what is...?

The cytoskeleton

The cytoskeleton is found throughout the cytoplasm of eukaryotic cells. Here cell biologist Rebecca Bridgewater explains how the cytoskeleton gives cells their shape, organises their contents, and enables them to move

Key words

Cytoskeleton
Cell shape
Intracellular transport
Cell migration
Mitosis

Cells do many amazing things, from secreting hormones to healing wounds. Their diverse shapes are important for the structure and function of different tissues. Some cells can move from one place to another — for example, immune cells move to sites of infection. And within a cell, different components are transported to parts of the cell where they are needed. None of these vital functions could happen without the cytoskeleton.

The cytoskeleton is an organised network of proteins. It has three components (see Table 1):

- actin filaments
- intermediate filaments
- microtubules

These are all proteins assembled into long, fine threads. The three types each have different mechanical properties as well as different functions. Some cells also have specialised structures made up of cytoskeletal proteins — for example, the flagella that propel sperm, and the cilia that sweep mucus up the respiratory tract (see this issue, pp. 20–21 and Biological Sciences Review Vol. 27, No. 3, pp. 22–26).

The cytoskeleton is dynamic — it is continuously being partially destroyed and rebuilt. This is important because it allows cells to change shape and to move. Without this, cells would be unable to divide and wounds would not heal.

Shaping up

Cells come in a huge variety of shapes, which are crucial for their function — from long, thin nerve cells (see this issue, pp. 2–5) to box-like cells lining the small intestine (see Table 2). The cytoskeleton gives cells the mechanical strength needed to maintain their shape. This is the main function of intermediate filaments.

There are many types of intermediate filament, made up of different proteins, such as keratin and lamin. The proteins are organised as chains, which are twisted together

Table 1 Properties of three types of filament that make up the cytoskeleton

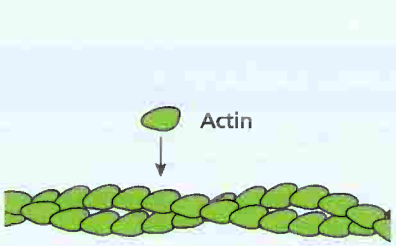
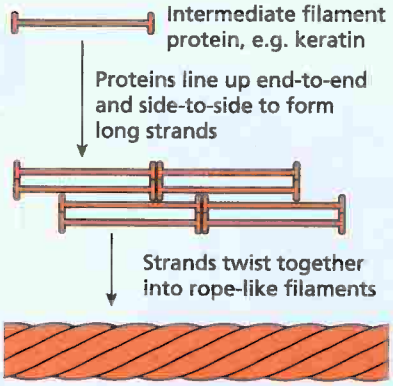
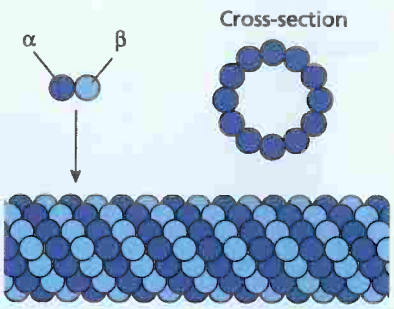
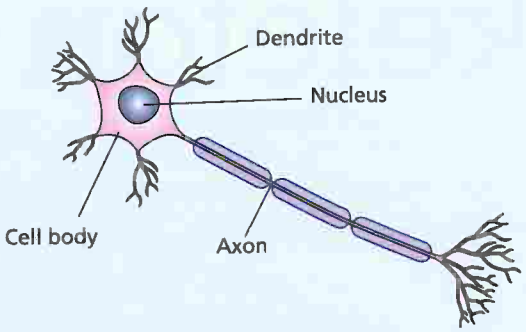
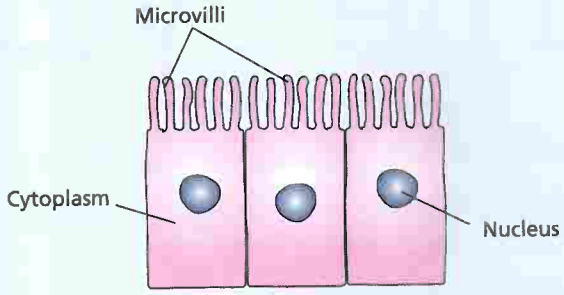
	Actin filaments	Intermediate filaments	Microtubules
			
Protein(s)	Actin	Various (e.g. keratin, lamin)	α-tubulin and β-tubulin
Diameter	7 nanometres	10 nanometres	25 nanometres
Structure	Twisted chain of actin molecules	Rope-like fibres composed of eight protein strands twisted together	Hollow tubes of tubulin
Function	Cell movement Cell division	Cell shape Mechanical strength	Internal cellular organisation and transport Specialised structures

Table 2 Cell shapes and functions

Neurone	Intestinal epithelial cells
	
Basic cellular functions take place in the cell body Dendrites receive and **axons** transmit electrical signals, sometimes over long distances	Cells form a continuous sheet lining the small intestine Microvilli increase the surface area — more nutrients can be absorbed

like a rope to form a long, durable filament (see Table 1). Intermediate filaments form a network, extending from the nucleus outwards, and often attaching to the plasma membrane (see Figure 1).

Cells that undergo mechanical stress, such as **epithelial cells** that form the outer layer of the skin, have many intermediate filaments. Intermediate filaments made of keratin (the same family of proteins that gives fingernails and hair their strength) help prevent these cells from tearing apart when the skin is stretched, during everyday movements such as bending a knee, or smiling. They form a continuous network from one cell to the next (see Figure 1), linked by special structures in the plasma membrane, called desmosomes.

They also bind to a dense protein network underneath the epithelium, known as the basement membrane, anchoring the cells in place. The networks of filaments allow stretching, while providing enough strength to prevent the cells breaking apart. When the gene for an intermediate filament protein is defective due to a mutation, the networks are disrupted. In the inherited condition epidermolysis bullosa simplex, faulty intermediate filaments are unable to form networks (see Figure 1). Even the softest touch can tear the skin cells apart, causing blistering.

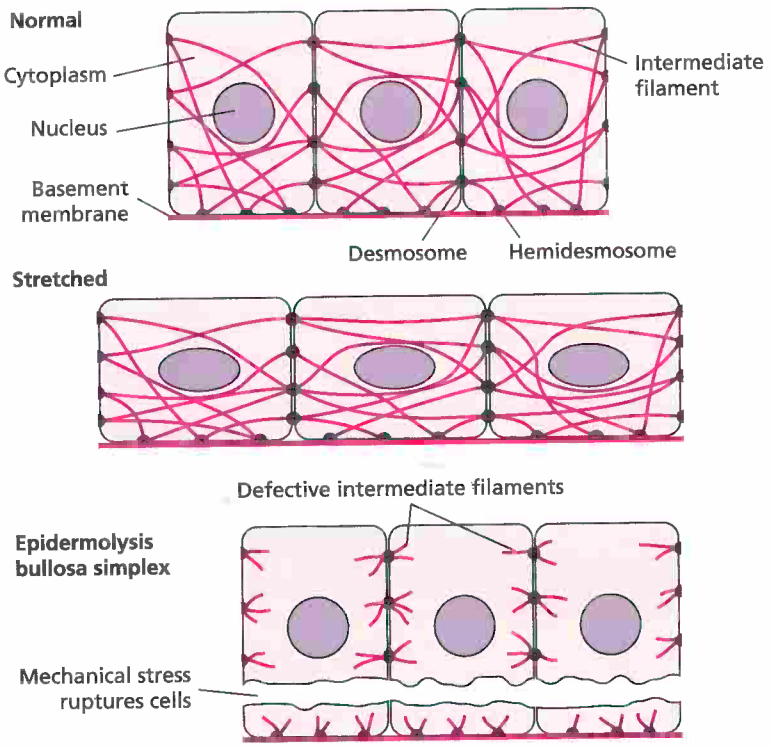


Figure 1 Intermediate filaments form a continuous network within epithelial skin cells. In the genetic disease epidermolysis bullosa simplex, faulty intermediate filaments are unable to form networks. The cells rupture in response to mechanical stress, causing blistering

Internal organisation

The cytoskeleton has an important role in organising the inside of the cell. Microtubules are made up of two proteins called α-tubulin and β-tubulin, joined together to form long, hollow tubes (see Table 1). Microtubules form a system of 'tracks' throughout the cell that anchor and move organelles about.

Terms explained

Axon A long extension of a neurone that conducts electrical impulses away from the cell body.

Chromatid One copy of a chromosome that has been duplicated prior to cell division.

Epithelial cell Animal cell type that lines surfaces and cavities in the body, forming a barrier to the outside world.

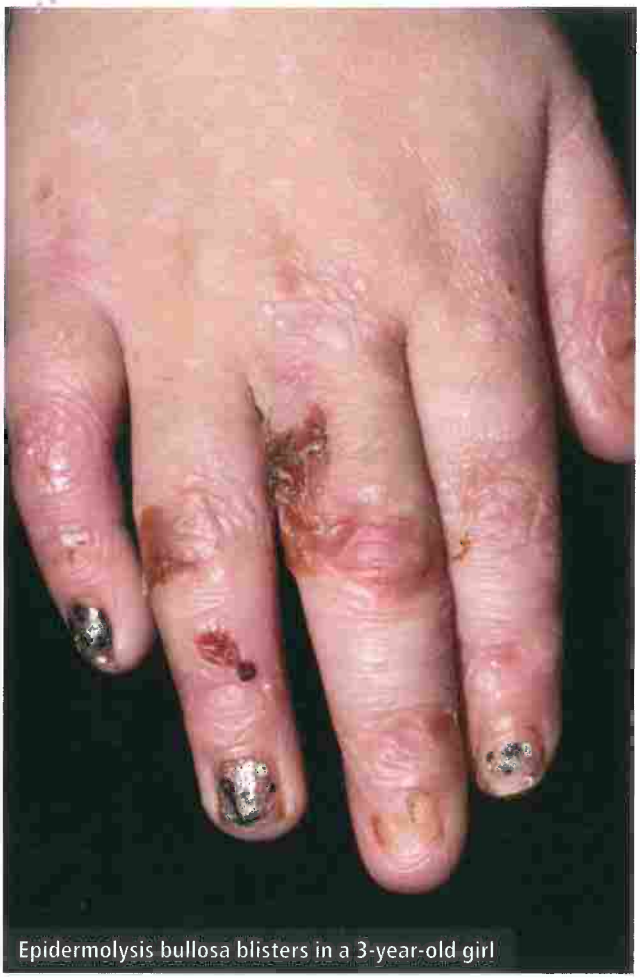
Eukaryotic cell Cell containing a nucleus and other membrane-bound organelles (e.g. animal and plant cells).

Mitosis Nuclear division producing two new nuclei that are genetically identical to each other and to the original.

Mitotic spindle Structure inside a dividing cell that segregates chromosomes into the two daughter cells.

Motor protein A type of protein that uses ATP to power movement along cytoskeletal filaments.

Nuclear envelope Double-layered lipid membrane surrounding the cell nucleus.



Epidermolysis bullosa blisters in a 3-year-old girl

They grow continuously from a structure called the centrosome, which is located close to the nucleus (see Figure 2) and is composed mainly of a third type of tubulin called γ-tubulin. They grow outwards in random directions, and then shrink back again. Sometimes a microtubule attaches by chance to another structure — for example, the plasma membrane. This stabilises the microtubule, preventing it from shrinking back.

Microtubules attach to cell organelles via motor proteins, which bind to the organelle on one side and the microtubule on the other. Powered by adenosine triphosphate (ATP), the

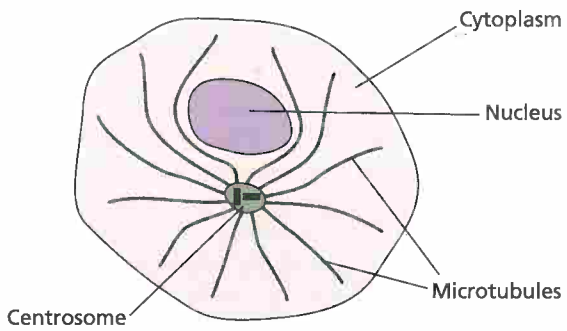


Figure 2 Microtubules grow outwards from a single centrosome, composed mainly of γ-tubulin

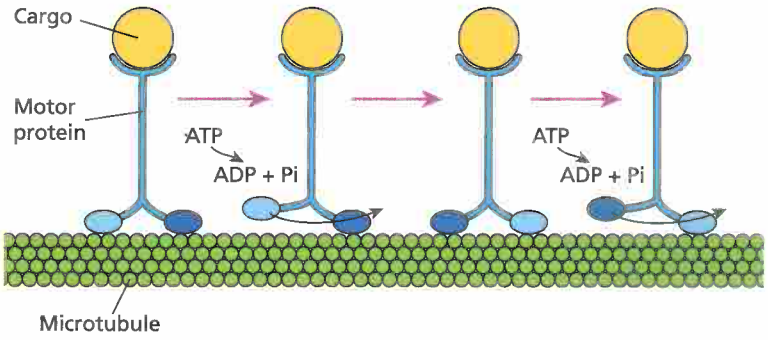


Figure 3 Cargo-carrying motor proteins 'walk' along microtubules, powered by the conversion of ATP to ADP plus inorganic phosphate (Pi)

motor proteins 'walk' along microtubules, carrying their cargo around the cell (see Figure 3 and **www.youtube.com/watch?v=y-uuk4Pr2i8**). There are two types of motor protein:

- kinesins carry organelles away from the centrosome
- dyneins carry organelles towards the centrosome

The stable microtubules and **motor proteins** work together to ensure correct positioning of the organelles (see Box 1).

Motor proteins also transport molecules around the cell in vesicles consisting of a lipid bilayer membrane surrounding a fluid interior. Vesicles carry materials such as hormones to the plasma membrane for secretion from the cell.

In neurones, materials synthesised in the cell body may be needed far away at the tip of the axon — sometimes as distant as a metre in a large animal. These materials include

Box 1 Formation of the endoplasmic reticulum

The endoplasmic reticulum (ER) is an organelle that processes proteins. It comprises an extensive network of membranes that spreads outwards from the nucleus (see Figure 1.1) and includes rough ER and smooth ER. The ER is held in place by motor proteins. Kinesins pull the ER along microtubules away from the nucleus, spreading it like a net. Meanwhile, dyneins pull the ER back towards the nucleus. This tug-of-war ensures that the ER is distributed throughout the cell.

Figure 1.1 Endoplasmic reticulum

proteins required for growth, and neurotransmitters for use at synapses (see this issue, pp. 2–5). Microtubules run the whole length of the axon, allowing kinesins to transport vesicles to its tip, and dyneins to transport them in the opposite direction. Depending on the length of the axon, transport can take several days. Some viruses, such as the rabies virus, take advantage of this system. The virus binds dynein, which carries it from the site of entry — e.g. a dog bite to the hand — to cell bodies in the brain, where it causes potentially fatal inflammation.

Moving along

For some cell types, movement is a vital part of their function — for example, for crawling across surfaces to heal wounds. These movements rely on actin filaments — the thinnest filaments of the cytoskeleton (see Table 1). These are made up of twisted chains of the protein actin, linked together, giving them extra strength. Actin filaments are most concentrated just inside the plasma membrane, where they are arranged into a network to provide strength. Like microtubules, actin filaments are continuously growing and shrinking and cell movement occurs when the organisation of the actin network changes.

White blood cells move through tissues to sites of injury or infection, and skin cells crawl towards wounds to close them. This movement over a surface is called cell migration.

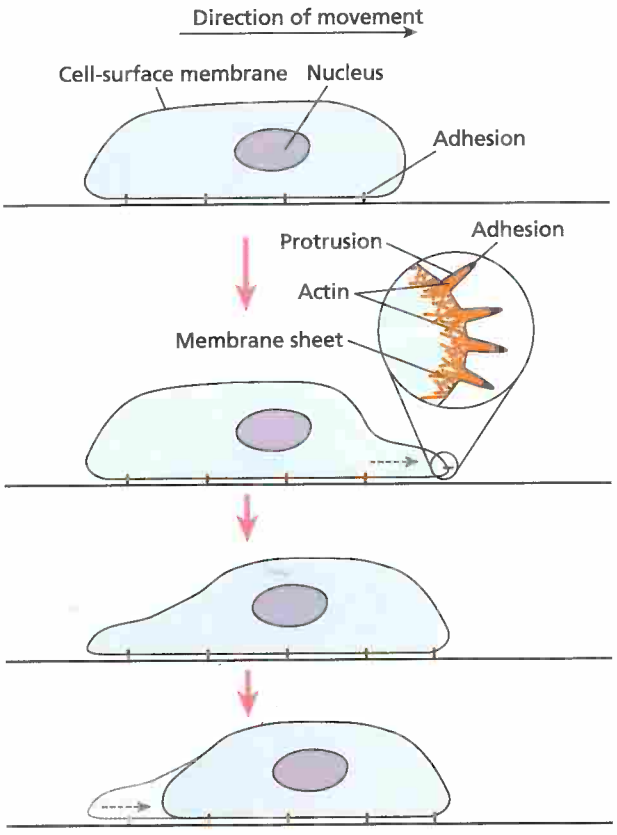


Figure 4 Cells use actin to crawl over surfaces. The front of the cell pushes forwards and sticks down to the surface using specialised adhesions. Actin filaments contract to pull the back of the cell forward, releasing adhesions

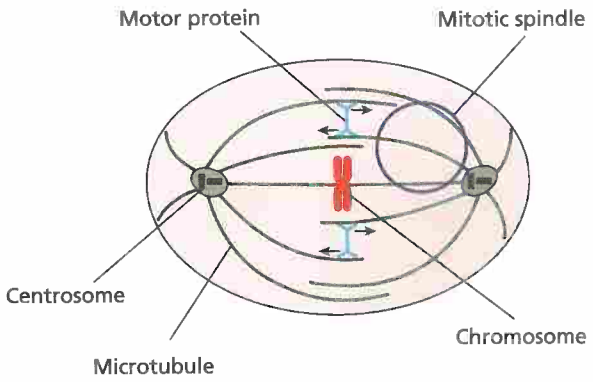


Figure 5 Formation of the mitotic spindle. Microtubules grow from both centrosomes. Motor proteins attached to microtubules from each centrosome 'walk' towards their ends, pushing the centrosomes apart. The mitotic spindle captures chromosomes, and pulls the sister chromatids to opposite ends of the spindle

In the first step of cell migration, a thin sheet of plasma membrane at the front of the cell reaches forward and sticks down to the surface. The cell then uses these strong sticking points — adhesions — to pull itself forward, releasing adhesion points at the back of the cell (see Figure 4 and www.youtube.com/watch?v=TB6H8RoyPh0). This process is repeated, moving the cell forwards.

Adhesion points consist of proteins in the plasma membrane called integrins, which bind to proteins on the surface over which the cell is crawling, anchoring actin filaments down at the same time. The plasma membrane sheet contains a dense network of actin filaments. These grow quickly, pushing the plasma membrane out in front. This region also pushes out thin, stiff protrusions containing parallel bundles of extending actin filaments. The sheet and protrusions are continuously growing and shrinking back, exploring their surroundings. When they find a suitable surface, they stick down to it. The forward pulling force is achieved by the actin filaments contracting, acting rather like a muscle to pull the rear of the cell forward.

Cell migration is an effective means of getting cells to where they need to be. For example, when skin is wounded, epithelial cells migrate over the wound during healing, and can close a centimetre-wide wound in just a few days.

Working together

Different types of cytoskeletal filament have distinct roles, but complex cellular processes such as **mitosis** require all three to work together. The chromosomes of **eukaryotic** cells are normally contained within the membrane-bound nucleus. A network of intermediate filaments, called the nuclear lamina, provides structural support for the **nuclear envelope**. During mitosis, the nuclear envelope breaks down. This involves disassembly of the nuclear lamina, through weakening of the binding between the filaments.

Just before mitosis, the centrosome is duplicated. Microtubules grow out of both centrosomes in all directions. When microtubules from the two centrosomes come into contact, they anchor together using the motor protein kinesin

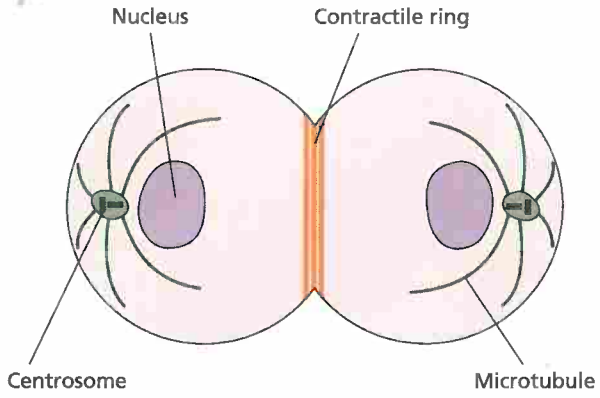


Figure 6 At the end of mitosis, a ring made of actin forms around the middle of the cell. It contracts, separating the two daughter cells

(see Figure 5). Kinesin then 'walks' towards the growing ends of both microtubules, pushing the centrosomes apart to form the **mitotic spindle**. Microtubules within the spindle attach to chromosomes and, once all of the chromosomes are attached, they are pulled apart into **chromatids**. This separation is achieved by the microtubules drawing them back towards the centrosomes at the opposite ends of the cell. The nucleus reforms and the cell divides in two.

Division of animal cells is dependent on actin filaments, which assemble in parallel bundles around the middle of the cell to form a contractile ring (see Figure 6), which gradually tightens to pinch the cell in two. Contraction is achieved by a motor protein called myosin — the same protein that works alongside actin in muscle cells to cause contraction. Myosin pulls the parallel actin filaments in opposite directions to shorten the bundles of actin. So, the complex process of mitosis requires all three types of cytoskeletal filament working together.

The cytoskeleton is essential for many aspects of cell function. Knowledge of its role in these functions will help us to understand better how diseases work, from viruses travelling along microtubules in a nerve cell axon, to cancer cells migrating to distant parts of the body to establish new tumours.

Further reading

Intermediate filaments: **http://tinyurl.com/5obdur**

Microtubules: **http://tinyurl.com/pk3d57o**

Actin filaments: **http://tinyurl.com/ykfmlw9**

Intracellular transport of vesicles: **http://learn.genetics.utah.edu/content/cells/vesicles/**

Rebecca Bridgewater studied cell biology at The University of Manchester. She is now writing her PhD, on how transport of proteins within cells controls the production of milk.