Exploring & Understanding Science

fascination

CONTENTS

ALICE’s Breakthrough
3D drug target structures
OCTOPUS
Science Breakthrough
Leap in hospital X-rays
STFC’s Photowalk

If you would like to register to receive Fascination automatically please visit http://www.stfc.ac.uk/fascination

Image: Human epithelial cells
Welcome to the ‘STFC Science in Healthcare’ issue of Fascination. We hope to share with you some of the awesome and truly revolutionary science that STFC researchers are contributing to the world of healthcare. Breakthroughs can come about through collaboration with medical researchers, experiments on STFC supported research facilities or through technological advances intended for other areas of science that innovative researchers can see the potential to apply in healthcare. While the articles in this edition cover a broad range of biological applications that STFC science is helping to improve, it is by no means a complete list as we are only able to bring you a selection of the scientific highlights.

This issue is split into four sections; Fundamental Research and Technology, Diagnosis Techniques, Treatments and STFC Highlights. Even though each of the articles highlights fundamental scientific breakthroughs there is still much research needed in all the fields mentioned and therefore we are not yet at a stage for commercial use or human trials.

Joint STFC Futures and IPEM workshop - cancer care: computing for imaging, early diagnosis and therapy – 19 and 20 March.
The joint workshop between STFC Futures and the Institute of Physics and Engineering (IPEM) will be held in Cambridge. The purpose of the workshop is to bring together the cancer community and the research community funded by STFC in areas where there is significant potential for STFC to contribute, and begin the formation of collaborative research partnerships.

Global Challenge Networks - Closing date for applications is Thursday 29 March.
Welcoming proposals to create new multidisciplinary healthcare research communities between STFC-funded researchers and appropriate science, technology and industry groups in the areas of:
- Detectors and sensors in cancer care
- Cancer imaging
- Early diagnosis of disease
- Regenerative medicine
- Information and health

STFC exhibition at the National Cancer Research Institute (NCRI) – 4 – 7 November, Liverpool.
NCRI cancer conference is the leading international oncology meeting in the UK and delivers a pioneering programme showcasing high-quality data and a multi-disciplinary approach to cancer research from basic research to prevention, diagnosis, treatment and survivorship.

STFC Contribution to Healthcare and Ageing Report - Published January 2010
The Physical and Life Sciences Committee (PALS) carried out a review of the STFC contribution to the grand challenge of healthcare and ageing to inform future STFC priorities and policy in this area which can be found at:
Experimental insight could explain why lizards don’t freeze

Researchers from the Dougan Research Group at the University of Leeds have been using neutron diffraction data from ISIS in combination with a computational model to understand the mysterious ‘anti freeze’ capabilities of glycerol – a property that is already successfully exploited by lizards when experiencing sub-zero temperatures.

Today the method of preserving cells or whole tissues by cooling to sub-zero temperatures (known as cryopreservation) is used in many industries, medical protocols and everyday items - from anti freeze for your car, treating embryos in fertility treatments, and even in reducing the amount of ice in your ice cream!

Animals like lizards that are ‘ectothermal’ have little to no ability to regulate their own body temperatures. When temperatures fall, their core body temperature also decreases, putting their tissues, cells and biological activity at risk of irreparable damage. Some choose to avoid the cold by migrating to warmer climates or hibernating, whilst others have developed adaptive techniques to overcome this situation and avoid becoming a lizard ‘ice statue’. Like humans, a significant proportion of a lizard’s body is made up of water, so during cold winters when they are exposed to sub-zero temperatures they are at risk of potentially lethal ice crystals forming in and between the cells in their bodies as the available water and body fluids begin to freeze.

To overcome this, lizards have evolved using chemical compounds such as glycerol to reduce the temperature at which the water in their bodies will freeze. Glycerol is a common cellular component in many cold blooded organisms. It is often used as a cryoprotectant compound, providing protection by limiting the damage to cells and tissues during prolonged periods of sub-zero temperatures.

Thanks to this ‘anti freezing’ technique, cell activity is effectively paused while in freezing temperatures, yet when temperatures rise, normal cell activity can resume. Scientists have improved our understanding of this natural process and the way in which we use this technique over sixty years, yet we still do not fully understand the molecular mechanisms which allow glycerol to provide this essential protection. Researchers keen to discover glycerol’s secrets have previously used exploratory research methods such as thermodynamic measurements, infrared and Raman Spectroscopy to try to solve the mystery. And although these methods have greatly helped explain the dynamic behaviour of glycerol, they have not been able to provide us with the complete picture.

It is however known that the mechanism by which glycerol provides its cryoprotectant properties involves a delicate interaction between its structure and dynamics. The Dougan Research Group, supported by the EPSRC, wanted to look deeper into glycerol’s molecular mechanisms, in particular how glycerol – hydrogen bonds form as this part of the interaction is currently poorly understood. When asked why the neutron diffraction technique at ISIS was selected for this work, Dr Lorna Dougan, from the University of Leeds, commented: “Neutron diffraction is an ideal probe for the structural study of liquid glycerol. Over the past decade, significant advances have been made in the methods of neutron diffraction and in the development of more powerful computational tools. This study provides the first detailed experimental, structural insight and allows a number of hypotheses to be tested for the first time.”

The data revealed that the presence of only small quantities of glycerol in the solution had the same impact on water structure as increasing the pressure – reducing water’s freezing temperature. One possible explanation for glycerol’s molecular mechanism as a cryoprotectant is that glycerol works by driving water towards this high pressure structure, at which point its freezing temperature reduces, thus preventing ice formation.

Dr Dougan says: “The knowledge generated in this area will improve our fundamental knowledge of cryopreservation which may lead to improved storage and recovery of tissue for fertility treatment, better storage of drugs in the pharmaceutical industry, transport of organs for surgery and better storage of food in the agricultural industry.”

The team has now begun a new collaboration with Dr Giovambattista from City University of New York, an experienced researcher in the fields of supercooled and glassy systems and are engaged with researchers who use cryopreservation for fertility treatment in reproductive medicine and in the storage of transplant organs. They hope that while cryopreservation protocols to freeze-stores these cells and complex tissues are already in use, the methods used would greatly benefit from further investigation and optimisation.

The EPSRC are supporting this research to enable the full team (PhD student James Towey, ISIS scientist Professor Alan Soper and group leader Dr Lorna Dougan, School of Physics, University of Leeds) to conduct this research. For more information you can look on the Dougan Research groups’ website (http://www.mnp.leeds.ac.uk/dougan/research.html)
First of its kind – Diamond helps reveal 3D drug target structures for improved medicines

The Membrane Protein Laboratory (MPL) at Diamond Light Source is one of a kind – it is the only laboratory used for researching membrane protein structures that is situated adjacent to a synchrotron. There are estimated to be over 7,000 membrane proteins within the human body. Solving their complex 3 dimensional crystal structures remains a very real and significant challenge to biologists as over 50 per cent of current drugs target these membrane proteins. Using Diamond’s Macromolecular Crystallography (MX) beam-lines, scientists have been able to solve some of these protein structures using X-ray crystallography - making invaluable contributions to structural biology, pharmacology and medicine.
Symptoms but doesn't have any side effects. Understanding to develop an 'ideal' drug: that stops the effects. They hope that by finding the answer to questions how the histamine drugs cross-react with other membrane should have fewer adverse side effects for patients.

‘Third generation’, much more selective, antihistamines which Diamond, it has opened up the way for the development of to prevent this reaction."

It took a considerable team effort," says Professor Iwata said: "Now that we know the shape and size of the drug-binding site within a bacterial model of the protein it should enable the design of improved drugs which are much more targeted and will 'fit' much better."

The team were surprised to find that the structure of ASBT was similar to the sodium proton antiporter, NhaA as they had had no previous suggestion that this would be the case. NhaA moves sodium ions and protons passively across the membrane rather than the much larger bile acid which is actively transported by ASBT. An important contributing factor to the discovery was the team's access to the specialised equipment at Diamond, which dehydrates the protein crystals before they are screened, improving the more accurate results.

The researchers are now continuing to work on ASBT to try and understand the mechanism that allows the protein to transport bile across the membrane. The hope is that in the future pharmaceutical companies will use this structural information in drug design programmes.

**Case Study: Histamine H1 receptor protein structure**

Histamine is found in the cell membranes of various human tissues including airways, vascular and intestinal muscles and the brain. An essential step in an immune reaction is histamine binding to the H1 receptor. However, in susceptible individuals who can have a hypersensitive immune system, this binding can trigger allergic reactions such as hay fever, food and pet allergies. Anti-histamine drugs, administered to treat this often uncomfortable reaction, work as they prevent histamine attaching to H1 receptors.

Dr Simone Weyand, post-doctoral scientist at Imperial College London, explains, “First generation antihistamines such as Doxepin are effective, but not very selective, and because of penetration across the blood-brain barrier, they can cause unwanted side effects including sedation, dry mouth and (the heart condition) arrhythmia”.

A team made up of leading experts from Diamond and Imperial College London, UK; The Scripps Research Institute, California, USA; and Kyoto University, Japan worked on the problem. Sixteen months and three continents later, the 3 dimensional structure of the human Histamine H1 receptor protein was solved! The protein was produced in cells at Kyoto University and then the processed cell material was flown to Professor Raymond Stevens at The Scripps Research Institute. Here the crystals took around two months to grow. Once each batch of around 100 was ready, they were frozen and flown to the UK where Professor So Iwata, David Blow Chair of Biophysics at Imperial College London and Director of the MPL, and Simone worked with Diamond’s scientists to analyse over 700 samples using MX beam-line I24 - a unique instrument capable of studying tiny micro-crystals using an X-ray beam only a few microns wide. The team was pleasantly surprised by just how clear and detailed the images were from this technique.

“It took a considerable team effort,” says Professor Iwata, “but we were finally able to elucidate the molecular structure of the Histamine H1 receptor protein and also see how it interacts with antihistamines. This detailed structural information is a great starting point for exploring exactly how histamine triggers allergic reactions and how drugs act to prevent this reaction.”

By using specialised structure defining techniques at Diamond, it has opened up the way for the development of ‘third generation’, much more selective, antihistamines which should have fewer adverse side effects for patients.

The research team is now working on understanding how the histamine drugs cross-react with other membrane proteins (which is why some people suffer adverse side effects). They hope that by finding the answer to questions like these scientists will someday soon have a great enough understanding to develop an ‘ideal’ drug: that stops the symptoms but doesn’t have any side effects.

**Case Study: Cholesterol reabsorbing ASBT protein structure**

Cholesterol helps your body build new cells, insulate nerves, and produce hormones. Normally, the liver makes all the cholesterol the body needs. But cholesterol also enters your body from foods such as milk, eggs and meat. Too much cholesterol in your body is a major risk factor for heart disease. According to the British Heart Foundation, in 2009, over 180,000 people died from cardiovascular disease (CVD) in the UK - one in three of all deaths.

About 50 per cent of cholesterol is eliminated from the body by its conversion into bile acids. However, bile acids released from the bile duct are constantly recycled in the body, being reabsorbed in the intestine by the Apical Sodium-dependent Bile acid Transporter (ASBT). It has been shown in animal models that plasma cholesterol levels are considerably lowered by specific inhibitors of ASBT, so it is not surprising that ASBT is a drug target for hypercholesterolemia drugs.

A team of researchers from Imperial College London and Diamond Light Source used the Diamond synchrotron’s MX beam-lines I02 and I03 to determine the structure of the ASBT protein for the first time. Professor Iwata said: “Now that we know the shape and size of the drug-binding site within a bacterial model of the protein it should enable the design of improved drugs which are much more targeted and will ‘fit’ much better.”

The team were surprised to find that the structure of ASBT was similar to the sodium proton antiporter, NhaA as they had had no previous suggestion that this would be the case. NhaA moves sodium ions and protons passively across the membrane rather than the much larger bile acid which is actively transported by ASBT. An important contributing factor to the discovery was the team’s access to the specialised equipment at Diamond, which dehydrates the protein crystals before they are screened, improving the resolution of their diffraction data, thus leading to much more accurate results.

The researchers are now continuing to work on ASBT to try and understand the mechanism that allows the protein to transport bile across the membrane. The hope is that in the future pharmaceutical companies will use this structural information in drug design programmes.

Dr. Simone Weyand working on Microfocus Macromolecular Crystallography beamline (124) at Diamond.
OCTOPUS provides cancer breakthrough

A breakthrough in understanding an everyday biological process that occurs within the cells in our bodies, in some cases causing cancer when a mutation occurs, can lead to the possibility of improved cancer drugs. A collaboration between STFC’s Central Laser Facility (CLF) and the Computational Science and Engineering Department (CSED) has solved a puzzle that scientists have been working on for 30 years!

Molecules known as EGFRs (Epidermal Growth Factor Receptors) are an antenna for living cells. They receive chemical signals from other cells that tell them when to grow and when to divide. Sometimes mutations occur in EGFRs stopping them from functioning properly and leading to uncontrolled cell division, causing a tumour to grow. Cancer drugs block all signals from the EGFRs halting tumour growth, but the body can find ways of bypassing the blocked signal system allowing cells to grow again.

The CLF facility OCTOPUS (Optics Clustered To Output Unique Solutions) at STFC’s Rutherford Appleton Laboratory is a new concept in laser imaging where multiple light sources are linked to multiple imaging stations allowing a combination of techniques to be used on samples under investigation. OCTOPUS enabled scientists to examine the shape of these molecules while they were still in the cells. This was not possible before as previously X-rays were used to examine the structure of molecules. The X-ray system described a purified crystallised version of the protein instead of the actual form the protein takes in the cell, and as a result the structure identified in the crystallised molecule didn’t match what was known about how the protein worked.

OCTOPUS consists of a central hub that fires laser beams via fibre optics for exact precision to a cluster of eight microscopes surrounding it. This enables the scientists to use different imaging techniques as well as chemical research to piece together information about the molecules structure and function. From this process the researchers discovered an unknown molecular shape which is partly responsible for transmitting the signals that instruct cells when to grow and when to divide, until now it wasn’t known how EGFRs transmit these key messages in the development of cancer, which means drugs designed to stop them transmitting these cancer inducing signals may have also been limited in their effectiveness.

This new found molecular shape shares key features with the better understood EGFR molecules in fruit flies. This is also a result of the research providing clues how EGFRs have changed over evolution. Teamwork and close collaboration have been key in this vital discovery; the CLF used the OCTOPUS facility to take nanoscale measurements of EGFRs, then CSED used high performance computing to determine the measurements and calculate the receptors’ high resolution structure, highlighting the similarities with the fruit fly. The discovery is a significant breakthrough and may provide information for cancer treatment, but there are still a lot of unanswered questions regarding EGFRs. The findings provide knowledge of ways to access the EGFR in cells which may lead to new insights on how to target EGFR to treat human cancers.

Professor John Collier, Director of the CLF comments “Breakthroughs like this have the potential to really pay dividends in terms of saving lives and maximising the value of healthcare expenditure. By constantly pushing forward the boundaries of what laser technology can do, we can deliver real world-benefits that tangibly improve people’s lives.”
Could this be the future of diagnosing diseases

Breath tests are a cheap, quick and non-invasive diagnostic tool for some diseases, allergies and ailments which affect many people’s daily lives. Doctors can now test for allergies and gastric ulcers, just by analysing your breath!

The theory that characteristics of a person’s breath can give signs of health problems has been used since the time of Hippocrates about 400BC. Back then, the methods were more basic and instead relied on recognising distinctive smells in exhaled breath. For example, the fruity aroma of acetone signalled untreated diabetes (a result of excess sugar in the blood) and the aroma of sulphur suggested liver impairments.

Gases such as CO₂, hydrogen and Volatile Organic Compounds (VOCs) diffuse from the blood, through the lungs and are then exhaled out of the body, providing clues about what is taking place inside the body. A modern breath test measures the minute differences in the concentrations of specific compounds, looking for signs and links with certain medical conditions. It is an emerging field which is heavily reliant upon new and more sensitive methods and equipment being developed to gain more sensitive and detailed measurements and better diagnosis.

A team of STFC researchers at RAL Space are working to improve one of the current breath test methods using laser spectrometry. They aim to collect quantitative measurements of the difference between the exhaled carbon isotopes 12 CO₂ and 13 CO₂ in real time. CO₂ is needed for all metabolic processes and a low level can change the body’s pH level and create the perfect conditions for pathological infection. CO₂ level is currently used in other, commercially available breath tests to diagnose asthma, but isotopic information provides further insights on organs’ functions.

There is a real possibility that with further investigations like this, breath tests could more routinely be used for diagnosis to save many people from the current, widely used invasive prick tests, stool sampling or endoscopy which could lead to more early diagnoses and more people being diagnosed and offered timely treatment.
Excellent progress has been made at Daresbury’s ALICE accelerator over the past few months resulting in exciting advances in cancer diagnostics. The most significant advance is in research that will eventually lead to a diagnostic test for oesophageal cancer. Current understanding has now reached a point where there could be considerable improvements in both diagnosis and prognosis of this cancer.

Oesophageal cancer is the ninth most common cancer in the world and around 8000 people are diagnosed every year in the UK. It is an extremely difficult cancer to diagnose and is highly aggressive. Patients often present when the tumour is at an advanced stage, when surgical removal is no longer possible.

Led by Professor Peter Weightman from the University of Liverpool, a collaboration of researchers have been using the InfraRed Free Electron Laser (IRFEL) on ALICE. They have been able to collect the first scanning near field images of oesophageal cancer. The aim of the collaboration is to develop a diagnostic test by imaging tissue obtained by endoscopy from patients with a precursor condition called Barrett’s oesophagus. The images they have collected using the IRFEL will enable them to develop a diagnostic test for oesophageal cancer. The group are now developing improved instrumentation capable of obtaining images from larger areas of specimens.

Professor Weightman said: “Eventually we hope to develop a diagnostic test that can be used in an endoscope. The most promising approach may be to develop a test using the intense terahertz light also generated by ALICE. ALICE is Europe’s most intense band source of terahertz light and the only one in the world equipped with a tissue culture facility for research on cancer. This would lead to much cheaper and more efficient diagnosis of the disease. However this development is some way off.”

The collaboration involves Daresbury’s Cockcroft Institute (including accelerator physicists from University of Liverpool, Daresbury Laboratory’s ASTeC department), The National Research Council – ISM, of Rome, Tor Vergata, The Institute of Translational Medicine and the departments of Physiology, Gastroenterology and Physics of the University of Liverpool and the Royal Liverpool and Broadgreen University Hospitals NHS Trust.

The human stem cell stained to show the nucleus (blue) and internal structure (green).
Nuclear physics offers earlier detection of tumours with just one scan

Earlier detection of tumours could soon be achieved thanks to the Nuclear Physics groups at the University of Liverpool and STFC’s Daresbury Laboratory. Together they are working on a project called ProSPECTus which will offer patients fewer appointments and earlier, more effective diagnosis of tumours which will give a higher probability of effective treatment.

Project ProSPECTus is developing the technology for the next generation SPECT (single photon emission computed tomography) imaging. SPECT detects gamma rays emitted by a tiny amount of radioactive pharmaceutical which is injected into the body. It is mostly used to test the functioning of the heart and for detecting tumours and provides 3D information about the body presented as cross sectional slices through the patient. The current generation of SPECT imaging machines uses a device called a collimator, which filters some gamma rays through and pin points exactly where they are coming from using geometry, building a picture of the biological process happening inside the patient.

The ProSPECTus technology doesn't use the collimator. Instead the researchers developed technology based on a ‘Compton camera’, which can identify the origin of the gamma rays without the use of a collimator. This results in less radiation and hence less information wasted. Not only is the radiation used more efficiently but the Compton camera is one hundred times more sensitive than the current SPECT imaging system. The increase in the sensitivity offers benefits in two different ways; either the dose of radiation administered to the patient could be reduced which is beneficial for patients who require frequent scanning, or more patients could be scanned by one machine in a day using the current dose enabling a higher throughput of patients in hospitals.

ProSPECTus is truly unique and offers the possibility to operate simultaneously with MRI (Magnetic Resonance Imaging). This has never before been an option due to the strong magnetic field of the MRI. This provides the possibility that this SPECT system may fit onto the 350 existing MRI scanners in the UK. Both Nuclear physics groups are working closely with STFC’s technology team and Liverpool’s Magnetic Resonance Imaging Analysis Research Centre who provide MRI expertise.

This is an exciting example of how technology emerging from fundamental nuclear physics research can have a direct and positive impact on the future and wellbeing of our society and generate knowledge exchange into health security and energy applications.
Leap in hospital x-rays

X-ray machines that can travel quickly and easily to patients in hospitals, care homes and accident sites.

The revolutionary technology being developed by Radius Diagnostics Ltd (‘Radius’) will transform X-ray systems. The machines based on MAX technology (Micro emitter Array X-ray, an ‘X-ray source on a chip’) will be 20 times lighter than any existing portable X-ray machine. Current movable X-ray machines weigh 250 kg or more and can take time to position and set up, however the new X-ray machines will weigh less than 10 kg and will be no bigger than a laptop allowing quick and easy access to patients. The lightweight technology could be used by paramedics at patients’ own homes, by the armed forces in the field and at the scene of accidents. Radius imagines that patients could be imaged ahead of transportation and that hospital staff will be reading the X-rays before the patient arrives, or even before being moved if a spinal injury is suspected, saving vital time in treating critical injuries. In addition, the machines will be easily operated at a bedside, avoiding discomfort for patients, which often occurs when moving them to X-ray suites.

Production costs will be less than half of any current equivalent which means the new technology will be affordable for widespread use which may result in doctors’ surgeries having their own X-ray systems.

Radius has recently become a tenant of the European Space Agency Business Incubation Centre (ESA BIC) at Harwell where they are working on the technology originally developed by STFC and the California nanoSystems Institute (CnSI) which incorporates the MAX technology. The design was originally developed for use on space satellites but now Radius is bringing the technology one step closer to everyday use.

Mark Evans, CEO and co-founder of Radius, said “MAX will transform many applications of X-rays and we are thrilled that one of its first application, allowing truly portable X-ray systems to travel to the patient, will improve patient comfort, prevent unnecessary hospital admissions and save lives. The transformation that MAX will achieve is as great as the shift from the old-style TVs to today’s flat screens. However, it will be the reduction in cost and the opportunity for miniaturisation that will create a revolution. Many of the applications in healthcare, security and industry that MAX will make possible have not even been envisioned yet”.

X-ray machines that can travel quickly and easily to patients in hospitals, care homes and accident sites.
Treatment

Treatments can be preventative (and work to prevent the condition occurring, like a vaccine), stop the condition from developing further, be supportive (not treating the condition but instead treating the symptoms) or cure the condition; returning the individual to good health. All of these treatments require an accurate diagnosis the available knowledge as to how the condition and medicine work (a fundamental knowledge).

Antibiotic process for disease that causes half a million deaths a year

Scientists are researching an antibiotic that will treat a strain of meningitis that is responsible for over half a million deaths a year.

The severe strain of the disease called Cryptococcal Meningitis is diagnosed in nearly a million people a year worldwide and particularly affects AIDS patients. Over 600,000 of these cases are fatal. Until now, the fungal disease has been effectively treated by the antibiotic Amphotericin. However recent reports indicate that the fungi causing the infections are developing a resistance to Amphotericin and there are fears that if new drugs cannot be found, it could become untreatable.

Dr David Barlow and his team from King’s College, London have been using the ISIS neutron source to carry out experiments to find an improved antibiotic for the disease. Using neutrons to look at the effects of Amphotericin, they need to gain an understanding of how the antibiotic works before finding new and more effective treatments. The aim is to create a new drug that will work in a similar way to the old drug; however, it will need to stop the fungus which is causing the disease developing a resistance to the antibiotic.

The current drug has little effect on human cells as these cells are surrounded by membranes containing the steroid cholesterol. The fungi cell’s membranes also contain a related steroid, ergosterol. However, it is unclear how the difference in membranes is affected by the workings of the Amphotericin. So in early 2011, the scientists spent a couple of days at ISIS looking for differences at the speed in which the drug enters the human and fungal cell membranes.

Further progress is currently being made; the team returned to ISIS in December to carry out more investigations. They performed stopped flow experiments on the SANS-2D (small angle neutron scattering) instrument to study the interaction between the antibiotic and their model cell membranes over very short timescales. This was to specifically look at what happened within seconds of the membranes exposure to the drug. The results of this research are currently being analysed.

Extending the life of hip implants

With average life expectancy rising the life span of a hip implant needs to keep pace. Research led by Dr Rehan Ahmed and his team from Heriot-Watt University in Edinburgh has been using the ISIS neutron source to investigate how to extend the life of implants. Over 50,000 hip replacements are performed in Britain each year, this number is suspected to roughly double by 2030. Although the life of human implants is dependent on a number of factors including the quality of implant, surgical procedures involved and patient’s medical condition etc. for hip implants recent studies have shown a typical life span of 15 to 20 years.

Using the neutron beams, researchers have been investigating causes of implants failure. Commonly, implants are made using titanium which is coated with a thin layer of hydroxyapatite coating. Hydroxyapatite is the main component of human bone, which means that the coating encourages bone growth into the implant and bonds the bone to the implant holding it in place.

The thin coating is sprayed onto the titanium, however, due to the difference in properties between the titanium and hydroxyapatite, residual stresses form between the two materials which can cause the implants to fail.

Neutron beams allowed the researchers to study both the hydroxyapatite coating and the titanium together without having to remove material from titanium. Neutrons were used to look at implant coatings and researchers were able to collect experimental data to develop a stress profile for computer models of stress generation. Dr Ahmed explained, “Up to 18 per cent of implants can fail, for a number of reasons, including stress. If we are going to be able to provide long-lasting implants, it is crucial to have experimental data to back up our computer models”.

The Engin-X instrument at ISIS allows researchers to carry out accurate studies of microscopic stresses. It provides high resolution experimental data to back up the computer models, which will support the design of long lasting implants in the future. “The experimental data we collected at ISIS is vital for the validation of our model and it is not currently possible to get this quality of data using other techniques such as X-rays” added Dr Ahmed.
EMMA has proven technology that could revolutionise cancer treatment

Results from the EMMA Accelerator at Daresbury were published in Nature Physics in January confirming the proof of principle underlying its technology that could revolutionise cancer therapy and lead to cleaner, safer nuclear reactors in the future.

Professor Susan Smith, Director of ASTeC at STFC’s Daresbury Laboratory said: ‘It is fantastic news that EMMA’s concept has now been proven and published in Nature Physics. We’ve demonstrated for the first time a new type of particle accelerator that could be used in many different areas of our lives, and one which will hopefully allow for more widespread use of accelerators to tackle some of the most challenging problems facing our society.’

EMMA is a prototype for a brand new type of accelerator. It is an experiment to prove the principle of a new acceleration technique that will change the way accelerators across the world are designed and built in the future. Modern day accelerators were constructed and operate on principles developed over 50 years ago. This limits their potential for use outside of large scale laboratories due to their size, complexity and cost.

Hadron therapy targets cancer tumours more accurately and speeds up the treatment process. Unlike traditional radiotherapy treatment the hadron therapy would not damage healthy tissue around the tumour. Engineered and constructed at Daresbury Laboratory, EMMA’s breakthrough technology was designed by a group of scientists involved in the CONFORM project. CONFORM is funded by BASROC, where the ultimate aim is to build a complete hadron therapy facility.

EMMA is the world’s first non-scaling fixed field alternating gradient (NS-FFAG) accelerator. This technology combines the attractive features of the two types of accelerator currently used for research, the synchrotron and the cyclotron.

Synchrotrons, such as the Large Hadron Collider, are able to achieve high beam energy but with low beam intensity. Cyclotrons such as those used to provide hadron beams for cancer therapy, are able to produce high beam intensities but only at low energies, also the large magnets required make them prohibitively expensive. The rapid acceleration technique used in EMMA is capable of providing high energy and high intensity simultaneously, opening the way for a variety of applications for particle accelerators.

EMMA is a ring of interleaved magnets and accelerating cavities. The magnets simultaneously steer and focus the beam while the cavities accelerate the beam to 20 million electron volts. As this occurs the beam moves towards the outside of the ring, but due to the strong focusing, this movement is only a few millimetres. This makes EMMA smaller and cheaper than other machines with fixed magnetic fields. It is this compact, affordable design that will enable the acceleration of particle accelerators in hospitals and industry.

EMMA’s experimental work is ongoing, with more detailed studies being undertaken. The next step is to apply this technology to a range of applications not only with a view to improving medical treatment but also to provide better security scanning and create new solutions to tackle the energy crisis. It may in the future allow hospitals to implement newer and more effective form of particle beam technology to help treat some of the most difficult cancers as it is more cost effective and operationally simpler.
**ISIS reveals the secret to killing the *E.coli* bacterium**

*E.coli*, commonly found in the intestines of humans and animals, is generally considered to be a helpful bacterium that aids digestion. However, in some cases, it can be harmful to humans and is most commonly associated with food poisoning causing vomiting and diarrhoea which it can be particularly serious for young children, the elderly and people with weak immune systems. A team working on ISIS at RAL have made a breakthrough that could help combat such illnesses and help develop new ways of treating food poisoning and other diseases including meningitis.

The *E.coli* bacteria fight each other in competition for food and space; recent studies at the ISIS neutron source have highlighted how this happens and will be fundamental in developing new ways to treat illnesses. The results revealed that Colicin, toxins released from *E.coli* bacteria, travel across a protective waterproof membrane to kill their target cells.

During the neutron experiments the Colicin protein was tracked as it travelled through the membrane. The Colicin hijacks the pore-forming protein OmpF in the outer membrane of the bacteria and then squeezes down the side to reach the inner membrane, which it then attacks. This is a truly remarkable discovery as the Colicin is too big to fit through the narrow food entry pores in the outer membrane of *E.coli*.

This experiment was carried out at ISIS by a team from Newcastle University and was funded by the Wellcome Trust. The results of the research have been published in the Journal of Biological Chemistry and will be used to develop new, more effective ways to treat life threatening illnesses and save lives.
STFC’s Photowalk to be made into an annual event!

Over 200 amateur and professional photographers were given unprecedented access to three STFC sites; UK Astronomy Technology Centre (UK ATC), Daresbury Science and Innovation campus and Rutherford Appleton Laboratory. A number of working facilities, laboratory work spaces, science and site landscapes were photographed resulting in over 500 images submitted into the competition.

The event has proven to be a huge success and a very enjoyable day for participants. Positive feedback was received from each site, ‘it really presented a unique chance to shoot the various environments’, ‘from a photographic perspective there was no lack of subject matter.’, really outlines what a unique and fascinating experience the photowalk was. At each site the photographers were provided with the chance to see the facilities behind cutting edge science in the UK.

Following such positive feedback as ‘I hope this becomes a laboratory tradition’ and ‘what a fascinating morning’. STFC are going to make this an annual event that will also include Chilbolton Observatory in 2012 so get your cameras at the ready as you could have the chance to take part in this amazing opportunity and see ground breaking science at its best! Details about the next photowalk and last year’s winning images can be found by visiting our website on this address http://www.stfc.ac.uk/38366.aspx.
The winner of the public online vote

Dark Sky

In issue 8 we announced that Dark Sky Discovery was launching nine new and spectacular sites to explore the wonders of the night sky across England. The hope is that communities across the country will be inspired to identify their own ‘hot’ spots to view some of the wonders of the Universe.

Since then, Dark Sky Discovery have announced the opening of a further six sites on the hugely successful BBC ‘Stargazing LIVE’ series. Millions of viewers tuned in to watch while groups from each community demonstrated just how fun, inspiring and simple it is to explore the wonders of the night sky.

People from all backgrounds and age groups took part. Some of the sites will be used by astronomers to run regular stargazing events while others are good spots for local people, or tourists, to stargaze by themselves.

People can find out how to nominate their local Dark Sky Discovery Site by visiting www.darkskydiscovery.org.uk. For a full list of BBC Stargazing LIVE events please visit the BBC’s website: http://www.bbc.co.uk/thingstodo/project/stargazing-live.
A new facility that will allow scientists to see the properties of materials more clearly at the atomic level was launched in January.

The SuperSTEM consortium launched the EPSRC National Facility for Aberration Corrected Scanning Transmission Electron Microscopy (STEM) at Daresbury. The facility will give researchers from universities in the UK and around the world easier access to highly sensitive electron microscopes that are tuned to take account of lens distortions.

The launch event held at Daresbury was attended by an audience of leading scientists, industrialists and politicians. The day involved many lectures and addresses by various people including Andrew Bourne (Head of the EPSRC Physical Sciences Programme) who addressed the official opening of the facility.

STFC’s Professor Colin Whitehouse, a member of the Daresbury Science and Innovation Campus Joint Venture Board, said: “As a partner in both national science and innovation campuses, STFC is delighted that the EPSRC National Facility for Aberration-Corrected Scanning Transmission Electron Microscopy will be located at Daresbury. This superb facility will be an important asset to both the academic and industrial communities, and make the Daresbury Science and Innovation Campus an even more attractive place to develop important new scientific ideas and products.”

SuperSTEM is an academic consortium consisting of the Universities of Glasgow, Leeds, Liverpool, Manchester and Oxford. It also has collaboration agreements with three further partner universities: Cambridge, Sheffield and Warwick.

Please could you take the time to fill in our feedback form on our website from the following link http://www.stfc.ac.uk/stfcforms/FascinationSurvey.aspx