Diamond Light Source Case studies.

Diamond Light Source has kindly put together these case studies about how the facility has been used by a range of people, doing a variety of exciting work.

Diamond diffraction

Understanding HIV

What was the problem?

Although scientists have worked on the HIV virus for over 20 years, the structure of the protein that allows the virus to infect cells was not known. This is important as several drugs already target this protein, but it is not known exactly how they work. With this information, they can develop new drugs, which will hopefully be more effective.

The scientists used Diamond to find the structure of a protein called integrase – this is the protein that allows the genetic information from the virus to be integrated into the genome of the host. Once this has occurred, the host starts producing new copies of the virus.

What did they look at using diamond?

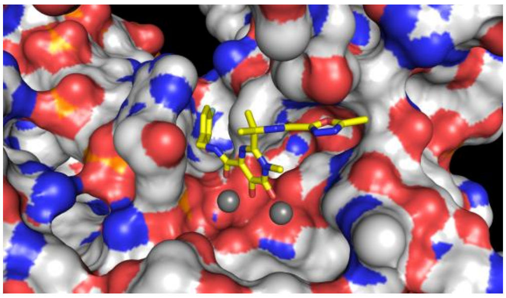
To study the protein, the team first had to produce a very pure solution of it, and then try to produce a protein crystal. The crystals are solid pieces of material produced by the protein molecules arranging into a very regular pattern. You can see crystals in nature – salt and sugar are both crystals. This can sometimes happen really easily, but often is very difficult.

In this study, it took over 40,000 attempts and four years of work to produce crystals suitable for studying.

When they finally succeeded, the team brought the crystals to Diamond to study using X-rays. The X-rays shine through the protein crystal, producing a pattern called a diffraction pattern. This pattern tells the researchers the position of the atoms in the protein. By taking many images, a 3D model can be created.

What did they find out?

The researchers succeeded in finding the structure of the protein. They also managed to soak the crystals in two drugs used to treat HIV, to see how the drug binds the protein. This information will hopefully allow them to develop new drugs which block the protein and stop it from working.



Isentress (Raltegravir) – a drug treatment, bound to the active site of the integrase-DNA complex

Application

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> *"It is a truly amazing story. When we started out, we knew that the project was very difficult, and that many tricks had already been tried and given up by others long ago. Therefore, we went back to square one and started by looking for a better model of HIV integrase, which could be more amenable for crystallization. Despite initially painstakingly slow progress and very many failed attempts, we did not give up and our effort was finally rewarded."*
>
> Dr Peter Cherepanov, Imperial College London

More info:

Retroviral intasome assembly and inhibition of DNA strand transfer Stephen Hare, Saumya Shree Gupta, Eugene Valkov, Alan Engelman, Peter Cherepanov, Nature January 2010

DOI: 10.1038/nature08784

Diamond materials

What becomes of the broken heart valves?

What was the problem?

The heart acts a powerful pump, pushing blood around the body. There are valves in the heart to ensure that blood is pumped in the right direction, but these can become damaged with age or disease. Damaged valves can be replaced with either an artificial valve, or a biological valve, usually from pigs. Over 200,000 people have valve surgery every year, and around 1/5th of these will need to have the valve replaced within 15 years.

Researchers are working to make valves more effective, by using different plastics called block co-polymers. These materials use different plastics bonded in tiny layers, which each contribute to the final properties of the valve. The properties of the material are complex, and finding out how they behave under repeated stress, as the heart will beat many many thousands of times over the life of the implant, is vital in deciding whether the material can be used in patients.

What did they look at using diamond?

The researchers, from Cambridge University, used Diamond to examine how three different materials behave under stress. They stretched the valves 10,000 times – the equivalent of a heart beating for just three hours, and took X-ray pictures every 10 milliseconds (1 millisecond is 1 thousandth of a second).

The technique they used showed how the polymers behaved at the molecular scale – looking at how individual polymer molecules move with each heart beat. Taking pictures so fast and so small is only possible using Diamond's X-rays.

What did they find out?

The researchers discovered that the new material behaves well under these realistic conditions. They also discovered that the direction of each layer was important to how the material behaves.

Application

The new materials will continue to be developed, and they can use the information from these experiments to improve them even more. It will be a few years before they are ready to test in humans.

> *"This study allowed us to examine the morphological evolution from the initial state to the stressed state and how this linked to the mechanical properties. We were able to observe real time micro-structural developments over the cycle time and over 10,000 cycles and measure the response of the material to applied mechanical stress on the ms timescale. It showed that these materials have both the long term stability and microstructural mechanical properties to be very promising for use in prosthetic heart valves."*
>
> Geoff Moggridge, University of Cambridge

More info

A real time SAXS study of oriented block copolymers during fast cyclical deformation, with potential application for prosthetic heart valves, Joanna Stasiak, Adriano Zaffora, Maria Laura Costantino and Geoff D. Moggridge, Soft Matter, 2011

DOI: 10.1039/C1SM06503C

Diamond Heritage

Saving silver with synchrotrons

What was the problem?

Silver leaf is commonly found on carved items from the medieval period. Many of the items decorated with silver leaf are rare and precious, but the silver leaf is prone to degrading and discolouring. The pieces were created by craftsman using complex techniques – there are many layers of adhesive, leaf and varnish. These are often made using materials such as animal based glues and varnishes, and the layers are extremely thin.

Scientists and conservators are trying to find the cause of the discolouration, so that better methods for preserving the pieces can be developed.

What did they look at using diamond?

Researchers looked at several tiny pieces of carved and flat wood with silver leaf decoration. They examined the samples using infra-red light, which allows the researchers to identify the biochemical signatures different molecules.

Because of the complexity of the materials, with multiple thin layers, made from organic materials, the synchrotron is a useful tool to use. The synchrotron can produce very focussed beams, allowing the scientists to identify the chemical composition of each layer in turn, to try and find the cause of the discolouration.

The infra-red technique used is a type of spectroscopy – the infra red light causes molecules in the sample to vibrate, and by looking at the vibrations we can see the 'signatures' of different molecules. This helps us find out what the material is made from.

What did they find out?

The researchers looked at several different materials, and it seems that in most cases the discolouration is produced by the layers on top of the silver leaf wearing away or cracking, allowing chemicals from the environment to react with the silver.

This is actually good news, as it means that the varnish isn't causing the problems in itself – if the varnish is intact, then the silver should not discolour.

Application

Understanding the way that historical objects are created gives us a better understanding of the techniques used by craftsmen and women. It also allows us to find new ways of preserving artefacts, and to make sure that the techniques we already use are not going to do more harm than good.

The synchrotron is a great tool for this, as it only required tiny samples, and is not destructive, so samples can be brought in whole if needed, or have very very small parts removed to be analysed.

More info:

Salvadó, N., Butí, S., Labrador, A., Cinque, G., Emerich, H. & Pradell, T. SR-XRD and SR-FTIR study of the alteration of silver foils in medieval paintings. Analytical and Bioanalytical Chemistry. 399, 3041-3052 (2011)