InsideDiamond

Science from the UK synchrotron Winter 2016

Next-Generation Nanotechnology

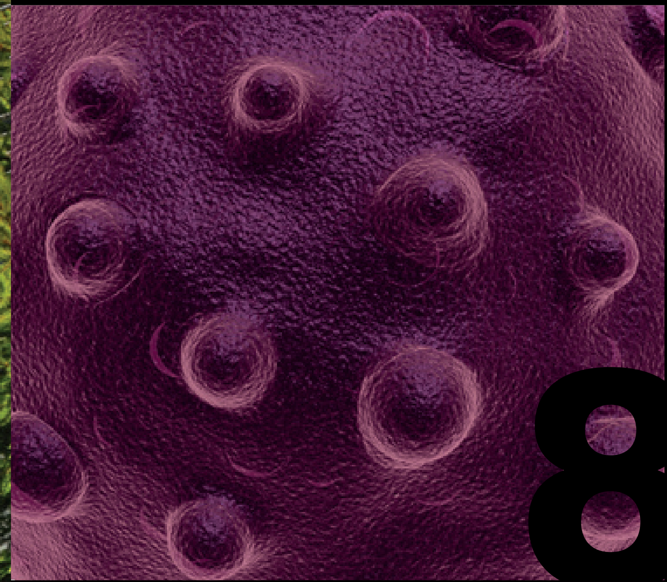
Bacterial Warfare

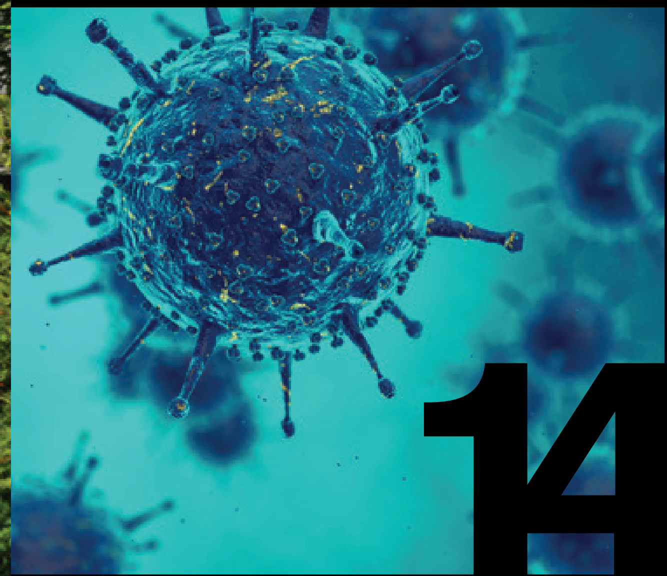
Heritage Science: Conserving History

Diamond 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: Light microscope image of crystals from a melt of an aspirin/phenacetin mixture, viewed with crossed polars. Courtesy of Spike Walker, Wellcome Images.





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Next-generation Nanotechnology

Spintronic devices will make technology faster, smaller, and smarter

Spintronic materials are the Holy Grail of nanotechnology. They have the potential to dramatically reduce the size of devices and improve their efficiency, creating the next generation of fast, powerful, and miniaturised technology. But we're not there yet. Scientists around the world are currently on the hunt for these special materials, looking for ways to make them usable in real-life conditions. At Diamond, scientists are joining the search for a perfect spintronic material with research that will help to shape the future of technology.

Moore's Law observes that the amount of processing power required by technology doubles about every two years. In the 1970s, a computer would have about 20,000 'transistors' – tiny devices that help to transfer data. These days, an iPhone 6 has two billion.

We're requiring more and more nanotech components to create our advanced devices, but we have a problem: more components require more space and more power. So we have two options: we can either reduce the size of these components, or we can make them more efficient.

In the past, we've been focussed on trying to bring down the size of technology components, but we've almost reached the limit for how small we can get them. And so fairly soon, we can expect to see devices getting bigger and hotter, as they eat up more energy to keep running. That's why scientists are looking to create transistors from new materials that use less power and transfer data more efficiently, allowing us to pack the same computing power into ever smaller devices.

Normal transistors work like tiny electronic switches. They transfer data and essentially enable all action to take place on devices: from opening up an app to making a call. But for transistors to work, they need to be exposed to a voltage.

If we can make these transistors out of a different class of materials – known as spintronic materials – it's possible to make them much more efficient. Instead of transferring information using electron charge, like regular transistors do, spintronic transistors could exploit another fundamental property of electrons: their spin. This would allow us to transfer data, not through charge, but by the flow of electrons with a specific spin, thus making spin-based transistors much more powerful than traditional ones.

Spintronics could allow future electronic devices to be faster and use less power without becoming bigger. We wouldn't need larger processors and massive batteries to get the same computing power and battery life out of laptops and mobile phones. We could also create devices that run for weeks or months on a single charge – no more having to plug in your phone every other day. With spintronic technology, the possibilities really are limitless, and learning how to exploit their potential could bring us into a new age of advanced computing power.

But to create transistors capable of this feat, we need to find the perfect material that can control electronic spin and also function in a real-life setting, at normal temperatures and pressures. Prototypes do exist, but this is a burgeoning field and no clear solution has yet been found. So scientists at Diamond are joining efforts to find this precious material and learn how to manipulate it.

Jonathon Riley is a joint PhD student between Diamond and the University of St Andrews. He's using Diamond's angle-resolved photoemission spectroscopy beamline, I05, to study spintronic materials. Here, Jonathon can probe these materials and investigate how electrons move around inside.

One of the samples Jonathon is studying is called tungsten diselenide, and it shows promise as a potential spintronic material. Using photoelectric techniques on one of Diamond's beamlines (I05), Jonathon shines X-rays generated by the synchrotron onto the tungsten diselenide samples, causing electrons to eject from the surface of the material. The ejected electrons retain a lot of their information and, by studying them, Jonathon can work out the complex pattern of how they were moving and the energies they had when they were inside the material.

Jonathon can also manipulate the electronic environment of the tungsten diselenide and record how the electron behaviour changes. In this way, he's able to find out more about the material and how it could be exploited for use in a spin-transistor.

But that's not all: in the future, Jonathon will scrutinise the behaviour of this material and others like it under different temperatures and chemical environments to ensure that it is workable under real-life conditions. With a deep understanding of how these materials behave, we will be in a better position to build a fully functioning spin-transistor.

Jonathon's research is part of a wider movement around the world to track down potential spintronic materials and, as Jonathon observes, this is very much a communal effort: "Scientists everywhere are really excited about the potential of spintronics, so it's little wonder that many groups are working on developing them.

"All this research is building up our understanding of these remarkable materials and bringing the age of spintronic technology closer."

He continues: "You never know when these things are going to happen, but new scientists are always joining the hunt. There's no doubt in my mind that we'll find the right material eventually."

Spintronics have the potential to revolutionise technology and completely redefine what devices can do. These materials are highly complex and making them usable will require more research and understanding. But every day science is bringing us closer to harnessing the power of spintronics and, with the combined efforts of bright minds around the world, finding that perfect substance is just a matter of time.

Heritage Science: Conserving History

How Diamond is helping to preserve Scotland's iconic historic buildings

History is all around us: and there are few more striking relics than the vast historic buildings that adorn ancient towns and cities in the UK and around the world. As of 2013, the UK tourism industry was estimated to be worth more than £125 billion. But work is needed to ensure the preservation of our cultural heritage – many of these iconic structures are at risk of being lost to time.

Over years of exposure, their basic materials become weakened, leading to deep structural damage. Uncovering the microscopic processes that lead to deterioration could help conservationists to develop a solution, but that's no easy feat. Sometimes the damage goes so deep that it's impossible to pick up on the surface. And so scientists are looking to Diamond to help ensure that the architectural legacy of the past lives on.

In the 1800s, Scottish workers were employed to quarry huge amounts of sandstone from the surrounding landscape. The attractive stone was a rich local resource and it was used to build some of Scotland's most recognisable buildings, bestowing the architecture of the country's towns and cities with a distinctive character that attracts visitors from far afield. But there was an issue with the sandstone that would only become apparent centuries afterwards. Hidden deep under the surface, there were millions of minute pores, and these tiny holes would later create big problems for conservationists.

A fairly absorbent material, sandstone sucks in moisture from the surrounding atmosphere. Small particles of salt are also absorbed, either from the sea air or from de-icing salts used to make paths accessible in winter. This water and salt mixture then gathers in the pores of the material, where it slowly dries out. As this drying process takes place, the salt particles multiply and crystallise, forming growing concentrations of crystals inside the stone. This is bad news for historic buildings; the pressure from inside can cause them to weaken and eventually crumble.

But if scientists can learn more about how and why this process takes place, it may be possible for them to counteract the sandstone deterioration and recommend suitable materials to help repair the damage that has already been done. Because this entire process takes place within the stone, scientists can't easily visualise it with standard lab equipment. That's where Diamond comes in – its bright beams are about 10,000 times more powerful than visible light microscopes, giving scientists exactly what they need: the ability to see beneath the surface.

Supported by the conservation charity, Historic Scotland, Callum Graham is a University of Glasgow PhD student leading the research into preserving Scotland's sandstone architecture. Callum is using Diamond to compare the differences between types of sandstones commonly used as replacements in damaged buildings: Locharbriggs and Cullalo sandstone, each quarried from different regions of Scotland.

Callum wants to explore differences in how the two stones respond to salt crystallisation damage. His aim is to find the perfect replacement stone to help remedy the architectural damage that has already occurred. To do this, Callum uses a technique more readily associated with hospitals than synchrotrons: computed tomography scanning, better known as CT scanning.

CT scanning is used to determine the density of a material. It works by exposing an object to X-rays and observing the amount of rays absorbed in different areas. This makes it medically useful in determining the site and shape of tumours or internal injuries. At Diamond, Callum uses the same technique to observe where pores exist within the Scottish sandstone and how salt crystals develop inside them.

This research has already yielded some important results. Using Diamond's Joint Engineering and Environmental Processes beamline (I12), Callum has been able to see inside the stone and view the salt crystallisation process taking place in real time, observing the damage as it occurs.

By scrutinising this process, Callum has discovered real differences in the way each stone distributes salt and moisture throughout the material. These differences are down to the stone's pore structure, which is influenced by how the stone was formed. For instance, Locharbriggs stone formed approximately 265 million years ago during the Permian period, when Scotland was an extremely arid, desert-like environment. Because of this, Locharbriggs is a very porous stone. Its many small pores can be found within distinct layers in the stone. These layers prevent water from spreading so far, keeping it confined to smaller pores in the material.

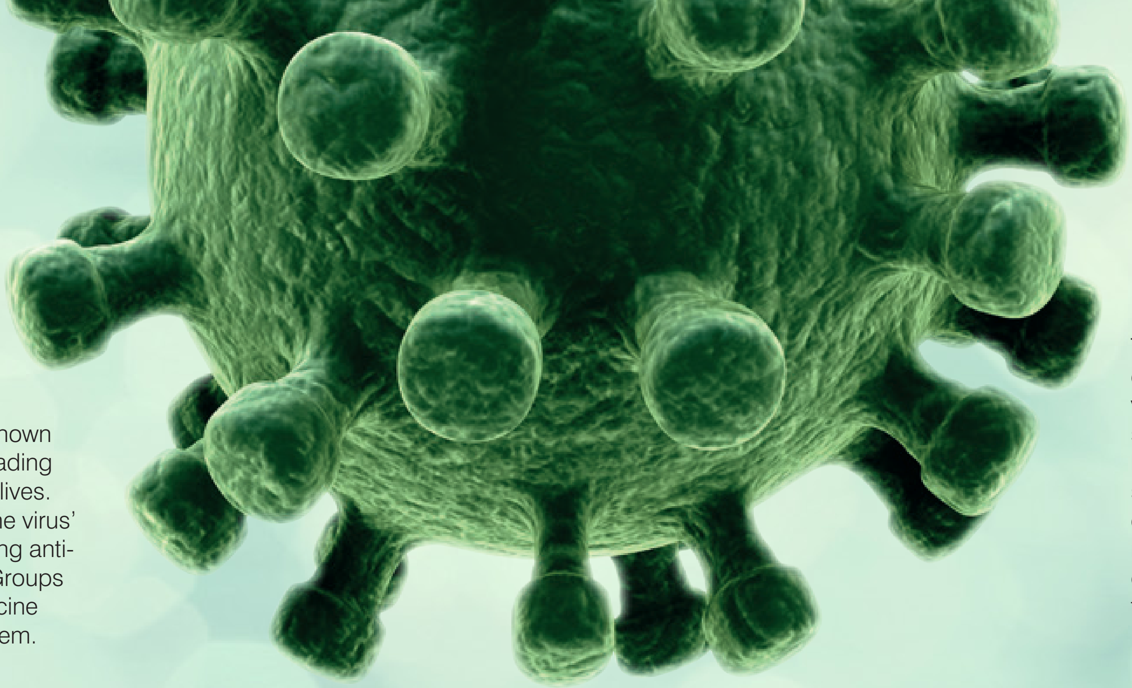
Callum also found that smaller pores are filled with moisture before larger pores, with crystallisation occurring in these pores more quickly than previously thought. This is particularly important because it means that just a small amount of moisture and salt can rapidly cause permanent damage to the stone. But there is an upside: with this information, Callum can recommend the best response from authorities to help preserve Scotland's historic buildings. His research will help to identify types of replacement sandstone that are more resistant to damage, and will ensure that councils develop a better formula for de-icing salts that don't have the same sort of detrimental impact.

Observing the impact of his work, Callum comments: "A historic building is so much more than bricks and mortar. It is a relic of our past and a reminder of where we have come from. To keep our cultural heritage alive, we need to understand more about the microscopic processes taking place way below the surface, and this depth of insight is only possible using the facilities based at a synchrotron."

He continues: "I'm keen to share our experiences so that other people can appreciate how powerful the facilities at Diamond are, and how they are helping to solve real-world problems that are of great value to our national heritage."

Our history is important. It links us back to our past, and we have a duty to preserve relics of our national heritage. Although they may seem like unlikely bedfellows, science plays a vital role in safeguarding history through the preservation of the monuments and artefacts from our collective past. And this is vital work. The lasting impact of Callum's research will be the preservation of his ancestors' architectural triumphs so that they can live on, to be enjoyed by future generations for years to come.

"A historic building is so much more than bricks and mortar. It is a relic of our past and a reminder of where we have come from."



HIV>

Human immunodeficiency virus targets the immune system, making hosts susceptible to infections and disease. HIV is currently incurable, but the use of drugs known as anti-retrovirals can prevent the virus spreading and allow HIV-positive people to live normal lives. Scientists are using Diamond to scrutinise the virus' molecular machinery so as to improve existing anti-retrovirals and counteract drug resistance. Groups are also exploring ways of developing a vaccine against HIV using T cells in the immune system.

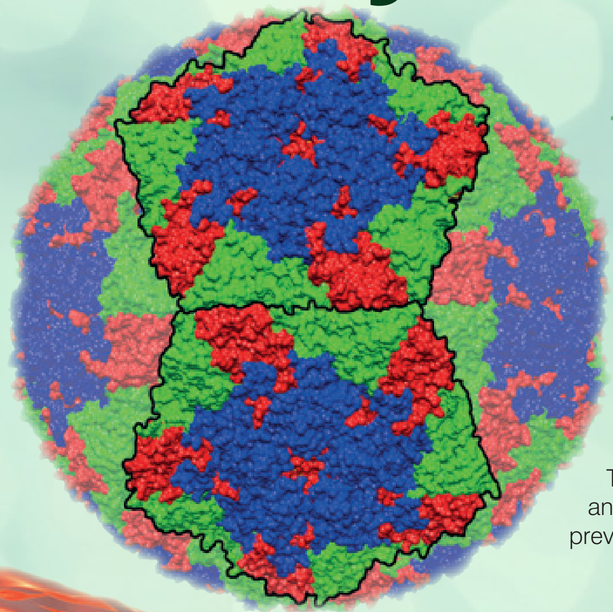
Ebola>

The 2014-15 Ebola outbreak in West Africa is estimated to have killed over 11,000 people. The virus, which leads to fever, muscular pain, and sometimes internal bleeding, is spread through bodily fluids. Scientists are using Diamond to study the viral receptor proteins involved in cell entry as well as the enzymes involved in the replication and spread of Ebola with hopes of designing anti-viral drugs and vaccines against the disease.

Rogues Gallery: Viruses

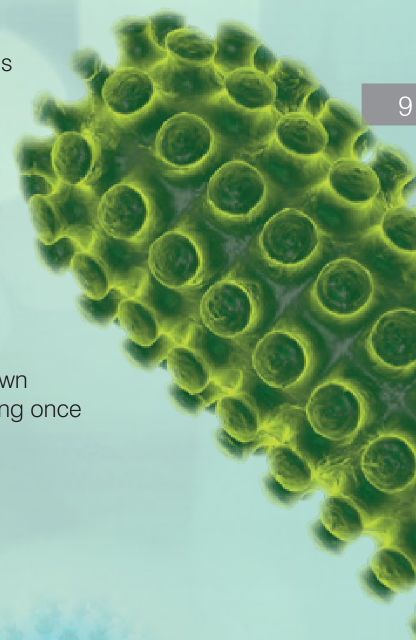
<Hep A

Despite an effective vaccine, Hep A continues to infect 1.4 million people each year. It causes infection of the liver, and symptoms can include diarrhoea, vomiting, yellow skin, fever, and abdominal pain. Scientists at Diamond have deciphered the atomic structure of Hep A, research that could contribute to new vaccines and anti-viral drugs that work better and are easier to produce and store.



<FMDV

Foot-and mouth disease virus is a devastating disease of cattle that is endemic in much of the world. The 2001 outbreak in the UK led to the culling of millions of animals at an estimated cost of £8 billion. Scientists have now used Diamond to develop a new vaccine for the disease that is safer and easier to use. Now in trials, the vaccine mimics the atomic structure of the virus but contains no RNA. This means that it induces immunity without any risk of infection, a vital characteristic for preventing viral spread in livestock.

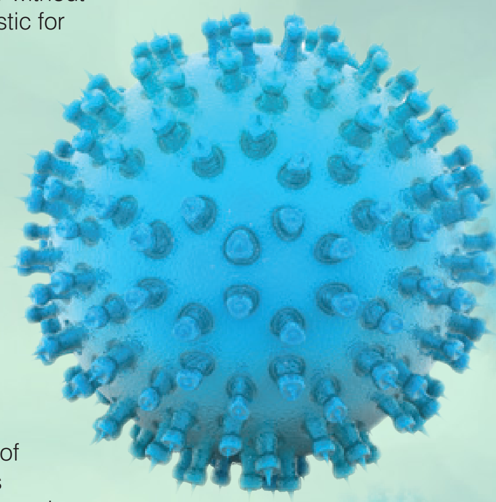


Rabies>

A virus that infects both humans and animals, rabies causes inflammation of the brain leading to anxiety, paranoia, aggression, and confusion. The virus has an extremely high mortality rate once symptoms appear. At Diamond, scientists are studying the processes involved in viral replication in an effort to shut them down and prevent rabies spreading once infection has occurred.

Polio>

Up until the mid-1950s, when an effective vaccine came to market, Polio was a devastating disease that affected hundreds of thousands of people worldwide, mostly children. Although it has been wiped out in the west, the virus remains endemic in Nigeria, Pakistan, and Afghanistan. Scientists at Diamond are working on creating a next-generation vaccine that contains no viral RNA – this will make it safer to produce and easier to transport and store in hot climates. If it is successful, a synthetic vaccine could be instrumental in eradicating polio, once and for all.



Herpes>

There is no available vaccine for herpes and, once infected, there is currently no cure. The virus causes blisters and ulcers, and in some cases fever, muscle pains, swollen lymph nodes, and headache. Scientists using Diamond have discovered a protein complex at the heart of cellular transport networks used by herpes to travel to the nerve cells, from where it spreads. This understanding could support the development of new therapies for the disease that involve regulating these transport networks to prevent the spread of the virus.

What does Diamond do? Engineering

Getting a reaction

Catalysis is at the heart of the chemical industry, speeding up reactions and helping to create useful substances. Catalysts are used in everything from cars, to pharmaceuticals, to manufacturing; and the need to understand catalysis at the atomic level is driven by both economic and environmental concerns. Scientists use Diamond to study catalysts in great detail and under real-life conditions in order to get the structural information they need to formulate improved versions that are stronger, cheaper, and more effective.

Navigating drone technology

Scientists are using Diamond to study the eyes of orchid bees in an attempt to determine how they navigate dense tropical forests. The orchid bees have a small brain the size of a sesame seed, but five eyes, two of which have thousands of lenses, make up for this lack of thinking power. This blue sky research could help support a range of future advances, including improved automated navigation technology for drones.

Combatting casting cracks

The technique of manipulating a liquid alloy and then allowing it to form a solid is one of humankind's oldest engineering processes. But defects can occur in this casting process that can ultimately lead to failure; not good news if your component is critical to safety, like an engine or a building material. With research performed at Diamond, scientists have been able to study why cracks occur during casting. Findings can be used to develop improved manufacturing techniques and safer alloy materials, and to improve modelling for maintenance so that we know when to service and replace components.

Shaping hydrogen storage

Hydrogen has immense potential as a powerful and environmentally-friendly fuel source. However it is currently only possible to store and transport hydrogen either as a liquid at very low temperatures or as a gas under very high pressure; both of these have serious implications for weight, cost, and safety. And so scientists are using Diamond to look into novel ways of storing hydrogen under low pressures to help make it feasible as a more widely-used fuel.

Advancing automotives

Diamond is a leading centre for research into automotive engineering. Groups from academia and industry are exploring different routes for creating next-generation motor cars. Current projects include streamlined chassis design, enhanced fuels and lubricants for diesel and unleaded automobiles, as well as technology for improved electric vehicles.

Boosting biofuels

Many naturally-occurring processes involve transforming waste products into sources of fuel. But harnessing the potential of sustainable biofuels on an industrial scale can prove a real challenge. Scientists are currently using Diamond to study different sources of biofuel, including natural enzymes that create liquid fuel from products like wood and mould.

Epidemiology: Piecing Together the Puzzle

Using scientific detective work to help fight disease

In the 1980s, scientists and clinicians were grappling with one of deadliest outbreaks in modern history. Large numbers of patients were dying from uncommon types of pneumonia, cancer, and infections of the lymph nodes. It seemed that some sort of immune system disorder was sweeping through the population. This was the official beginning of the AIDS pandemic, an outbreak that would go on to kill an estimated 39 million people worldwide.

The surge in AIDS cases in the early 1980s caused a great deal of fear and confusion in affected areas. People didn't understand where the disease had come from or how it was transmitted, and the prevalence of HIV/AIDS amongst the gay community and intravenous drug users led to the stigmatisation of HIV-positive individuals.

Epidemiologists were absolutely central to combatting misinformation during this period. Their work helped to lift the veil on HIV, allowing scientists, clinicians, and officials to help manage the condition. Literally translated from the Greek meaning 'the study of people', epidemiology is the practice of tracking the patterns, causes, and impact of diseases within populations. Epidemiologists are the detectives of science, and their work draws on many different areas, including medicine, public health, social sciences, statistics, and policy.

When an outbreak occurs, scientists look to study the pathogen and its structure and processes in intense detail. At Diamond, we are the ultimate reductionists, exploring the structure and characteristics of pathogens on an atomic and molecular level – this helps us to develop medicines to fight back.

Epidemiologists operate on the opposite end of the scale, looking at the impact of disease at the population level. Who is affected? What behaviour leads to transmission? What are the impacts of medical interventions? These are questions that epidemiologists help to answer, sometimes going beyond molecular cause and effect and exploring social issues like poverty and cultural practices to help get a bigger picture of healthcare issues.

Epidemiologists and scientists working at research facilities like Diamond may look at disease from different angles, but you need both sides – the fundamental biological knowledge and the population impact – to really understand a problem.

We see the effects of epidemiology everywhere, from the decline in smoking rates, to the increased use of sunscreen. The findings of epidemiologists inform government policy, treatment plans, and public health campaigns; and their work helps to optimise the response to healthcare issues and disease outbreaks around the world. Epidemiologists were integral to recent efforts to wipe out Ebola in West Africa; they're also at work investigating the effect of attempts to combat malaria.

Epidemiology often directly informs research at Diamond. In the late 1990s, a new type of hip implant came into use around the world. Metal on metal implants were thought to last longer than other types and be a solution for younger patients whose implants would need to be more durable. But data gathered by epidemiologists indicated that the failure rate for these implants was much higher than for other types. Scientists then discovered that when the metal implant parts rubbed against each other they caused small metal particles to enter into the body's bone cells, where they could have a toxic effect.

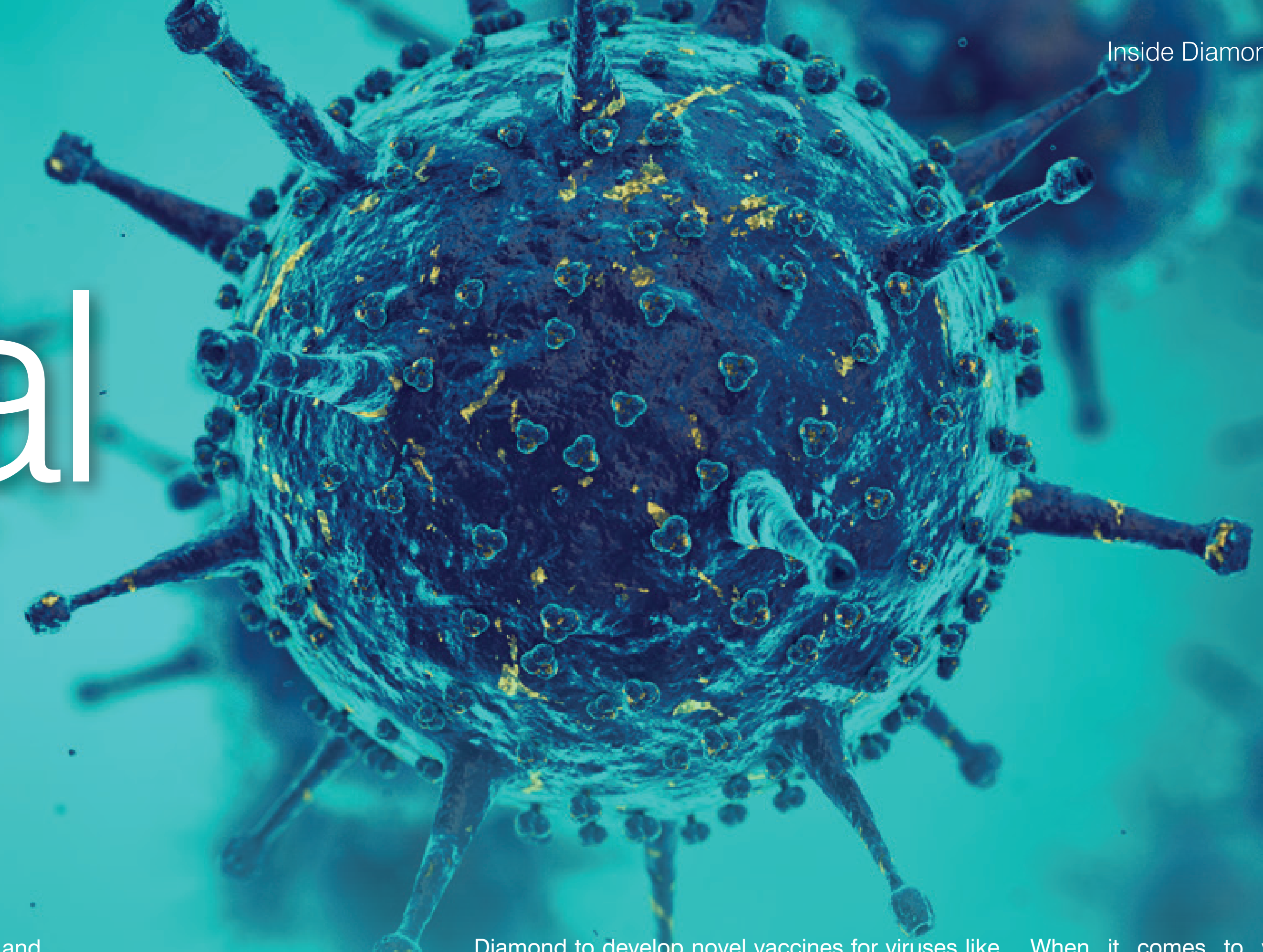
Using Diamond, researchers were able to study the course and impact of this process. Armed with this knowledge, we have been able to explore new drugs that could help to prevent toxicity and improve the reliability of implants. Epidemiologists were central to this work, helping to provide scientists using Diamond with the information they needed to begin exploring the problem.

But epidemiology doesn't just cover tracking, prevention, and control; it also assists with prediction. Pathogens can evolve and emerge really quickly, and when a new strain of dangerous virus or bacteria is found, it's important to get a picture of its impact, virulence, and existing status amongst the population as quickly as possible. The data gathered by epidemiologists helps to answer these questions and augments our understanding of what level of threat new pathogens are. This informs research priorities at Diamond and other facilities, arming us with the knowledge to act quickly to stem outbreaks.

Back in the 1980s, the work of epidemiologists helped to restore understanding and clarity around HIV. They tracked the spread of the disease, building up a picture of the relationships and commonalities between sufferers. Their work stemmed the tide of infection by informing people of how to prevent transmission. Government policies were developed to introduce healthcare campaigns and treatment services for those affected. The dawn of the AIDS pandemic in the 1980s was a dark time for many communities, but epidemiologists helped to expel some of the dread and anxiety surrounding the virus and improve the lives of those affected.

Science doesn't begin and end with the laboratory. Around the world, epidemiologists are building up the bigger picture of how healthcare issues play out within the population. Their work goes hand in hand with the sort of lab-based research that takes place at Diamond, and helps scientists to solve the puzzles presented by disease, one piece at a time.

Epidemiologists and scientists working at research facilities like Diamond may look at disease from different angles, but you need both sides – the fundamental biological knowledge and the human impact – to really understand a problem.



Going Viral

Unpicking the mysteries of viruses

Viruses are one of the oldest and most pervasive components of the natural world. There are more of them on Earth than all bacteria, plant, and animal life combined, and they evolve faster than any living thing. Because of this diversity, treating viral infections and predicting their future evolution can be a challenge. But thanks to cutting-edge technology, scientists are unpicking the mysteries of these molecular machines, virus by virus; atom by atom.

Diamond is a hub for virus studies, attracting some of the leading researchers in the field. Diamond's CRYSTAL beamline allows scientists to use synchrotron light to experiment on viruses under a higher level of containment than other life science beamlines at Diamond. Containment Level 3 means that scientists can study treatable pathogens that can be fatal to humans in a safe and secure environment.

Thanks to these capabilities, scientists are able to scrutinise viral components in unprecedented detail. The knowledge they generate helps to identify drug targets and provides an insight into how viruses evolve – information that could help us to better manage outbreaks like the recent Ebola epidemic in West Africa.

Prof Jonathon Grimes is a Diamond Fellow and Professor of Structural Biology at the University of Oxford. He uses Diamond to study a variety of viruses, and is particularly interested in how they replicate. An integral component of the replication process, polymerases are enzymes made up of long strings of amino acids. They help to copy the viral genome and reproduce messenger RNA which is then used to reproduce the virus's genetic code.

Using Diamond's capabilities (MX beamlines and B21), Jon has successfully identified the structure of the polymerase involved in influenza C, a Containment Level 2 variety of flu which, together with influenza A and B, infects approximately 3 to 5 million people every year, leading to between 250,000 to 500,000 deaths around the world. Understanding the atomic structure of the influenza C polymerase could be a major step forward in developing new treatments to fend off the spread of flu.

Jon explains: "Polymerases are just one component of the replication process, but if we can design compounds to stop it working, then it may be possible to develop a cocktail of drugs that together target different elements of the process and thus stop the virus in its tracks."

The structural information Jon has uncovered may now be used to develop pharmaceuticals that target the influenza C polymerase and counteract viral replication. His findings could also provide insight into polymerases of other viruses in the same family, including the more aggressive and dangerous influenza A and B types. Meanwhile, Jon is now using Diamond to study the polymerases for rabies and Ebola, in an attempt to determine their structure and open up new avenues for the treatment of these diseases.

Shutting down the replication process is one way of combatting viruses, but another approach involves purposefully replicating the virus in a non-virulent form to act as a vaccine. Professor Dave Stuart is Director of Life Sciences at Diamond and Professor of Structural Biology at Oxford. His group is using Diamond to develop novel vaccines for viruses like foot-and-mouth disease and polio by mimicking the atomic structure of the virus shells.

All viruses contain RNA, and it is a genome, often made from RNA, that allows viruses to replicate and spread. Most vaccines use an attenuated version of a virus to build up the body's immunity, so that when exposed to the actual virus, the immune system will recognise it and be able to defend against it. However this approach requires high containment production facilities and is not always effective – the attenuated vaccines can themselves sometimes produce infection, and they are difficult to transport and store, particularly in hot climates.

Dave's group are looking to create 'empty' virus shells that mimic the atomic structure of viruses but contain no RNA. Exposing the immune system to these empty shells would produce a response and induce immunity to the virus without any risk of infection. The group have already successfully produced a potential 'empty' vaccine for foot-and-mouth disease, which is currently being trialled in livestock in South Africa, and are now looking to develop the approach to work against polio.

Whilst Dave's research focusses on specific viruses, his findings are also contributing to our wider understanding of viruses as a whole. There's a lot of variety when it comes to viruses. They've been around for many millions of years, so they've had a fairly long time to adapt and evolve. But whilst viruses differ in terms of their structure, effect, and components, just like other species they can be grouped into families based on shared characteristics.

When it comes to viruses, understanding the bigger picture is vital. Dave observes: "Knowing the structure of viruses and viral elements is pivotal to combatting particular infections, but that knowledge can also help us to predict the structure and treatment options for other diseases.

We can study how the structure changes between different viruses and virus families, and as we build up that wider understanding, we become better equipped to anticipate what to expect, so that when we come to look at tackling another virus, be it an existing pathogen or something entirely new, we already have a base level of understanding which we can build on."

Both Dave and Jon are at the forefront of efforts to track the evolution of viruses and the relationships between different families so that we can build up an evolutionary family tree. The team have solved the structure of many different viruses and virus components – some extremely ancient and some far newer. Their work is helping to shape our understanding of the viral world and providing us with the insight to respond to future outbreaks in a quick and effective way.

Exploring the atomic structure of viruses is key to developing more effective medical responses, both to existing pathogens and to those that may emerge in the future. Viruses are as varied as they are pervasive, but the work of scientists like Jon and Dave is helping to create a clearer picture of how they operate and evolve. And in this way, science will continue to make viruses a little less mysterious, and a lot easier to manage.

Diamond Snapshots

Meet Our Users

Colin Pulham, Professor of High-Pressure Chemistry and Head of School of Chemistry, University of Edinburgh

1 What are you studying at Diamond?

We study several types of material, including pharmaceuticals, fuels, and energetic materials at very high pressures. We've also recently been studying phase-change materials that operate at normal pressures. These chemical compounds absorb heat on melting and release it on cooling, and so they are able to act as heat-storage systems. Compared to traditional methods of storing heat, like hot-water tanks, these materials can store much more energy. Forty-two per cent of UK energy consumption is in the form of heat, so these materials could help dramatically reduce energy usage.

2 Why does this research require synchrotron light?

We use X-rays to probe the crystal structures of our phase-change materials – essentially, we are able to see how the atoms are arranged in the structures. The very high intensity of the beam allows us to collect data in a matter of seconds, so we are able to follow structural changes of the materials in real time and investigate their properties and performance.

3 What do you hope your work will achieve?

This technology has the potential to reduce CO_2 emissions and reduce domestic fuel bills, thereby contributing to the alleviation of fuel poverty. In partnership with a small local company (Sunamp Ltd.), we are incorporating these phase-change materials into "heat batteries" that are able to store thermal energy for hot-water and heating applications. The work at Diamond enhances our understanding and provides confidence that the materials will continue to function over extended periods – essential if heat batteries are to be installed in a domestic environment.

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

Go for it! You have the opportunity to change people's lives and really make a difference to the world. Stay curious about science and your environment – there are so many unanswered questions. Cherish those "that's interesting" moments – they so often lead to new discoveries. Make sure that you choose the appropriate subjects at school in order to keep your options open, and talk to young researchers about what motivates them in their scientific careers.

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

Up until I was nine years old, I wanted to be a surgeon. But then I realised that I didn't like the sight of blood or the smell of hospitals!

Scientist in the Spotlight

Tina Geraki, Senior Support Scientist on I18

1 How did you first become interested in science?

From when I was younger than 10 years old, I remember walking under the Milky Way with my dad explaining the Big Bang to me. I also recall my best friend talking to me about atoms and molecules during long coach drives to the beach. What were my chances of not becoming a scientist?

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

The fact that everything around us, materials and processes, is reduced to a small number of elementary particles and their interactions is something that I still find fascinating; even more if you expand this concept to live objects such as biological systems.

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

I only realise now that I don't have any specific heroes. I believe a lot more in the power of collective contribution rather than extraordinary individuals that stand out.

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

They should remember they are very lucky to have a passion for science – you won't earn a fortune, so passion is really important. Many other paths that seem attractive are ephemeral, but being curious about the world around you keeps you young for much longer.

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

I would be a dedicated surfer hunting big waves all over the planet. But because not every day can be about fun I would also like to get to know different parts of the world by being embedded and working in their communities.

Aerial image courtesy of Harwell Campus

Bacterial Warfare

The scientists tackling antibiotic resistance

The threat of antibiotic resistance is one of the greatest challenges facing humankind. Since their advent in the 1940s, antibiotics have saved millions of lives around the world. But bacteria are fighting back. As more and more bugs become resistant to antibiotics, we have to find a way of making drugs more effective again or else risk reverting to a pre-antibiotic age, when minor infections could kill. So scientists are on the hunt for new weapons in the war against pathogenic bacteria, and Diamond is helping to illuminate chinks in the armour. Tenacious and quick to evolve, bacteria are a formidable enemy but, in this fight, science is our secret weapon.

Bacteria survive because they evolve, not in the traditional sense, over thousands of years, but extremely quickly, sometimes in an instant. Bacteria replicate in vast quantities. They also multiply very quickly. So beneficial mutations are more likely to occur, and when they do, they spread fast. This means that they can quickly learn how to bypass drugs. It's much harder to hit a moving target, and bacteria have a real evolutionary advantage: they can change faster than we can develop drugs.

To add to the problem, very few new antibiotics have come on to the market in recent decades. Because the drugs only work for a short time, the financial incentive for pharmaceutical companies to create new antibiotics is limited. And without new approaches to tackling bacteria, we'll soon be left with drugs that simply don't work anymore.

Diamond is a hub for research into new drugs and strategies for overcoming resistance. The synchrotron's bright beams allow scientists to look at the interaction between drugs and their target at the atomic scale – with this level of understanding, we can design drugs that bypass bacteria's defences.

Researchers from the University of Southampton and Diamond are working on an entirely new approach to tackling bacteria. The team brings together expertise in microbiology, biochemistry, and structural biology to aid a fuller understanding of biofilms: huge collections of bacteria that cluster together to create a thick and slimy mass.

Biofilms are the predominant life form of bacteria. In this state, bacteria grow in organised colonies and become immobile – this can make them really difficult to get rid of. Biofilms can cause chronic infections, such as non-healing wounds, and persistent infections that affect people with cystic fibrosis. They also represent health threats through growth on implants or catheters.

Jeremy Webb, the lead microbiologist from Southampton, explains: "Biofilms are extremely common, in fact they account for around 80% of all bacterial infections. But when antibiotics were developed, they were designed to target single cell bacteria. Biofilms represent an entirely different mode of bacterial growth, and they can be made up of complex and structured communities of bacteria. The biofilm state and the heterogeneity within biofilms mean that they can tolerate up to 1,000 times more antibiotics than a single-celled bacteria."

However biofilms do have an Achilles heel. In order to aggregate – that is, transform from free-living single cells into a biofilm cluster – they have to use a biological mechanism to change state. Once they're aggregated in a biofilm, the bacteria can still separate again; and the fact that this reverse mechanism exists means that we can exploit it. By triggering the dispersal mechanism, it's possible to break up the biofilm, leaving the individual bacteria on their own, ready to be destroyed by antibiotics. And this mechanism exists within all bacteria, which means that, if we can harness it, dispersal offers an entirely new approach to combatting bacterial infections.

Using Diamond life science beamlines, the team are studying the atomic structure of bacterial molecules involved in triggering biofilm dispersion. Not all biofilms are the same, and different triggers for dispersion are currently being investigated. In Southampton, the team have developed their own method of dispersing biofilms using a common gas: nitric-oxide. For humans, nitric-oxide is known as a signalling molecule in many physiological and pathological processes, but for bacteria, it's a signal to break up biofilms.

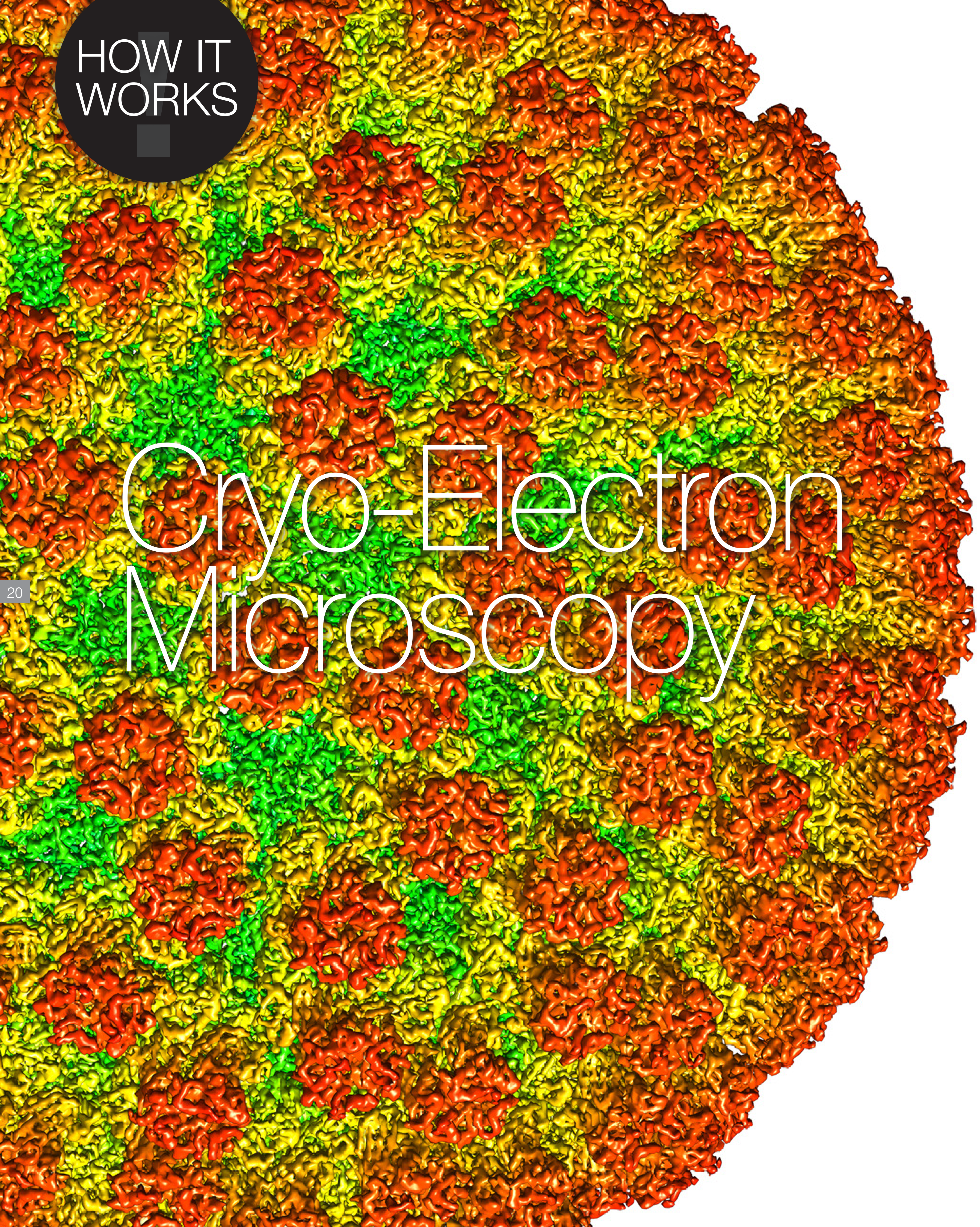
Ivo Tews, who leads the structural work at Southampton, explains: "The nitric-oxide induced dispersion is our own discovery and we are keen to understand how this works and further explore the process. Diamond has transformed the way we approach the problems presented by biofilms. With synchrotron light, we can study the proteins of the bacteria involved in dispersion."

The Southampton group have joined forces with Martin Walsh's group at Diamond who also are using structural biology techniques to understand the molecular basis of biofilms in bacterial respiratory pathogens. Andy Hutchin, a Southampton/Diamond jointly funded PhD student, enables the team to combine the use of Diamond and the powerful infrared lasers at the Central Laser Facility to observe how nitric oxide binds to the protein molecules involved in this dispersal process, leading to the reaction. The group also plan to use super-resolution microscopy to study bacterial cell surface receptors. Ivo notes: "Having access to technology is central to advancing our understanding of biofilms and how to combat resistance."

We now know that biofilm dispersal restores the effectiveness of antibiotics. We also know how to trigger the mechanism in biofilms that causes them to break up. But there's something else that makes this finding really significant. Jeremy explains: "The biggest barrier to treating bacteria has always been their astonishing capacity to evolve. But because dispersion isn't a direct threat to bacteria's existence, they won't evolve to overcome drugs that induce it." He continues:

"That's what makes this new approach really exciting. Instead of engaging in this constant battle against bacteria, we may be able to take it out of the fight altogether. And as soon as they stop evolving resistance, bacteria become much easier to treat."

Drugs that use this approach are already in clinical trials and are showing great promise in reducing resistance. There's still work to be done on investigating the various mechanisms of dispersal in different biofilms and designing drugs that work effectively with antibiotics, but the team's strategy of divide and conquer looks set to provide a powerful new weapon in the war on bugs. It's a tough battle: bacteria are astonishingly complex and resilient, but we have the upper hand, because we have science on our side.



HOW IT WORKS

Cryo-Electron Microscopy

Electron microscopes function on the basic principle that electron wavelengths are shorter than photons', and thus generally are able to pick up more detail. Photons are the basic particles of light and everything we see around us is the result of these particles reflecting off of objects and into our eyes. However some objects are smaller than the wavelength of photons, so they don't really interact and our eyes just can't see them.

But never fear: because their wavelength is so minute, electrons can interact with tiny objects. So by using electron rather than light microscopes, we can delve even deeper into cellular and molecular structures – about 5,000 times deeper to be precise. Cryo-electron microscopy, or cryo-EM, is exactly what it sounds like: using this method under really cold conditions, at -200 °C using liquid nitrogen. This amazing technique can help us to uncover even more about the minute, hidden elements in matter, leading to advancements in medicine, bio-engineering, and our fundamental understanding of the world around us.

What is it?

Electrons are the tiny charged particles that make up the outside of atoms, and they're able to help us see minute components of matter like cells, microorganisms, molecules, and the up-close structure of materials.

Electron microscopes work by generating a beam of electrons. Electromagnetic lenses are used to focus the beam, which is then fired at a sample. The electrons then interact with nano-scale components, allowing us to investigate and visualise samples in astonishing detail.

There are different varieties of electron microscopy, and cryo-EM is a relatively new field. Regular electron microscopy requires samples to be prepared in complex ways – techniques include coating samples in substances that protect them from radiation, sectioning them into tiny slices, or dehydrating them to prevent the interaction between electrons and water molecules.

But with cryo-EM, samples don't require this sort of preparation – they can simply be frozen and then studied in their normal state. This means that scientists can see biological elements as a whole and in an active state. Furthermore, rather than studying individual components of a sample and piecing a wider picture together, cryo-EM enables scientists to look at big, complex biological systems.

Cryo-EM isn't perfect. It produces lower resolution images than some other techniques, like X-ray crystallography. But the real strength of cryo-EM lies in its versatility. The technique allows scientists to study objects that – because of their size, complexity, or sheer awkwardness – would be virtually impossible to scrutinise with other techniques. It's quick and flexible; and when used in tandem with other techniques, cryo-EM is a supremely powerful tool.

The History

The first microscope was invented in the 1600s, but the first electron microscope wasn't developed until about 300 years later, and cryo-electron microscopes are even newer than that – they've only been about since the 1980s.

When the first commercial electron microscope became available in the 1930s, electron microscopy wasn't immediately popular as a scientific technique. People recognised their potential to be more powerful than a standard light microscope, but the electron microscopes tended to seriously damage samples. To solve the problem, scientists began treating and preparing their samples to protect them prior to experiments – this development suddenly made electron microscopy much more useful, and it shot onto the scientific scene.

In the 1980s scientists began working on an entirely new approach to counteract the sample-destruction challenge. In 1984, a European team discovered a method of carefully cooling samples without compromising their structure or usability. This was the birth of cryo-EM, and from here, the technique grew and grew. There are now cryo-EM facilities all over the world – and that's where Diamond comes in.

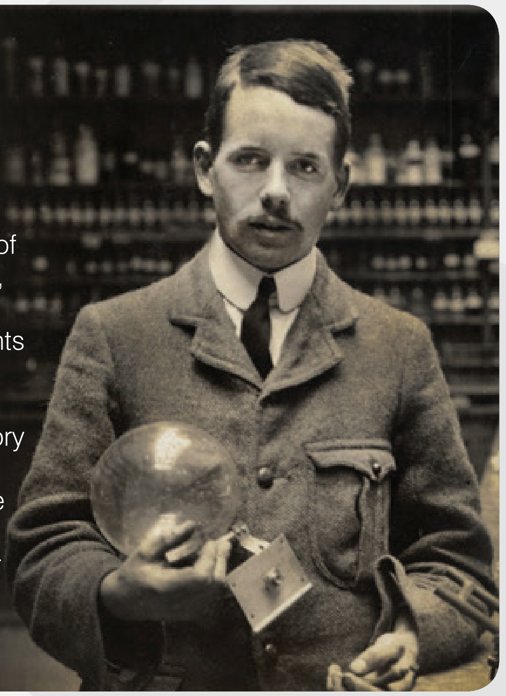
Cryo-electron microscopy at Diamond

Cryo-EM is an amazing technique with the power to add an entirely new level of insight to biological science, but the infrastructure to support the latest generation of electron microscopes can be prohibitively expensive. Cryo-EM requires specialist equipment, advanced software, and scientific staff who have specialised as electron microscopists, so it makes sense for facilities to be centralised at places like Diamond experienced in running very valuable equipment 24 hours a day.

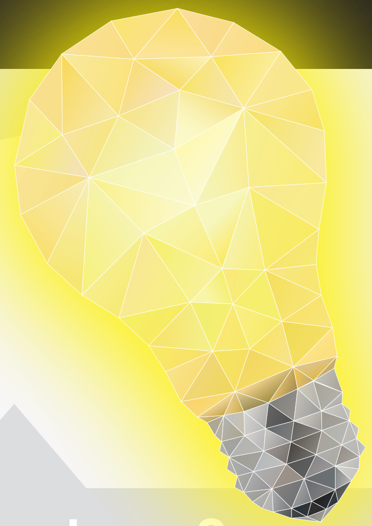
At Diamond, scientists can access state-of-the-art cryo-EM facilities through the electron Bio-Imaging Centre (eBIC). An onsite cryo-electron microscope is currently being used by scientists to study everything, from complex virus structures, to never before seen proteins. It will soon be joined by a second microscope to serve the growing needs of the science community: a development that will further augment Diamond's ability to support advances in medicine and healthcare.

Cryo-EM has real potential as a tool for the biological sciences. Its ability to quickly and simply illuminate large and complex components makes it a profoundly useful addition to the arsenal of techniques that scientists use to explore the world and generate advances. With cryo-EM behind us, we can study more comprehensively, see more deeply, and come to understand more fully.

Hero from History



Henry Moseley is regarded as one of the most important scientific heroes that never was. At the age of 26 he solved one of chemistry's greatest conundrums, determining what distinguishes elements from one another and developing a means of identifying elements based on their atomic characteristics. Moseley's work revolutionised chemistry and spawned a vital and widely-used technique: spectroscopy. However his story is a tragic one. Moseley lost his life during fighting at Gallipoli in World War One; he was just 27. But despite his short career, Moseley left behind a rich legacy of scientific accomplishment and laid the groundwork for the evolution of modern chemistry.



Did you know?

When it's running, Diamond is one of the brightest lights in the solar system.

Recommended viewing

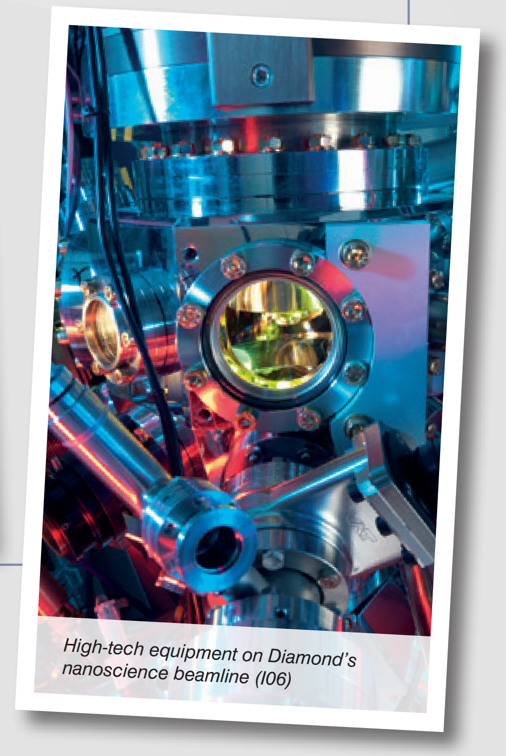
Want to learn more about our Hero from History, Henry Moseley? Diamond's film, *Henry Moseley: Scientist Killed in Action,* celebrates his life and legacy. You can watch it online at:
http://www.diamond.ac.uk/films

*A micrometre is 1 millionth of a metre; a nanometre is 1 billionth, and a picometre is 1 quadrillionth!

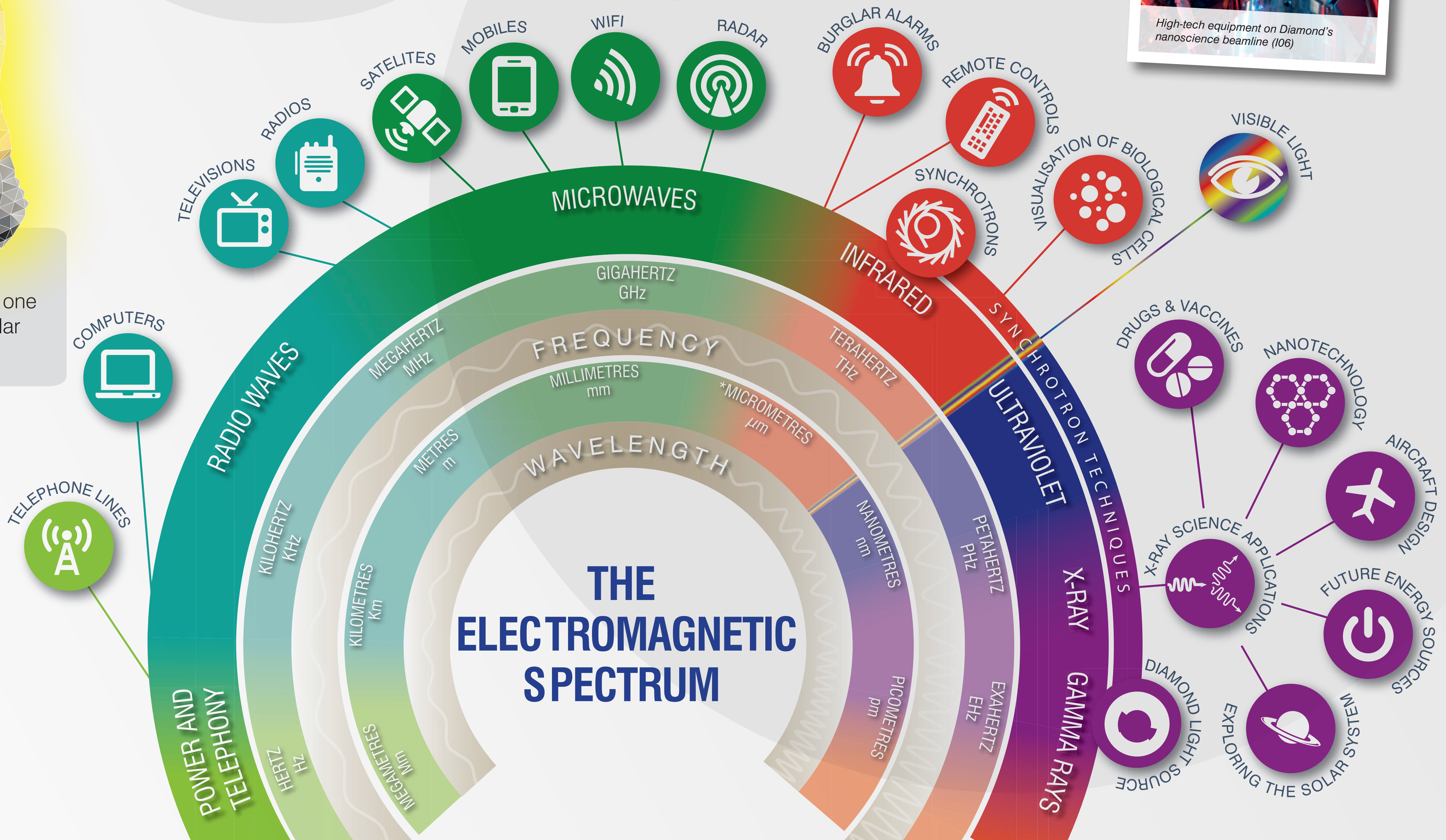
Diamond Captured

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

Principal Beamline Scientist, Chris Nicklin, on XENA (I07), a surfaces and interface diffraction beamline



High-tech equipment on Diamond's nanoscience beamline (I06)



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