell theory**, a general acceptance that all living things are made of cells. Modern cell theory has three central ideas:

- The cell is the smallest independent unit of life.
- The cell is the basic living unit of all organisms – all organisms are made up of one or more cells.
- Cells arise from other cells by cell division. They cannot arise spontaneously.

As you study biology in more detail, you will discover that there are exceptions to every rule. In the case of cell theory, that exception is the **virus**. Viruses do not have a cellular structure or organisation, and whether they are actually living organisms is a subject of debate.

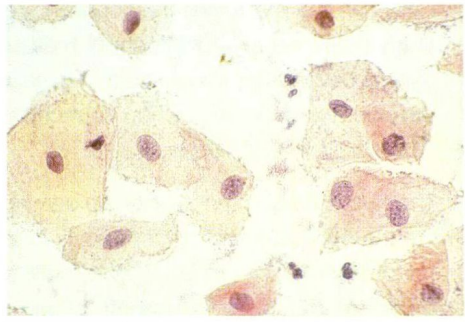


Fig 1.2 The light microscope can reveal the basic features of animal cells; this is what cheek cells look like

3 USING CELL STRUCTURE TO CLASSIFY ORGANISMS

Organisms can be classified on the basis of the internal organisation of their individual cells. With the exception of viruses, all organisms are either **prokaryotic** or **eukaryotic**. Prokaryotic cells are relatively simple, they have no separate nucleus and show little organisation. Bacteria are prokaryotes. In contrast, eukaryotic cells are larger and show much more internal organisation. Animals, plants, fungi and protoctists are all eukaryotes. The main differences between prokaryotes and eukaryotes are shown in Table 1.1.

Table 1.1 Differences between prokaryotes and eukaryotes

	Prokaryotes	Eukaryotes
organisms	bacteria	plants, animals, protoctists, fungi
diameter of cells	0.1–10 µm	10–100 µm
site of genetic material	DNA in cytoplasm	DNA inside distinct nucleus
organisation of genetic material	DNA is circular; no histone proteins; DNA does not condense at cell division	DNA is linear; attached to histone proteins; condenses into visible chromosomes before cell division
internal structure	few organelles	many organelles with complex membrane systems
cell walls	always present	present in plants and fungi and some protoctists; never in animals
flagella	have simple flagella	have modified cilia that consist of microtubules in a distinctive '9 + 2' arrangement

4 PROKARYOTES – THE FIRST ORGANISMS?

A few billion years ago, the first living organisms to evolve on Earth were probably prokaryotes. The term literally means 'before the nucleus' because the genetic material (DNA) of these organisms is not enclosed by a membrane, and therefore they do not have a true nucleus.

It is tempting to think of prokaryotes as inferior to eukaryotes, but in some ways they have achieved greater success. They have been on Earth more than twice as long as eukaryotes, they are present in greater numbers (there are more bacteria living on your skin than there are people on Earth) and they occupy an enormous number of different habitats. Some bacteria, for example, are able to live in volcanic springs at temperatures as high as 90 °C.

REMEMBER THIS

No matter how far you take the study of biology, all you need to know about microscopic distances is these two simple facts:

- 1 mm = 1 000 µm
  1 millimetre = 1 000 micrometres
- 1 µm = 1 000 nm
  1 micrometre = 1 000 nanometres

HOW SCIENCE WORKS

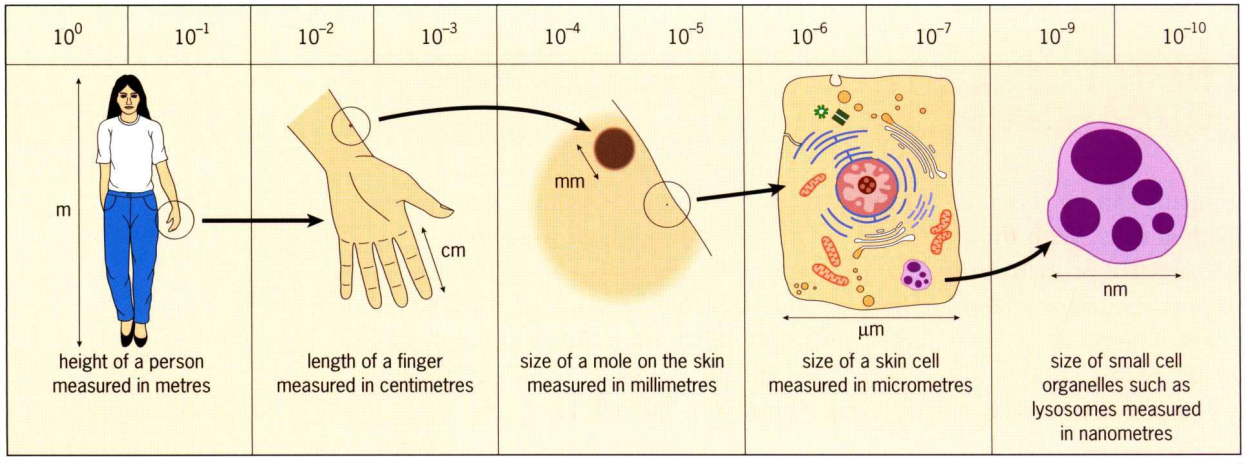
How small is small?

Cells and the molecules they contain are very small. When we study them, we must think about measurements that are minute beyond our imagination. It is easy, for example, to develop a mental block when confronted by the statement 'The nanometre is 10^{-9} m.'

The two units commonly used to describe microscopic objects are the **micrometre** (μm) (commonly called the micron) and the **nanometre** (nm) (Fig 1.3). Starting with a familiar unit, the millimetre (mm), one thousandth of one millimetre is known as a micrometre (μm). The micrometre is used to describe cells and organelles. An average animal cell is 30 to 50 μm across; the nucleus has a diameter of about 10 μm. Plant cells can reach 150 μm or more in length.

When describing small cellular components and molecules, the useful unit is the nanometre (nm). A nanometre is one thousandth of a micrometre. As a rough guide, the light microscope reveals structures that can be measured in micrometres, but you need an electron microscope to see objects measured in nanometres.

Fig 1.3 Units of measurement; how they are used and how they relate to each other

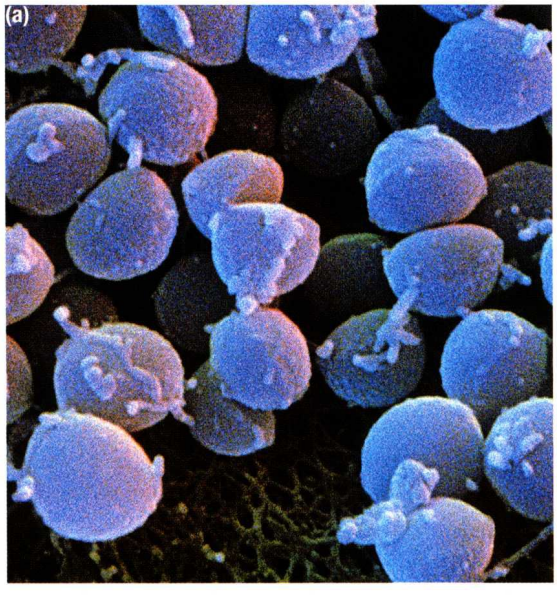


? QUESTION 1

1 **a)** Estimate the diameter (in micrometres) of a full stop on this page.
b) How many nanometres are there in one millimetre?

BACTERIA

Most bacteria are spherical or rod-shaped cells, and several micrometres long (Fig 1.4). Their rigid protective **cell wall** is made of **peptidoglycan**, a substance unique to bacteria. Beneath the cell wall is the **plasma membrane**, which is similar in structure to the membrane of eukaryotic cells. This completely encloses the contents of the cell.



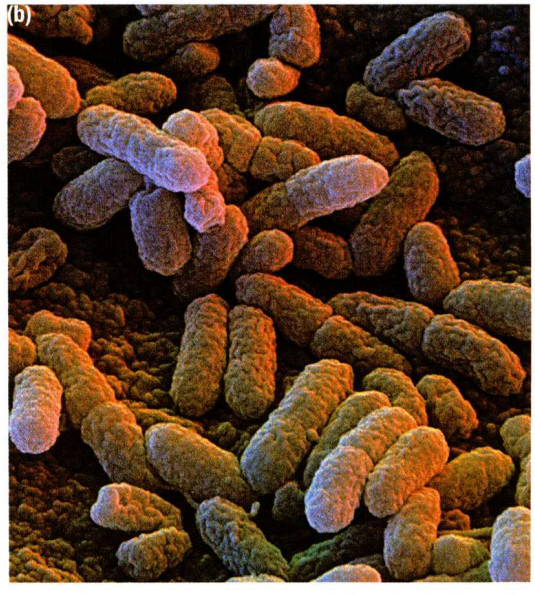


Fig 1.4(a) Scanning electron micrograph showing *Staphylococcus aureus* cells. These spherical cells are called cocci (singular coccus), and are one of the two main types of bacterial cell (the others are bacilli – (singular bacillus); see Fig 1.4b) *S. aureus* is commonly found on human skin where it usually does no harm. However, it can cause serious infection if it enters the body through a cut or wound

Fig 1.4(b) Scanning electron micrograph showing *Salmonella enteritidis* cells. These sausage-shaped cells are called bacilli. This species of *Salmonella* can cause severe food poisoning

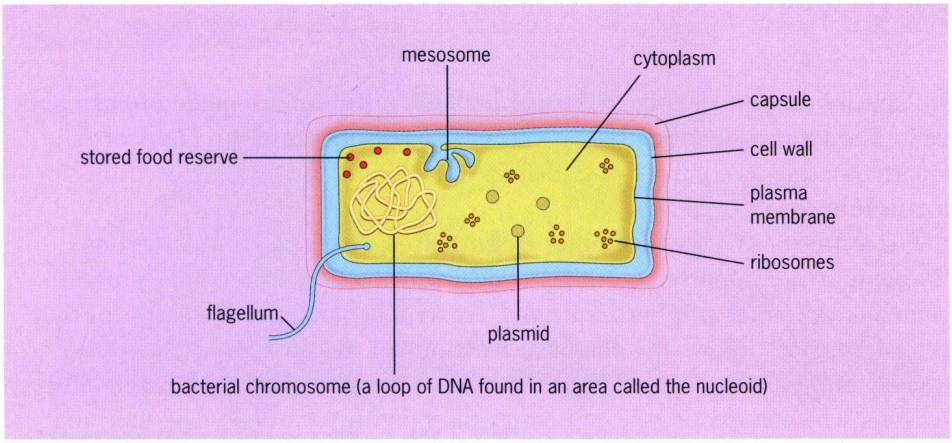


Fig 1.5 The basic structure of a bacterium

Some types of bacteria, such as *Neisseria meningitidis*, which can cause meningitis, also have a **capsule**. This is a sticky coat outside the cell wall that prevents the bacterium from drying out, from being digested by host intestinal enzymes, or from being attacked by the host's immune system.

Fig 1.5 shows the internal structure of a rod-shaped bacterium, *Escherichia coli*.

Inside the plasma membrane, the bacterial cell is a single cytoplasmic compartment that contains DNA, RNA, proteins and small molecules. Bacteria have a circular piece of DNA in a region of the cytoplasm known as the **nucleoid**. There are smaller rings of DNA, known as **plasmids**, elsewhere in the cytoplasm. Plasmids are of great interest to biologists because they often contain genes that code for antibiotic resistance, and can be used to carry genes between cells in genetic engineering.

Bacteria feed by **extracellular digestion**. They release enzymes into the surrounding medium and absorb the resulting soluble products. **Glycogen granules** and **lipid droplets** often occur in the bacterial cytoplasm and provide a limited store of these polymers. Bacteria can synthesise a wide variety of enzymes, and some species are able to digest unlikely substances such as oil and plastic. Proteins are synthesised on **ribosomes** (page 13), and cell respiration occurs on **mesosomes**, inner extensions of the plasma membrane.

Some bacteria are **motile**: they can swim. They have thin fibres called **flagella** (singular flagellum) that are corkscrew-shaped and that rotate, propelling the bacteria in different directions. Other fibres, called **pili**, enable the bacteria to perform a primitive form of sex, as shown in Fig 1.6. During **conjugation**, the pili become joined and form a channel to allow plasmids to be copied and transferred to other individuals.

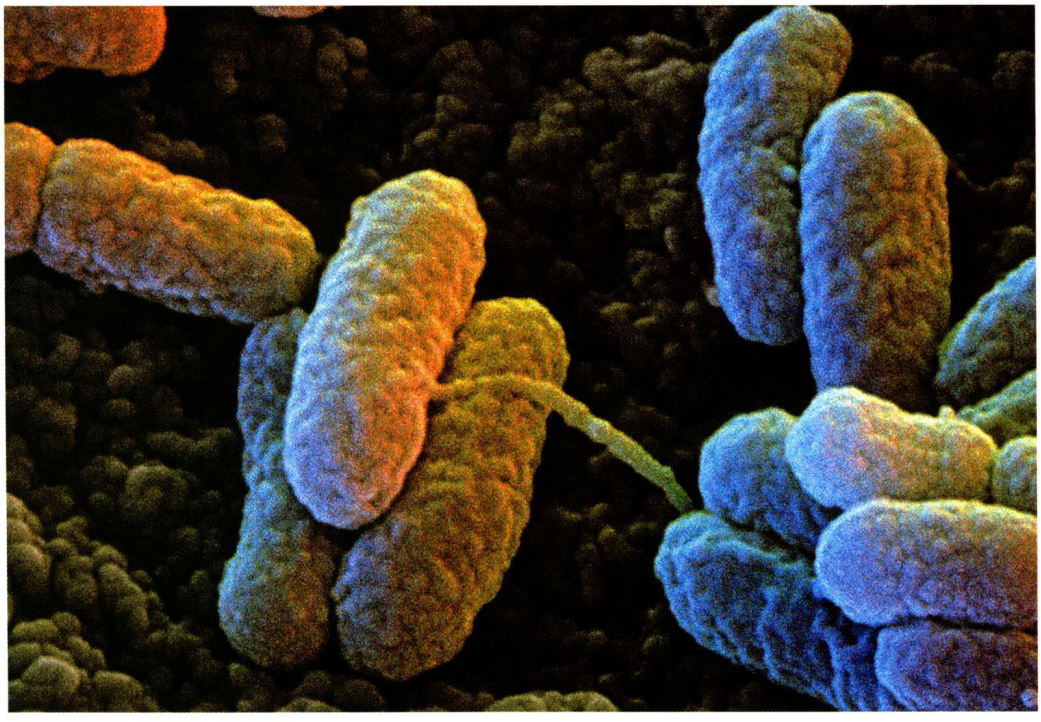


Fig 1.6 SEM showing conjugation in two bacterial cells

? QUESTION 2

2 Some bacteria can digest, or break down, oil and plastic. Suggest how this could be useful to people.

The role of plasmids in genetic engineering is further discussed in Chapter 31.

✔ REMEMBER THIS

Until the invention of the microscope, people had no idea that cells existed. They knew nothing of bacteria and had no idea about how infectious diseases spread.

The role of bacteria in the environment is discussed in Chapter 37.

5 EUKARYOTES: ANIMAL CELLS

All species of animals, plants, **fungi** and **protoctists** are made of eukaryotic cells. The term **eukaryote** means 'true nucleus', because the DNA of eukaryotic cells is confined to a definite area inside the cell enclosed by a **nuclear envelope**.

Eukaryotic cells also have other **organelles** that form compartments. By being in a compartment, the chemicals involved in a particular process, such as respiration or photosynthesis, are kept separate from the rest of the cytoplasm. This allows the chemical reactions of the process to take place quickly and efficiently. This high degree of internal organisation is one of the reasons why eukaryotic cells are larger than prokaryotic cells. The fluid that occupies the space between organelles is the **cytosol**, a solution containing a complex mixture of enzymes, the products of digestion (amino acids, sugars, etc.) and waste materials.

INSIDE AN ANIMAL CELL

If you look at an animal cell under a **light microscope**, the right staining and illumination techniques and a good quality microscope should allow you to see the **nucleus, nucleolus**, the **chromosomes** in a dividing cell, and even the **Golgi body**, **mitochondria** and food storage particles. But to make sure you see the inside of a cell in more intricate detail, you really need an **electron microscope**.

The **electron micrograph** in Fig 1.7 (opposite) shows the internal structure of an animal cell. You can see far more of the cell's components – the **endoplasmic reticulum** (**ER**), the internal features of the mitochondria, the plasma membrane, **lysosomes, ribosomes** and **cytoskeleton** are all now visible.

In this chapter, we look at the detailed structure of each individual organelle and find out how each type contributes to the function of the cell as a whole.

Table 1.2 summarises the functions of some of the major organelles and structures in the eukaryotic cell.

Table 1.2 Summary of the functions of major eukaryotic cell organelles and structures

Organelle	Occurrence	Size	Function
nucleus	usually one per cell	10 µm	site of the nuclear material – the DNA
nucleolus	inside nucleus	1–2 µm	manufacture of ribosomes
mitochondrion	numerous in cytoplasm; up to 1 000 per cell	1–10 µm	aerobic respiration
rough endoplasmic reticulum	continuous throughout cytoplasm	extensive membrane network	isolation and transport of newly synthesised proteins
smooth endoplasmic reticulum	usually small patches in cytoplasm	variable	synthesis of some lipids and steroids
ribosome	free in cytoplasm or attached to rough ER	20 nm	site of protein synthesis
golgi body	free in cytoplasm	variable	modification and synthesis of chemicals
lysosome	free in cytoplasm	100 nm	digestion of unwanted material
chloroplast	cytoplasm of some plant cells, e.g. mesophyll	4–10 µm	site of photosynthesis
vacuole	usually large, single fluid-filled space in plant; smaller and more numerous in animals	up to 90% of volume of whole plant cell	storage of salts, sugars and pigments; creates turgor pressure by interaction with cell wall
plasma membrane	encloses the cytoplasm of all cells	7–10 µm	exchange and transport of materials into and out of the cell
cell wall	surrounds all plant and fungal cells (but of different structure)	thickness varies	provides rigidity and strength

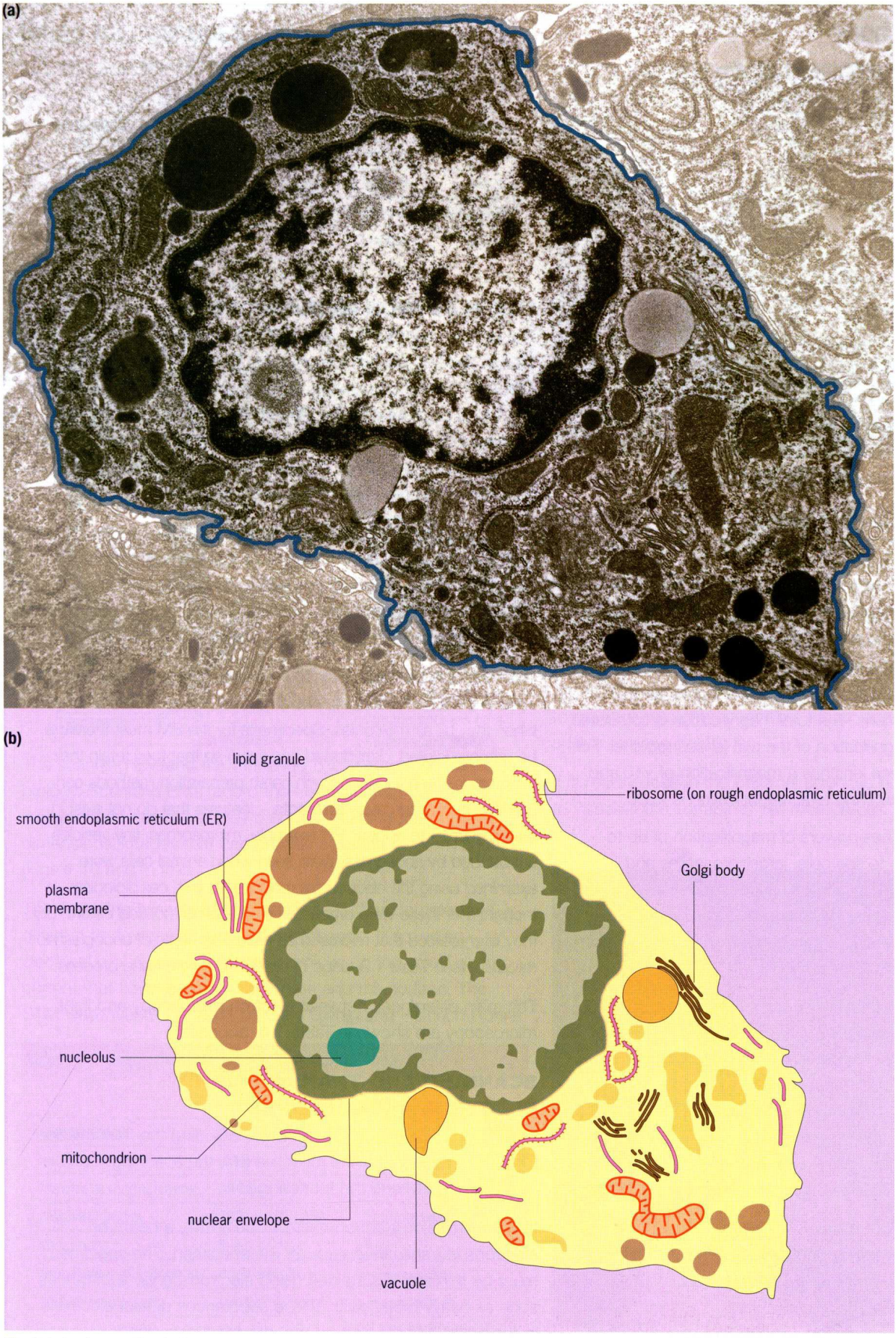


Fig 1.7 A micrograph of a human cell **(a)** with an interpretive diagram **(b)**. It shows that the cytoplasm of animal cells contains a complex system of membrane-bound organelles

HOW SCIENCE WORKS

Using microscopes

THE LIGHT MICROSCOPE

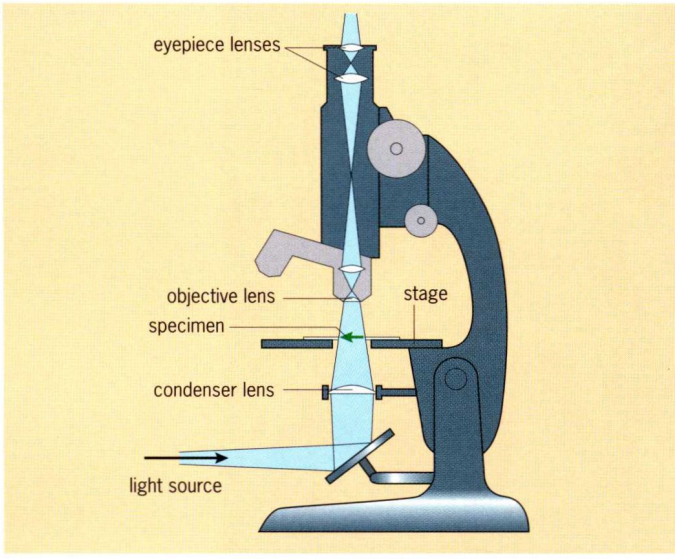


Fig 1.8 The standard compound microscope

Fig 1.8 shows the structure of a **light** or **optical microscope**. This instrument is also known as a **compound microscope** because two lenses, the **eyepiece lens** and the **objective lens**, are combined to produce a much greater **magnification** than is possible with a single lens. The total magnification is calculated by multiplying the magnification of the two lenses together. For example, if the eyepiece lens has a magnification of ×10 and the objective lens is ×50, the total magnification is ×500.

The light microscope has powers of magnification of up to ×1 500, good enough to see cells, larger organelles and individual bacteria, but not powerful enough to reveal smaller structures such as plasma membranes, viruses or individual molecules. Table 1.3 shows organelles in animal and plant cells that are visible with a light microscope.

An important feature of a microscope is its **resolving power**, which should not be confused with the magnification. Two objects close together may appear as one single image when viewed under the light microscope. Increasing the magnification does not allow you to **resolve** the two objects into separate images; the objects just appear to be a larger single image. Resolving power is as important as magnification when investigating structural details.

The limitation of the light microscope is due to the nature of light itself. The wavelength of light determines the maximum effective magnification and the resolving power. The wavelength of visible light is around 500–650 nm and the resolving power – the resolution – of the light microscope is 200 nm (0.2 µm), so two objects separated by less than 200 nm appear as one object.

Table 1.3 Structures normally visible in animal and plant cells with the light microscope

Organelle	Function	Animal cells	Plant cells
nucleus	control of cell activities	✓	✓
vacuole	storage and support	✗	✓
chloroplasts	photosynthesis	✗	✓
cell wall	support	✗	✓

THE ELECTRON MICROSCOPE

The electron microscope (EM) (Fig 1.9) was invented in the 1930s. Today's modern transmission EMs can magnify up to 50 million times and can resolve two objects that are 78 picometres apart (one picometre is one trillionth of a metre). They can visualise individual atoms. The development of the EM has had a huge impact on biology. Organelles inside cells can be seen in great detail and new ones have been discovered.

While the light microscope uses lenses to focus a beam of light, the EM uses electromagnets to focus a beam of electrons. The wavelength of the electrons is much smaller than the wavelength of light, so the resolving power of the EM is much greater than the light microscope.

The main disadvantage of the EM is that the electron beam must travel in a vacuum because, being so small, electrons are scattered when they hit air molecules. Specimens for the EM must therefore be prepared (killed, dehydrated and fixed) so that they retain their structure inside a vacuum. Such harsh preparation methods can damage cells, and cause **artefacts** – features that do not exist in the living cell – to appear. For example, microsomes, tiny vesicles surrounded by ribosomes, were seen when animal cells were examined using the electron microscope. At first, cell biologists thought that these were organelles they had not noticed before, but they later realised that microsomes were fragments of endoplasmic reticulum (see Table 1.2, page 6) produced by the fixing process.

The main differences between electron microscopy and light microscopy are shown in Table 1.4, opposite.

SCANNING AND TRANSMISSION ELECTRON MICROSCOPES

There are now several types of EMs, including the transmission EM, the scanning EM, the reflective EM, the scanning transmission EM and the tunnelling EM.

In a transmission electron microscope (TEM), a beam of electrons is transmitted through the specimen. The specimen must be thin and it is stained using electron-dense substances such as heavy metal salts. These substances deflect electrons in the beam and the pattern that the remaining electrons produce as they pass through the specimen is converted into an image (Fig 1.7a, page 7).

HOW SCIENCE WORKS

Using microscopes

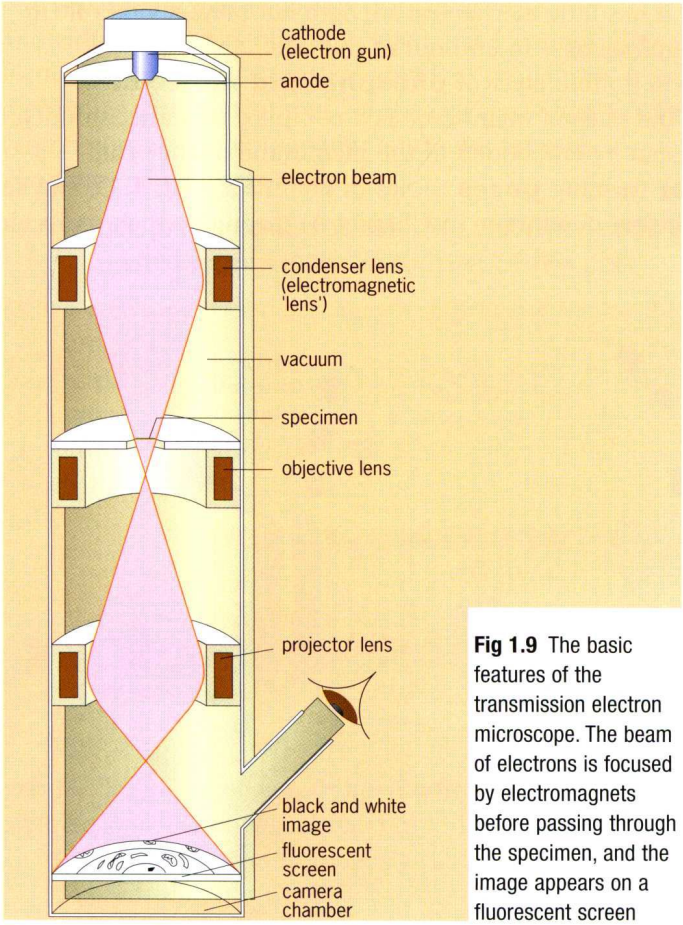


Fig 1.9 The basic features of the transmission electron microscope. The beam of electrons is focused by electromagnets before passing through the specimen, and the image appears on a fluorescent screen

The scanning EM and the tunnelling EM are the most useful in biology. Scanning EMs record the electrons that bounce off the surface of an object, so they produce stunning three-dimensional images that can provide a wealth of information (Figs 1.10 and 1.11).

The **scanning tunnelling microscope** (STM) is completely different to a scanning electron microscope. It scans an electrical probe over a surface and picks up the weak electric current that flows between the probe and the surface. The STM was invented in 1981 by Gerd Binnig and Heinrich Rohrer who worked for IBM at the time. They won the Nobel Prize for their development of the STM in 1986.

Table 1.4 Comparing light and electron microscopes

	Light microscope	Electron microscope
illlumination	light	electrons
focused by	lenses	magnets
maximum magnification	×1 500	×50 million
resolving power	200 nm (0.2 µm)	78 picometres
specimens	living or dead	dead
preparation of specimens	often simple	more complex
cost of equipment	relatively cheap	very expensive
images in colour	yes	no (colour is added by computer)

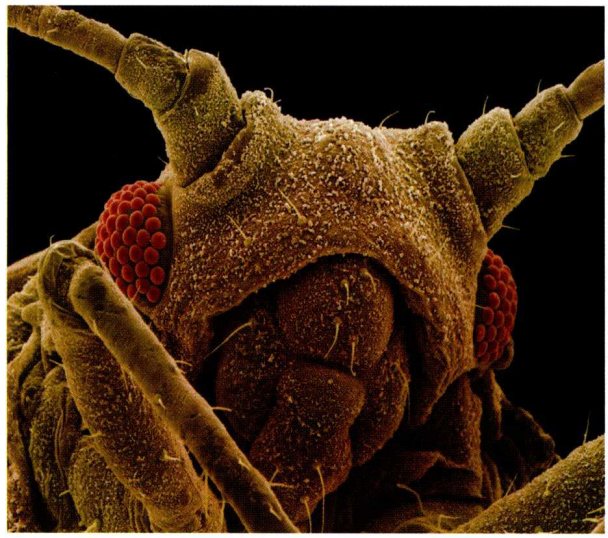


Fig 1.10 Scanning electron micrograph (SEM) of the head of an aphid

The STM is special because it allows scientists to 'see' individual molecules and even atoms. The three-dimensional images produced can show the individual atoms within a crystal lattice, for example. This kind of EM can resolve to a distance of 0.2 nanometres and it is interactive. It can be used to manipulate atoms, control or trigger chemical reactions or add or remove electrons.

It is mainly used in the physical sciences but has been used to visualise the surface of cell membranes.

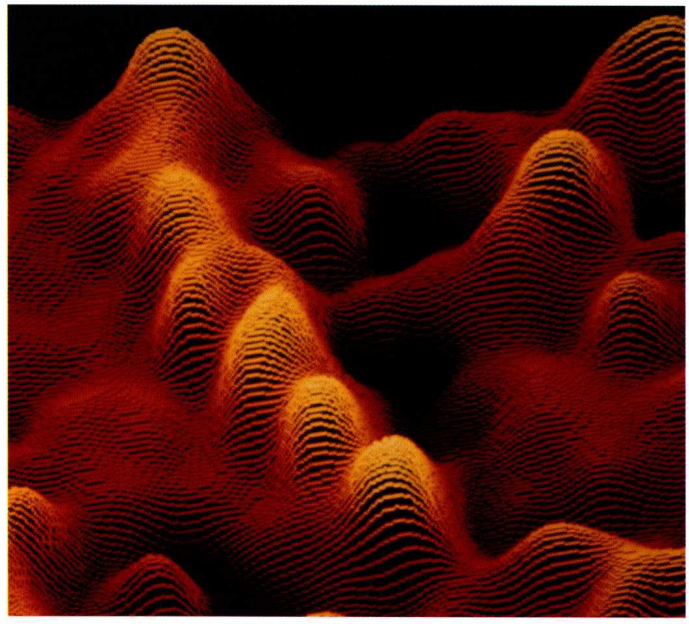


Fig 1.11 False-colour scanning tunnelling micrograph (STM) of double-stranded DNA

? QUESTION 3

3 If a light microscope had an eyepiece lens of ×25 and an objective lens of ×40, what would the total magnification be?

Chapter 4 covers the structure and function of the plasma membrane in detail.

THE PLASMA MEMBRANE

The **plasma** or **cell surface membrane** is the boundary between the cell and its environment. It has little mechanical strength but plays a vital role in controlling which materials pass in and out of the cell.

Although basically a double layer of **phospholipid molecules**, arranged tail to tail, the plasma membrane is a complex structure, studded with proteins. These can be embedded in the membrane or they can penetrate the **bilayer** forming **pores** (holes or channels – Fig 1.12 and see the section on the plasma membrane in Chapter 4) through which molecules can pass.

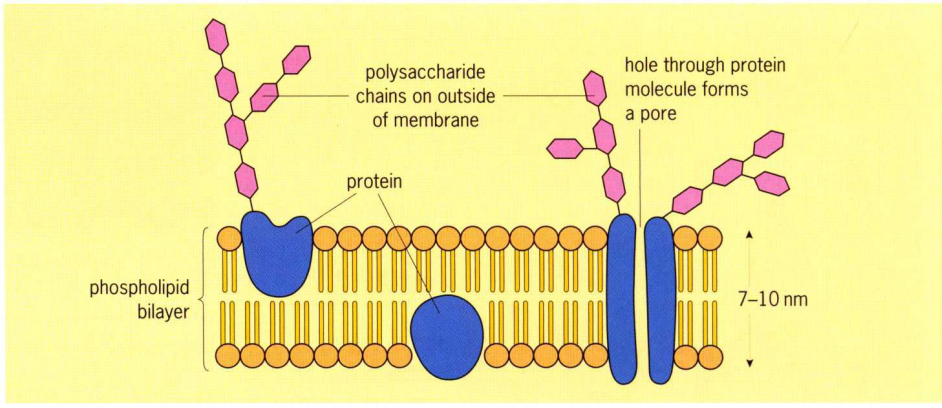


Fig 1.12 The plasma membrane is a complex organelle but its structure can be represented by this simplified diagram

THE NUCLEUS

The **nucleus** is the largest and most prominent organelle in the cell. Almost all eukaryote cells have a nucleus – red blood cells in mammals and phloem cells in plants are exceptions. Every nucleus is surrounded by a **nuclear envelope**. As Fig 1.13 shows, this consists of two membranes that are separated by a gap of 20 to 40 nm.

The nucleus is usually spherical and about 10 µm in diameter. It contains the cell's DNA, which carries information that allows the cell to divide and carry out all its cellular processes. When the cell is not actively dividing (as in Fig 1.13), the DNA is spread throughout the nucleus as chromatin. Close examination of the chromatin reveals two different levels of density. Dark-staining chromatin, consisting of tightly packed DNA, is known as **heterochromatin**; the lighter, more loosely packed material is called

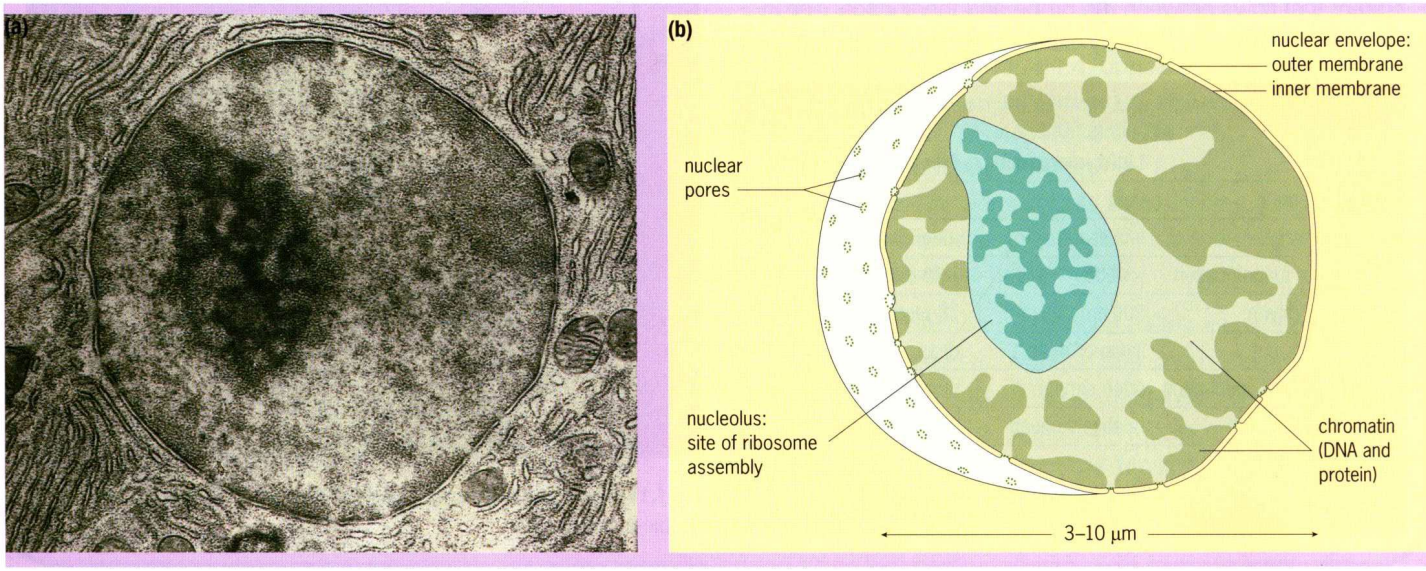


Fig 1.13 As the electron micrograph **(a)** and the interpretive diagram **(b)** show, the nucleus is bounded by the nuclear envelope, a double membrane which contains many pores, each one about 100 nm in diameter. The nuclear pores represent about 15 per cent of the total surface area of the nuclear envelope, indicating the heavy traffic of materials in and out of the nucleus. The nucleus contains the cell's genetic material that exists as chromatin, loosely packed DNA attached to proteins called histones. The nucleolus is clearly visible

euchromatin. Euchromatin contains the DNA that is being actively read to produce proteins; in heterochromatin, the DNA is packed together, and is not being read.

Individual segments of DNA called genes contain the information necessary to make individual proteins, including the enzymes that control most of the cell's activities. In fact, a central concept in biology that is true for all cells, prokaryotes and eukaryotes, is that:

Many genes code for making enzymes that, in turn, control the activities of the cell.

When a cell is dividing, its chromosomes become visible, as Fig 1.14 shows.

Nuclei also have one or more nucleoli (Fig 1.15). These dark-staining, spherical structures are ribosome-producing centres: they synthesise ribosomal RNA and package it with ribosomal proteins to make ribosomes.

Fig 1.14 When a cell divides, its DNA condenses into visible chromosomes

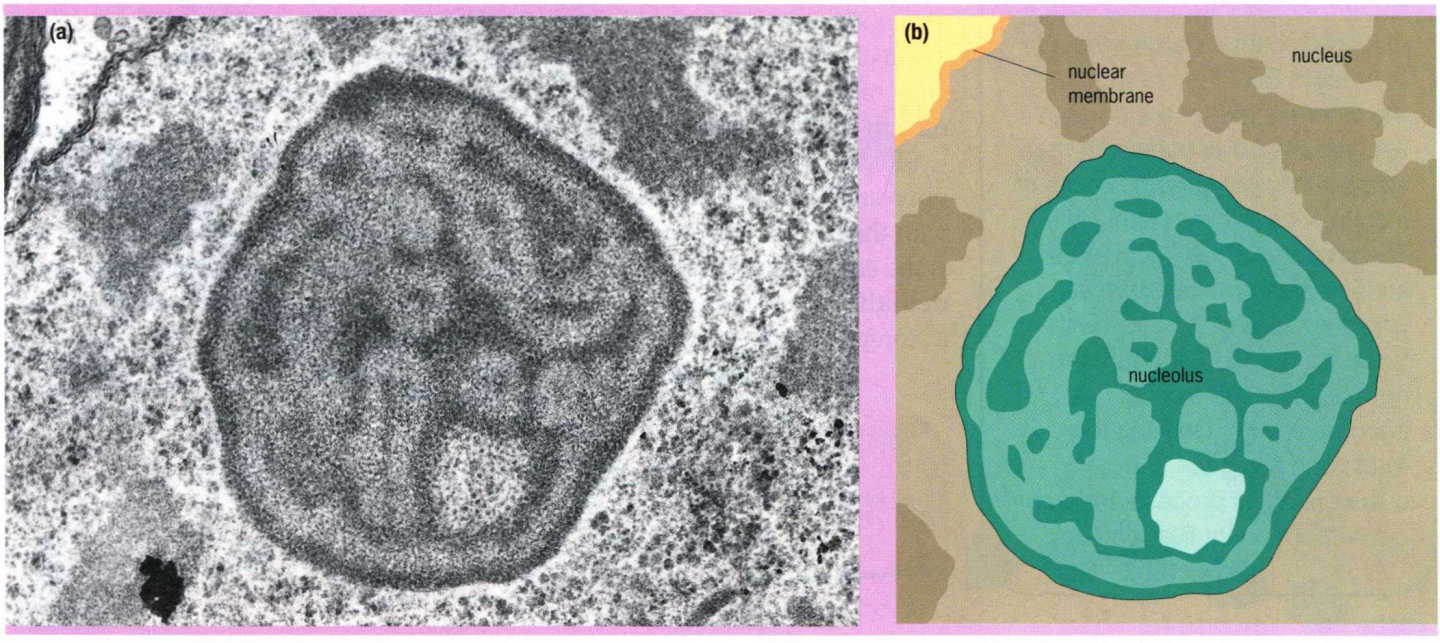


Fig 1.15 As the electron micrograph **(a)** and interpretive diagram **(b)** show, the nucleolus has a highly organised structure; its DNA codes for the RNA and proteins that are used to make ribosomes

ENDOPLASMIC RETICULUM

The nuclear envelope joins with the membrane of the **endoplasmic reticulum** (ER), a system of complex tunnels that are spread throughout the cell.

On much of the outside surface of the ER in a eukaryotic cell are the sites of attachment for ribosomes. This gives it a grainy appearance (Fig 1.16, overleaf) and its name, **rough ER**.

The main function of rough ER is to keep together and transport the proteins made on the ribosomes. Instead of simply diffusing away into the cytoplasm, newly made proteins are threaded through pores in the membrane and accumulate in the space called the **ER lumen** (Fig 1.17, overleaf). Here, they are free to fold into their normal three-dimensional shape. Not surprisingly, a mature cell that makes and secretes large amounts of protein – such as one that makes digestive enzymes – has rough ER that occupies as

Enzymes are discussed in Chapter 5 and protein synthesis in Chapter 28. Cell division is covered in detail in Chapter 26.

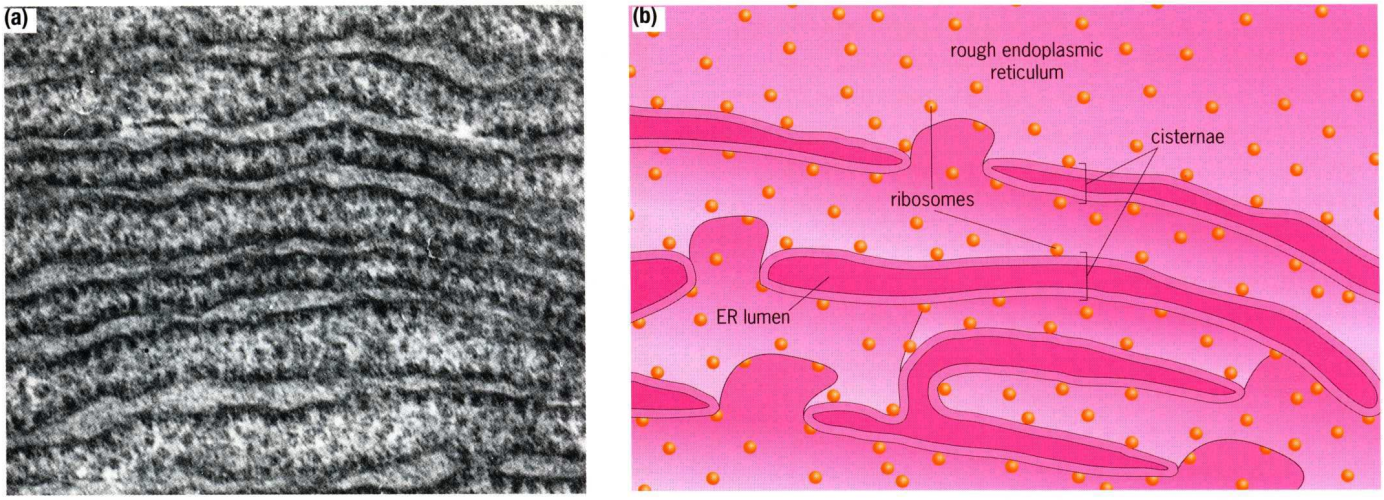


Fig 1.16 Electron micrograph **(a)** and interpretive diagram **(b)** showing rough ER. The ER is a large sheet of membrane that is folded over on itself many times, forming stacked layers called cisternae. The space inside the cisternae, the ER lumen, forms an extensive transport system throughout the cytoplasm

much as 90 per cent of the total volume of the cytoplasm. The rough ER is also a storage unit for enzymes and other proteins.

Small vesicles containing newly synthesised proteins pinch off from the ends of the rough ER and either fuse with the Golgi body or pass opposite directly to the plasma membrane.

ER with no ribosomes attached is known as **smooth ER** (Fig 1.18, opposite). Smooth ER tends to occur in small areas that are not continuous with the nuclear membrane. Smooth ER is not involved in protein synthesis but is the site of steroid (lipid hormone) production. It also contains enzymes that **detoxify**, or make harmless, a wide variety of organic molecules, and it acts as a storage site for calcium in skeletal muscle cells.

SCIENCE IN CONTEXT

The smooth ER in a binge drinker

Liver cells contain large amounts of smooth ER. The enzymes on the inner surface of the smooth ER help the body cope with the sudden influx of large amounts of alcohol – as in binge drinking. The smooth ER can double its surface area and its enzymes within a few days to cope with the extra demand. It returns to normal when the alcohol has been dealt with. Drinking too much and too often can overwhelm this process and can cause permanent liver damage.

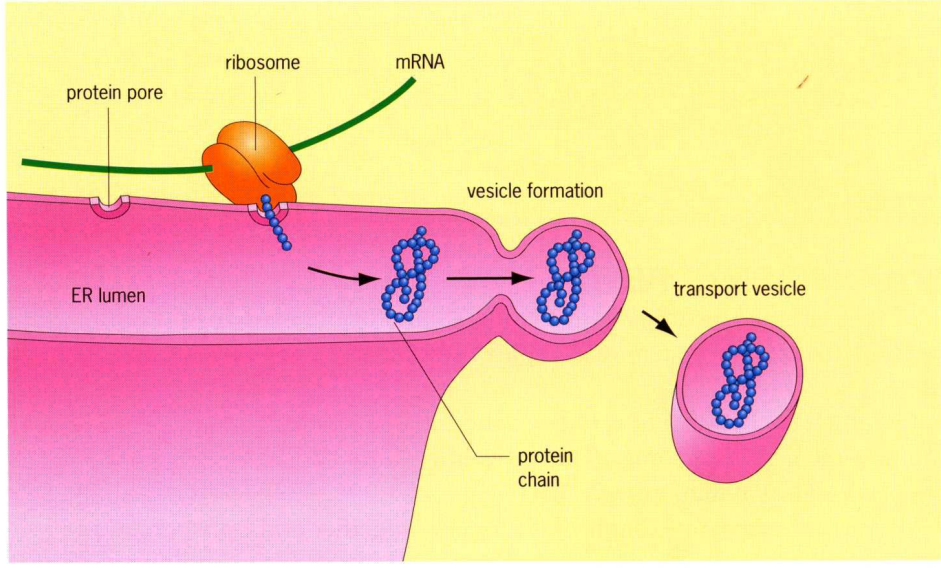


Fig 1.17 Accumulation of proteins in the ER lumen. Many proteins made on the ribosomes are threaded through pores in the ER membrane

? QUESTIONS 4–5

4 What function might the cells of the liver, gut and glands have in common? How could you recognise such cells from electron micrographs?

5 Why was ER not discovered until after the invention of the electron microscope?

RIBOSOMES

Ribosomes are small, dense organelles, about 20 nm in diameter, present in great numbers in the cell. Most are attached to the surface of rough ER but they can occur free in the cytoplasm, as in Fig 1.19. This artist's impression of protein synthesis shows the ribosome's distinctive shape. Ribosomes are made from a combination of ribosomal RNA and protein (65 per cent RNA : 35 per cent protein).

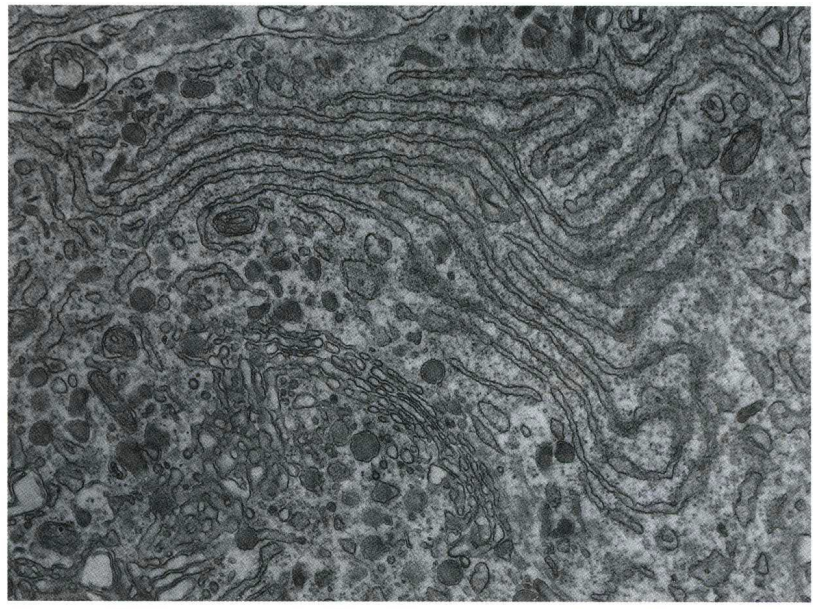


Fig 1.18 EM of smooth ER, which has no attached ribosomes. It is usually not as abundant as rough ER, although it is common in the cells of the liver, gut and some glands

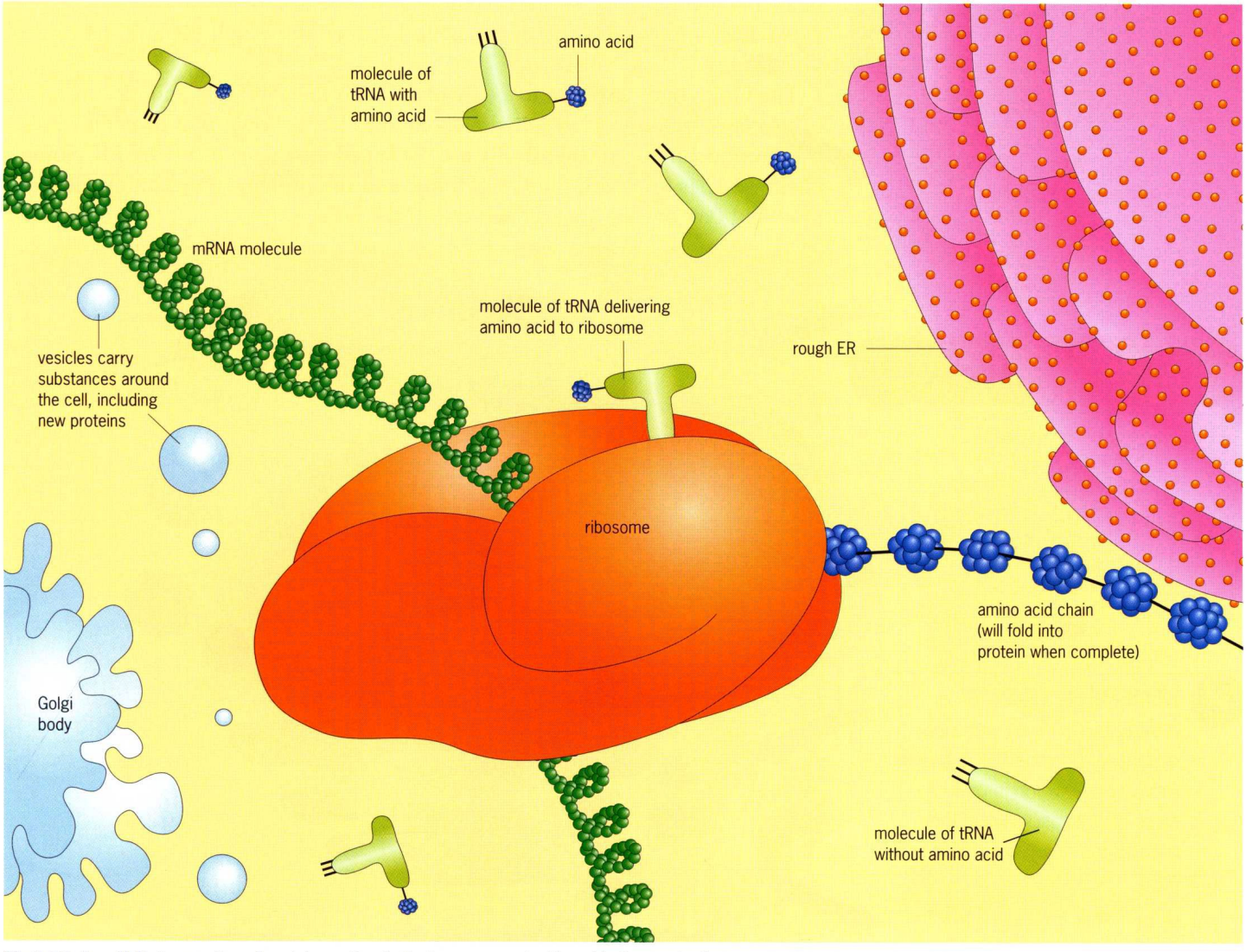


Fig 1.19 An artist's impression of protein synthesis. A ribosome can be thought of as a giant enzyme on which a protein is assembled. Transfer RNA molecules (tRNA) bring specific amino acids to the ribosome. Each one is added to the growing amino acid chain according to the code on the messenger RNA molecule