

# InsideDiamond

News from the UK synchrotron Summer 2015



Pioneering Cancer  
Treatments

The Story of the Solar  
System

Super Smart Materials

**D**iamond Light Source is the UK's national synchrotron science facility. It's shaped like a huge ring, and works like a giant microscope. Diamond speeds up electrons to near light speeds, producing a light 10 billion times brighter than the sun. These bright beams are then directed off into laboratories known as 'beamlines'; here scientists use the light to study everything from viruses and vaccines to fossils and jet engines. Diamond is one of the most advanced scientific facilities in the world, and its pioneering capabilities are helping to keep the UK at the forefront of scientific research.

Inside Diamond brings you research highlights and thought-provoking insights, showcasing the wonders that lie within the walls of the synchrotron.

*Front cover image: An artistic representation of a dried droplet of human serum diluted with physiological water. The patterns are due to salt crystallisation and the natural coffee ring effect that occurs upon drying. Courtesy of University of Strathclyde and Universite de Reims Champagne-Ardenne.*



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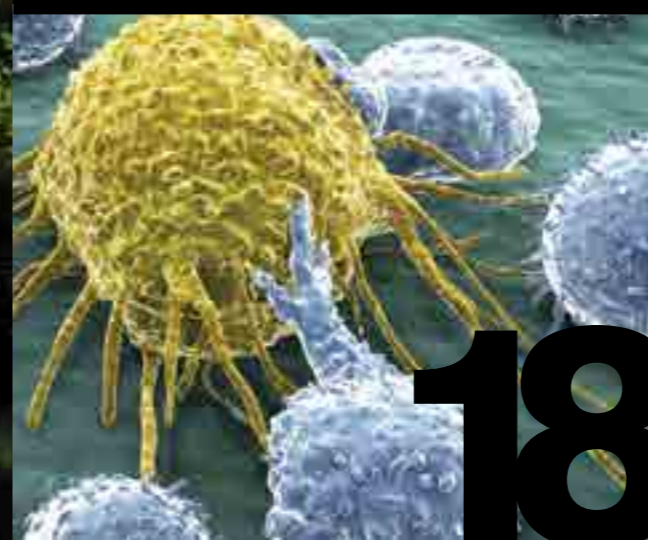
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# The Science of Pain

Physical suffering starts at the cellular level; but what can we do to stop it?

**T**he processes involved in pain are astonishingly complex. This intricacy means that combatting physical suffering can be a real challenge; but with so much on the line, it's important that we get it right.

For that reason, a lot of work goes into investigating the science of pain. We're already quite good at dealing with short term pain; however there is still a very serious problem with chronic pain. Whilst painkillers exist, we don't yet know precisely how they work; this means that we're not sure how to make them more effective or how to reduce side effects. It's become clear that the best way to create next-generation drugs is to understand biological systems at the atomic level. So instead of playing a game of trial and error, scientists now do a lot of research before they design pharmaceuticals so that they know exactly what biological component or system the new drug needs to target to be effective.

This new approach, known as 'targeted drug design', requires us to know as much as possible, right down to the atomic structure of the component we're targeting. When it comes to pain, advances in scientific technology are starting to make this level of knowledge more attainable. Scientists are continuing to scrutinise the process by which pain signals are generated and transferred from the site

of injury to the brain. With an in-depth knowledge of how this reaction takes place, it might be possible to design drugs that intervene at certain stages and prevent us from becoming conscious of discomfort.

A key element in all of this is the ion channel; this tiny cellular component looks as though it might be just the kind of target that scientists have been looking for. But to understand exactly why the channel is so important, it helps to know a bit about what pain actually is and how it works.

Our experience of pain results from electrical signals being sent from our nerves to our brain. When our body meets with a painful sensation, it activates the nerves, which fire off charged particles called ions. These ions then enter into the nerve cells through a hole in their surface, and it's this microscopic hole that we refer to as the ion channel. Once through, the charged particles pass from one side of the cell membrane to the other, creating a charged current which then flows through the nerve cells. When charged with this current, the nerve cells are equipped to send electrical signals to the brain telling it that the body is in pain.

So this is why the ion channel is such a key piece of the puzzle, because it is here that the current is

generated to fire electrical signals to the brain. If scientists can find a way to close the channel and block the entry of charged particles into the cell membrane, they can then prevent electrical current being generated and stop those messages being sent on.

Until recently though, there was a problem: we didn't actually know that much about the structure of the ion channel. Prof Liz Carpenter and her team from the University of Oxford have changed all that. The group has been using four of Diamond's macromolecular crystallography beamlines – I02, I03, I04, and I24 – to study the channels. Although there are lots of channels, all responsible for processing different stimuli, Liz's group were particularly focussed on a channel called TREK-2 which is one of the channels that is strongly linked to the pain response.

Using X-ray crystallography, Liz and her team were able to get atomic images of the ion channel in both an open and closed position. They were even able to capture an image of the channel with Prozac bound to it. Prozac is an antidepressant and is not designed to interact with this protein, so it binds very weakly.

But by chemically modifying the drug, the team could potentially improve binding and blocking of the channel, thus opening up new avenues for the design of next-generation painkillers.

This is an exciting moment for research into pain and pain visualisation. Thanks to Diamond's bright beams and the bright minds behind them, we now have an atomic picture of how this ion channel is structured. That brings us one giant leap closer towards developing drugs that can hook into the nooks and crannies of the channel and keep it firmly closed.

But Liz and the team aren't done yet; they now want to move on to decoding other ion channels, some of which are responsible for migraine and a host of genetic diseases. It seems that these tiny cellular components have a big impact on our lives, helping to determine how we sense the world around us. The work of Liz and her team provides a vital framework that scientists can build on. Because of them, we know what the target looks like; now we just need to take aim and fire.

# Stardust and the Story of the Solar System

Using traces of ancient comet to explore the history of the solar system

**S**pace: the final frontier – never were truer words spoken. We have currently explored less than 0.01% of the universe; in fact, it's much less than that. We've actually explored about as close to zero percent as it's possible to get. With so much left to discover, space is likely to remain a mystery for quite some time. But with the support of technological advances, scientists are making real progress, particularly when it comes to what planetary scientists regard as remainders from the 'building blocks of the solar system' – comets.

Composed primarily of ice and dust, comets are billions of years old. Preserved within the ice are believed to be the materials that the solar system formed from. Some theorists even believe that comets may have been responsible for bringing water to Earth. That's why scientists are so keen to study them up close,

because comets could reveal extraordinary insights into the origins of the solar system and life itself.

In late 2014, the Rosetta Mission successfully landed a probe on the surface of a comet named 67P/Churyumov-Gerasimenko. They were looking to analyse changes to the comet's material composition as it travelled through the solar system. The mission captured the imagination of the world, and drew international attention to the ways in which comets might provide a window onto the origins of the universe.

Back on Earth, Diamond was being used to study comet samples gathered in another NASA mission: Stardust. Launched in 1998, the sample gathering mission flew directly behind a comet called Wild2, trapping particles of the comet's coma – the envelope around the nucleus of the comet – inside an aerogel

package. The samples were then returned to Earth in 2006, to the delight of experts like Prof John Bridges and his team at the University of Leicester, who set about trying to unravel the mysteries they contained.

In 2008, John visited Diamond to examine the comet samples. John's experiments yielded some important insights into the composition, but he didn't find direct evidence for the action of water on the comet.

During the six years that followed, technology shot forward, and so John returned to Diamond in 2014 to analyse Wild2 samples newly harvested from the aerogel collector, exploiting the world-leading set up on one of Diamond's spectroscopy beamlines, I18. Using X-ray diffraction and X-ray absorption, the University of Leicester team discovered the mineral magnetite. Magnetite is formed from the reaction between iron magnesium silicates and water, so the discovery of this mineral showed that the comet had once contained water.

What's more, the nature of the comet suggested that it was formed billions of years ago in the outer solar system, beyond Neptune. This makes the existence of water on the comet even more of a surprise; you might expect liquid water to be present in the inner solar system, but not in the cold outer solar system.

John's work has provided the space science community with entirely new information about this far out area of the cosmos, and the discovery of the effects of water on this ancient comet is helping to change our understanding of the early solar system. But the research doesn't stop there; John's next step is to study meteorites – fragments of Mars or an asteroid that have fallen to Earth. This will provide new perspectives on the evolution of asteroids and the planets.

John highlights why he's so keen to expand his research:

*“There's just so much more left to discover, and the technology is now there to help us push forward with space science.”*

He continues: “We really need Diamond for this sort of work; the intense beams allow us to see far more in our samples than we otherwise could. Sample return missions from a comet, an asteroid, and in future years from more asteroids, Phobos, the Moon, and ultimately Mars mean that Diamond can have a crucial role in this field of scientific exploration. And that's why this field is so exciting; because it really is the case that the more we look, the more we'll find.”

When it comes to space science, the research will never be finished. Each breakthrough inches us towards a greater understanding of the cosmos, but it also opens up new questions and avenues for enquiry. We still only understand an infinitesimal portion of the world around us, but from a scientist's perspective that's no bad thing; after all, the universe could be infinite, but that also means that the possibilities for exploration are endless.



Stardust - An image of magnetite tracks within samples of comet retrieved on the Stardust mission. Courtesy of John Bridges, University of Leicester

Nanoparticle treatments could prove a powerful new force against cancer

# Nanomedical Cancer Innovations

**N**anomedicine is going to be big; really big. This rapidly emerging field of research is likely to have a massive impact on 21<sup>st</sup> century healthcare. Some scientists even compare it to the Industrial Revolution in terms of the effect it's expected to have. Billions of dollars are pumped into this field every year, and that investment is beginning to pay off as the first nanomedicines start to hit the shelves. Meanwhile, scientists are busy at work trying to uncover more about nanoparticles and how they could be used to address some of the greatest challenges of modern medicine; and one of the most formidable of these challenges is cancer.

About the same size as most natural biological molecules, nanoparticles have a number of qualities that make them excellent medical devices. They're very small, which means that they can pass easily through the body to the site of interest. What's more, their size, shape, and composition can all be adapted to suit different environments and purposes; this means that nanomedicine is extremely useful, particularly when it comes to cancer, where non-invasive, adaptable therapies are particularly important.

There are many ways that nanoparticles could prove a useful weapon in the fight against cancer. The particles could be used to carry drugs directly through to cancerous areas of the body, allowing stronger concentrations and smaller amounts of drugs to be administered. Nanoparticles might also be used as a contrast material to help identify tumours quicker, or as a form of thermal therapy, conducting heat so as to destroy unhealthy tissue.

Work currently being carried out at Diamond focusses on one area of nanoparticle cancer therapy that looks especially promising: using the particles to enhance the effectiveness of existing radiation treatments. Radiotherapy is a commonly used technique for combatting cancer, but there are some significant pitfalls.

Radiotherapy works by exposing the patient to radiation in the form of photons. The photons damage cancerous cells and can kill a tumour, but they also have a very narrow therapeutic window; this means that the amount of radiation needed to destroy the cancer can be very close to, if not more than, the amount that also kills lots of healthy cells. That's why patients often start feeling really unwell, and if a patient needs more radiation than can safely be administered without killing too many healthy cells, then radiotherapy ceases to be an option.

But nanoparticles could help to change this situation. They react intensely to photons, damaging surrounding cells; this means that they could enhance and better target radiation treatments so that much less exposure has a greater effect. This approach has an added advantage because the facilities are already in place. Doctors would simply need to introduce nanoparticles to the site of the tumour prior to beginning radiation treatment. This small addition to the current process could dramatically improve the effectiveness of radiotherapy.

More work is needed to bring this research into a clinical setting, and the first step towards developing effective nanoparticle cancer therapies is to work out how exactly they kill tumours. Using Diamond's I15 and B16 beamlines, Dr Fred Currell and his team from Queen's University Belfast have determined that the process begins when photons from the radiation treatment knock electrons off of the atoms inside the nanoparticles; a chain reaction then causes many other electrons to leave the atom, resulting in a release of energy that destroys surrounding cells. This makes the radiation treatment much more localised and much more effective.

Radiation treatments also cause a chemical reaction that transforms water in the body into a more toxic component called hydroxyl (OH). It is well known that OH is responsible for about 70% of DNA damage, and hence cancer cell death, in conventional radiotherapy.

The addition of nanoparticles could potentially increase the amount of OH produced in a localised area, increasing the effectiveness of the radiation.

Diamond enables the scientists to visualise both of these processes taking place. What's more, the synchrotron allows the team to adjust the energy of the photons being emitted; this means that they can expose nanoparticles to photons carrying different energies, and observe how the behaviour of the particles changes. The team's goal is to identify mechanisms at work which will in turn indicate the perfect size and composition of nanoparticles.

But this is no simple feat. There are many different kinds of cancer and the type of nanoparticle and radiation dose that tumours respond to is different depending on the variety of cancer you're working with. Fred and his team are currently focussing on breast, brain, and prostate cancer, but they hope to eventually create therapies for a wide variety of different cancers.

Fred observes why I15 and B16 are so useful in this work: "Diamond gives us something we can get only at a synchrotron. By using the machine to precisely manipulate the energy that hits the nanoparticles, I can turn on and off certain processes, test hypotheses and, ultimately, point the way to developing more effective therapies." He continues: "Modern medical research often starts with fundamental atomic processes and that's what we're doing here."

Nanoparticle cancer treatments are already in clinical trials, but the work of Fred and his team could help to further improve the effectiveness of these next-generation therapies. Fred is well aware of what his research could mean for patients. He explains: "My daughter became ill some years ago. I was sitting in the hospital feeling very useless, but seeing amazing feats of science and technology saving her life. This got me thinking – 'you can contribute to this'."

And so Fred moved from studying fundamental physics to researching novel cancer treatments. "The science I was doing before was important and fascinating, but I suppose I just began to feel a sense of urgency with these issues. The skill set I'd developed from fundamental physics gave me a really useful perspective, and I think it's helped me to push forward some important discoveries about the way nanoparticles behave at the atomic level and how we can harness that behaviour as a cancer therapy." He continues:

*"If we get this right, it will help people for years to come, well beyond my lifetime."*

Fred concludes: "I think it's the idea that this research will go on to benefit our children's lives and their children too; that's the best thing for me. That makes everything completely worthwhile."

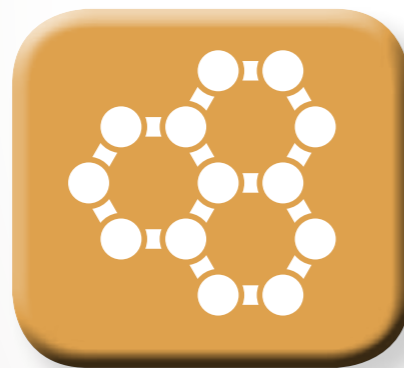
Fred and his team are part of one of the most important medical movements in history. Their work could redefine the way we approach cancer therapy and significantly improve the way those therapies impact on the lives of patients. There's still work to be done, but it looks as though nanoparticles have the potential to augment current cancer therapies and improve outcomes for patients; and for people like Fred who dedicate their lives to cancer research, that is most certainly a cause worth striving for.

# What does Diamond do? Materials



## Chemical Sponges

Metal organic frameworks (MOFs) are man-made chemical sponges that can trap certain materials while leaving others untouched. Researchers at Diamond are trying to learn more about MOFs so that we can use them for carbon capture and hydrogen storage, as well as in catalysis and drug delivery.



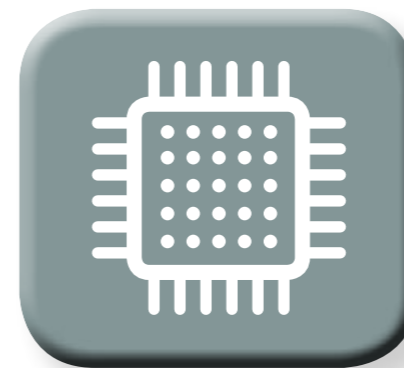
## Graphene 2.0

Scientists at Diamond have uncovered the properties of a new material which could revolutionise consumer technology. The super-material is a hybrid of graphene and something called a 'topological insulator', but unlike graphene it is three dimensional, making it easier to use. The new material carries huge amounts of information and could soon lead to gadgets that are smaller, quicker, and less power hungry.



## Photovoltaics

Photovoltaic materials are the driving force behind solar power; they use photons emitted by the sun to excite electrons in the material, creating electrical current. Research at Diamond is looking at making these materials even more effective by manipulating their components and structure. From reordering nanocrystals in the materials, to investigating solar cells made from organic matter, scientists at Diamond are driving forward solar technology with ever more advanced photovoltaic materials.



## Superconductors

Superconducting materials have the incredible capability of being able to transmit an electrical current that flows forever so long as they are cooled to freezing cold temperatures. They can create extremely powerful electronic circuits without ever needing to be topped up, and they're already used in magnetic Maglev trains, electric power lines, MRI machines, and synchrotrons! Researchers at Diamond are now trying to find ways to create superconducting materials at room temperature; this could vastly broaden their applications, making superconductors a widely available source of power.



## Super Strong Welds

In welding, work-pieces are melted to form a pool of metal that cools and solidifies into a joint. Welds hold together our bridges, buildings, ships, planes, pipelines, and reactor vessels, so we want them to be faultless. Scientists at Diamond are exploring how welds form inside the weld pool at the atomic level; they want to develop improved welds that are even stronger and more durable, leading to safer and longer-lasting structures.



## Radioactive Waste Storage

The issue of radioactive waste storage is a pressing challenge for governments around the world. Scientists are using Diamond to study strong and durable materials capable of storing this waste as it decays over tens of thousands of years.

# From Accident to Design

## A short history of life, death, and drug discovery

**The history of drug discovery is woven into our everyday lives. Whenever we use painkillers, antibiotics, anaesthetic, or vaccines, we are benefiting from a string of incredible accomplishments. Over the past 250 years, pioneering men and women have researched and developed drugs that have altered the course of human history and saved billions of lives. This work continues today and, with the help of advanced technology, scientists are developing new ways of creating drugs based on our in-depth understanding of chemical and biological processes. Their work builds on a legacy of accident, discovery, and design that has shaped the world as we know it.**

The first written documentation of any kind of medicine appears in around 3000 BC. Records suggest that the ancient Sumerians, living in what is now Iraq, brought the world arithmetic, domesticated agriculture, and early astronomy; what's more, they may have introduced the use of herbs to treat medical ailments.

The early Greeks, Chinese, Egyptians, and Romans all incorporated animal or plant-based drugs into their civilisations. But this folk medicine would usually be administered by a sage or religious icon, and treatments would often incorporate spiritual elements. The drugs themselves would have had an effect, but this would have been much less pronounced because the active ingredients were diluted by other elements in the natural product.

These drugs were developed by chance, and knowledge of them was spread between different civilisations and continents by traders and travellers. By the renaissance period, great minds were turning their attention to medicine, and scientific thought was being applied to the concept of medicinal drugs. But still no scientific, systematically-tested drugs existed. This state of affairs remained right up until the end of the 18<sup>th</sup> century, when Edward Jenner made a discovery that forever altered human history and heralded the birth of modern medicine.

During the 18<sup>th</sup> century, vast numbers of people in Europe were dying from smallpox epidemics. Estimates suggest that 400,000 people were killed each year in Europe by the disease, which was fatal in

20-60% of adult cases. In 1796, Edward Jenner was a medical scientist working in England at a time when smallpox was killing huge swathes of the population. He was intrigued by the fact that milkmaids somehow seemed immune to the disease, and thought it might have something to do with their encounters with another virus: cowpox – a much less severe disease that rarely caused anything more than blisters and a mild fever.

Jenner expected that exposure to cowpox could make individuals immune to smallpox. Whilst this would never happen today, he was so sure of his theory that he injected his gardener's son with cowpox, resulting in a mild infection. He then exposed the boy to a small sample of smallpox; thankfully the child remained unharmed. Despite using methods that would be unthinkable today, Jenner had successfully proved the efficacy of vaccination: using a safe substance to induce immunity to a more dangerous one. In 1979, the WHO declared smallpox eradicated, and a host of other infections are now far less prevalent thanks to his vaccine research. Indeed, Jenner's work is thought to have saved more lives than the work of any other human in history.

Vaccination was discovered at the close of the 18<sup>th</sup> century; in the one hundred years that followed, scientists would uncover more and more about the nature of disease, laying the foundations for modern drug discovery. Between 1860 and 1864, Louis Pasteur's investigations into germ theory uncovered how microorganisms spread and contamination occurs, leading to the development of the first vaccines for rabies and anthrax. About 15 years later, German physician Robert Koch discovered that diseases could be transmitted by bacteria. His work pioneered the fields of bacteriology and microbiology, revealing that infection begins at a very small level in the human body.

However, whilst more was known about the nature of disease and the impact of chemicals on the body, very few actual drugs existed by the mid-1800's. Throughout the latter part of the century, scientists began exploring how common natural remedies worked. The first pharmacological department was set up by Rudolf Buchheim at the Estonian University

of Dorpat in 1847; there they tried to determine the chemical and biological processes by which these early drugs produced their effects, and scientists began trying to identify and isolate key components.

By the turn of the 20<sup>th</sup> century, the pharmaceutical industry – previously nothing more than a distributor of botanical remedies – began engaging in research. The industry started looking at purifying chemicals in natural agents and combining different chemicals to create compounds with interesting effects. Over the one hundred years that followed, scientists' understanding of key chemical agents grew and the drive to synthesise more effective drugs really took off.

The first decades of the 20<sup>th</sup> century were an era of trial and error; researchers made minor chemical changes to the composition and structure of drugs, and then tested the impact of these changes to determine the most effective compound. By the 1930's, this work had resulted in the development of epinephrine for asthma and congestion, phenobarbital for epilepsy, and arsphenamine for the treatment of syphilis.

But perhaps the biggest achievement of 20<sup>th</sup> century drug discovery came in 1928, when Alexander Fleming returned to his lab after a holiday to find that a strange mould had grown on his samples of staphylococcus. The bacterium, which causes a wide variety of diseases including food poisoning, was being eaten away by the mould. This discovery laid the foundations for a biomedical revolution, for Fleming had inadvertently discovered penicillin. The drug was researched and mass produced by Howard Florey and Ernst Boris Chain and, by the 1940's, it was in regular use to treat bacterial infection. Penicillin saved millions of lives in World War Two and, along with the string of other antibiotics that followed, it has transformed humankind's relationship with disease, making once fatal ailments far more manageable.

By the mid-20<sup>th</sup> century, scientists were using groundbreaking new methods to uncover the structure of drugs and the diseases they targeted. Using an advanced technique called crystallography, scientists were able to use X-rays and diffraction to determine the atomic framework of matter. This was an extremely slow process – it took Dorothy Hodgkin

35 years to work out the structure of insulin. But in this way, determined scientists elucidated the exact structure of the biological components involved in drug interactions. This technique is still in use today, and provides the foundation for modern drug design.

Technology advances towards the end of the 20<sup>th</sup> century had a tangible impact on the pace of new drug discovery. In the 1980's, computational advances allowed scientists to use technical algorithms to predict the success of drugs prior to development. Improvements to robotics in the 1990's saw the semi-automation of drug discovery, so that thousands of different chemical compounds could be tested in a short space of time.

And that brings us right up to the present day. Modern drug design rests on this extensive history of research and discovery, and we've come a long way. Today, scientists use powerful machines like Diamond to determine the atomic structure of key biological and chemical components. The structural work on insulin that took Hodgkin 35 years could now be done at Diamond in a single hour. These capabilities are allowing scientists to work out the exact shape of receptors on our bodies' cells and on disease cells, so as to design drugs that slot perfectly into place. This is leading to drugs that have fewer side effects – because they act on nothing except the intended target – and that are much more effective. This approach to drug discovery is known as rational drug design, and work at Diamond has already contributed to research into potential new antibiotics, a polio vaccine, and novel treatments for cancer, HIV, and other prevalent diseases.

The world we know today is undoubtedly safer for the work of medical scientists throughout history. These pioneers helped to create drugs that have since saved countless lives and improved living conditions for people around the world. Drug discovery continues today, supported by advanced technology and facilities, and whilst it may be a challenging and relentless task, each small step adds to this legacy of knowledge, improving the lives of all those who follow after us.

# Extreme Science

## Exploring nature's most brutal environments

**S**ometimes science means taking things to the edge, and nowhere is that more the case than in extreme conditions research. Scientists in this field explore the impact of nature's most intense environments in order to learn more about the planet, the solar system, and the world around us.

But to safely study environments that are completely inaccessible to human beings, like Earth's mantle and outer space, scientists have to mimic some very extreme conditions; and extreme means extreme – we're talking about pressures that could crush any life forms instantly, and temperatures that are as hot as the sun's surface. To create that sort of environment in a controlled scientific setting, you need something special, something like I15: Diamond's extreme conditions beamline.

On beamline I15, scientists can use specially designed pressure cells and powerful lasers to create extraordinary pressures and temperatures. To recreate extreme pressures, researchers can place their samples between two diamond anvils and then squeeze them together. Diamond is one of the strongest elements on Earth, and with enough force, the anvil cell can exert pressures on the sample similar to those found at the Earth's centre. If it's heat you want, shining powerful laser light onto the compressed sample can heat it to several thousands of degrees. I15 allows scientists to see the impact of these conditions at the atomic level, capturing the way the arrangement of atoms changes and distorts. This allows scientists to gather information about extreme conditions environments that would be impossible to get virtually anywhere else.

If you want to know about extreme environments, Prof David Dobson can tell you a thing or two. He and his team from University College London are using I15 to

study conditions deep inside the Earth, where the lower mantle meets the core. This area of flowing mass, called the D double prime (D'') region, plays an important role in affecting life up on the surface of Earth. It forms a big part of the convection system that produces earthquakes and volcanoes. The consequences of these events can be devastating, so it's really important to understand exactly how this environment behaves.

David is using I15 to study a mineral called perovskite that makes up 80% of the Earth's mantle. The arrangement of the atoms in the perovskite crystal structure changes under extreme pressure, transforming into post-perovskite and then back again as the pressure lowers. David is using I15 to put perovskite crystals under extreme pressure and examining the atomic changes that take place. He's looking at how pressure alters the mineral's texture and what this can tell us about the way in which the mantle flows.

David highlights why this research is so important:

*“The entire natural history of the surface of the Earth has been driven by mantle convection. It's created our atmosphere, our waters, everything.”*

He continues: “The interior controls the surface conditions, and that's why it's so important to understand what's going on down there. It's all interrelated, and the more we understand about the centre of the Earth, the more we understand about the world we experience around us.”

It's not just conditions on Earth that I15 can recreate; some users on the beamline want to study environments that are literally out of this world. Dr Ross Howie is the team leader for a University of Edinburgh research project exploring the conditions on two of Saturn's icy moons, Dione and Rhea, which are freezing masses of ice, surrounded by a weak oxygen atmosphere. Ross is using I15 to explore the interaction between oxygen and water on the planet and the clues that this provides about the moons' brutal environments and whether life could ever exist there.

Ross also uses a diamond anvil cell to recreate the pressure levels within Dione and Rhea. This device is able to create enough pressure on the liquid water and oxygen to force them to chemically react and form a solid, known as a clathrate hydrate. It is this material that may exist within the icy mass of the moons. Ross then uses I15 to determine the atomic structure of this material. In this way, he can uncover complex information about the composition of celestial objects from hundreds of millions of miles away.

From the centre of the Earth to outer space, I15 recreates environments that humans could never otherwise access. The Extreme Conditions beamline enables users to explore the behaviour of materials under extreme circumstances in astonishing atomic detail. In this way, it affords scientists the opportunity to work with even the most hostile conditions in the attempt to make the unknown known.



# Diamond Snapshots

## Meet Our Users

Matthew Baker, Senior Lecturer at the Department of Pure and Applied Chemistry at the University of Strathclyde (@ChemistyBaker)



Matthew Baker

### 1 What are you studying at Diamond?

We are trying to develop accurate disease diagnostics using serum samples and infrared spectroscopy. Serum is the carrier of biochemicals – like hormones and other chemical messengers – around the human body, and infrared is an easy to use method that can quickly analyse any biochemical differences between different serum samples.

### 2 Why does this research require synchrotron light?

Our aim is to develop hand held analysers that doctors can use to diagnose patients in the clinic or at the hospital bed. But before that we need to understand what is occurring when we process the serum; synchrotron light enables us to look at smaller regions and analyse biochemicals that may be present at lower serum concentrations.

### 4 What advice would you give to young people who are interested in a career in science?

Stick to it. Science is great! I often get adults and mates saying that they didn't know chemistry was this interesting when they were at school but now they wish they had carried on. So keep on going, and these basics will open up a hugely interesting and creative world.

### 3 What do you hope your work will achieve?

We want to create a robust preparation technique and make it possible to use serum to diagnose lots of different diseases when you visit your GP or consultant. This could provide accurate early diagnosis of disease, and treatments are generally much more effective when disease is caught at an early stage.

### 5 If you hadn't been a scientist what else would you be?

I very nearly chose different careers at different stages leading up to my PhD, including aerobics instructor, chef, and paramedic!

## Scientist in the Spotlight

Emily Longhi, Senior Insertion Device Physicist at Diamond



Emily Longhi

### 1 How did you first become interested in science?

I can't really remember not being interested in science. I have always been curious about how things work, and I was always encouraged by the grownups around me to ask questions.

### 3 Do you have a scientific hero? Who and why?

Johannes Kepler: the ultimate data junkie. He spent years looking at hand recorded data about the position of planets until he finally found patterns and now he has laws of planetary motion named after him for his effort. And it was quite an effort to see that the square of one set of data was equal to the cube of another - in the 1600s with no calculator or spreadsheets!

### 2 Your key areas of expertise are physics and engineering. Why do you find these fields so fascinating?

I enjoy making things. I like the challenge of making and measuring very precisely. We build magnet arrays that need to be aligned to a few microns (thousandths of a millimetre) over a few metres. How well we do this makes our devices some of the brightest X-ray sources in the world. It's really satisfying to start by designing the magnets, and finish a couple of years later with seeing the first light on the beamline where the users can use it to do experiments.

### 4 What advice would you give to young people who are interested in a career in science?

Take as many different kinds of science and maths classes as you can. Try out coding and chemistry and biology even if you think you want to do physics or astronomy. Science is a way of thinking and working, but the details can make a huge difference to how much you enjoy it, so try as much as you can until you find something you like best.

### 5 If you hadn't been a scientist what else would you be?

I wanted to be a detective when I was growing up. Then I wanted to be a car mechanic when I was in my twenties, but I only wanted to work on antique cars, so I decided to do experimental physics instead. I build magnetic devices for a living so I've really ended up in a combination of physics and engineering.

# Cancer-Killing T-cells

Enhancing the body's own immune system to fight diseases like cancer and HIV

**F**orget your pals, your parents, or your partner; your immune system is the best friend you will ever have. Thanks to this collection of organs and processes, our bodies really are fortresses. We may still get sick, but we successfully fight off vast numbers of microbes and viruses every day. Yup, our immune system is pretty great, and right at the centre of this defensive force are T-cells, the white knights of the body.

T-cells are a type of white blood cell responsible for finding and destroying unwelcome cells. These incredible cells are covered in little fingers known as 'receptors', which allow them to identify anything out of the ordinary. All cells are covered in tiny proteins: long chains of amino acids all strung together. Proteins control a huge variety of functions inside the cells. But bacterial and viral proteins look very different from normal, healthy proteins. When the T-cell receptors come across cells infected with these invaders, they call in reinforcements and get other cells to come and help; then the army of T-cells latch on to the proteins and shoot out toxic granules that punch holes in the infected cell, neutralising the threat.

These little scrappers are extremely powerful; in fact, they can sometimes be too powerful. Autoimmune diseases like type 1 diabetes occur because T-cells wrongly attack healthy cells. In the case of diabetes, they destroy insulin-producing cells, leaving the body insulin-deficient. But there's a bright side; because they are so powerful, T-cells could be a major weapon against disease, particularly as a cancer therapy. That's why scientists are working hard to try and harness the potential of T-cells and make them usable as a medical treatment.

Two people who are at the forefront of this mission are Dr Pierre Rizkallah and Dr David Cole from Cardiff University. Pierre and David are using Diamond's macromolecular crystallography beamlines, I02, I03, I04, I04-1, and I24, to study the interaction between T-cells and cancer cells in an attempt to make super T-cells capable of eradicating cancer from the body.

There are many different types of T-cell, and a very small number of them are already capable of picking out and destroying cancerous cells. Unfortunately there aren't enough of the cancer-killing variety, and they're also not effective enough to always successfully destroy cancer. So Pierre and David are looking at ways of increasing the number of cancer-killing T-cells that the body produces.

Pierre describes the process of picking out those key T-cells from all of the other types of T-cell in the immune system: "It's a very small number that are actually effective against cancer, but if we can find that needle in the haystack and pick it out, then we can leave the haystack and concentrate on replicating the needle."

But it's not just a case of isolating the cancer-killing T-cells; Pierre and David also need to make them more effective at binding to the cancer cell proteins. This means manipulating the fingers on the outside of the T-cell so that they're better at hooking on to the cancerous proteins. To do this, they need to know the exact shape of the cancer cell proteins down to the individual atoms; they can then alter the shape of the T-cell fingers so that they latch perfectly on to the target proteins.

*A T-cell (green) interacting with a cancer cell (grey) via the T cell receptor.*

And this is where Diamond comes in. David comments: "That's the power of the synchrotron. We use it to identify the atomic structure of the target. We can then modify the T-cells and come back to Diamond to see close up the changed reaction between the modified T-cells and their target. Diamond is there the whole way through. Without that you're just fumbling in the dark. The synchrotron allows you to see what's really going on so that you can direct what you're doing to those molecules in the proper way instead of just taking guesses and using trial and error, which is what you would be doing otherwise."

Based on the research carried out at facilities like Diamond, we're now closer than ever to seeing T-cell therapy used on patients. In a medical setting, clinicians could take T-cells out of a patient's body, pinpoint the cancer-effective T-cells, mutate them to create stronger fingers, and then replicate the enhanced, cancer-killing variety before injecting them back into the patient's body, where they can begin destroying cancerous cells.

This form of cancer therapy has real advantages over existing treatments. Firstly, T-cell treatments are a form of 'personalised medicine', which means that they work around the genetic differences between individuals. Because we're all made slightly differently, existing cancer treatments work better on some people than others. But T-cells are something that we all have in common, and so the results of T-cell therapy would be much more consistent. What's more, because the T-cells are from the individual's own immune system, there's no risk of the body rejecting them.

But there's another key advantage of T-cell therapy over existing treatments: they are highly targeted to only destroy cancerous cells and nothing else. Existing treatments like chemotherapy destroy large numbers of healthy cells – that's why patients often lose their hair and feel nauseous. With T-cell treatment, there would

potentially be no collateral damage to healthy cells and thus no side-effects.

All cancer cells are different and so are the proteins on the outside of them. That means that there's still a lot of work that needs to be done to create different types of highly-effective T-cells for each cancer. But astonishing progress has already been made, and T-cell cancer therapies are already in clinical trials.

"I really believe it's going to be available in the next 10 years." David comments. "It's already happening now. There's a lot of investment from bio-tech companies in T-cell treatments." He comments:

*"We all know how powerful these cells are, and our ability to harness that power is increasing with the research we're doing at Diamond."*

Cancer is a highly complex group of diseases, and T-cells won't be a magic bullet, but they are likely to provide robust new options for patients undergoing cancer therapy. There's still work to be done, but in the meantime, T-cells will continue fending off the nasties that try and invade our bodies every day. So be grateful for these little warriors, going in to battle time after time as they tirelessly fight to keep us safe.

# Small Angle Scattering

**D**espite being a cutting-edge technique, the concepts behind scattering are actually fairly simple to grasp. Everything that we see is the result of light bouncing off objects. And if we use the right wavelength, then the light can scatter off much smaller elements within objects, so we can learn more about their microscopic structure. It's really quite straightforward, but scattering is a powerful technique and an essential tool for helping scientists to explore the hidden world that, for most of us, remains just out of sight.

## What is it?

We can't see cells, bacteria, and molecules with the naked eye because the wavelength of visible light is relatively large compared with these objects. Some basic principles: light moves like a wave, and so it only catches objects that fall within the path of the wave. If an object is smaller than the length of one wave then it gets lost.

X-ray photons and neutrons both have very short wavelengths, so they will scatter off very small objects, like molecules. The angles at which the light scatters can be very small – hence the name 'small angle scattering' (SAS); so scientists need powerful machines capable of both producing intense, well collimated forms of light and measuring very small changes in the direction of that light.

The angles may be small, but SAS experiments can uncover huge amounts of information. From determining the shape and density of molecules in a sample, to exploring the behaviour and chemical composition of materials, SAS can reveal a whole lot.

But that's not all; it's the samples SAS can study that make it really cool. The technique works well on 'disordered systems', where the arrangement of atoms is random. Other techniques involve freezing or modifying samples so that the atoms line up in an ordered way, but SAS doesn't need order to produce information.

This makes it very quick and easy to use – SAS doesn't require much in the way of sample preparation. It also means that it can be used to study some really interesting samples. Liquids, gels, and all sorts of other goopy stuff can all be studied with the technique. From mud to rubber, SAS allows scientists to get stuck in to all sorts of messy samples and still garner valuable structural information.

And if you weren't yet convinced, SAS has some other really interesting properties. It's usually non-destructive, so samples remain intact. It's also a great

all-rounder; useful in many fields, from archaeology to nanotechnology. And although it produces quite low-resolution images of the samples it targets, SAS can pick up more at once, so it's perfect for macromolecules or big complex systems. For what it offers in convenience, breadth, and unique insight, there's no doubt about it: SAS is pretty darn cool.

## The History

SAS has its origins in 1930's France. In the midst of the Great Depression, André Guinier was busy at work trying to determine the relationship between particles' size and the intensity with which they scatter light. The equation he came up with, known as Guinier's Law, opened up an entirely new way of studying the microscopic nature of matter.

SAS exploded onto the scene and, over the next 50 years, the technique grew as advancements in light-producing technology made it even more effective. But the biggest boost to SAS came towards the end of the 20<sup>th</sup> century. With the advent of powerful X-ray and neutron sources like synchrotrons and other particle accelerators, scientists had access to radiation that was much more powerful and detectors that could pick up very subtle changes in particle direction. Better equipment created clearer scattering patterns, and these advancements led to what we have today: a vital tool for scientific research.


## X-ray SAS at Diamond

As X-rays are shone onto samples, the photons scatter clearly, even from very small elements in objects. That's why scattering experiments at the synchrotron are referred to as SAXS, or 'small angle X-ray scattering'. Diamond has many beamlines that support SAXS studies and two entire beamlines dedicated to these experiments. Each year, I22 and B21 welcome hundreds of scientists who are keen to use the powerful synchrotron light for SAXS.

At Diamond, the technique is currently being applied to a range of areas. Researchers are looking into advanced polymers that may help to create flexible solar cells that can be painted onto windows and glass. SAXS is also being used to explore the origins of life on Earth by investigating the possible mechanisms behind early cell formation on our planet.

Over the past 80 years, SAS has burgeoned into an invaluable tool for scientific enquiry. By exploiting the natural physical phenomena of light scattering, scientists continue to uncover hidden aspects of our world, allowing us to see more, go further, and explore the unknown.

## Hero from History



**Dorothy Hodgkin** was a pioneer of X-ray crystallography who worked out many important atomic structures, creating an entirely new scientific field: structural biology. Hodgkin's work on penicillin aided the ongoing development of antibiotics, whilst her research into insulin was a huge step forwards in understanding and treating diabetes. She was awarded the Nobel Prize in Chemistry in 1964 for work on Vitamin B12. Hodgkin's legacy lives on in the structural biology research that today takes place at facilities like Diamond.

## Harwell campus open days

On July 11th 2015, Harwell campus will open its doors to 10,000 visitors, who can explore a range of world-leading scientific facilities and see first-hand where some of the world's most pioneering research takes place. Here, people can meet the scientists and engineers who deliver the breakthroughs and discoveries that are shaping all of our lives in the 21<sup>st</sup> century. To register, visit [www.opendaysatharwell.org](http://www.opendaysatharwell.org)



### Did you know?

The Diamond storage ring isn't a circle; it's a 48 sided polygon known as a tetracontakaiioctagon

## Recommended viewing

The Harwell campus has been a scientific research centre since the 1940's, when it was used for nuclear research. This archive British Pathé footage shows the reaction of local villagers when the facility came to their area: [www.britishpathe.com/video/didcot-atom-village](http://www.britishpathe.com/video/didcot-atom-village)

Have memories or photographs of your own to share? Contact [Mary.Cruse@diamond.ac.uk](mailto:Mary.Cruse@diamond.ac.uk) with your stories of past life at Harwell.

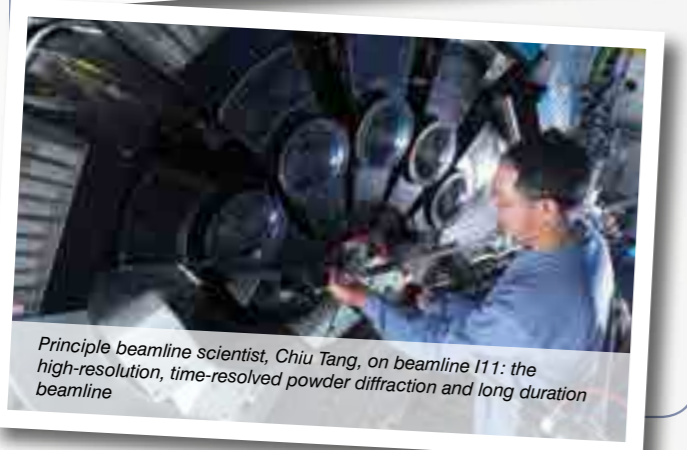
## Harwell Campus Heritage

Diamond sits on the Harwell campus in Oxfordshire, a world class science and innovation hub. But the site also has a fascinating past:

- 43-410AD**  
Under the Roman occupation, Harwell and the Ridgeway are used as a key road linking the south coast to the rest of Britain
- Stone Age**  
Ancient peoples settle on site, where they remain until the Iron Age
- 5-15th Century**  
Harwell becomes a prominent medieval trading route known as 'The Golden Mile'
- 18th Century**  
The site is used as a racehorse stables, breeding prize-winning steeds
- 1935**  
The RAF takes over the site and creates a base, from which pathfinders set off for D-day
- 1945**  
PM Clement Attlee announces plans to transform site into an atomic research establishment
- 1950's**  
Spy scandals as two site employees are revealed to be spies for Russia
- 1994**  
Harwell moves from being government labs to a campus housing multiple scientific organisations
- 2015**  
Harwell now hosts some 200 organisations, and over 5000 people work at this world-leading science and research hub.

## Diamond Captured

Diamond is one of the UK's most impressive structures, but here's a side of the synchrotron you wouldn't normally see.



### Research at Harwell has led to:

- Europe's first nuclear reactor
- Discovery of the structure of bucky balls
- Support for the Rosetta Mission
- The world's first all-transistorised computer
- Discovery of lyonisation: important to genetics
- A potential new vaccine for foot-and-mouth disease
- ...and much more



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