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Fighting malaria

How science works in Africa

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Catalyst

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The front cover shows a haematologist pipetting a blood sample to be analysed from a test tube. African scientists have a major role to play in developing new approaches to tackling local diseases. See the article by Alom Shaha on pages 7-8. (Photographed at St. Mary's Hospital in Lacor, Gulu, Uganda; photo credit: Mauro Fermariello / Science Photo Library)

Contents

A bigger vision

Science changes the way we look at the world around us. The Big Picture in this issue looks at the invention of microscopy. Felicity Henderson of the Royal Society describes how the ability to see small details revealed an unexpected world which captured the imagination of people in the late seventeenth century. In particular, the discovery of tiny organisms and their means of reproduction gave a vital clue to the mechanisms of many diseases.

This work is carried on today in labs in every continent. On pages 7-8, Alom Shaha describes the work of Alexis Nzila, a Kenyan biologist who has won awards for his innovative approach to the problem of malaria.

This issue of Catalyst has another theme – light and electricity. On pages 14-16, three young researchers from Imperial College London describe their current work on photovoltaic cells which turn sunlight into electricity. On pages 17-19, another young researcher from Cambridge University describes how high-efficiency light-emitting diodes are being developed and the impact they may have on our consumption of electricity.

Answers to the puzzle on pages 2-3:
Human female: coniferous resin and beeswax; ibis: bitumen; crocodile: frankincense

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Molecules from the past

Archaeology meets chemistry

Lucy Cramp and Fiona Gill

Modern archaeology uses analytical chemical techniques to answer questions about ancient civilisations and animals. Scientists working at the University of Bristol match compounds present in archaeological materials to those in modern plants and animals which were likely to have been used in ancient times. These techniques allow diverse questions to be answered. Here Lucy Cramp describes how she has identified the substances used by ancient Egyptians to preserve their dead, and on page 4, Fiona Gill reveals the likely diet of a long-extinct mammal.

A partially unwrapped mummy

Key words
analysis
chromatography
mass spectroscopy

Egyptian mummies

The Ancient Egyptians perfected the technique of preserving the bodies of their dead which was used for over three thousand years. Not only have human mummies been remarkably preserved, but also a range of animals, including cats, dogs, ibises (a type of bird), crocodiles, fish and even scarab beetles were mummified and placed into the tombs. These animals may have been pets or symbolic animals during their lifetime, or perhaps were ritual offerings to particular gods. Some animals were even placed in the tombs as joints of meat, in order to provide food for the deceased during the afterlife.

The Egyptians mummified animals as well as people – this is a mummified cat.

Many Egyptologists have tried to reconstruct the ways in which the Egyptians mummified their dead, and experimental work has even been performed (usually on rabbits and birds, rather than humans!) in order to test out some of the techniques and materials that they think the Egyptians may have been using. It is thought that after the internal organs were removed, the bodies would first have been cleaned and then dried out using natron (a naturally-occurring mixture of sodium carbonates, sodium sulphate and sodium chloride) before the body was anointed with various oils, waxes and resins and spices in order to scent the body and provide it with a waterproof coating to prevent decay. Diodorus, a Greek historian who visited Egypt in 59 BC, reported that:

> *'...they carefully dress the whole body for over 30 days, first with cedar oil and certain other preparations, and then with myrrh, cinnamon and such spices as have the faculty not only of preserving it for a long time but also of giving it a fragrant odour...'*

Chemical analyses can be performed on tiny samples of the mummy balms which allow us to identify the various substances which still remain attached to human and animal mummies from Ancient Egypt. These samples are dissolved into organic (non-water) solvents and analysed using gas chromatography and gas chromatography/mass spectrometry (see Box) in order to identify **biomarkers** for particular ingredients that may have been mixed together to make the balms. This biomarker approach involves looking for distinctive parts of molecules, called carbon skeletons, in the ancient samples which can be used as a fingerprint to compare with modern reference materials.

BOX Gas chromatography-mass spectrometry (GC-MS)

GC-MS is a powerful analytical tool for identifying molecules in archaeological and geological samples. The gas chromatograph consists of an oven containing a long, thin, silica tube through which helium gas flows continuously. Compound mixtures extracted from samples are injected at one end of the column and the oven starts to heat up slowly.

Each compound in the mixture behaves differently; some tend to stick to the stationary phase (the lining of the tube) while others remain in the mobile phase (the helium gas). This means that, as the molecules flow down the tube, the mixture starts to separate into its individual components. Usually, smaller, lighter molecules travel down the column faster than larger, heavier molecules, but the functional groups of the molecules can also affect their affinity for the stationary phase (how much they stick to it).

Each compound in the mixture reaches the end of the column at a slightly different time and passes into the mass spectrometer. In the mass spectrometer the molecules are bombarded by a stream of electrons and break into fragments. The fragments formed depend on the chemical structure of the molecule and are characteristic for each compound. They can therefore be used as a 'chemical fingerprint' to identify the molecule.

A GC-MS machine, closed and open. The chromatography takes place in the oven on the right; molecules are detected by the mass spectrometer on the left.

The analysis of the composition of mummy balms allows scientists to reconstruct the often-complex mixtures of substances that were applied to the bodies. This means that the trade routes of more exotic substances can also be reconstructed. For example, resin from conifer trees was probably imported from the eastern Mediterranean or Near East, whilst bitumen may have come from the Dead Sea. These more exotic ingredients were probably added to fats, oils and waxes that would have been locally available. Chemical analyses have revealed that whilst certain ingredients such as coniferous resin and beeswax were relatively common, there was no single formula that was in use throughout the period of mummification. This suggests that different embalmers had their own ideas about the best recipe to use!

Preparing archaeological samples for GC-MS analysis in the lab at Bristol University.

What is a biomarker?

A biomarker is a term that is used in many different fields of research, but in organic geochemistry it means a molecule of biological origin that can be directly linked to the plant, animal or microbe that produced it, on the basis of its chemical structure or stable isotopic signature. Many biomarkers are lipids, because these are common components of cell membranes and are therefore abundant in living things.

Table 1 *Analysis of samples from a number of mummies*

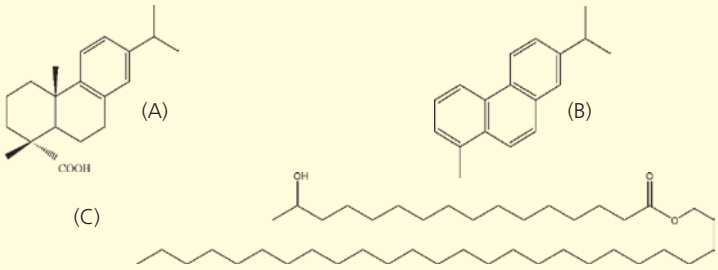
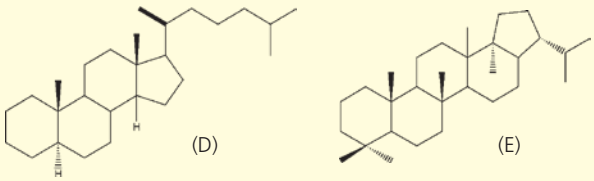
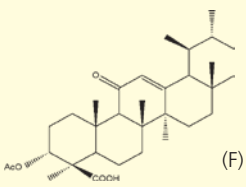
Mummy	Biomarkers present in sample
Human (female) Date: 250 BCE	
Ibis Date: 500 BCE	
Crocodile Date: 675 BCE	

Table 2 *Biomarker Guide*

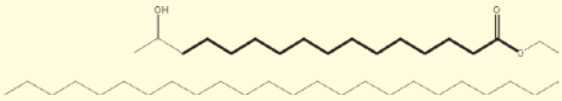
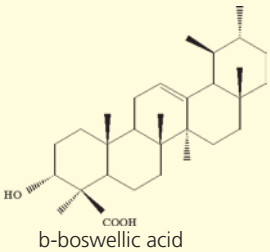
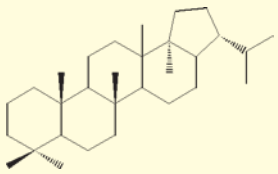
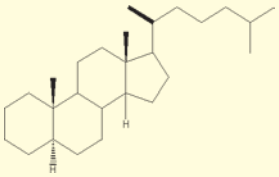
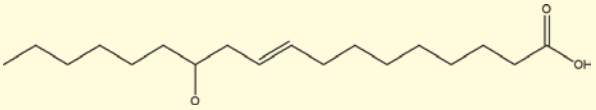
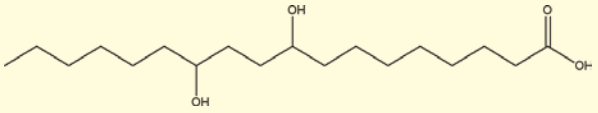
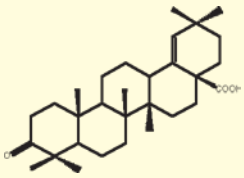
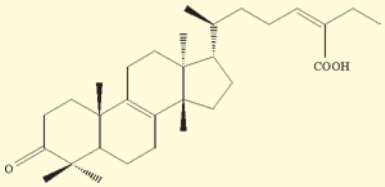
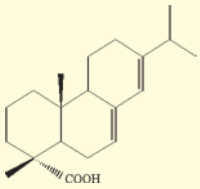
Substance	Origin	Composition	Biomarkers
Beeswax	Honeycomb	Palmitate wax esters and hydroxy wax esters; long-chain alkanes, fatty acids and alcohols	 Hexacosanyl palmitate (hydroxy wax ester)
Frankincense	Gum-resin from Boswellia shrubs growing in Arabia and parts of Africa	Plant sugars, triterpenoids (polycyclic compounds containing 30 carbon atoms)	 b-boswellic acid
Bitumen	Petroleum, derived from heat and pressure acting upon ancient organic marine matter over millions of years	Straight, branched and cyclic hydrocarbons	 17a(H), 21b(H)-hopane  a, a, a-cholestane
Castor oil	Oil from seeds of castor plant, believed to be indigenous to parts of Africa (possibly including Egypt) and the Near East	Fatty acids; mono- and dihydroxy fatty acids	 Ricinoleic acid (12-hydroxyoctadecenoic acid)  9,12-dihydroxyoctadecanoic acid
Mastic or terebinth resin	Various species of *Pistacia* shrubs, found in North Africa, Mediterranean and Near East	*Triterpenoids* including oleanonic, moronic and masticadienonic acid	 Moronic acid  Isomasticadienonic acid
Coniferous resin	Resin from pine, cedar, fir etc growing in the eastern Mediterranean and parts of the Near East	*Diterpenoids* (polycyclic compounds containing 20 carbon atoms), in particular, abietic and pimaric acids	 Abietic acid

Table 1 shows some of the diagnostic biomarkers that were discovered in three ancient Egyptian mummies. To find out which substances were used to preserve the mummies, use Table 2, the biomarker guide. Look for molecules which have a similar shape and structure to the ones in the sample. For example, biomarker C in the mummy looks like it came from beeswax. Can you work out which substances were used in each mummy? Answers on inside front cover.

What did ground sloths eat?

Imagine if, in 11 000 years time, someone could figure out what you ate for lunch today. This is what we were able to do, by looking at molecules preserved in dung from a Pleistocene ground sloth!

Alain Beneteau

A reconstruction of a ground sloth of the species Nothrotheriops shastensis – extinct for the last 10 000 years.

Dr E. Loeffler

Ancient dung – a sloth coprolite taken from Gypsum Cave, Nevada

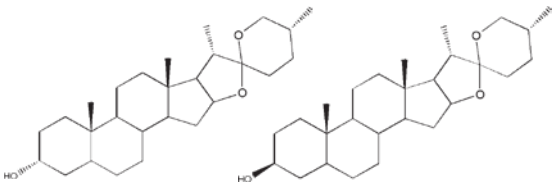
Ground sloths are bear-like creatures that lived in North and South America between 35 million and 10 000 years ago. Caves in these areas often contain dung deposits from the animals that lived in the region and because caves are cool, dry environments, the dung tends to be very well preserved. Scientists have investigated the diet of ground sloths by identifying fragments of leaves, seeds and other plant structures that survived the trip through the animal's digestive tract and are preserved in the dung. From this, and from studies of their teeth, we know that ground sloths ate only plants. However, some plants are more resistant than others to the physical and chemical processes of digestion and not all are preserved as recognisable remains in dung. Analysis of lipid (fat) biomarkers preserved in fossilised dung provides an alternative way of determining the diet of extinct animals.

Archaeologists prepare to enter Gypsum Cave, Nevada, to analyse the deposits laid down over thousands of years.

The dung that we analysed came from Gypsum Cave, Nevada, USA and was produced by a species of ground sloth called *Nothrotheriops shastensis*. Identical dung from the same locality was radiocarbon dated and found to be between 11 000 and 29 000 years old and we believe that the dung we analysed also lies within this age range. We took 1 g of the desiccated (dried) dung and ground it into a powder, extracted the organic molecules from the dung by heating it with organic solvents and separated the resulting mixture according to the chemical structure of the compounds. The sample was analysed using gas chromatography-mass spectrometry (see Box on page 2).

Environmental scientists have previously studied the organic molecules in faeces from modern domestic animals (and humans) to identify sources of faecal contamination in water supplies. We expected the organic molecules from the sloth coprolite to be similar to those found in modern herbivores such as cows or sheep, with the most abundant compounds being general plant biomarkers such as β-sitosterol (the plant equivalent of cholesterol) or 5β-stigmastanol. We did see those compounds in the sample, but they were in very low abundance. The most abundant compound was a sapogenin compound called epismilagenin. Most sapogenins are plant secondary metabolites, molecules produced by plants for non-essential functions (i.e. not growth, development or reproduction). Epismilagenin itself isn't found in plants, but is produced by the chemical alteration of another sapogenin called smilagenin. Smilagenin in dietary plants is known to be converted to epismilagenin in the digestive tract of (modern) sheep, and we believe the same thing happened in *Nothrotheriops shastensis.*

We searched published reports to compile a list of all the plant species that contain smilagenin. We then looked at reconstructions of the climate of the Gypsum Cave area and found that only two plants from the list of smilagenin-producers would have been likely to grow there at that time, namely Yucca and Agave. We therefore concluded that Yucca and/or Agave had formed a major component of the sloth's diet, at least for the few days before it produced the dung that we analysed! Future research will include analysing more dung from *Nothrotheriops shastensis* to find out whether Yucca and Agave were typical components of the diet of this species.



Epismilagenin *Smilagenin*

***Lucy Cramp** and Fiona Gill are archaeology researchers working in the Chemistry Department at Bristol University*

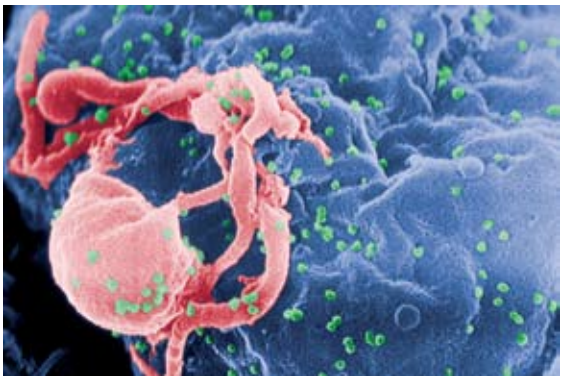
Helen Fry

When the drugs don't work

There are millions of bacteria everywhere – on your skin, in your guts, on your lunch. Bacteria have been troubling us for as long as we've been around, so we have put a lot of effort into finding ways to fight back at them.

We have developed thousands of different antibiotics since their discovery in 1928, to treat everything from boils to leprosy. However, bacteria are not the most abundant nor the most troublesome of microbes – this dubious title belongs to the virus. Viruses cause colds, flu, cold sores, AIDS, chicken pox, measles and a host of other common or serious diseases.

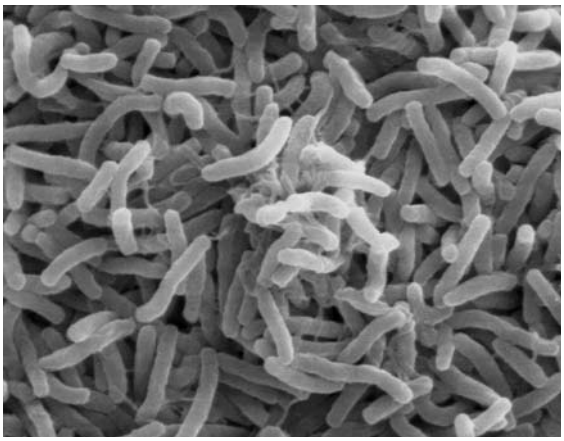
With the swine flu pandemic well under way, it has become even more obvious how defenceless we are against viral adversaries. To put this in context, if you have a bacterial chest infection there are over 100 antibiotics available to treat this. If you get influenza, there are only two. Of the hundreds of viruses that cause disease in humans, there are effective drugs against just six of them.



A human cell infected with HIV (shown in green) which causes AIDS.

Developing antivirals

So why are there so few decent drugs, when viruses are clearly such a pest? Firstly, in order to make a drug against a particular virus, it needs to be well understood, so that a specific part of its lifecycle can be targeted. However, researching viruses is difficult, as they will not simply grow in a dish like most bacteria, they have to be grown inside living cells, and they cannot be seen with a normal microscope.

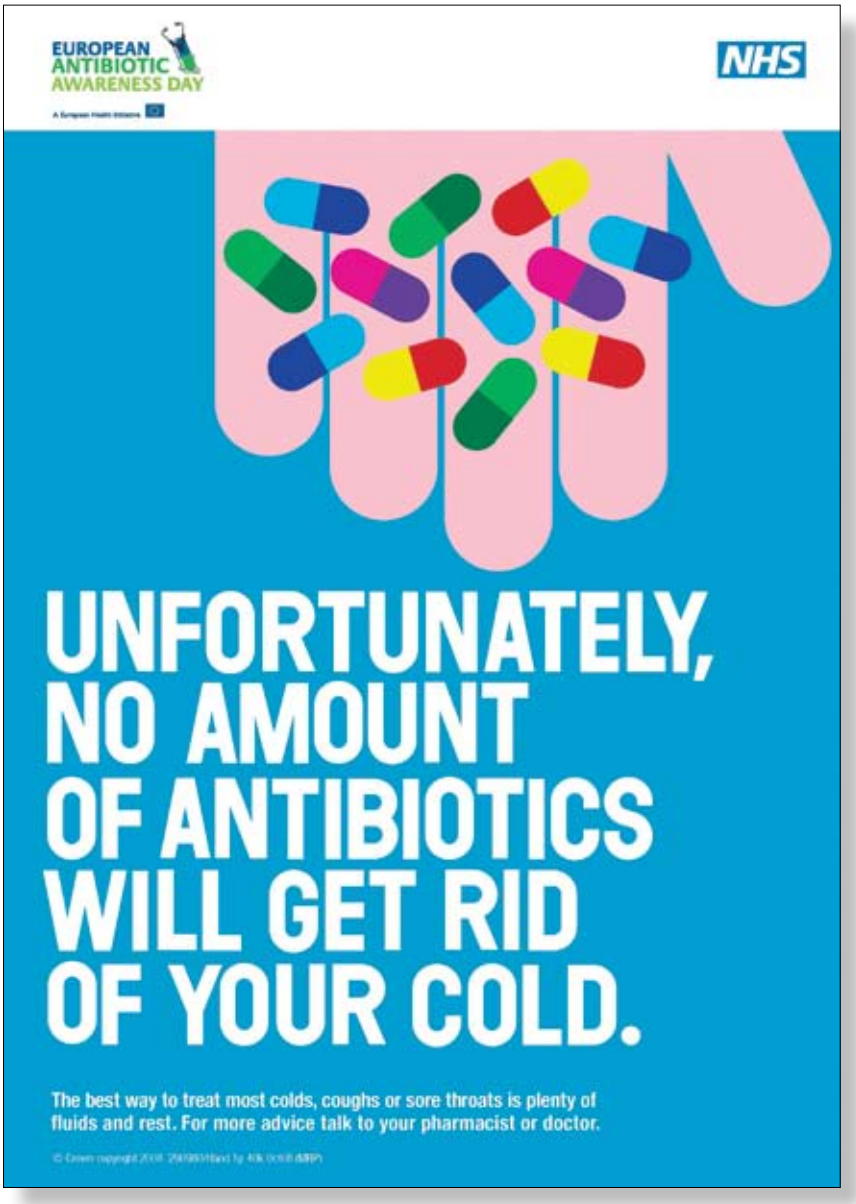


Cholera bacteria, seen using a scanning electron microscope.

They do not produce any toxins or compounds of their own which could be detected, so they are very hard to study well. On the other hand, they have very small genomes, which can be easily sequenced, so some information can be gained this way. The difficulty of studying viruses means that not a lot is known about them, making it hard to find ways of killing them.

Even when a virus is well studied, it is still difficult to make good antivirals. This is because viruses live and multiply inside host cells, so for a drug to be

Key words
bacteria
viruses
antibiotics
antivirals



This poster attempts to persuade patients that there is no point in asking for antibiotics to cure a viral infection.

effective it needs to enter the host cell to find the virus. However, if a drug enters a cell it is likely to harm it, so a drug has to target cells infected with virus. This is difficult to do, so antivirals are often quite toxic, generally killing off cells that are dividing rapidly, such as bone marrow and hair follicles. In fact, the side effects of some drugs can be worse than the disease itself.

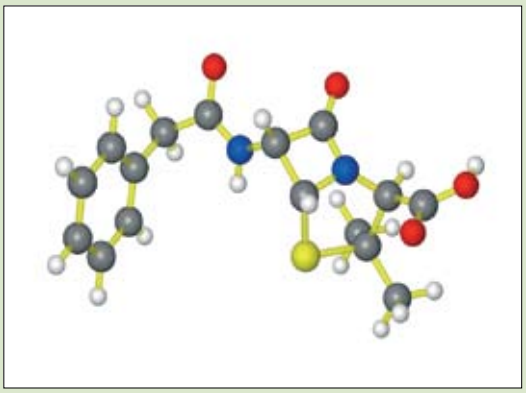
There is also, of course, the issue of money. It takes millions of pounds and close to 15 years to make a drug and bring it to market, partly due to strict safety tests. Drugs are developed by companies, so have to be profitable. Most profit comes from drugs that have to be taken for a long time, so drugs for all kinds of infectious diseases are under-researched as they generally require a short course. The exception to this is HIV, which requires life-long drug therapy and is therefore more profitable and better researched. There are more agents to treat HIV than any other virus.

Helen Fry is a microbiology graduate and medical student

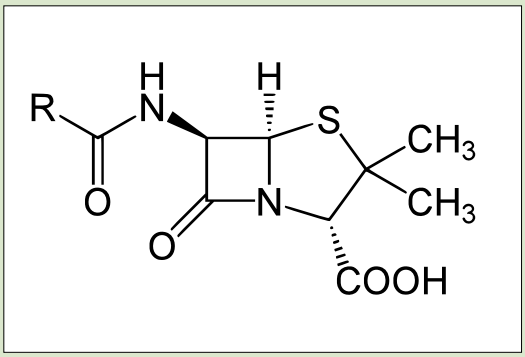
Antiretrovirals are drugs developed to fight retroviruses such as HIV, which causes AIDS.

Antibiotics

- The first antibiotic to be discovered was penicillin, by Alexander Fleming in 1928.
- Penicillin was first purified during the Second World War and made available for general use.
- Penicillin is a natural substance; most modern antibiotics are chemically-modified versions of natural substances.
- Antibiotics work either by killing bacterial cells (bactericides) or by preventing their growth (bacteriostatics).
- Bacterial cells are rather different from mammalian cells so antibiotics can attack bacteria without affecting the host mammal (such as a human).



The chemical structure of a penicillin molecule.
Key: grey = carbon; white = hydrogen; red = oxygen; blue = nitrogen; yellow = sulphur.



How science works in Africa
Tackling malaria in Kenya

Alom Shaha

"For the common man, research is just a matter of mixing chemicals in a test tube, but modern science requires technology that is not available in most African labs." Alom Shaha meets Dr Alexis Nzila, a senior research scientist based in Kenya, to hear about the challenges of doing science in Africa.

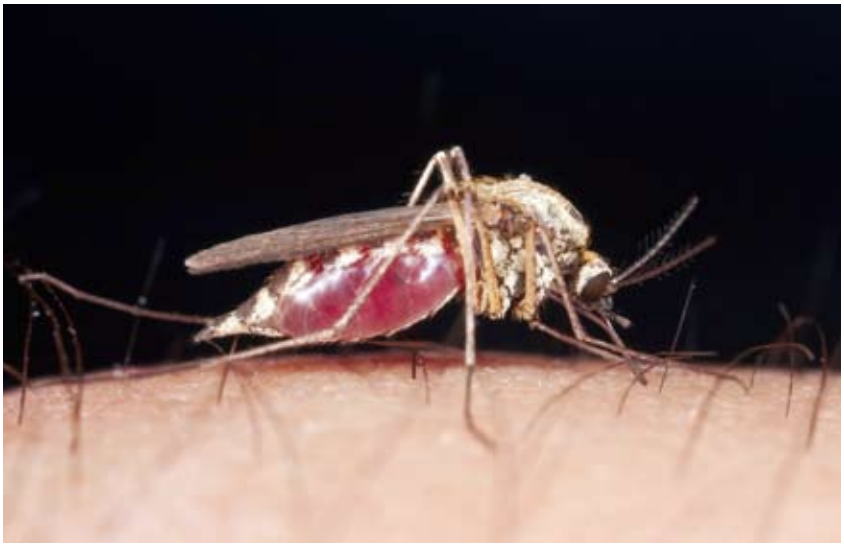
I met Alexis in 2006, when I was asked to make a film about him to celebrate his being awarded the Royal Society Pfizer Award for "an outstanding, innovative contribution to biological science, including basic medical science, which contributes significantly to capacity building in Africa." Making the film gave me the opportunity to get to know a remarkable man and provided me with an insight into how science works, or often doesn't, in Africa.

Alexis chose to specialise in malaria research because it is one of the biggest problems facing Africa today – it kills more than a million Africans a year. Malaria also makes hundreds of millions of Africans sick, which impacts on the economic well-being of the continent.

Drug resistance

One of the big problems with malaria is that the parasite which causes the illness has a remarkable ability to quickly select for resistance against the drugs we use. So, it is important to understand how the parasite develops resistance to existing drugs and to identify alternatives which work in different ways.

Alexis decided to look into a family of drugs called antifolates. These block the synthesis of folate molecules, which are essential for cell multiplication. Alexis explained that, "Highly dividing cells, such as cancer and the malaria parasite, rely heavily upon the availability of folates for growth. So, inhibiting the availability of folates is an effective way to stop these cells multiplying. Since malaria causes illness by the growth of parasites within our red blood cells, antifolate drugs offer an effective weapon against malaria."



The blood-sucking mosquito transmits the malaria parasite from person to person.

One of Alexis' main contributions to science has been to improve our understanding of how the malaria parasite develops resistance to a drug called Fansidar. He did this by developing "simple ways of tracking and predicting resistance". Whilst he was innovative in his experimental approach, Alexis based his work on existing research in the field of cancer, where there was already a lot of work done on folate biochemistry. Through this work, Alexis came up with a method to increase the efficacy of Fansidar by combining it with another drug, Probenicid. He tested his ideas in vitro and human trials have since shown that he was right.

Alexis' work exemplifies the way in which scientists build on prior knowledge and come up with and test their own hypotheses. However, perhaps a more important aspect of Alexis' story is that it provides us with a valuable insight into the challenges faced by anyone wishing to be a scientist in Africa.

Lack of funding

Alexis and his team are just some of the African scientists who have shown that internationally recognised science can be done from within Africa. But he is all too aware of the difficulties his fellow African scientists face, mostly due to a lack of funding – African countries spend on average 0.3% of their GDPs on research and development, compared with 1.8% in EU countries and over 2.6% in the US and Japan.

Universities in most of Africa simply do not have the resources to turn out well-trained scientists;

young scientists are forced to travel abroad to complete their training. Often, they do not return, for reasons that Alexis understands: "Scientists who leave Africa cannot be blamed... they get frustrated trying to do science here and give up and move to the west... there are better opportunities to follow a successful and rewarding scientific career in Europe or the US."

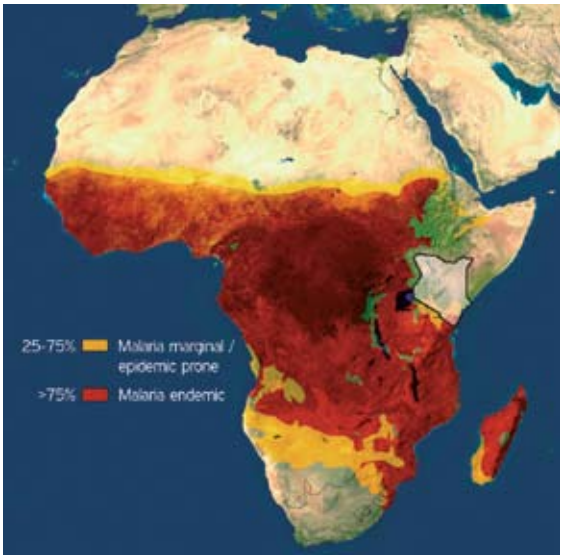
A commitment to a continent

Alexis is committed to staying in Africa because he wants his work to make a direct difference to the lives of his fellow Africans; he feels the best way to do that is to be based in Africa.

Leah Mwai, research student in Alexis' lab.

Alexis (right) discusses problems with local doctors while family members tend a young patient.

Nursing a young malaria victim in a Kenyan hospital.



Alexis believes firmly that "there will not be lasting solutions to malaria without a strong contribution from African scientists. Controlling malaria is not simply a matter of distributing bed nets and medication. It also requires planning and research so we can predict what the situation may be like in 5 or 10 years from now. To tackle malaria at a national level, governments need scientific evidence to make effective policy decisions. Without strong research groups, government programmes for malaria control cannot work."

Alexis has already made an invaluable contribution. His research promises cheap new drugs that may save millions from the ravages of malaria. Dr Kevin Marsh, director of the KEMRI research laboratory in Kilifi, says, "It is not an exaggeration to say that Dr Nzila's work is by far the most innovative in the area of defining possible new approaches to anti-malarial drugs to come out of Africa in the last ten years."

Results from Alexis' work have also been used to inform government policy. Dr Willis Ahkwale, Head of the Kenyan Government's Division of Malaria Control told me, "Scientists like Alexis are essential to malaria control in Africa, his work has helped us to evaluate whether our drug policy is working. It is crucial that we can keep scientists of Alexis' calibre in Africa."

Alexis has every intention of staying in Africa. However, it will take more than good intentions to ensure that Alexis and other talented African scientists remain in Africa; simply put, the biggest problem in doing science in Africa, like so many of the other problems in that troubled continent, is a lack of funding.

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

Look here!

You can watch Alom's film about Alexis' work at: *http://www.vimeo.com/6607065*

Small wonders
The invention of microscopy

Felicity Henderson

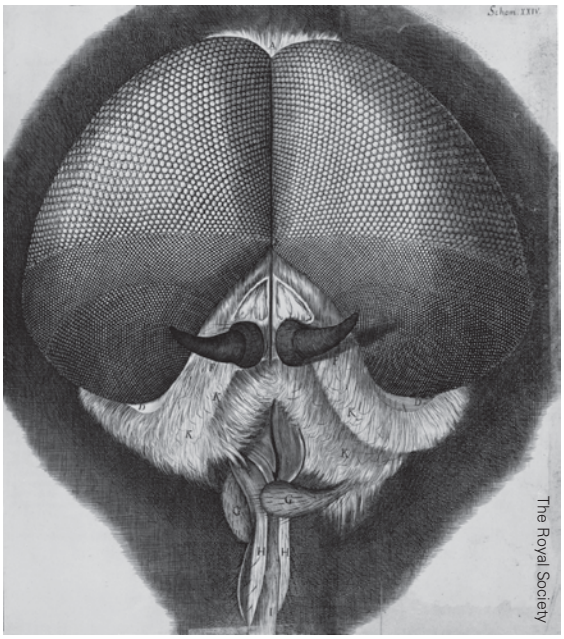
Key words
microscope
Royal Society
cells
lens

Summer, 1665. London was hot, dirty and smelly – and so were Londoners. They rarely changed their clothes, and the bathroom hadn't been invented yet. Fleas and lice lived in houses, beds and hair – they were hard to see, but their bites were a constant annoyance.

One man was investigating these tiny animals more closely. Robert Hooke was one of London's best early scientists, making discoveries in chemistry, geology, engineering, medicine and many other areas (Hooke's Law of elasticity is named after him – see the previous issue of CATALYST).

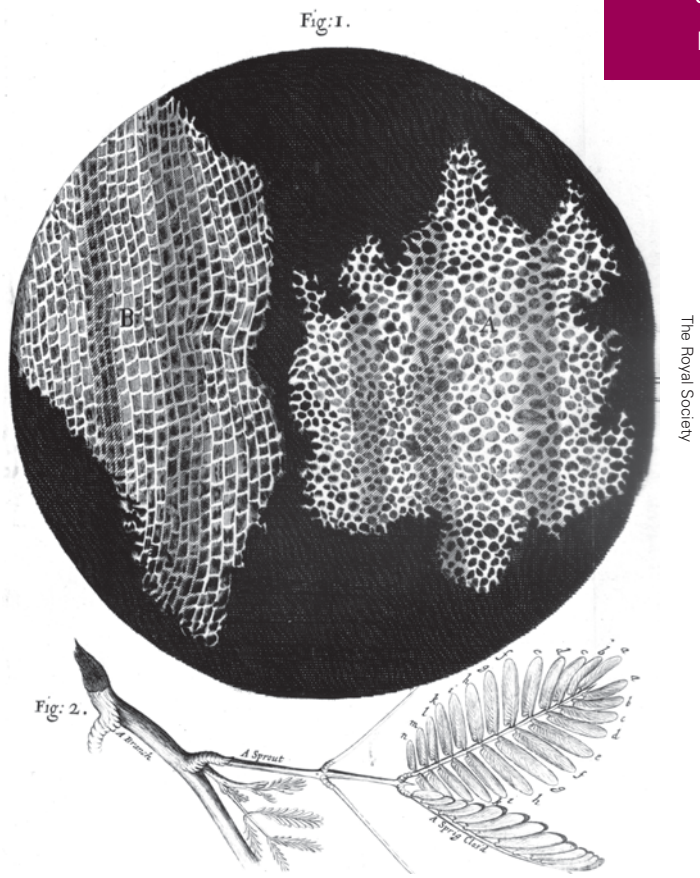
Hooke was fascinated by the miniature world that existed beyond human sight. He designed an improved microscope, and used it to study anything he could find: snowflakes, the tip of a needle, mould on bread, flies, lice and fleas, and a full-stop on a printed page.

These were all common, everyday things – most people wouldn't give them a second thought. But through the microscope, they were transformed into something mysterious, wonderful, and perhaps even beautiful. Hooke was excited to find that snowflakes grew in regular, hexagonal shapes, each one different from the next. A razor's edge that seemed perfectly smooth was actually marked with impurities and nicks. A fly's eye contained a multitude of tiny facets, allowing it to look in many directions at once.



The Royal Society

Hooke's image of a fly's eyes, from Micrographia *(1665)*



The Royal Society

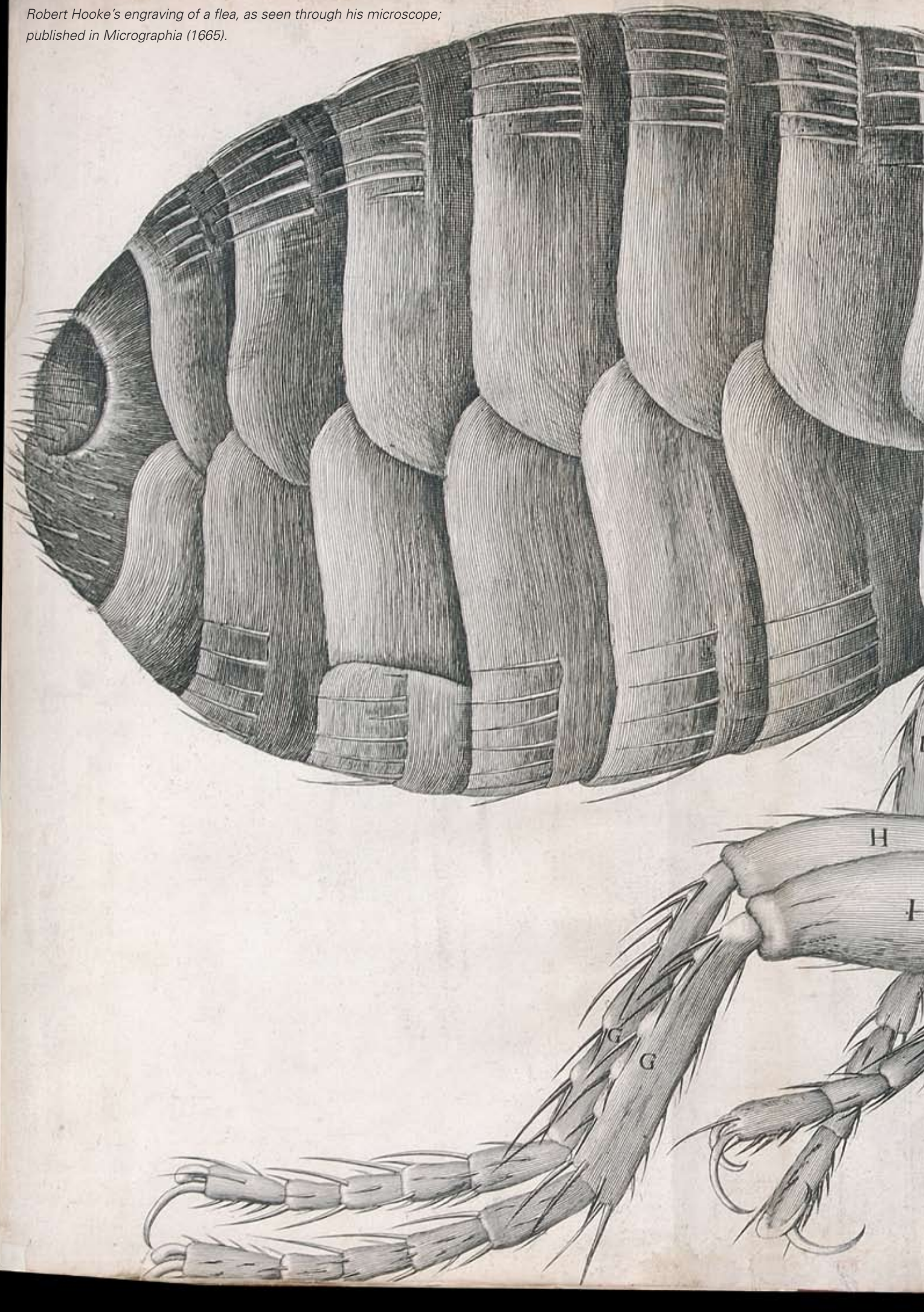
Hooke's drawing of cells in a slice of cork, from Micrographia (1665)

Hooke made an important discovery when he inspected a thin slice of cork. He noticed that the wood was made of many tiny individual compartments bunched together. He called these compartments 'cells' (thinking they looked like a honeycomb). We now know that cells are the fundamental unit of all life.

Hooke's great achievement was not just to see these things for the first time, but to show them to others. His book, *Micrographia*, published in 1665, was filled with beautiful, intricate drawings. They made the microscopic world visible to non-scientists for the first time, and people have been fascinated by it ever since.

On pages 10-11 you can see Hooke's drawing of a flea. The original engraving is considerably larger than these pages although the flea itself was only about 3 mm in length.

Robert Hooke's engraving of a flea, as seen through his microscope; published in Micrographia (1665).



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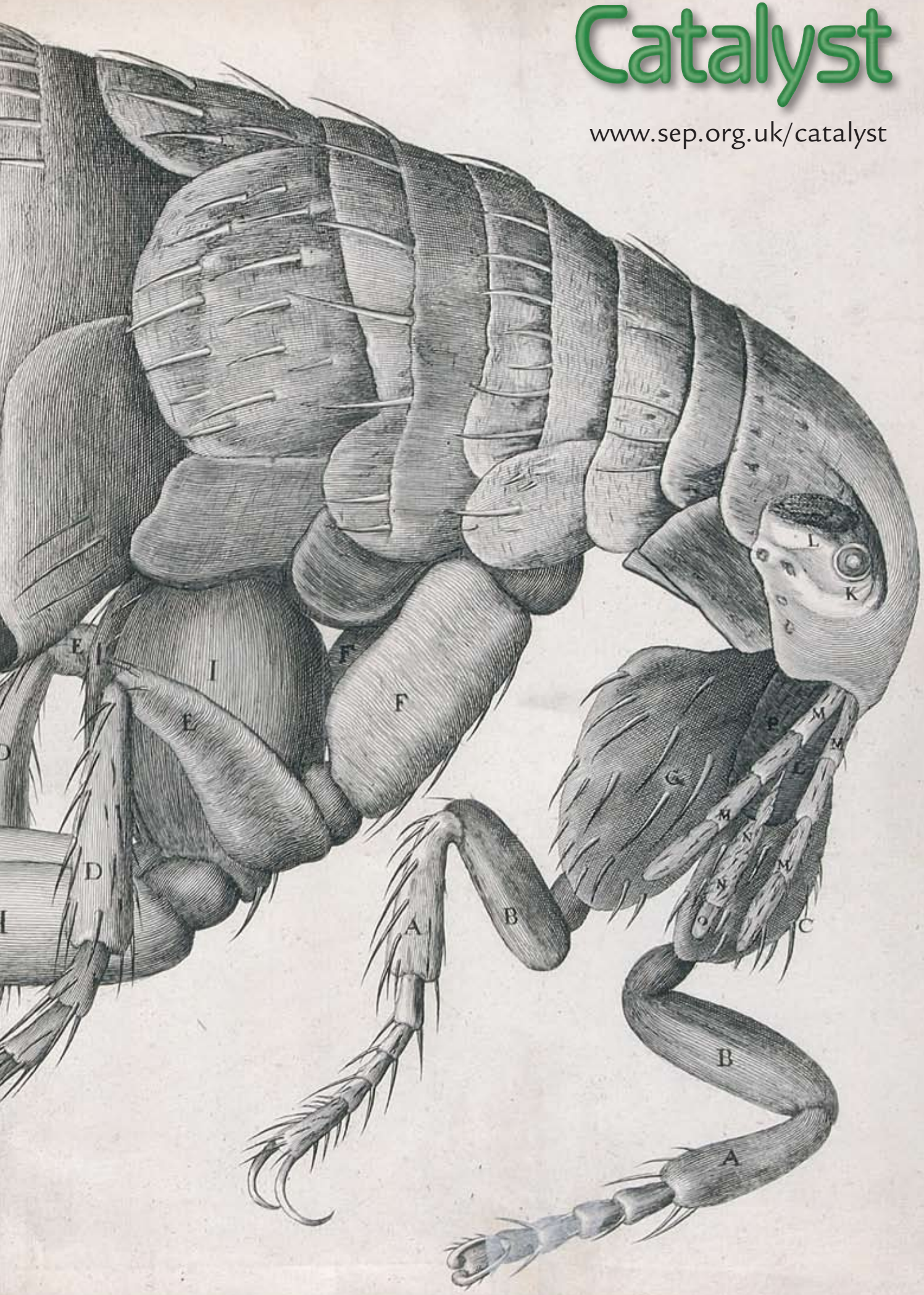
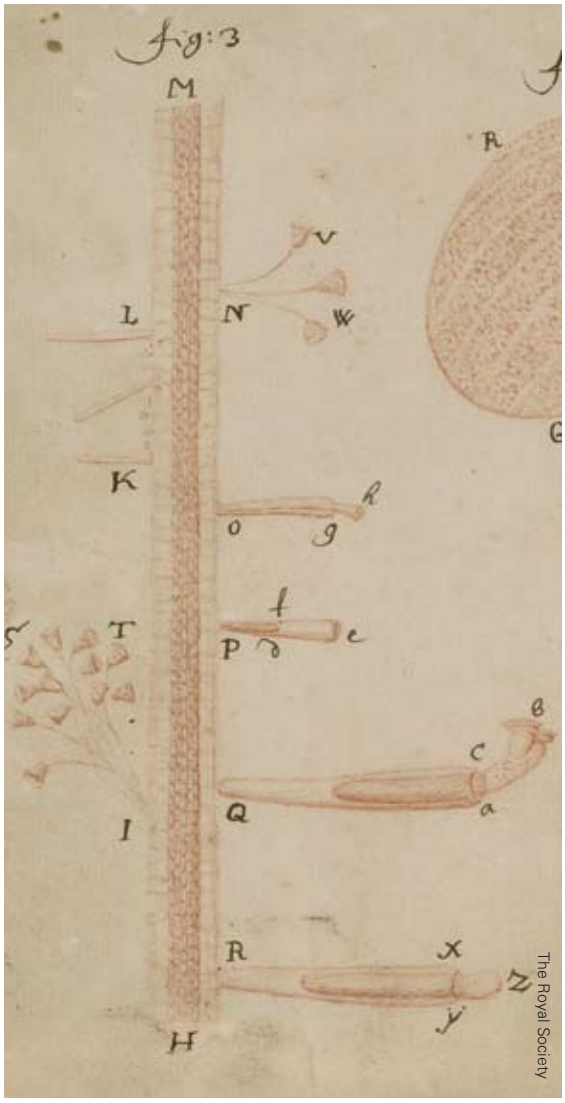


The Royal Society of London for Improving Natural Knowledge

Robert Hooke was employed by the Royal Society, Britain's first scientific institution. It was founded in 1660 by a group of men who wanted to understand more about the natural world. At the time, most 'natural knowledge' had been passed down from ancient philosophers such as Aristotle. The Fellows of the Royal Society wanted to test this knowledge for themselves, using personal observations and experiments to prove or disprove ancient theories. They were among the first to do what we would call 'science' today. Find out more about the Royal Society and its history at royalsociety.org.

While Robert Hooke was at work in London, a Dutchman living in Delft was making exciting discoveries of his own. Antoni van Leeuwenhoek (pronounced Lay-wen-hook) used a very small, very powerful lens. It was simple, just a single tiny drop of glass made at home by Leeuwenhoek himself.

Leeuwenhoek used his lenses to study a huge range of natural objects, from animal tissue and plant structures to saliva, vinegar and blood. He was the first to systematically investigate the tiny eel-like creatures he found swimming in drops of water and other liquids. Today we would know them as bacteria and other protozoa.



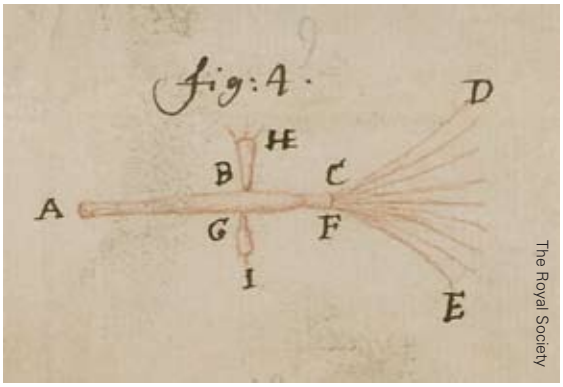
A strip of pondweed (MH in the figure) with 'animalcules' attached, from Leeuwenhoek's letter to the Royal Society in December 1702. The organisms have been identified as Vorticella (NVW), Carchesium or Zoothanium (IST), and the rotifer Limnius ceratophylli (RXY and cba).

On the opposite page, Felicity compares the microscopes used by Leeuwenhoek and Hooke.

Leeuwenhoek wrote to the Royal Society with news of his discoveries, but it took Robert Hooke a long time to reproduce his results. When he did, he was amazed, saying,

I was very much surprised at this so wonderful a spectacle, having never seen any living creature comparable to these for smallness.

He showed the little animals to the other Fellows, who were equally surprised. Sadly, it took almost 200 years – and millions of deaths from cholera, dysentery and typhoid – before scientists understood the significance of the creatures swimming in their drinking water.



A drawing of a Hydra species, first described by Leeuwenhoek in his letter to the Royal Society in 1702.

Spontaneous generation

Leeuwenhoek discussed his discoveries with another Dutch microscopist, Jan Swammerdam. Although he trained as a doctor, Swammerdam was particularly interested in insects. He dissected them at every stage of development, from larvae to adult, and showed that the same insects underwent a series of developmental stages. He also investigated insect reproductive organs. His research provided evidence against the long-standing theory of 'spontaneous generation'. This theory suggested that insects (and some small animals) simply appeared out of rotting vegetation rather than being the offspring of parents.

Swammerdam dissected a queen bee and other insects and was able to see microscopic eggs inside their bodies. He argued that all animals, no matter how small, came from eggs like the ones he had seen. He was correct, but the theory of spontaneous generation was only finally proved wrong in an experiment by Louis Pasteur in the 19th century.

Hooke, Leeuwenhoek and Swammerdam were all fascinated by the microscopic world, but they didn't just want to see it – they wanted to understand it, and they wanted to describe it to other people. They knew that if they could explain structures and processes that existed on a small scale, they would have the key to understanding more complex organisms. Scientists have built on their work ever since.

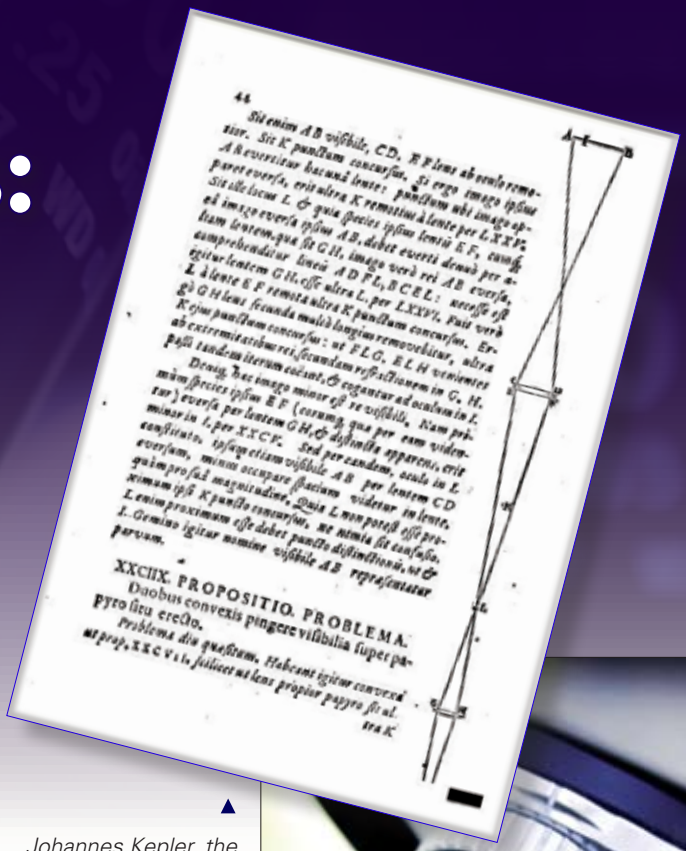
Dr Felicity Henderson is a researcher at the Royal Society Centre for the History of Science

Microscopes:
Simple or Compound?

Hooke and Leeuwenhoek were both using microscopes, but they were very different instruments.

- **Leeuwenhoek** used a 'simple' microscope, with a single lens – just a tiny drop of glass about five millimetres in diameter. He mounted the lens in a thin piece of metal – like a very small magnifying glass.
- **Hooke's** microscope was a much larger, 'compound' instrument. It used three lenses: a small double-convex eye-lens at the top, then a large plano-convex field-lens, and another double-convex lens with a short focal length at the bottom of the tube.

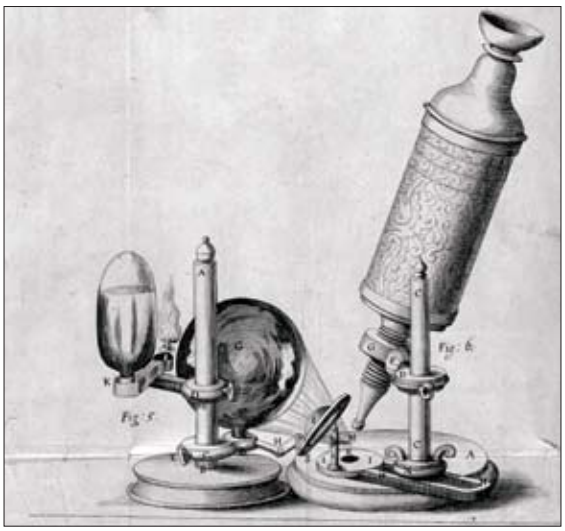
Which was better? Some of Leeuwenhoek's simple microscopes could magnify objects more than 250 times, but Hooke's compound microscopes only magnified somewhere between 20 and 50 times. Leeuwenhoek's instruments were more powerful, so why did Hooke not use one? He knew how to make and use a simple lens, but he chose not to. They had to be held very close to the eye, and Hooke was concerned that he would damage his eyesight if he used a simple microscope regularly.



Johannes Kepler, the astronomer, was also interested in microscopy. Above is his publication in which he explained (in Latin) how a compound microscope works, complete with a ray diagram.

The Royal Society

A modern lab microscope usually has a choice of objective lenses which gives a choice of magnifications.



A drawing of Hooke's microscope, from Micrographia (1665). He used a glass globe filled with water to focus light from a small flame onto the specimen, to counteract the darkened images caused by lens aberrations.

The Royal Society

A replica of Leeuwenhoek's simple microscope. Specimens were fixed to the sharp point and viewed through a tiny lens mounted in the small hole.

Jessica Adams, Rahul Bose and Ben Browne

Solar cells

Turning sunlight into electricity

Key words
photovoltaics
solar cell
energy efficiency
semiconductor

Every minute enough sunlight strikes the Earth to power our civilisation for a year, yet less than 1% of global energy generation is provided by solar energy. Solar cells convert sunshine directly to electricity, but to make them more attractive they have to perform at higher efficiencies and lower costs. Physicists around the world are working on a myriad of new technologies so that in the future we will be able to harness the Sun's energy on a scale that matches its potential. Ben Browne, Jessica Adams and Rahul Bose take you on a tour of these exciting technologies.

Energy from the Sun

Sunlight may appear yellow, but in fact the solar spectrum is made up of a broad range of colours. As well as the visible colours that the human eye can detect, sunlight is also made up of ultraviolet (UV) and infrared (IR) light. More energy is contained in the sunlight that hits the Earth's surface in an hour than is used by humans in a year!

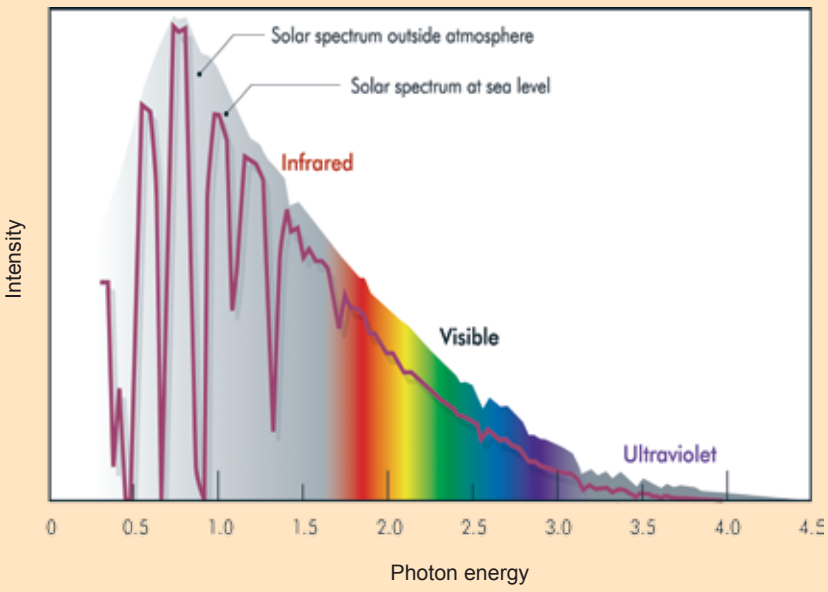
You may be used to thinking of light as a wave, but it can also be thought of as a particle. We call particles of light photons, and each photon can be classified according to its energy. IR photons are low energy, UV photons are high energy, and visible photons have an intermediate energy.

How a solar cell works

When sunlight hits a solar cell, it can be absorbed. The energy of the photons can knock loose electrons from their host atoms such that they can move freely within the material. These free electrons can be made to flow round an external circuit. A flow of electrons is an electric current, and the energy carried by each electron determines the voltage. The electrons in the circuit can be made to do electrical work, such as charging a mobile phone.

In physics terminology, the field of solar cell research is known as **photovoltaics**. This word comes from the Greek *photo*, meaning light, and the name of Alessandro Volta who performed pioneering research into our understanding of electricity.

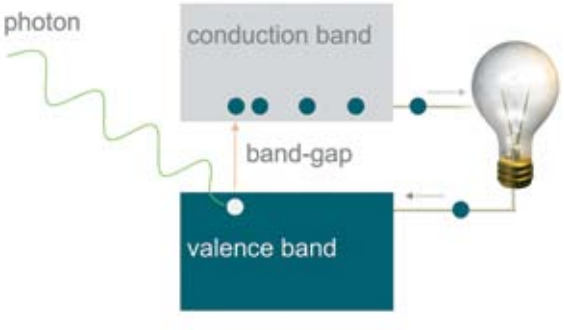
Solar cells are typically made from a group of materials called **semiconductors**. As the name suggests, a semiconductor has electrical properties halfway between those of insulators and those of conductors. In an insulator, such as rubber, all electrons are bound to the atoms and are said to be in the "valence band". In a conductor, such as a metal, there are many electrons that are free to move across the material, and these are said to be in the "conduction band". A material only conducts when electrons can move within it. A semiconductor acts as an insulator unless enough energy is injected, for instance through the absorption of photons, to allow electrons to jump up from the valence to the conduction band. The energy imparted to each electron has to be large enough to bridge the **band-gap**. This band-gap energy varies between different materials.



Box 1: Sunlight

The Sun emits light from its surface, which is at a temperature of nearly 6000 kelvin. The light we receive on the Earth's surface is much less intense that at the Sun's surface and is almost parallel due to the large distance to the Sun. Certain parts of the spectrum are also absorbed in the Earth's atmosphere. On a sunny day at noon with the Sun directly overhead, the intensity of sunlight is about 1000 watts per square metre. This means that a square metre of 20% efficient solar cells, for instance, would generate a power of 200 W at peak hours.

The spectrum of light from the Sun is made up of photons covering a broad range of energies. Besides the visible spectrum with which we are familiar, the Sun also emits light in the infrared and ultraviolet energy ranges.



An electron is freed from its atom when it absorbs a photon with enough energy. It can then move within the conduction band and perform useful electrical work in a circuit – lighting a bulb, for example.

If the incoming photon has an energy that is lower than that of the band-gap, it will not be able to free an electron and the light will simply pass through as though the solar cell were transparent. If the photon has a greater energy than is necessary to free the electron, the extra energy will be wasted as heat. The solar cell efficiency is the ratio of power produced by the solar cell to the power of the incident sunlight. Because the solar spectrum consists of photons with a broad range of energies, a solar cell can never be 100 % efficient at converting all the energy contained in sunlight into useful electrical energy.

The efficiency of a solar cell depends strongly on its band-gap. A cell with a low band-gap can absorb a lot of light, but this comes at the cost of producing only a low voltage. A high band-gap on the other hand leads to a high voltage but a small current since only a small high energetic component of the solar spectrum can be absorbed. There is an ideal band-gap energy that strikes the right balance, and in theory an efficiency of 31% is possible with a simple solar cell. In practice one has to find or engineer materials with suitable properties.

Solar cell technologies

The first practical solar cells were invented in 1954 in the Bell Laboratories where a 6% efficient silicon cell was made, referred to then as a 'solar battery'. Initially solar cells were mainly used to power satellites, and until recently the silicon used to make common cells was taken from offshoots from computer chip manufacturers.

Silicon

The most common type of solar cell is made from crystalline silicon. These are the type that you may have seen on rooftops. Silicon is found as its oxide, silica, which is the most abundant material in the Earth's crust. However, to make a solar cell, the silicon needs to contain no more than a few impurity atoms for every million silicon atoms and these atoms must then be neatly arranged into regular crystal structures millions of atoms thick.

A crystalline silicon solar module

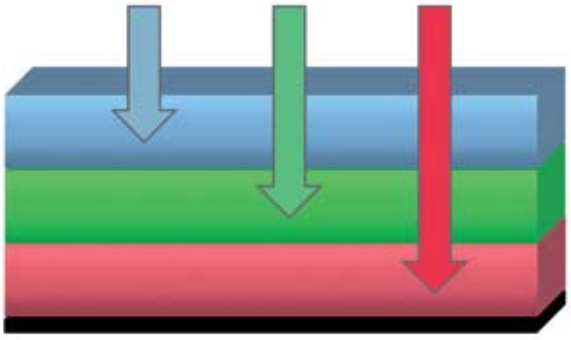
Thin film

There are several technologies which are cheaper to manufacture per square metre than silicon and which are becoming more common. The solar cells sometimes incorporated into calculators are an example of these. These types of solar cells are referred to as 'thin film' because they are deposited in a very thin layer, a few microns thick – hundreds of times thinner than crystalline silicon solar cells. They work because they use 'direct band-gap' semiconductors, which absorb light very strongly. These devices are only around half as efficient as crystalline silicon but may still prove cheaper to produce per unit of rated power because they can be deposited quickly and with less energy onto cheap materials like glass, plastic and metal. One relatively recent approach, still confined primarily to laboratories, is to make thin film cells out of plastics.

A lab sized thin film solar cell

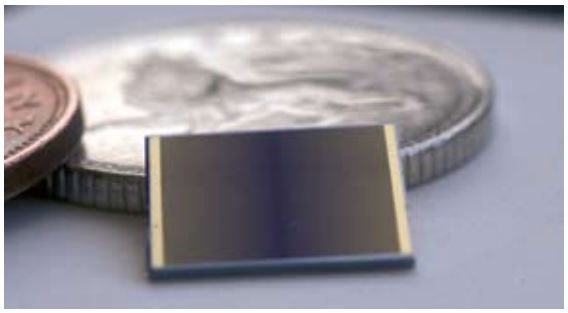
Multijunction

At Imperial College London, we are working on a way to make better use of the broad solar spectrum by stacking two or more solar cells of different band-gaps. This type of solar cell is called a multijunction cell, and to date the highest recorded efficiencies of over 40% have been achieved with designs that use three sub-cells. The order of the band-gaps in the stack is crucial. The first (top) cell in the stack has the highest band-gap and therefore absorbs only the high energy photons. Photons with lower energy travel straight through this cell and are absorbed by the next cells, which have successively lower band-gaps. In general, the more sub-cells included in the stack, the higher the achievable efficiency.



Multijunction solar cells use sub-cells with different band-gaps to absorb and convert different parts of the solar spectrum. The highest energy photons (blue light) are absorbed in the top layer while the lower energy photons pass through to be absorbed in lower layers. This method yields much higher efficiencies than simple solar cells.

The theoretical efficiency limit under normal solar illumination for this design is 68%, when the stack has a large number of sub-cells. One of the main challenges lies in developing materials with the right band-gaps. Multi-junction cells are also made of direct-gap semiconductors using exotic elements such as gallium, arsenic, germanium, phosphorus and indium rather than silicon. Besides the multijunction solar cell, several other advanced concepts are being researched at Imperial and elsewhere that could push the limits of photovoltaic conversion efficiency closer to the theoretical limit.



One of the high efficiency solar cells under development at Imperial College London. Because these cells are designed for concentrated sunlight they have areas from only 1mm^2 to 1cm^2.

Solar concentration

The Sun's rays can be concentrated directly onto a solar cell using lenses and mirrors. This method is called concentrator photovoltaics and has advantages over conventional photovoltaics. The bulk of the relatively expensive solar cell material can be replaced with inexpensive lenses or mirrors. Typical solar concentrators focus several hundred times the intensity of normal sunlight onto the cells. Moreover, an increase of efficiency is achieved through concentration. If we increase the light concentration by a factor of 100, the electric current produced by the solar cells increases by 100, but at the same time the voltage increases as well. Consequently, the electrical power and the efficiency are increased. Under concentration a simple solar cell can in theory reach 40% efficiency and multijunction cell 87%.

A solar concentrator like this one in Australia has a photovoltaic cell at the focus of the reflector dish. It uses direct sunlight and needs to track the Sun over the course of the day. To be cost-effective, these systems are usually quite large and are built in areas with a lot of sunshine, such as Spain.

Jessica Adams, Rahul Bose and Ben Browne are research students in the Department of Physics, Imperial College London

Box 2: Solar cell efficiencies

The first practical solar cells, invented more than half a century ago, had an efficiency of 6%, meaning that 6% of the power from incident light was converted into electrical power. Today, typical silicon solar cells achieve efficiencies between 15% and 20%, while the cheaper thin film cells are around 10%. Concentrator cells have significantly higher efficiencies, generally achieving 35% and above. However cells that are currently being developed in laboratories around the world are several years ahead of what we see on the market, with top efficiencies exceeding 40%. This is higher than a typical power plant or a car engine.

Compared to fuel-burning power plants, photovoltaics is a very young technology, and while the former are already operating very close to their theoretical optimum, photovoltaics still has a lot of untapped potential as its theoretical efficiency limit lies at 87%.

Look here!

More about our work on nanostructures in high efficiency solar cells:
www.imperial.ac.uk/quantumphotovoltaics

Detailed explanations of photovoltaic technology: *http://pvcdrom.pveducation.org*

Solar Systems is an Australian company manufacturing concentrator photovoltaic systems:
http://www.solarsystems.com.au/projects.html

Michelle Moram

LEDs
lighting up a brighter future!

Like food, water, clothing and shelter, light is essential to our lives and is needed by most people for most of their waking hours. Michelle Moram of Cambridge University describes the latest, energy-efficient lighting technologies.

Currently, about 20% of our electricity supply is used for lighting, but scientists and engineers hope to reduce this amount by developing more efficient ways of generating light. This is important because electricity generation is currently the single biggest source of man-made carbon dioxide emissions: at the moment, the energy used in lighting is enough to power all the world's aircraft three times over!

What's wrong with the light we've already got?

Right now, many people still use the old-fashioned incandescent bulb, which was invented by Thomas Edison in 1879. This works by passing an electric current through a very thin tungsten wire, which then gets so hot that it glows – around 3200 °C! Unfortunately, about 95% of the electrical energy that goes into the light bulb is wasted as heat, whereas only 5% is converted into light.

A more modern option is the fluorescent lamp, invented in the 1970s. This works by filling a tube with mercury vapour and passing an electrical current across it, generating ultraviolet (UV) light. This UV light is then converted to white light by a special fluorescent coating on the inside of the lamp. However, even the best fluorescent lamps waste about 80% of the electrical energy that is put into them. What's more, many people don't like the light they produce, which flickers and which tends to make colours look different to the way they look in daylight. Also, they are not always as reliable as the manufacturers claim!

Box 1 on page 18 describes how the eye responds to light of different colours.

What are the alternatives?

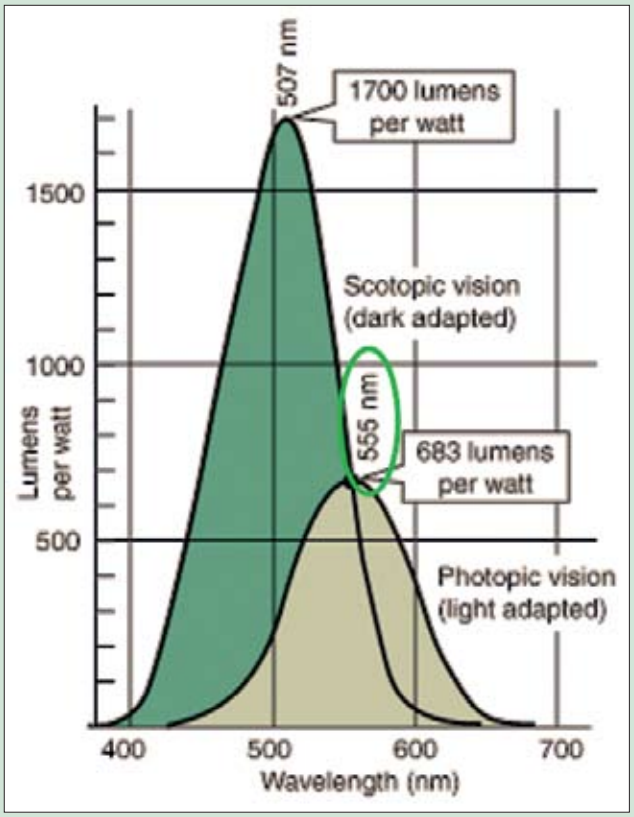
Many different technologies have been proposed as replacements, such as organic polymer light emitting panels, halogen lamps and semiconductor light-emitting diodes (LEDs). However, out of all of these options, LEDs are emerging as the most promising.

This torch has 12 white LEDs instead of a single incandescent bulb.

Railway signals are increasingly being converted to use LEDs because they are brighter than conventional lamps, cheaper to run and require less maintenance.

Key words
lighting
efficiency
light-emitting diode
semiconductor

Box 1



The sensitivity of our eyes to light of different wavelegths under bright daylight conditions (photopic vision) and moonlight conditions (scotopic vision)

What you see is what you get – or is it?

The efficiency of a light source is simply defined as the ratio of the light output power to the electrical input power. Simple, right? Actually, the efficiency isn't really a fair measure of how good a light source is, because we can't see all colours equally well. In fact, our eyes detect green light far better than they detect red or blue light. This is why night vision goggles, radar screens and other equipment that might be operated in the dark usually have bright green screens or displays.

A green night vision device display

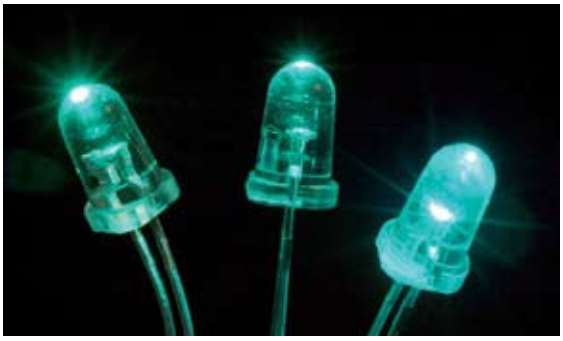
To account for the differences in our ability to detect light of different colours, we usually measure light output in lumens, which are an indicator of how much light we can actually see. Now we have a better way of defining how good a light source is – its luminous efficacy, which tells us how much useful light in lumens (lm) is produced per watt (W) of electrical input power. A green light of wavelength 555 nm has the maximum possible luminous efficacy of 683 lm/W, but in order to make white light, we are obliged to add some red and some blue light as well, which our eyes can't detect so well. This means that white light sources will always have lower luminous efficacies, reaching a theoretical maximum of around 240 lm/W. The world record for white LEDs currently stands at 186 lm/W. When we compare this to fluorescent lamps (60 lm/W), ordinary incandescent light bulbs (12 lm/W) and oil lamps (0.1 lm/W), it is easy to see just how much potential LEDs have for saving electricity!

How does LED lighting work?

LEDs work by creating a junction between two slightly different versions of the same kind of semiconductor. Each type contains a low concentration of different elements which either add extra electrons to the material, making it n-type (n for negative) or remove electrons (p-type). When the two types are joined together and a voltage is applied in the right direction, the extra electrons move from the n-type material to the p-type material, filling in the missing electron 'holes' and releasing light.

The wavelength of the light produced depends on the kind of semiconductor used. To create light of different colours, we need different materials: red LEDs are based on GaAs and blue LEDs are based on GaN. To make white light, we can either combine red, green and blue LEDs, or we can take a blue LED and coat it with a phosphor which converts some of the blue light into yellow light. However, we don't yet have materials which can emit green light efficiently enough, so at the moment, white LEDs are made by the second method.

You can already find these LEDs for sale in torches and bike lights. If the phosphor isn't coated evenly, then you can see the individual blue and yellow components when you shine the light onto a piece of white paper (go on, try it!).



Blue-green LEDs made at Cambridge

Ga = gallium
As = arsenic
N = nitrogen
So GaAs is gallium arsenide and GaN is gallium nitride.

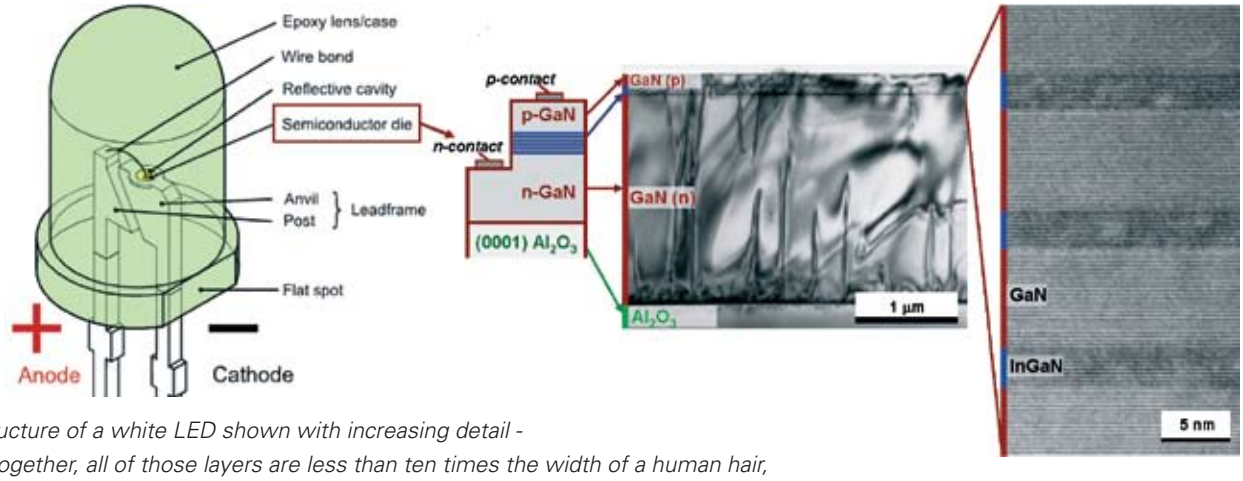
Box 2

How are white LEDs made?

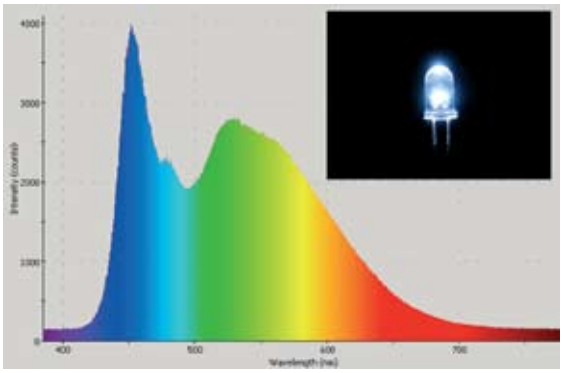
We start with a cheap, thin crystalline wafer of silicon or aluminium oxide. Very thin layers of GaN are deposited on the wafer using gaseous chemicals, which react on the surface of the wafer when it is heated to around 1000 °C.

$$Ga(CH_3)_3 + NH_3 \rightarrow GaN + 3\ CH_4$$

Firstly, we make an n-type GaN layer by adding very small amounts of SiH_4 to the reactor, which allows silicon (an electron donor) to be incorporated into the GaN. Then we deposit a very thin film of InGaN, just a few atomic layers thick. The composition of this film determines the exact colour of the light produced. Then we add a top layer of GaN, which contains very small amounts of magnesium (an electro acceptor) to make the GaN p-type. Then we cut up the wafer into individual pieces and coat them with yellow phosphor. Finally, each piece is packaged up into a finished LED.



The structure of a white LED shown with increasing detail - Taken together, all of those layers are less than ten times the width of a human hair, but it takes a machine the size of a classroom to make them!



The spectrum of light emitted by a white LED

Equipment used to make LEDs. It is so big, we had to knock down the wall of the laboratory to bring it indoors!

Why aren't we using LED lighting in our homes?

It takes a lot more energy to light a whole room than it does to light up a small area. Unfortunately, when we try to get more light out of each LED by passing a lot of current through it, the efficiency drops and a lot of heat is generated. This means we have to use more LEDs in each lighting unit, making them too expensive for many people to buy. To encourage people to use LED lights, we have to make them cheaper by making each LED extremely efficient, even under high power operation. At Cambridge, our research concentrates on reducing the density of crystal defects in the light-emitting region of the LEDs, because these are the main cause of low efficiencies.

Box 2 above describes how we go about making high-efficiency white LEDs.

So what does the future hold?

As efficiencies rise and LED costs go down, we can expect to see LEDs appearing in our homes and offices. This is good news for everyone, because LED lighting has been shown to cure the 'winter blues' and can help to prevent depression, eating disorders and immune system problems. This is because the light that LEDs produce is much closer to daylight than that from other light sources. Indeed, this combination of health benefits and energy efficiency points to a brighter future for us all!

Michelle Moram is a Research Fellow in the Department of Materials Science and Metallurgy at the University of Cambridge

Helen Roy

Encounters with aliens
Invasive species – they're here!

Key words
biodiversity
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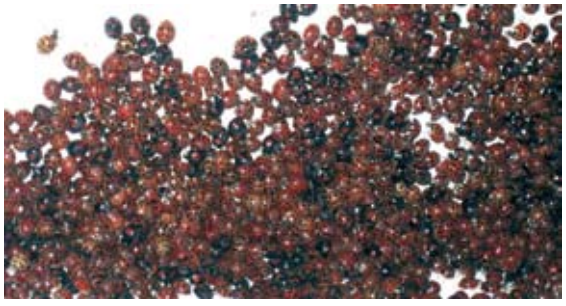
You can find Helen's survey at www.ladybird-survey.org.

Over the last century there has been a dramatic increase in the movement of so called alien species around the world as a consequence of international trade and travel. Invasive alien species, alongside climate change and habitat destruction, are considered to be one of the main drivers of biodiversity loss. Helen Roy asks: what are alien species and what threats do they pose?

Alien (or non-native) species are ones which are introduced by humans, intentionally or unintentionally, to a new region of the world. For example, the harlequin ladybird (Harmonia axyridis) is native to Asia but alien to Europe and America.

It was introduced to these continents by humans to control pest insects such as aphids (greenfly). Only ten percent of alien species will survive and reproduce in their new locality. If they do they are termed 'established'. The harlequin ladybird reproduces prolifically in Britain and so is an established alien. Only one percent of alien species will cause problems and this small but significant subset is termed 'invasive'. The harlequin ladybird poses a threat to biodiversity because it not only eats pest insects but also some the native species such as other ladybirds. See the Box for a definition of biodiversity.



Shirley Taylor

Harlequin ladybirds – prolific breeders

Alien impact

We live in a dynamic world. If we were to travel back in time and arrive in the Jurassic period the landscape would look very different to the one we experience today; the component species of Jurassic ecosystems are obviously not the same as recent times. So why does it matter if the species we see today comprise those we consider native and those we consider alien? To some extent it doesn't. Many of the alien arrivals are undoubtedly exquisite additions to our biodiversity. However, the rate of change is worrying.

The number of alien species arriving in countries around the world has escalated dramatically and is showing no signs of slowing. So in 1800 there were about 600 alien plant species in Europe, in 1900 about 1000 alien plant species and by 2000 a staggering 2500 alien plant species. Some consider the arrival of alien species a simple evolutionary process but this recent escalation is not on a time scale we would conventionally think of as evolution.

The invasive alien arrivals are only a small percentage of the total alien population but this not reflected in the magnitude of the problems they cause. Some species cause economic problems. Buddleia (butterfly bush) is costly to the railway network because it has to be cleared from the tracks. Rabbits are thought to cost the Australian economy $200 million a year. Others cause ecological problems. The Chinese mitten crab damages riverbanks and so threatens habitats. The large and aggressive signal crayfish not only out-competes native white-clawed crayfish but also carries a disease which has devastated white-clawed crayfish populations in Europe. Most invasive alien species cause both economic and ecological impacts.

Biodiversity

The official definition is:
Variability among living organisms from all sources, including, among other things, terrestrial, marine, and other aquatic ecosystems, and the ecological complexes of which they are part: this includes diversity within species, between species and of ecosystems

This means it is made up of

- **genetic diversity**
- **species diversity**
- **ecosystem diversity**

Looking at ladybirds

The harlequin ladybird is an invasive alien species that I know well. I jointly lead the UK Ladybird Survey, in collaboration with scientists from the University of Cambridge and Anglia Ruskin University, and have been monitoring the harlequin ladybird since it arrived in England in 2004 through an online public participation survey.

The survey has received more than 30,000 records of the harlequin ladybird, and particularly notable are the very large numbers of the beetle which are commonly reported in the autumn each

year, when this species enters buildings to locate suitable overwintering sites. From the data we have received we have calculated that the harlequin ladybird has spread at a staggering 100 km per year. We also know it has up to three generations a year in Britain (many native ladybird species have only one generation per year).

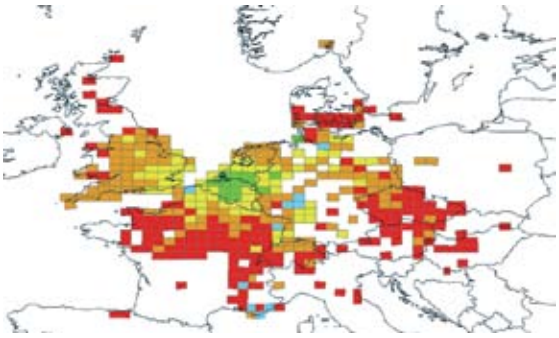
> Invading ladybirds breed up ecological storm for UK species
> *Guardian, 30th June 2009*

> **Harlequin ladybird threat to 1000 species**
> *Daily Mirror, 30th June 2009*

> **Beware the plague of smelly ladybirds**
> *Daily Express, 27th October 2009*

The harlequin ladybird has generated considerable press coverage. But what is the story behind these headlines?

The harlequin ladybird was introduced into continental Europe in the 1980s as a biological control agent of scale insects and aphids. It was never intentionally introduced into Britain, but arrived in the county of Essex in 2004. It remains abundant in the south east of England, but there are many records from central and northern England, Wales and also a few records from Scotland, as far north as Orkney.



We know that this species has the potential to threaten native biodiversity because we have carried out lots of laboratory experiments which show that the harlequin ladybird will eat many different types of insect, from other ladybirds to butterflies.

A harlequin ladybird larva eating eggs of noctuid moths.

Not much eats the harlequin in return! It is protected by an impressive cocktail of distasteful chemicals and its larval (immature) stage is very spiky. Laboratory studies give us a glimpse of potential problems and allow us to assess the risks but to get a picture of the extent of these problems in the wider countryside we have to head outside, away from the laboratory. We do this through carefully designed field surveys but the Ladybird Survey team can only look at a few habitats in a few locations across Britain. That is where you come in. People from all over Britain send in their ladybird observations using the on-line survey form on the Ladybird Survey website www.ladybird-survey.org or text "ladybird" to 83040 to complete the survey form. It doesn't take long.

So what is happening in the parks and gardens where you live?

- Are harlequin ladybirds very numerous or do you see lots of other ladybirds?
- Have you ever seen a harlequin ladybird eating something? What did it eat?
- Have you ever seen another predator or perhaps a parasite attacking the harlequin ladybird?

In the winter time, window frames and attics often harbour large groups of harlequin ladybirds and also 2-spot ladybirds. You could send in photos of the ladybirds you see in your house or school this winter. How many harlequins are residing in your house? How many 2-spots?

Harlequin ladybirds overwintering in the author's house alongside native 2-spot ladybirds.

Invasive aliens: the one-percent problem

In conclusion, non-native species are often thought of negatively but actually it is only one percent of them that are actually known to be problematic (although we could argue that the introduction of non-native species is part of the large impact humans are having on the Earth typified by climate change). The harlequin ladybird is reported as an invasive alien species with far reaching ecological impacts, and there is no doubt that it has the potential to threaten biodiversity. However, it is critical that we gather more evidence to enable us to have a thorough understanding of the extent of any effects this invasive alien species will have on other species. Records from people across the UK are essential in helping us to assess the threat of the harlequin ladybird to British wildlife.

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On the back page Helen introduces some other non-native species which have made their homes in the British Isles.

Meet the aliens

There are approximately 3500 non-native species in Britain but only a very small proportion (about 1%) cause ecological and economic problems and are therefore termed invasive alien species. The notable ones include:

NNSS

Grey squirrels have displaced native red squirrels through much of England and Wales. They damage trees by gnawing young bark and are also predators of birds' eggs and chicks.

FERA

Citrus longhorn beetles have occurred sporadically in England since 2005. The immature larval stages of this beetle create tunnels in host trees through feeding and make trees susceptible to diseases and wind damage.

NNSS

Creeping water primrose is known from only a few British sites. It has been introduced to Europe as an ornamental and water garden plant but causes severe negative impacts because it out-competes native species and clogs waterways.

FERA

Chinese mitten crabs are large crabs that have characteristic dense mats of hair on their claws. They are very good predators and have large appetites and so compete with native species leading to impacts on fish populations and other aquatic species. Chinese mitten crabs burrow into river banks causing erosion and collapse of river banks.

NNSS

Muntjac are small deer which were introduced into Britain early in the twentieth century. They have become widespread because people have deliberately released them. Where muntjac deer occur in high numbers they cause damage to plants of conservation interest particularly in woodland.