Catalyst

Secondary Science Review

Volume 20
Number 2
November 2009

Cell surface

Targeting the invaders

Science Enhancement Programme

Catalyst

Volume 20 Number 2 November 2009

The front cover shows an artist's impression of the surface of a biological cell. You can see the double layer of round-headed phospholipid molecules which make up the membrane bilayer, with embedded proteins and lipids. The outer, upper surface carries sugar molecules which act as receptors for molecules coming from outside the cell, including hormones and toxins. See the article by Joshua Howgego on pages 13-15. (photo credit: Hybrid Medical Animation / Science Photo Library)

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Subscription information

Catalyst is published four times each academic year, in September, November, February and April. A free copy of each issue is available to SEP Teacher Associates by request. Teachers should visit www.sep.org.uk to find out how to register as an associate.

Individual annual subscriptions (4 issues) are available from SEP for £16.95. Bulk subscriptions (10 copies of each of 4 issues for £75) are also available from SEP. Visit www.sep.org.uk/catalyst/catalystbuy.asp for further details, or email subscriptions@sep.org.uk.

Big molecules

Sometimes we think of atoms and molecules as small, hard spheres. However, as several articles in this issue of Catalyst show, molecules (particularly large biological molecules) can have complex shapes linked to their functions.

How do we know about the structures of such large molecules? Dorothy Hodgkin was a pioneer in the field of X-ray crystallography. She used this technique to unravel the structure of the insulin molecule. See the article on pages 4-5.

Chemists are learning to build large molecules from scratch, as illustrated in Josh Howgego's article on pages 13-15. He describes work by colleagues at Bristol University to build the sort of molecule which intercepts invading viruses as they try to penetrate the cell membrane.

And on pages 6-8, you can read about the work done using a fluorescent protein molecule which allows researchers to see what's going on inside living fish embryos.

Published by the Gatsby Science Enhancement Programme
Gatsby Technical Education Projects
Allington House (First Floor)
150 Victoria Street
London SW1E 5AE

The Gatsby Charitable Foundation

ISSN 0958-3629
Design and Artwork: Pluma Design

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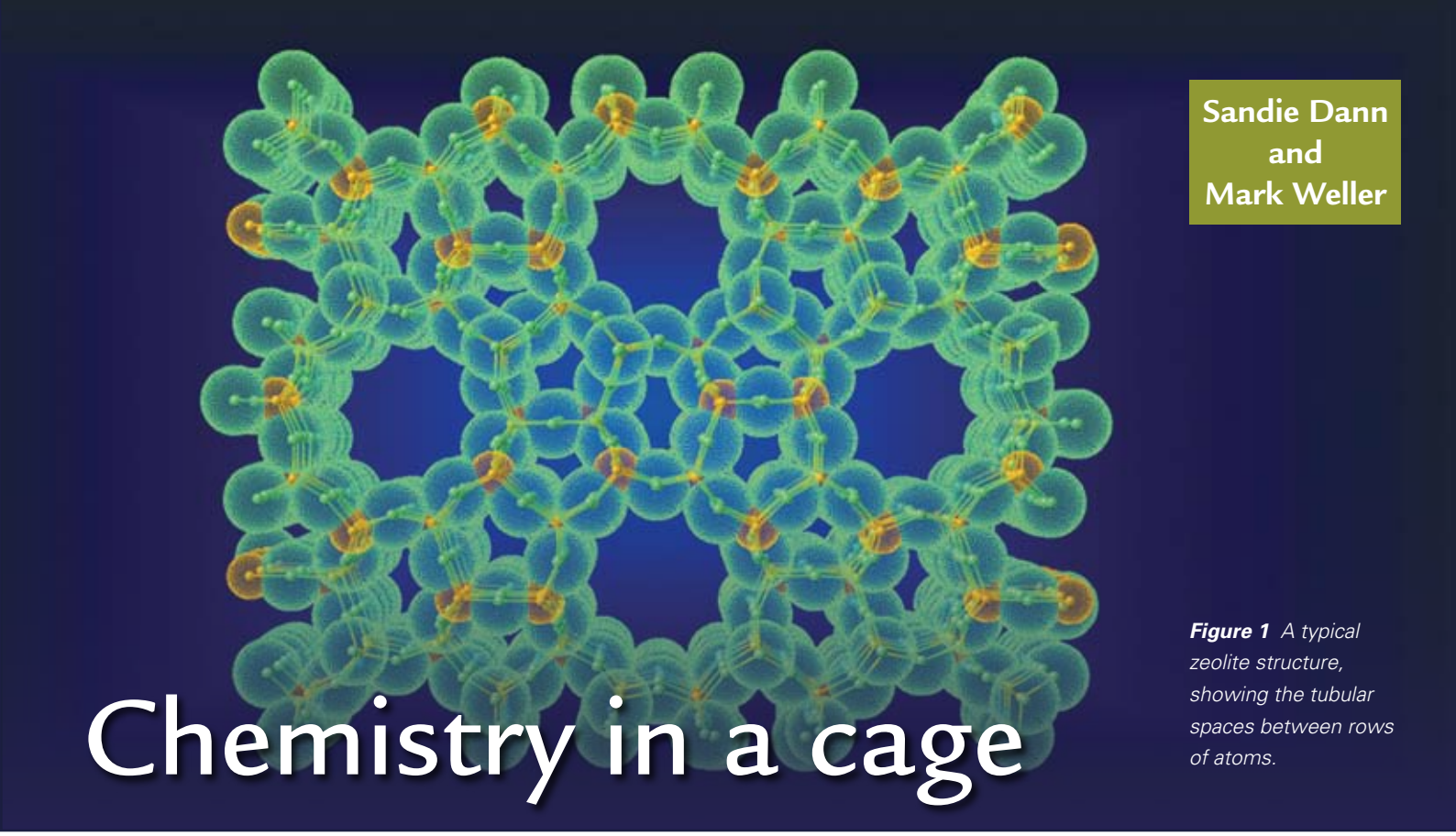


Chemistry in a cage

Sandie Dann and Mark Weller

Figure 1 *A typical zeolite structure, showing the tubular spaces between rows of atoms.*

Zeolites *are sponge-like materials developed from naturally occurring minerals. They have incredibly widespread applications. They are used in consumer products such as washing powder and cat litter while many of the petrochemicals used to make plastics and fibres will have been made using a zeolite. Find out here what zeolites are doing for you!*

Key words
zeolite
catalysis
ion exchange
hard water
nuclear waste

Atom trapping

Zeolites have diverse but hidden roles in the production and function of many everyday products. Washing powders, petrol, plastic drink bottles and deodorisers are all products which use zeolites directly or in synthesising the chemicals from which they are made. These applications of zeolites depend on their unique structures which, at the atomic scale, have holes and cages like a sponge, Figure 1. These holes or pores can trap molecules and ions and, once they are trapped inside the zeolite, it is often possible for the atoms to rearrange to produce a new, more useful substance.

What is a zeolite?

Many zeolites occur naturally as minerals; the first were described by geologists 250 years ago. Some natural zeolites grow as beautiful crystals (Figure 2); others as seams, thick deposited layers, that can be mined and around 5 million tons are extracted annually. Others are synthetic, made commercially for specific uses where a very pure material is needed or a natural equivalent is rare or non-existent.

Figure 2 *Crystals of a naturally occurring zeolite called scolecite*

Like many rocks, zeolites are made up of silicon, aluminium and oxygen atoms linked together, Figure 3. Each silicon or aluminium atom is surrounded by four oxygen atoms to form a tetrahedron of composition SiO_4 (or AlO_4); these tetrahedra then share the oxygen atom at each corner with the next tetrahedron. If these tetrahedra link so that there is very little or no space left in the solid then dense structures such as that of the mineral quartz (rock crystal) are produced. However, there are many other ways (it has been calculated there at least 1000 different stable possibilities!) of linking such tetrahedra together to form a three-dimensional network in which there are spaces in the structure called channels and pores (see Figure 3). When these spaces contain small molecules, such as water, the compounds are termed zeolites; they are also sometimes called 'microporous crystalline solids' because they have very small pores (around 1 nm in diameter) that contain ions and molecules. A good way of think of a zeolite structure is as a kitchen sieve shrunk to a millionth of its normal size.

A nanometre is roughly the size of an atom.

1 nm = 10^{-9} m = 1 millionth of a millimetre

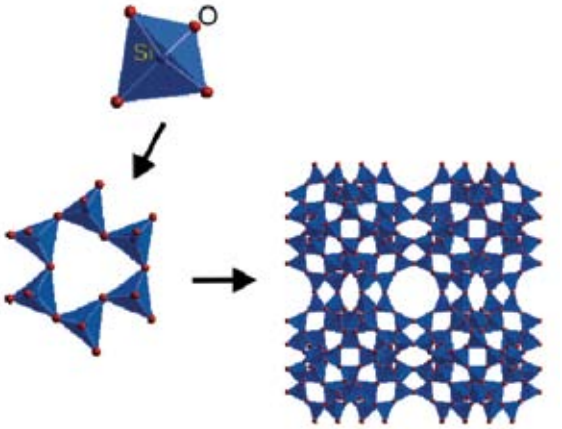


Figure 3 *A single silicate tetrahedron (pyramid) joins with several others to make a pore (hole). These pores then join together to form the extended crystal structure of a zeolite.*

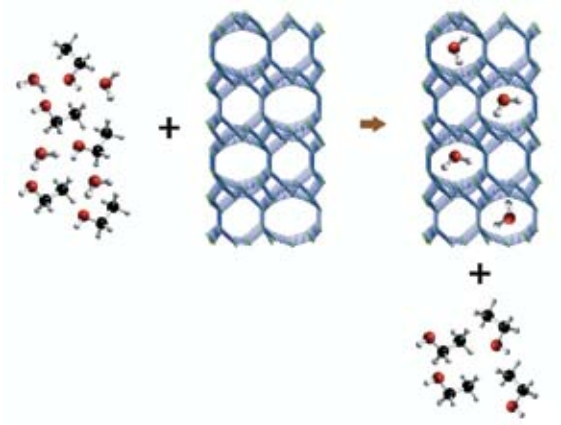


Figure 4 *A zeolite with correctly-sized pores acts as a molecular sieve to trap water.*

Around 200 different zeolites are known: 70 naturally occurring minerals and a further 130 which have been synthesised in research laboratories. Each one has a unique arrangement of the tetrahedra producing different sizes for the cavities and channels in the structure; one of the largest channels has 18 tetrahedra linked together into a ring. This flexibility in their structures leads to a fantastically useful feature of zeolites in that chemists can design them to have pores to undertake a specific function. Also, because the silicon- or aluminium-to-oxygen bonds are strong, these materials are very stable. This means that they can be heated to high temperatures and are only slowly attacked by acids and bases leading to their use in many chemical processes. It is this ability to produce very stable, microporous structures with a variety of different pore sizes that leads to the enormous range of applications.

So how and where are zeolites used?

Molecular sponges and sieves

The size of the micropores in a zeolite is similar to that of many small molecules, such as oxygen, water, ethanol and benzene. By choosing a zeolite with appropriately-sized pores it becomes possible for a molecule to enter the zeolite and then become trapped. In effect the zeolite acts like a sponge and, what's more, a beautifully-designed sponge that can select a single size or type of molecule that just fits inside the holes of that zeolite. This is exploited in applications that use zeolites to dry gases and solvents where a zeolite grabs hold of water molecules, Figure 4. A zeolite is first dried by heating it to 500 °C and any water it contains is driven out of the pores as steam (see the meaning of the word zeolite given on the left). If this dried zeolite is then placed in, for example, a mixture of water and ethanol then just the water molecules can enter the zeolite sponge and the dried solvent, pure ethanol, is left.

A similar process can be used to separate gas molecules where the zeolite acts a molecular 'sieve' allowing only one type of molecule to pass into and through its channels. This sort of process can be used to enrich the oxygen content of air to around 90% rather than relying on expensive liquefaction methods.

Zeolites can also be used to trap molecules. In some cases unwanted compounds such as the smelly molecules in urine and sweat can be trapped in the zeolite pores. This is used in some cat litter and odour removal products such as trainer insoles. There are also examples of molecules being temporarily 'stored' in zeolites and later released and there is research underway to try to store hydrogen in this way for future use as an energy source.

Washing powder and nuclear power

If you look at the list of ingredients on a packet of washing powder you will often find zeolite listed. It is there to help produce 'soft' water – that is, water from which calcium and magnesium ions have been removed. This is necessary for the detergent to work well, otherwise these ions attach themselves to the soap molecules that are needed to remove grease from clothing and so reduce their efficiency.

As mentioned above, zeolites usually contain both silicon and aluminium in their structures. The aluminium ions are negatively charged in the zeolite and so for every aluminium ion that is present an additional charge-balancing positive ion is incorporated into the pores. These are normally sodium ions, Na^+. When the zeolite is placed in 'hard' water that contains calcium ions, Ca^{2+}, these exchange places or 'ion-exchange' as the calcium ions have a stronger interaction with the zeolite – so we end up with sodium ions in the water and calcium ions in small particles of zeolite. The effluent produced by softening water in this way is a compound of calcium, aluminium, silicon and oxygen, much the same as many rocks and soils and so is environmentally very safe.

The word ***zeolite*** comes from the Greek words ζέιν (zein) meaning to simmer and λίθος (lithos) rock; that is, a rock that simmers. When a zeolite powder is heated it evolves water and particles move as if they are gently boiling.

Zeolites are also used to clean up radioactive waste at places such as Sellafield as they are excellent traps for some of the products of the nuclear fission of uranium. In particular caesium and strontium ions in nuclear waste are highly radioactive species which may be grasped with great efficiency by a natural zeolite mineral called clinoptilolite. After the Chernobyl accident this zeolite was fed to livestock, such as sheep and reindeer, to ensure that radioactive ions did not enter the animals' bodies from the gut but were excreted, trapped inside the zeolite pores.

Catalysis

The cracking of crude oil, where it is broken down to produce lighter more useful molecules, is carried out industrially using a zeolite. If the charge balancing cations in the channels of a zeolite are hydrogen ions, H+, rather than sodium or calcium ions, then the zeolites act as very strong acids – much stronger than sulfuric or hydrochloric – and as a result they are sometimes called solid acids. These acidic hydrogen ions attack the long carbon-chain hydrocarbons in crude oil and help break them down into the shorter molecules that are used as petrol or diesel and also in the production of many other petrochemicals such as plastics and man-made fibres.

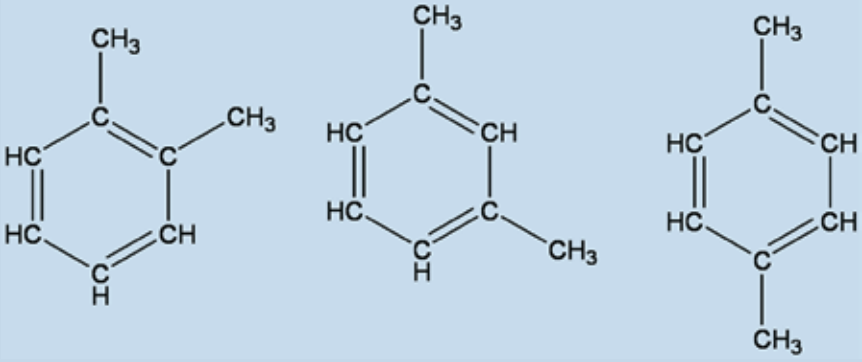
Zeolites may also be used in a similar process to convert one compound to another, more useful one – a reaction that combines their acid and molecular sieving properties, see Box below.

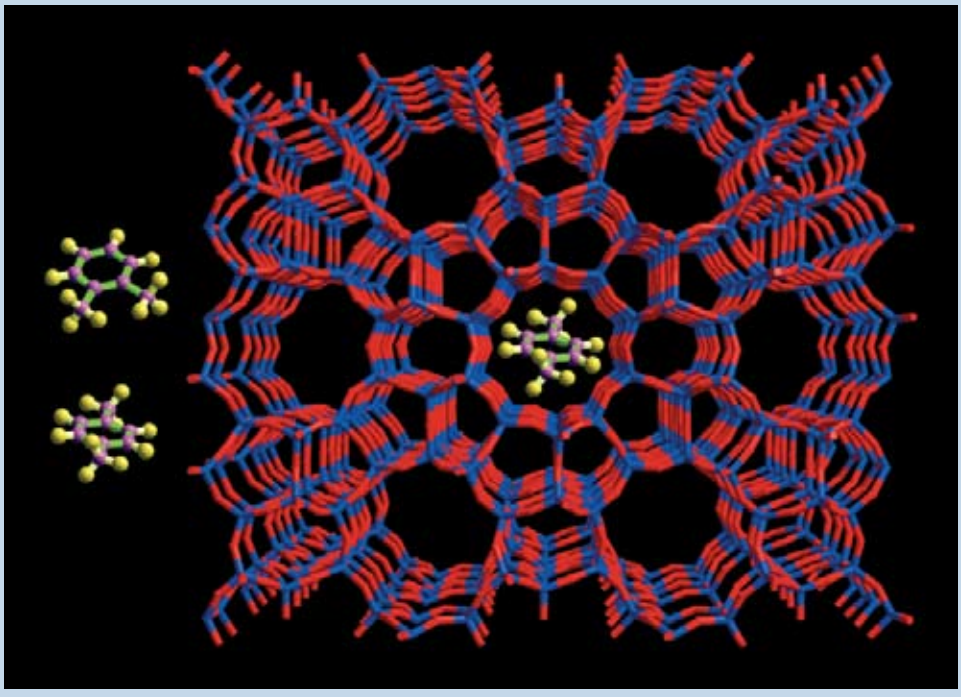
What next from zeolites ?

As well as developing better catalysts and molecular sieves, zeolites are being studied for storing hydrogen in the next generation fuel cell operated vehicles, for the controlled release of drugs or for producing isolated and environmentally-benign nanoparticles. New zeolites, with different pore sizes, are being developed for many of the applications described above with scientists often still learning from the zeolites that occur in Nature.

Mark Weller is a Professor of Chemistry at the University of Southampton and Sandie Dann is a Senior Lecturer in the Department of Chemistry at Loughborough University

Isomers are compounds with the same formula but a different arrangement of atoms.





Sorting and converting molecules

The compound dimethylbenzene can exist as three isomers – 1,2-, 1,3- and 1,4-dimethylbenzene (left to right in the diagram). Of these, 1,4-dimethylbenzene is much the most desirable compound as it can be oxidized to make terephthalic acid - which is then used to make terylene and PET (polyethylene terephthalate), the plastic used in many bottles.

If a mixture of the three dimethylbenzene isomers is passed through a zeolite known as ZSM-5, then the solid acid permits the three to rapidly interconvert inside its pores. The 1,4 isomer is a narrower molecule than the other two isomers and therefore moves through the zeolite channels faster and can quickly escape (as shown here), while the other two get stuck in the pores where they tend to react further, converting to more 1,4-dimethylbenzene. In this way the isomer mixture is quickly converted to almost pure 1,4-dimethylbenzene!

A life in science

Dorothy Hodgkin

Dorothy Hodgkin was a pioneering scientist, a peace activist, a mother of three and a Nobel Prize winner. Here we look at her Life in Science.

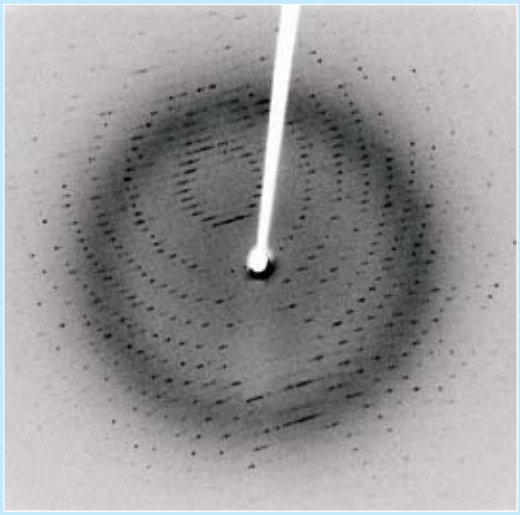
Dorothy Hodgkin was born in Cairo, Egypt in 1910. Her father was employed by the education service and also worked as an archaeologist. Her mother shared his enthusiasm for archaeology and was also a botanist and talented illustrator.

Dorothy was four when the First World War broke out. Her parents left her and her three sisters in England with relatives and returned to Egypt. After the war, her mother decided to stay at home and educate her children, which was a very happy time for Dorothy.

She began to study chemistry at school at the age of 10. She was one of only two girls who joined the boys' chemistry class as girls usually studied domestic science and physiology where the boys did pure science. The first lesson was in growing crystals. Dorothy enjoyed it so much that she set up a little lab at home and, with the help of the local chemist who sold her all sorts of chemicals, began growing them for herself. This was to form the basis for her future career.

After school, Dorothy studied Chemistry at Oxford University. Her father was not very keen on her studying Chemistry, but encouraged by her mother she stuck with her choice. After gaining her degree she went on to Cambridge to study for a further degree (a 'doctorate'). She chose to go into the new field of X-ray crystallography and was one of the first to apply it to biological molecules.

Box 1 Crystal structure



The X-ray diffraction pattern produced by a complex crystalline substance similar to insulin

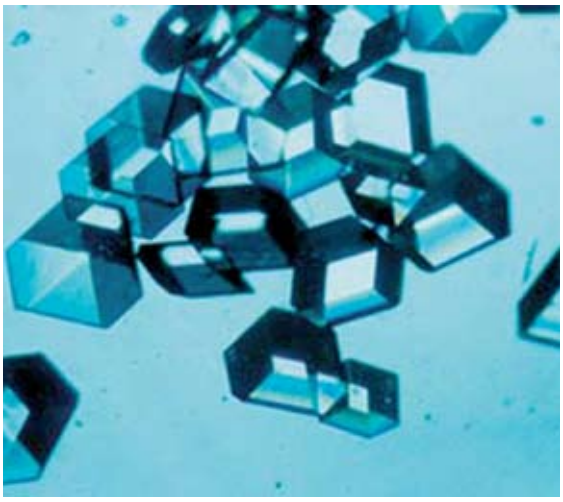
X-ray crystallography is the method used to determine the arrangement of atoms within a crystal. The first step is to grow a good quality crystal. A beam of X-rays is then fired at it and scattered into many different directions. From the angles and intensities of these reflected beams the crystallographer can calculate a 3-dimensional picture of the density of the electrons in the crystal. From this electron density, the positions of the atoms in the crystal can be worked out. As many different materials can form crystals it is useful in many fields of science.

A few years later, Dorothy returned to Oxford and continued to work on finding the structure of biologically important molecules. The molecules that she concentrated on were huge and without computers to do all the necessary calculations it was a very slow process to find their structure.

Dorothy always chose difficult and very time consuming projects. During the Second World War she was given some of the new and exciting antibiotic penicillin. Up to that point the drugs which were available for fighting infections were limited and there was much hope that penicillin would be a breakthrough. Initial trials were very positive, but without knowing the structure it would be difficult to synthesise (make artificially). It took 4 years, but Dorothy solved the puzzle of the structure in 1946, paving the way for mass production of the drug.

In 1953, Dorothy was one of the first people to see the model of DNA constructed by Francis Crick and James Watson. The structure of that, too, was solved with the help of X-ray crystallography (although that work was done by Rosalind Franklin).

The molecule insulin is the one for which she is best known. She considered solving the structure of it her greatest scientific achievement. She was first given some in 1934 and it fascinated her because it has such a wide-ranging effect on the body. At that time, however, X-ray crystallography techniques had not been developed far enough to be able to solve such a large and complex structure. Along with many colleagues she spent years improving and refining the processes until 35 years later in 1969 she finally resolved the structure.



Insulin crystals, as required for X-ray studies

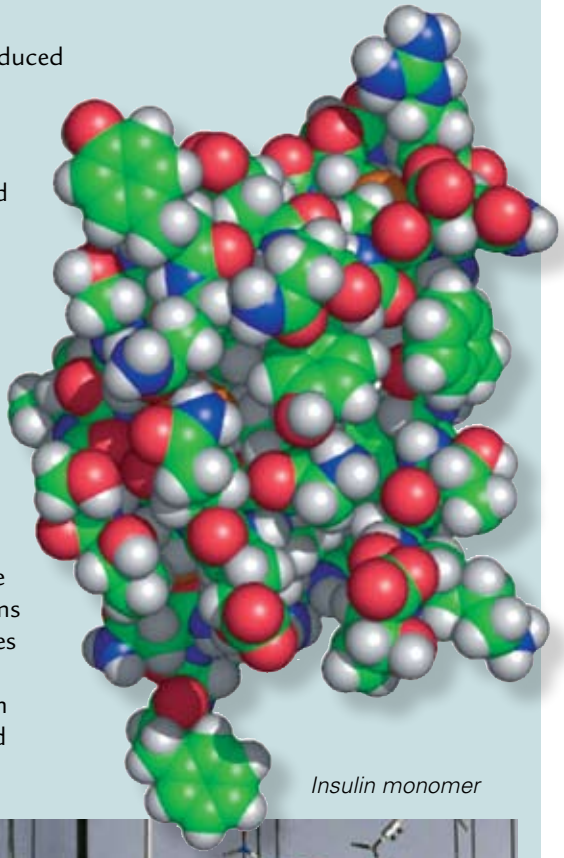
At the age of 24, Dorothy was diagnosed with rheumatoid arthritis. Even with this disability she achieved a huge amount in her chosen field. In 1964 she was awarded the Nobel Prize in Chemistry in recognition for her work. Aside from her scientific activities, Dorothy Hodgkin was a member of various international peace organisations. She died in 1994.

***Vicky Wong** is Chemistry editor of Catalyst*

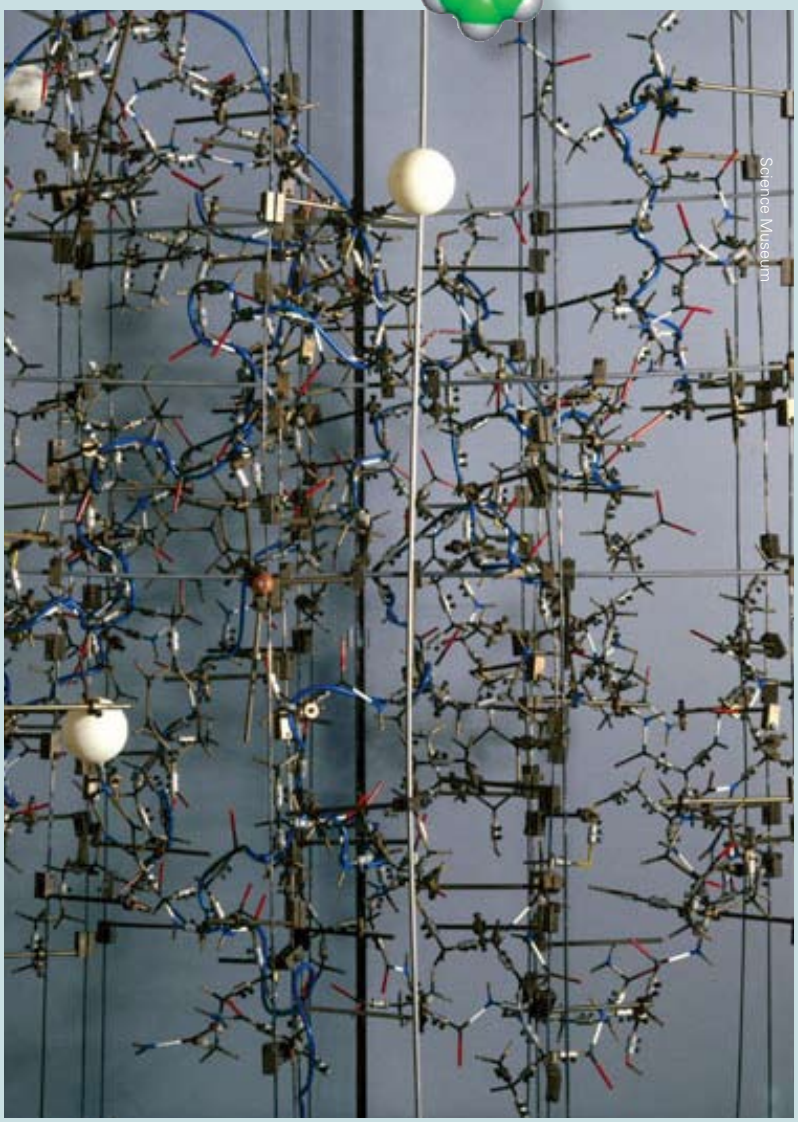
Box 2 Insulin

Insulin is a hormone produced by the pancreas. If not enough is made then the result is diabetes.

Dorothy Hodgkin worked out the structure of the insulin molecule over 35 years – below is her model which can be seen in the Science Museum. It consists of two peptide (amino acid) chains which are linked by bonds between two sulfur atoms. On the right is a space-filling model of the same molecule. The atoms are represented as spheres and are colour-coded: carbon (green), hydrogen (white), oxygen (red) and nitrogen (blue).



Insulin monomer



Caroline Parkin

Fishing for clues

Zebrafish as a model for human disease

Key words
zebrafish
genetics
development
model systems

Understanding how our bodies work and what causes human disease is the key to future medical breakthroughs. In this article, Caroline Parkin of Sheffield university describes how fishes can help us to learn more about our own biology.

Most discoveries in medical science are a result of experiments that cannot be performed on humans. We can use animal models to obtain vital clues about the causes and progression of human diseases. There are a range of model organisms to suit different topics; at the University of Sheffield we use zebrafish to model human disease.

Can we really study human disease in a fish?

Yes! Fish and humans are not so very different when you look closely - especially when you look at their blue-print for building their bodies - their DNA, or genetic code. By sequencing the DNA, we now know that there is a remarkable similarity between the genetic codes of different species, including zebrafish and humans.

Although you and I may appear to be very different to fish, the reality is that we're not that different at all. We have two eyes, a mouth, and a gut, for a start. And when we look closer - at all the cells inside them – there really are more similarities than differences.

This similarity between the genes of different organisms, which scientists call conservation, or genetic homology (from an ancient Greek word meaning 'to agree'), is the fundamental reason why we can use fish to learn about human diseases.

Zebrafish in one of the tanks at the Sheffield aquarium.

The genetic 'recipes' (genes) used to build particular body parts have often been conserved between species. For instance, the information to make an eye is stored in many different genes, but since human eyes and those of fish are built, and work, in much the same way, the 'recipes' are similar.

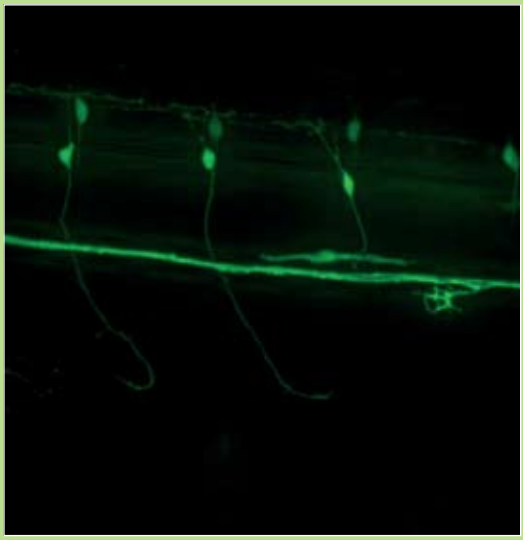
Why zebrafish?

Zebrafish are tropical fresh water fish from the minnow family. They are popular in home aquariums and you'll find them in many pet shops under the name 'Danios' (from their scientific name – *Danio rerio*, see Catalyst Vol 19, Issue 3, pp 7-8, What's in a Name?).

Most research is carried out using zebrafish embryos. The transparency of zebrafish embryos has become one of the leading reasons for using them for scientific research. Being able to see through the embryos allows us to watch changes that occur, both in normal development and when things start to go wrong. We can see cells move around, the heart as it beats, and the gut undergoing peristalsis, all in the living embryo. This transparency also means we can make use of a naturally fluorescing protein called GFP (Green Fluorescent Protein) – that can be used to label individual organs, cells or even compartments within a cell.

Green Fluorescent Protein

GFP is a protein, originally extracted from a species of jellyfish, which has proved vital in many fields of biological research. *Fluorescent* describes a substance which glows with visible light when another colour of light is shone on it. For example, white clothing may glow purple when (invisible) ultraviolet light is shone on it – you may have seen this in a night club. GFP glows green under blue light. The importance of GFP in Biology is that molecules of GFP can be used to show up particular organs, or to show that a gene has been successfully transferred into an organism. In 2008, three researchers shared the Nobel Prize for Chemistry for their discovery and development of GFP.



A muscle fibre (across the picture) with the motor neurons (nerve cells, above the fibre) which will control its operation, seen using GFP.

From genes to function... and back

When human genes involved in disease are identified, we are able to examine the function of the homologous genes in zebrafish. The zebrafish model also allows us to look at the disease processes more directly, for instance understanding the progression of a disease, or the precise cell or protein biology that underlies a disorder.

In Sheffield collaborations between medical doctors and scientists have helped establish a number of diseases models in zebrafish.

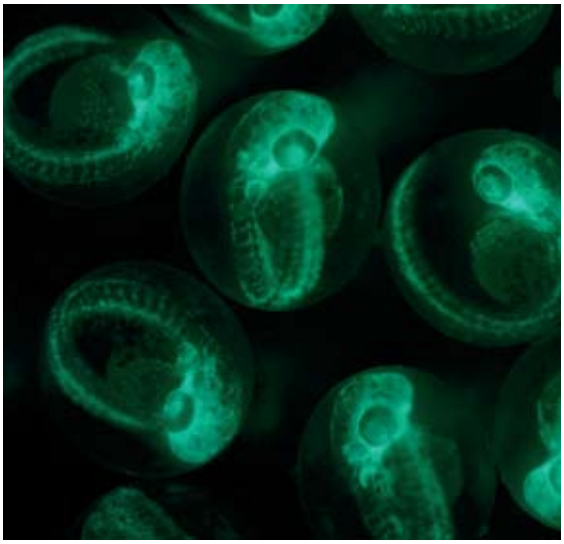
Using zebrafish to study hypoxic signalling and cancer

Cancer occurs when cells grow and divide out of control, even invading surrounding tissues and spreading to other areas of the body (metastasis). As tumour cells grow, they need oxygen to supply their needs.

A signalling pathway called the hypoxic signalling pathway allows tumour cells to survive under conditions of low oxygen supply ('hypoxia'), stimulating new blood vessel growth to the tumour. In this way, tumours become ever more dangerous, since they can get more oxygen and keep growing.

In addition, the new blood vessels can transport tumour cells to other sites in the body, where they can form metastases (new cancerous tumours).

We are using zebrafish larvae to study these processes. GFP allows us to follow blood vessel development in live fish larvae. We can also use GFP to show up the activity of the hypoxic signalling pathway in a living zebrafish larva and therefore study these processes as they are happening. Once we understand the normal events we can modify the environment around the larva in different ways, such as by changing the oxygen levels, introducing drugs that may affect blood vessel growth and we can manipulate genes to see what affect they have on blood vessel growth or oxygen sensing. In addition, we can search for chemicals that activate or inactivate the low-oxygen response.



These zebrafish embryos fluoresce because they contain GFP.

Understanding disorders of the nervous system

The central nervous system (CNS) coordinates the activity of the body. It includes the brain and spinal cord.

Neuronal network in a zebrafish larva.

Disorders of the CNS are severely debilitating and sufferers can be affected in profoundly different ways, through diseases such as Alzheimer's disease, Parkinson's disease, motor neuron disease and multiple sclerosis, or psychiatric disorders such as schizophrenia and bipolar disorder.

Work with zebrafish is bringing greater understanding of diseases of the central nervous system, bringing the hope of better treatments for patients such as this elderly Alzheimer's disease patient.

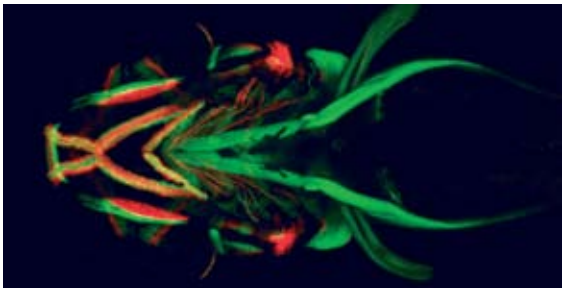
The zebrafish brain and spinal cord are very similar to those of a human. They develop in much the same way and require almost identical genes to make them. The genetic basis for some CNS diseases is only just beginning to be understood, and we can use zebrafish to understand much more about what goes wrong when particular genes are mutated.

But zebrafish can be even more useful, because we can use the fish to find new genes and then explore their roles in human disease. Another important use of zebrafish is to look at the effect of environmental factors, such as chemicals and toxins, on the development of neurodegenerative diseases.

Muscle disease and development

Muscular dystrophy is the collective name for a group of genetic diseases that cause the progressive breakdown of muscle in the body, which leads to weakness and subsequent loss of mobility. There is no known cure and treatment is limited.

We can use zebrafish models to investigate the genetic causes of muscular dystrophy and try to determine what changes are occurring in the cells when certain genes are mutated.



GFP shows up muscles in the head of a zebrafish embryo.

Duchenne Muscular Dystrophy, DMD, is caused by a defect in the gene coding for Dystrophin, a structural protein that provides support in the muscle cells. When the *dystrophin* gene is mutated the resulting protein is no longer fully functional. Over time the cells collapse and die. This leads to the muscle wasting characteristics of DMD.

We can model DMD and other muscular dystrophies by looking at fish that carry similar mutations to those found in humans. One such mutant is called *sapje* and has a mutation in the *dystrophin* gene. As in the human patients the muscle in the fish degenerates and dies.

To understand diseases such as muscular dystrophy we need to know how muscle normally develops in an embryo and how it functions in a living organism. Zebrafish have been used extensively to understand the development of muscle from single cells (called myocytes) into large bundles of contractile muscle fibres that allow a fish to swim or you and I to walk, run and even swim.

Muscle fusion and repair

To make large muscle fibres many single myocyte cells must fuse together to create what is called a syncytium, which may consist of thousands of individual cells. The syncytium is important as it allows coordinated contraction across the whole muscle.

Muscles don't only fuse during embryogenesis. When muscle is damaged, either through injury or normal wear and tear (think of how your muscles ache after lots of exercise), new muscle cells are able to fuse with the existing muscles to repair them. By understanding fusion in both adults and embryos it is hoped we can enhance the restoration of damaged muscle following disease or trauma.

Conclusion

The usefulness of this tiny tropical fish cannot be overstated. It has already provided many breakthroughs and expanded our knowledge of genetic interactions in the normal and diseased state. New techniques are constantly being developed that will enhance the strength of this model organism in our quest to understand and develop treatments for human diseases.

***Caroline Parkin** works in the Biology Department at Sheffield University.*

For more information about zebrafish and to see some great movies of the work in Sheffield, visit www.fishforscience.com

Jeff Banke/Bigstockphoto

Hooke's law of springs

The picture on pages 10-11 of this issue of Catalyst comes from a seventeenth century publication in which Robert Hooke outlined his findings on the behaviour of springs. Hooke was an employee of the Royal Society, Britain's recently-formed scientific society. His job was to present two or three different experiments each week to the assembled members of the society – and this was at a time when experimentation was new and there were no books of experiments to draw on. He had to think up the experiments and build the equipment himself.

What to look for

The picture is complicated because it contains several different diagrams. You can see the long, vertical spring on which Hooke experimented (*Fig 1*). It was fixed at point C, and weights were placed in the pan E. Below he has indicated the position of the pan as the weight was increased in uniform steps.

Also in the picture is a spiral spring (*Fig 2*). Hooke found that this showed the same pattern of extension as it was loaded.

On the right are Hooke's graphs of his results (*Fig 4 and 5*). If you have carried out a similar experiment, you will recognise the straight line graph which comes from plotting the spring's extension (increase in length) against the load (the weight in the pan).

Secrecy and publication

At the time, Hooke wasn't the only person experimenting on springs. He wanted to be the first to find the law which governed their behaviour but he didn't want to tell everyone else what he had discovered before he was ready to do so. His solution to this quandary? He published an anagram:

ceiiinosssttuv

Then, when he finally went public, he rearranged these letters to make the Latin phrase

Ut tensio, sic vis

which means: "As the extension increases, so does the force." In this way, he was able to establish the priority of his claim to the discovery. This relationship is what we know today as Hooke's law.

The illustration is complex because, at the time, illustrations were made by the process of engraving, and printing from engraved plates was expensive. As many illustrations as possible were crammed on to each plate – readers were used to this, and could easily focus on one illustration or another.

Hooke's notebook, rediscovered almost 300 years after his death. It includes a day-to-day record of his experiments and of his meetings with other scientists.

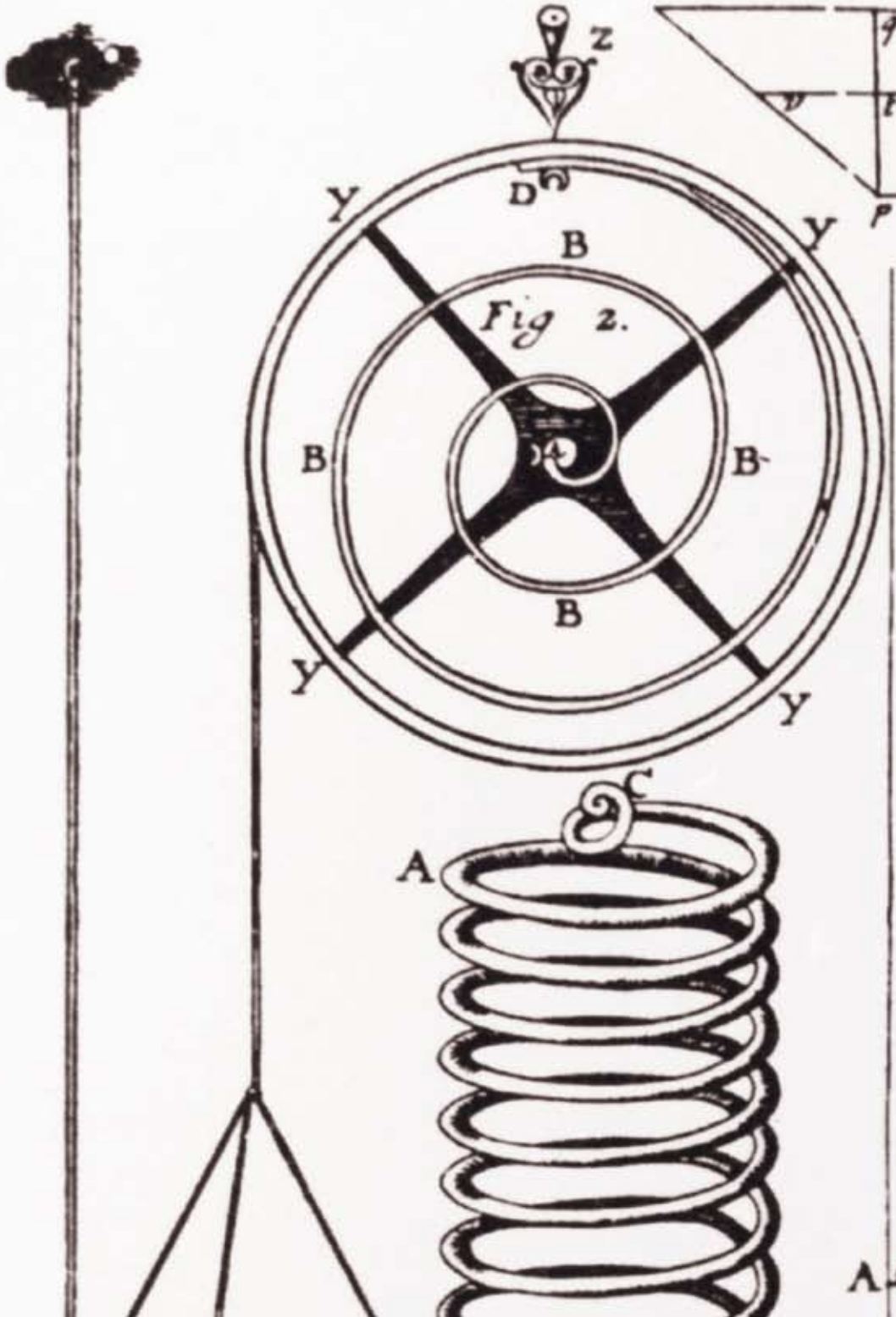


Fig 2.

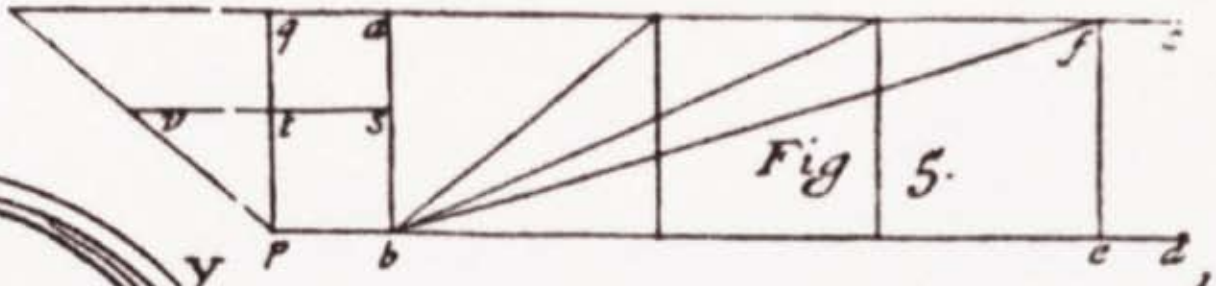


Fig 5.

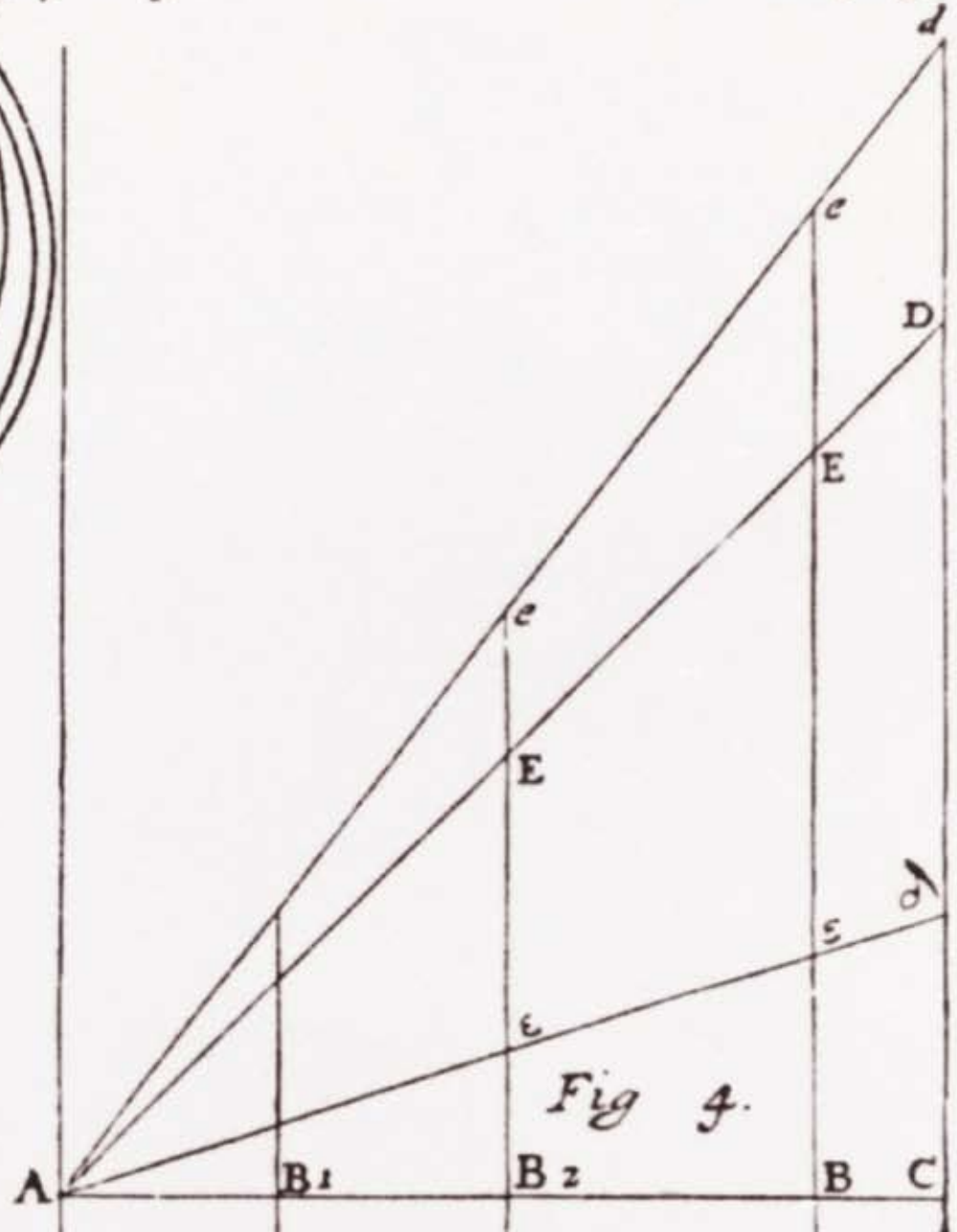
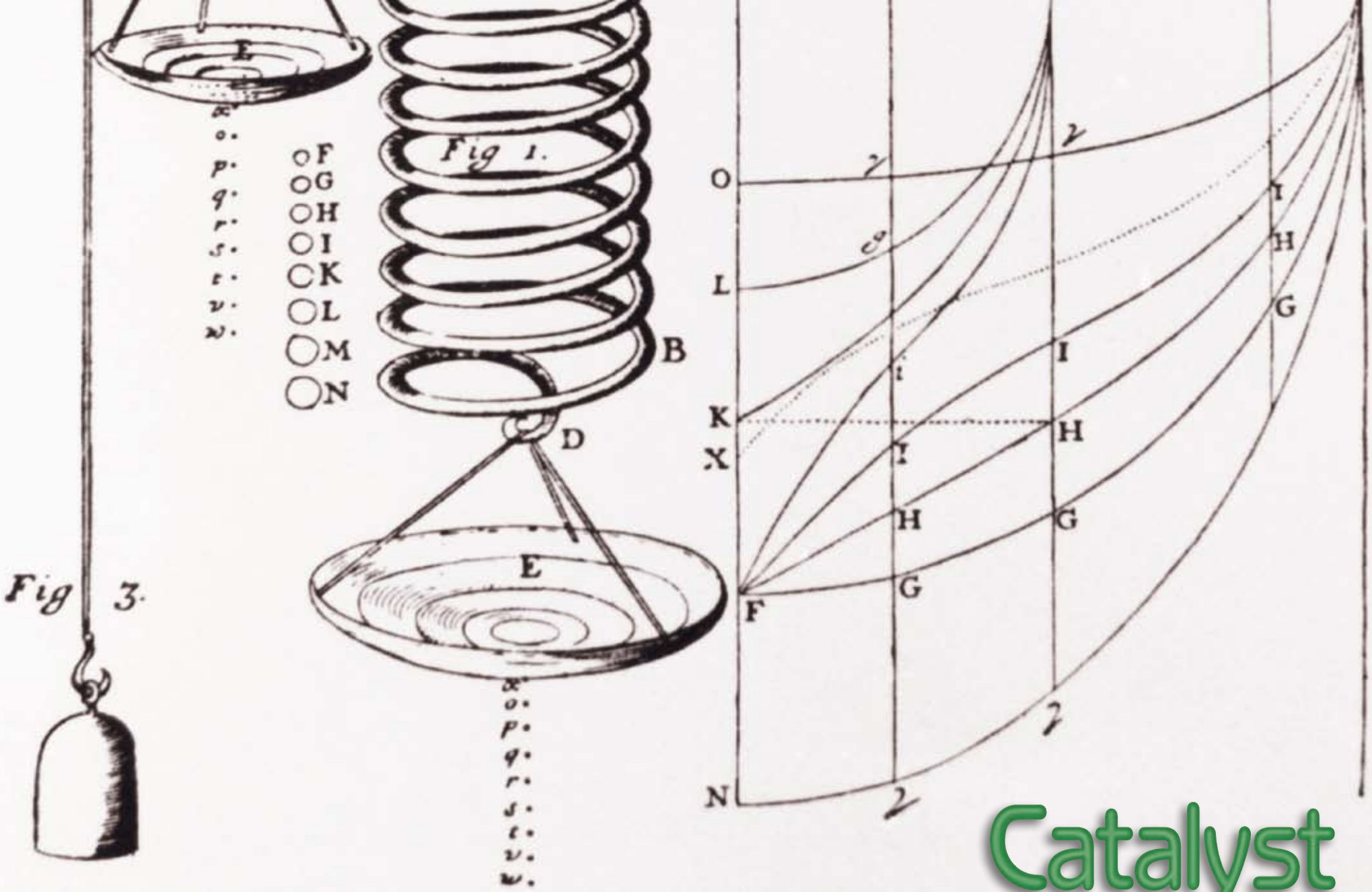


Fig 4.



Catalyst

www.sep.org.uk/catalyst

Robert Hooke's illustration of 1678, showing the equipment he used to establish the law which governs the behaviour of springs, with graphs of his results.

This image of Robert Hooke, made by Rita Greer for the Open University, shows Hooke surrounded by objects linking him to his many interests – there's a spring in the foreground. There is no historical portrait of Hooke – his great rival Isaac Newton saw to it that any images of Hooke were destroyed after his death.

'A mighty ingenious fellow'

Why was Robert Hooke interested in springs? One clue can be seen in the illustration on pages 10-11. He thought it must be possible to design a clock or stopwatch which used a circular spring to control its regular time-keeping movement. (Since Galileo's time, mechanical clocks had relied on the regular swing of a pendulum.) So Hooke had to show that a circular spring would vibrate with a fixed period, whether its amplitude was large or small.

This watch (from the Science Museum, London) was made around 1675 by Thomas Tompion in collaboration with Robert Hooke, and presented to Charles II. The face has been removed to show the mechanism.

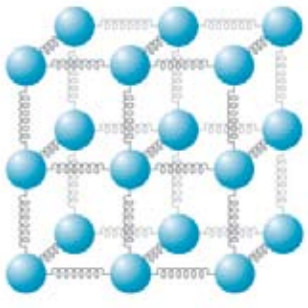
Hooke was a great inventor. He made great improvements in microscopes, telescopes, air pumps and other scientific equipment. He invented the universal joint which is in use in all vehicles today. He was also a fine architect – after the Great Fire of London in 1666, he worked alongside Christopher Wren in replanning the City of London and designing many of its important buildings.

A world of springs

But, to Hooke, springs were more than useful devices. They also related to the way he saw the world. He pictured the Earth and, indeed, the entire Universe as matter through which ran vibrations. This mechanical view of the world was different to that of his great competitor, Isaac Newton. For Newton, everything was to be explained by maths. He wrote equations for the force of gravity and for the orbits of planets, but he never gave a satisfactory physical explanation for these. When he tried to explain how light travels, he chose to describe it as particles. Hooke took the view that light, like sound, was a form of wave or vibration passing through matter.

Today, physicists agree that there was a lot of truth in Hooke's ideas. Sound waves are mechanical waves passing through matter. They can only do so because of the springiness of matter. Where does the 'spring' of stuff come from? We can picture matter as being made of atoms and molecules. Solid materials are held together by the bonds between these particles, and the bonds are springy. Stand on the floor and you squash the particles very slightly closer together. Move away and the bonds push back to their original positions.

In fact, Hooke's law of springs is really a reflection of the springy bonds between atoms. Pull on a spring and you stretch the bonds between the atoms of the spring. Let go and they spring back into place. So, in investigating springs, you are really investigating the forces between atoms.



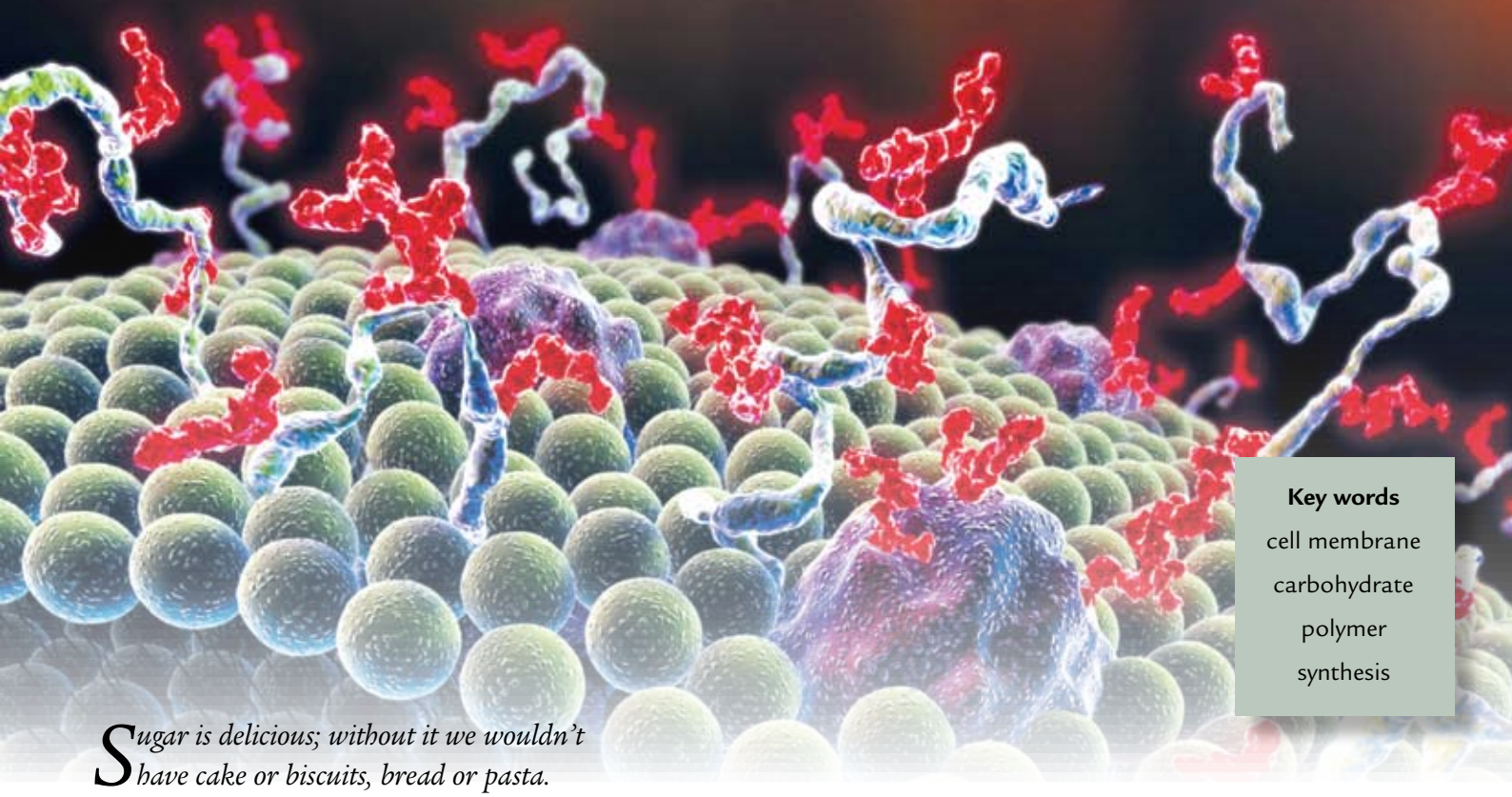
In this model of a solid, the atoms are joined together by springy bonds, rather like the springs that make up a mattress.

Look here!

More about the life of Robert Hooke:
CATALYST Vol 15 issue 1 p20-21

Blocking viruses with synthetic receptors

Joshua Howgego



Key words
cell membrane
carbohydrate
polymer
synthesis

Sugar is delicious; without it we wouldn't have cake or biscuits, bread or pasta. But to scientists, sugar is much more than a food; sugar molecules can also form polymers which act as 'molecular bar codes' to help cells recognise each other, as Josh Howgego explains.

A few decades ago carbohydrates were seen as the least important of the three types of molecule in biochemistry. Lipids (fats) make up our cell membranes and insulate the neurones which carry our brain waves. Proteins are the building blocks of life, forming enzymes which control all our cellular processes and the structural components of our hair, nails, skin. As for carbohydrates, we knew we needed a decent amount of them to burn up as fuel, but that was about where our interest ended.

Well, we were wrong to be bored with carbohydrates. It's now clear that every human cell is covered in a layer of molecules known as glycolipids; molecules which are part carbohydrate, part lipid (Figure 1). The glycolipids protrude from the surfaces of our cells as identifying markers to the rest of the body. It's vital that cells can tell each other apart, otherwise **phagocyte** cells might begin gobbling up bits of lung or heart, rather than concentrating on bacteria and other foreign material – which could be problematic, to say the least! These identifying glycolipid markers help to ensure this kind of tragedy doesn't happen.

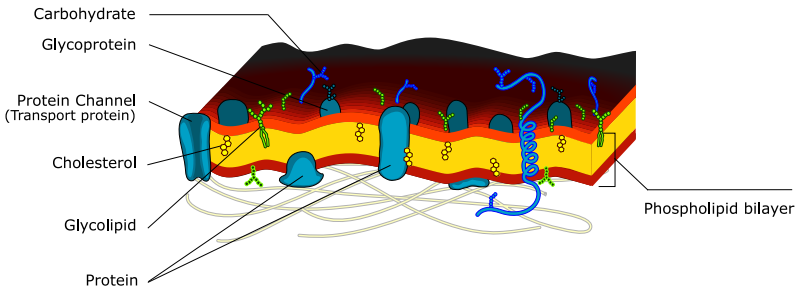


Figure 1 *Glycolipids (green branching molecules) on the surface of a cell.*

For these molecular bar codes to work, the glycolipids need to be complicated enough such that each type of cell can have its own unique identifying molecule. Although sugars themselves are quite simple molecules, they can join together to form polymers. Unlike conventional polymers (such as Nylon) where the **monomers** can join together in just one way, sugar polymers, or **oligosaccharides**, can be much more complicated. This is because sugars have several different hydroxyl (-OH) groups which may react. The bonds formed can also be different in space (see Box) so the resulting polymer can vary in lots of different ways – they're very complicated!

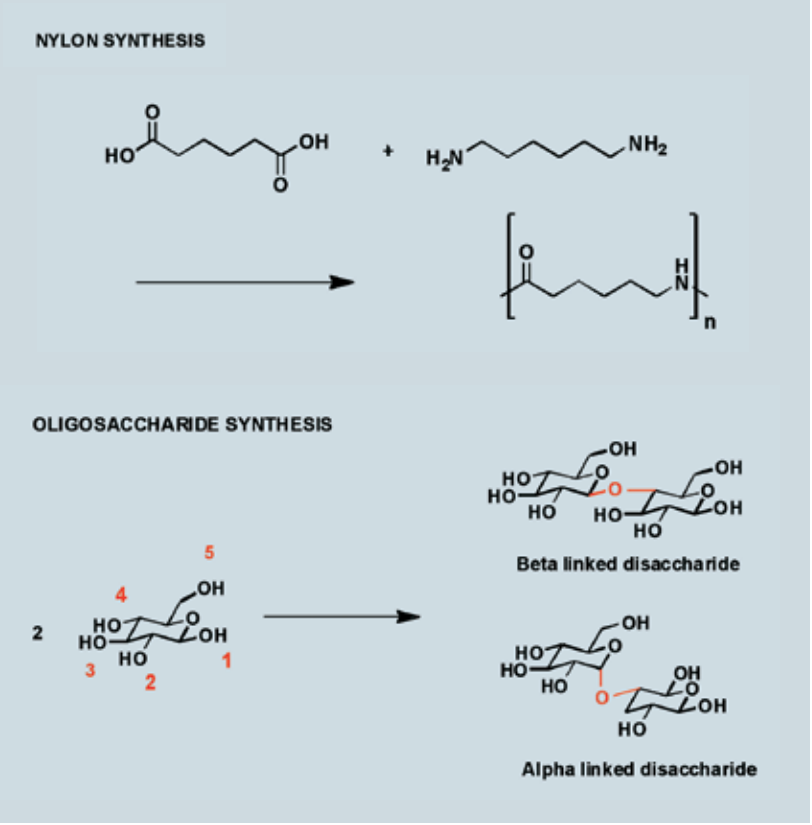
Monomers Small molecules which join together to form the repeating unit of a polymer.

Oligosaccharide A short polymer composed of a few sugar molecules joined together.

Phagocyte A type of white blood cell. These ingest and break down foreign cells and detritus in the body.

Polymerisation of sugars

The monomers which make simple polymers like Nylon can only react in one way, producing a long-chain structure. With sugars it's different though. Any of the 5 hydroxyl groups can react with another sugar and these linkages can also be different in space (alpha or beta). The diagram shows how just two sugar monomers join together; imagine how complicated the structures get when there are more!



'Lock and key' recognition theory

So we can see that by joining up lots of sugar monomer units we can generate a diverse range of complicated 3D structures – enough such that each type of cell in our bodies can have its own unique identifying molecule. But how can our cells 'read' these sugar patterns?

The process of recognition involves complex protein receptors; very large molecules which have a cavity of a specific size and shape (Figure 2). Only sugar markers which have exactly the right shape can bind inside the cleft, like a key into a lock. Since cells have these protein receptors as well as the glycoproteins built into their cell membranes (look back to Figure 1), they are able to recognise each other.

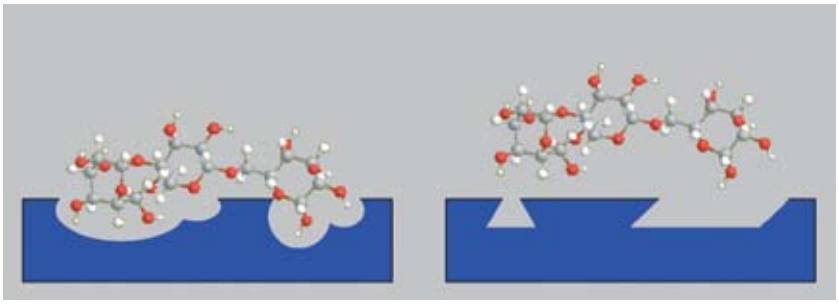


Figure 2 *Only an oligosaccharide (shown as a molecular model) and a receptor (blue) which have exactly complimentary 3D shapes can recognise each other (left). If the 'lock' and 'key' don't fit, then no recognition occurs (right).*

Alien invasion

Unfortunately, the glycoproteins also provide viruses and bacteria – not just the friendly cells from our own bodies - with an identifying handle to grab on to. This is precisely how many viruses (including HIV and influenza) identify their host cells; by using their surface receptor proteins to recognise and latch on to their unique 'bar codes'.

All this knowledge has led to a lot of scratching of heads among scientists. If only we could make something in our laboratories which could bind to specific cell markers it might be possible to block the recognition events which allow viruses to identify the host cells they are seeking to invade. It could be a way to cure lots of terrible diseases, such as HIV.

We are a long way from this goal, but chemists at the University of Bristol have now come up with a logical yet novel way of tackling this problem and have now reported the first artificial receptors for carbohydrates.

Professor Anthony Davis took another look at sugar molecules and recognised that have a cyclic core with just two main features emanating from it, as shown in Figure 3. These are –OH hydroxyl groups (blue) and C-H bonds (red), and they can lie either in the plane of the molecule (equatorial) or stick up from it (axial), depending on the type of sugar. Hydroxyl groups are hydrophilic – they prefer to dissolve in water – whereas C-H groups are hydrophobic and avoid water.

It ought to be possible, he thought, to build a molecule large enough to surround the sugar in a cavity and organise an array of polar hydrogen bonding groups and non-polar panels within it which would present complimentary surfaces to a sugar molecule in the cavity.

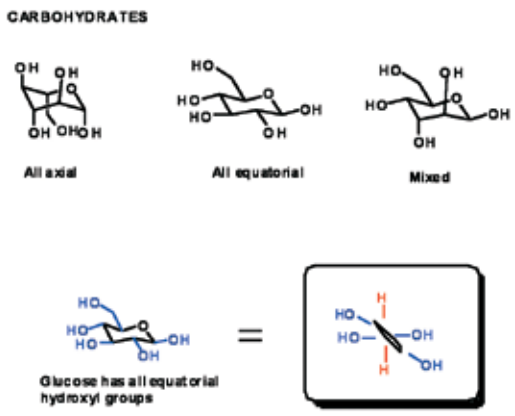


Figure 3 *Carbohydrate molecules have –OH hydroxyl groups which are polar (red) whereas their C-H bonds are non-polar (blue).*

To start with the chemists decided to target sugars which have all their hydroxyl groups pointing outwards to make things a little less complicated. They came up with a complementary scaffold for this and dubbed it a 'temple', due to its hydrophilic 'pillars' and hydrophobic 'roof' and 'floor' (Figure 4). The design also has outwardly directed polar groups which help make sure this large, otherwise non-polar structure can dissolve in water.

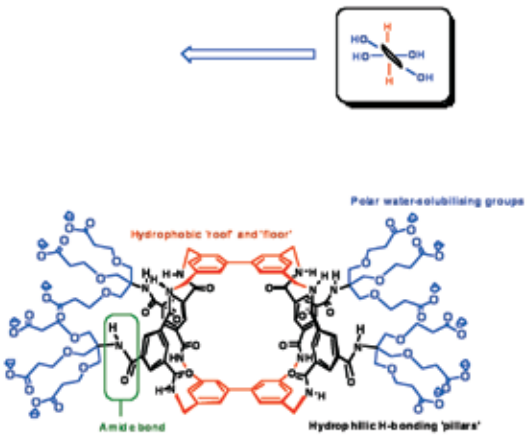


Figure 4 *A trap for a sugar molecule – the synthetic receptor designed by the Bristol team.*

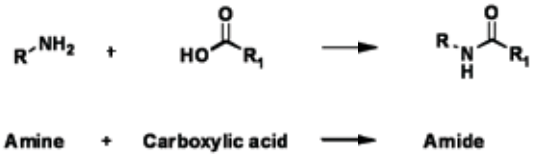


Figure 5 *Chemists use simple reactions such as the formation of amide binds to stitch larger molecules together, piece by piece.*

A chemist working in one of the research labs at Bristol University.

Building molecules

The chemists made the receptor using chemical reactions to build up the structure piece by piece. Although the structure may look frighteningly complicated, chemists use simple reactions to stitch the fragments together – in this case the formation of amide bonds, as shown in Figure 5.

Professor Davis' design worked well and the synthetic receptor was able to bind simple sugars with a strength approaching that of natural proteins. Figure 6 shows a sugar molecule trapped inside the receptor. There's a long way to go before we are truly able to put a cap on viruses – not least being able to bind sugar polymers, rather than just the monomer units. At last, though, the first step on the journey has been taken.

Josh Howgego *is a PhD student at the University of Bristol studying the design and synthesis of carbohydrate receptors.*

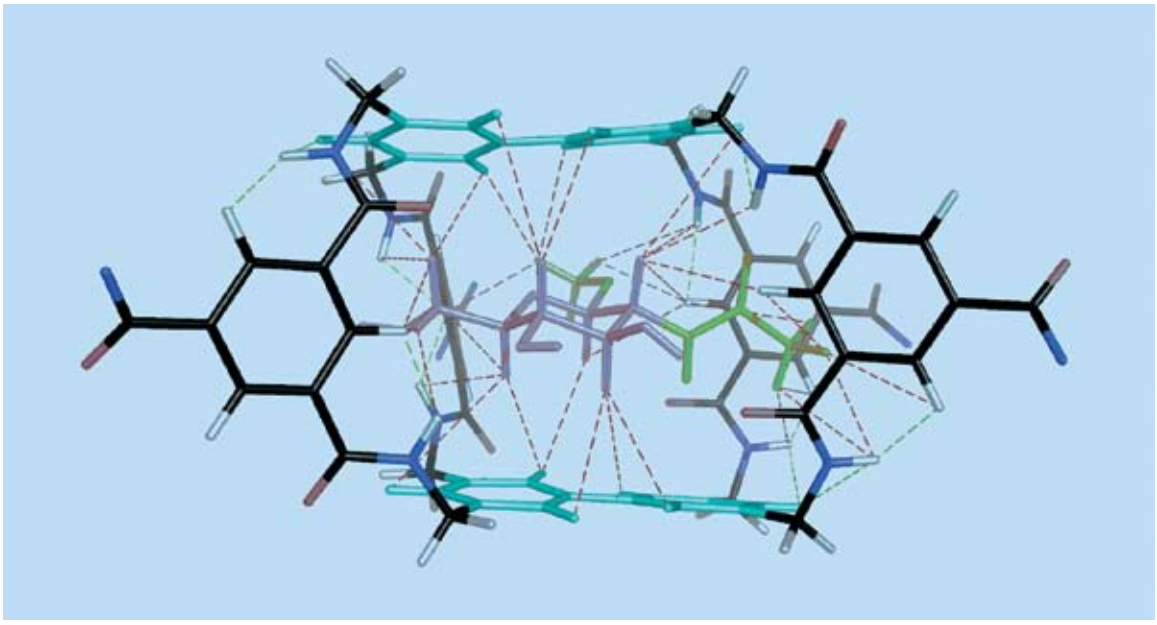


Figure 6 *A molecular model showing how the receptor can trap a single sugar molecule – (the purple and green structure in the centre).*

Alom Shaha

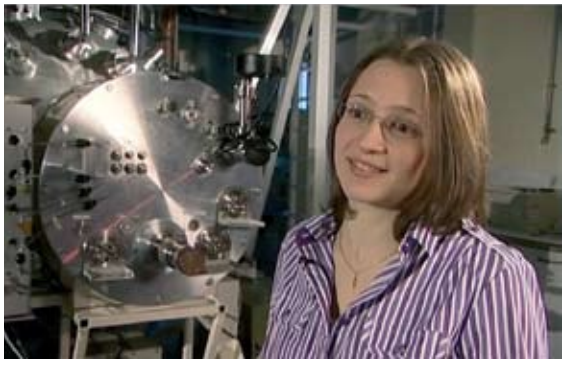
A love letter to science

"science, like art, surprises, delights and moves us"

Why study science? Why become a scientist? Alom Shaha, a science teacher and film maker, felt that his students needed an answer to these questions, so he set about making a film which would show many of the different answers people give to these questions.

For my film, I interviewed high profile scientists, writers and teachers. I also started up a blog, which very quickly took on a life of its own - people from all over the world were coming forward to contribute with their answers to the question "Why is science important?"

Over the course of about 6 months, I collected close to 100 responses in the form of essays, video clips and even a couple of comic strips.



Elaine Greaney, rocket scientist

The most bizarre answer had to be from Mark Miodownik, who argued in a video clip that "science is your mum" – you really have to go and watch his video if you want to understand this. I really loved the response from Maya Hawes, a 12 year old student of mine, who eloquently explains why science is "*not only about blowing up things and making potions*", that it's about finding cures for diseases, inventing new technology and ultimately, "*because we want to answer unanswered questions.*"

Science and technology

As the project developed, it was clear that most of the responses fell in to a few broad categories. The first category of response to stand out was one in which people explain how science has given us the technological world we live in. This response is typified by Jacob Aron who wrote: "*Without science, you would not be reading this. Without science, there would be no computers, no internet, and no blogging.*" Dr Chris Langley chose to respond to this type of argument with a video in which he asked us to consider whether it was the best use of science to be developing new mp3 players and jet planes when there were other, perhaps more pressing, needs to be met by technology.

Chris Langley, Scientists for Global Responsibility

Another type of response which emerged early on in the project, was the importance of science for the environment. Rosie Coates, a chemist at University College London (and a former student

of mine), made a video in which she showed her favourite chemistry demonstration, involving a 'giant technicolour test-tube' and used it to explain how science can provide us with useful knowledge about our environment. Dr Rhian Salmon wrote passionately about the role of science in tackling climate change and argued that "*without science, we wouldn't know where to start tackling this huge issue*".

The importance of science in medicine was emphasized by a number of contributors. Robin Weiss, Professor of Viral Oncology at University College London, spoke eloquently about the role science has played in the history of medicine and how it must continue to pervade all medicine today. Kat Arney, Science Information Officer at Cancer Research UK, stated simply that "*Science tells us whether a treatment actually works or not.*"

Robin Weiss, cancer scientist

A number of people emphasized the importance of science in a democracy – Martin Robbins, a science blogger, wrote, "*An understanding of science is vital to an understanding of politics*" and that "*Effective democracy depends on it*".

Getting to the truth

The most common responses to the question "Why is science important?" related to science as a way of thinking, as a way of looking at the world or, to state it more strongly, as a way of "arriving at truths about the Universe". Dr Susan Blackmore, a psychologist, stated that "*Truth is better than illusion...other claims...prevent people from using their natural curiosity to find out how things really are.*"

Susan Blackmore, psychologist

Gillian Dalgliesh, DNA researcher

Simon Singh, science writer and particle physicist, wrote: "*Being curious and addressing scientific questions is what makes us human.*"

Finally, my favourite response was from Dr Michael de Podesta, a former teacher of mine and a physicist at the UK's National Physical Laboratory, who went out on a limb and declared that "*Science is humanity's greatest achievement.*" I can't help but agree with him.

Working on this project was exhausting but it has been worth it. The website has become a kind of joint love letter to science and I hope it's one that is read by students all over the world.

***Alom Shaha** is a science teacher and film maker, based in London.*

Adam Hart-Davis, inventor and film-maker

Look here!

You can watch Alom's film and read the blog at www.whyscience.co.uk

What do you think?

The people who responded to Alom's blog had a variety of ideas about the value of science. They didn't all agree with one another.

Today, many people blame science for problems such as climate change and over-use of resources. Where do you stand?

For Debate

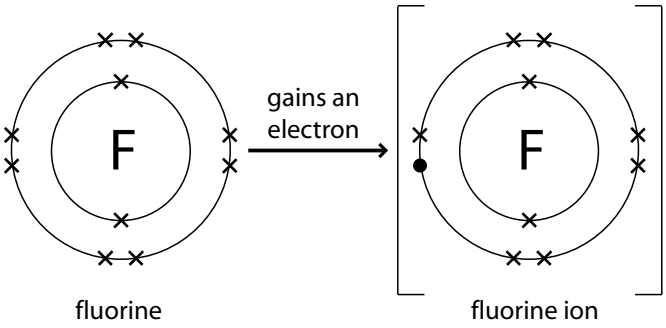
Fluoride in water supplies

Julija Sapic/Bigstockphoto

The UK health secretary recently announced that more water companies would be encouraged to add fluoride to the water supplies. Why is fluoride added? What are the advantages and what are the risks? Should it be put in our water? What do you think?

Fluorine or fluoride?

Fluorine is one of the most dangerous and toxic elements in the periodic table. In spite of this, the fluoride ion is used safely in toothpastes and drunk by most people in their water. Why?



When it is an element, fluorine has 7 electrons in its outer shell, which could potentially hold 8. This makes the fluorine atom very reactive as it grabs an electron from almost any other material. Once it has reacted and gained an extra electron it has a full outer shell. This is a far more stable arrangement and the fluoride ion is unreactive and safe.

Fluoride facts

- Fluoride is the naturally occuring ion of the fluorine atom and has the symbol F^-.
- It has been added to some water supplies in England since the 1960s, when statistics showed that in areas where water had naturally occuring high levels of fluoride children had fewer decayed teeth than in areas where the natural concentrations were low.
- The first places in the UK to have fluoride added to tap water were Birmingham and Solihull.
- Fluoride is also added to water in other countries. About 70% of tap water in both the USA and Australia has fluoride added to it.

How it works

Fluoride works to prevent cavities in teeth in two ways:

- When fluoride touches the enamel (the hard, white outer layer of the teeth) it becomes embedded in the mineral which makes up the main part of the teeth and bones (called hydroxylapatite). The F^- ions replace some of the OH^- ions which are naturally present in the enamel. This strengthens the tooth enamel and makes it more resistant to the acids produced by bacteria in the mouth.
- The fluoride also acts as a catalyst and helps the body to rebuild the enamel crystals if they are damaged by bacterial acids.

Arguments in favour

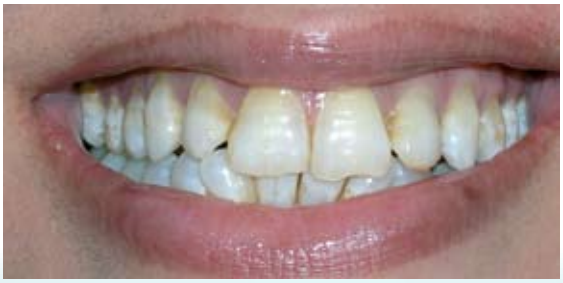
The Health Secretary and others believe that adding fluoride to drinking water is necessary to prevent

tooth decay among children who do not brush their teeth regularly. There is less decay in the teeth of children in more affluent families who tend to supervise the brushing of their children's teeth than households where children may not even have their own toothbrush. This is a chance to give children from poorer backgrounds a chance to have reduced tooth decay and cut down the amount of dental work which they may need in the future.

Children in Manchester, where water is not fluoridated, have twice the levels of tooth decay of those in Birmingham, where it is.

Arguments against

While a small amount of fluoride can help to prevent tooth decay, it is known to cause problems if too much is consumed. In drinking water with a fluoride content of greater than 4 mg/litre it can lead to a condition called fluorosis, the first sign of which is permanently discoloured teeth. Children are particularly susceptible to this. In more extreme cases fluorosis can cause a hardening of the bones which can lead to a deformed skeleton. In some parts of India and Ethiopia where the levels of fluoride in water can be naturally very high the condition is common.



Brown staining on the teeth of a child with fluorosis

There is also some research suggesting that too much fluoride could be a risk factor for certain types of bone cancer and possibly bladder cancer.

Part of the problem with adding fluoride to drinking water is that there is no completely accepted optimal (best) level for daily intake of fluoride. This means the amount that would maximise protection against tooth decay while minimising other risks. The range most often given by researchers is 0.05-0.07 mg of fluoride per kg of body weight per day. The trouble is that people do not just ingest fluoride from tap water – it is also found in toothpaste and numerous foods (see the table below). Exactly how much is consumed will vary from person to person depending on their diet, whether they swallow or spit their toothpaste and how much water they drink. This makes it is very hard to determine how much is consumed by the population.

Tooth decay has been decreasing throughout the last 50 years even in areas where fluoride is not added to drinking water. This could be due to increased use of fluoride toothpaste or better diet. The reasons are not entirely clear.

1 mg is a thousandth of a gram

Vicky Wong is Chemistry editor of CATALYST

Food	Fluoride content in parts per million (ppm)
Strong tea	3.73
Raisins	2.34
Fresh coffee	0.91
Diet coke	0.60 (average)
Mackerel and sardines	27 (fresh weight)
Vegetables	3-20 (dry weight)
Cheddar cheese	0.35

The debate - what do you think?

Adding fluoride is effectively adding medicine to the water supply. People are being medicated without giving their consent.

Fluoride is naturally present in many water supplies and artificially added to others. If children from these areas have better teeth then this benefit should be available to all children.

Not all doctors agree that it should be added. "Evidence on the potential benefits and harms of adding fluoride to water is relatively poor," according to The British Medical Journal.

We should do anything we can to help poorer children have good teeth. It's not fair that they should be at greater risk of dental health problems.

We do not know enough about the potential problems of consuming too much fluoride. We should leave it to parents to decide whether to give their children extra in their diet.

Fluoride is only being added to prevent tooth decay among a relatively small proportion of the population, mostly children in deprived areas who do not brush their teeth. These children are already being identified and treated in more effective ways.

We should concentrate on getting toothbrushes and toothpaste to children who are likely to have poor teeth, as well as access to a dentist, instead of adding fluoride to drinking water.

Try This

An *eggsperiment* on teeth

How is a tooth like an egg? Both contain calcium compounds which can be attacked by acid. When you put an egg in vinegar the shell is weakened by the acid making it soft and more fragile. When teeth are exposed to acids in the mouth they become more vulnerable to cavities. Teeth and eggs can both be protected by the use of fluoride.

You will need

- Small pot or ramekin dish
- Small glass jug or see-through plastic cup wider than an egg
- An un-cracked fresh brown egg
- Small tube of regular fluoride toothpaste (about 75ml)
- Distilled vinegar (colourless)
- Cling film
- Coloured nail varnish
- Paper towels
- Spoon

This experiment will take about 5-6 days.

Step 4 *The egg in the toothpaste*

Step 7 *The egg in the vinegar. The half which was not in toothpaste can be seen to be bubbling*

Step 8 *After about 3 hours the half of the egg which was in toothpaste remains the same; the other half has changed colour and the shell is clearly damaged*

What to do

1. Warm an egg to room temperature. Wash the egg and then dry it with the paper towel.
2. Empty the tube of toothpaste into the pot or dish. Pat the toothpaste down to remove any bubbles and level it out.
3. Put a dot of nail varnish onto one side of the egg.
4. Put the egg into the dish with the marked side down so that half of it is covered in toothpaste. Make sure that the egg does not touch the bottom of the dish.
5. Cover the whole thing with cling film and leave at room temperature for at least 4 days.
6. Rinse all the toothpaste off the egg with warm water and leave to dry overnight.
7. Pour enough vinegar into a clean cup or jug to cover the egg and then carefully lower the egg into the vinegar with the spoon. Rest the spoon on top of the egg to keep it under the vinegar. Cover with cling film. Watch the bubbles form on the unprotected side of the egg.
8. After at least 7 hours the unprotected side of the egg will soften. If it hasn't after 7 hours, keep checking every hour or two by tapping the shell lightly with a pencil or your finger.
9. When the unprotected side is soft, remove the egg and gently wash it. You should be able to see a noticeable difference between the protected and unprotected parts of the egg.

The fluoride in the toothpaste protected the half of the egg which was soaked in it. This is similar to the protection given to teeth by fluoride.

Step 9 *After several hours in the vinegar, the eggshell has become softened*

Look here!

For more information about how fluoride helps teeth visit the animated-teeth website: *http://tinyurl.com/pv9bmr*

Health and Safety *Raw eggs can be a source of salmonella (food poisoning). Wash your hands after handling them.*

Linking the world with light

David Sang

The Nobel Prize for Physics 2009 has been won by Charles Kao for his work in developing fibre optic communications systems. Born in China, he came to the UK to study at Woolwich Polytechnic and Imperial College in London.

Charles then worked as an engineer at Standard Telecommunications Laboratories in Harlow, Essex. He and a small team worked on the idea of sending telephone messages using pulses of light. They found that sending beams of light through the air didn't work because small currents in the air deflected and distorted the beams, so they turned their attention to using glass fibres.

Charles Kao at work in his lab in the 1970s. He is using an optical bench with a laser (left) to shine light through a variety of test materials.

Charles Kao today, with the next generation of science students.

Cleaning up glass

Most glass is slightly coloured, showing that it contains impurities. Charles and his colleagues developed high-purity glass fibres (99.999 999 9% pure!) through which light can travel for over 100 kilometres without being absorbed.

At the same time, he had to develop tiny solid-state lasers which would work for years without failing. Up until then, these lasers-on-a-chip had a lifetime of just a few hours.

Today, fibre optic systems are the basis of most long-distance telephone systems – there are over 1 billion kilometres of fibre in daily use. A beam of light or infrared radiation can carry many more messages than an electric current in a wire, allowing for the transmission of vast amounts of information for business, science and domestic consumers.

Overleaf we look at how the fibre optic revolution is bringing broadband internet access to the African continent.

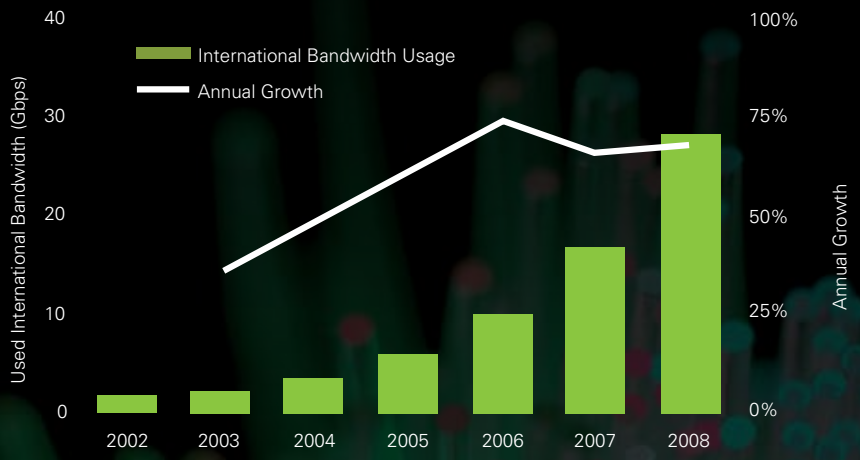
Charles Kao shared the 2009 Nobel Prize for Physics with two American physicists, Willard S Boyle and George E Smith. They are the inventors of the charge-coupled device or CCD, the electronic chip which replaces film in digital cameras (including mobile phone cameras). A CCD is an array of tiny light detectors which convert photons of light into an electrical signal which can then be manipulated, stored and shared digitally.

It is unusual for a Nobel prize to be awarded for such practical discoveries as these. You can see complete lists of Nobel Prize winners for Physics, Chemistry and Medicine at *nobelprize.org*

A video camera – the lens assembly has been removed to show the CCD.

Bringing broadband to Africa

The SEACOM fibre optic cable is bringing high-speed internet access to much of Africa, replacing expensive satellite systems. It is hoped that this will give African countries better access to world markets for their products, as well as bringing them closer to vital sources of technical information.



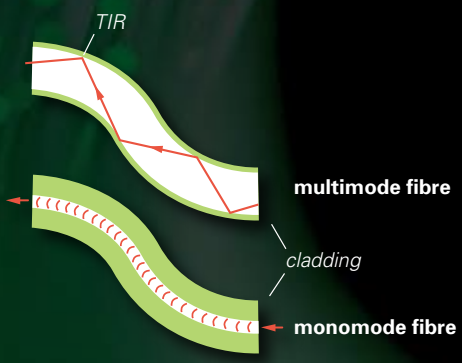
The SEACOM cable will link major centres in West and South Africa with Europe, Arabia and India.

The cable-laying machine is dragged slowly across the seabed, laying the fibre optic cable as it goes.

The optical fibre through which light travels is as thin as a human hair.

The armoured cable must withstand decades on the seabed.

Laying the cable across rural Uganda.



Bringing a SEACOM link cable ashore from the cable-laying ship.

Jordi Arrieta/Bigstockphoto

Electrical cables and optical fibres run side-by-side in a data handling centre.

Light travels along a multimode fibre by total internal reflection. For this to happen, the cladding must have a lower refractive index than the core.

The thickness of a monomode fibre is close to the wavelength of light so that diffraction causes light to follows its twists and turns.