SAXS Appeal Reveals a Broken Heart

The latest beamline to reach "first light" at the Australian Synchrotron uses an intense beam of X-rays that allows researchers to take a wide view and a narrow view of their sample simultaneously. One of its first users will use it to visualise the biochemistry of the beating heart.

The SAXS/WAXS beamline produces about as much X-ray light as all the current beamlines combined, and has near-instantaneous imaging – just a few milliseconds – repeated a few hundred times a second. It's like a molecular slow-motion camera able to capture the smallest steps in chemical and biochemical reactions in liquids and solids. And it takes a wide (500 nm) and narrow (0.1 nm) look at the same time.

"We can look at proteins in their natural state," says Nigel Kirby, the proud father (beamline scientist) of the small-angle X-ray scattering (SAXS) and wide-angle X-ray scattering (WAXS) beamline.

"The X-ray diffraction beamlines require the proteins to be in crystal form, but many proteins can't be crystallised," he says. "This beamline can visualise them in solution, revealing not just their structure but also how they react with other compounds. So we can watch how small drug compounds react with large proteins.

"Another application is looking at how insulin forms fibres and decays in storage. The study could lead to insulin with a longer shelf-life."

But the beamline's not just good for biology. SAXS/WAXS has been used to study plastics with real- time observations of injection moulding to make plastic bottles and parts. "You can actually mould on the beamline and see how the polymer molecules change in the process," Kirby says.

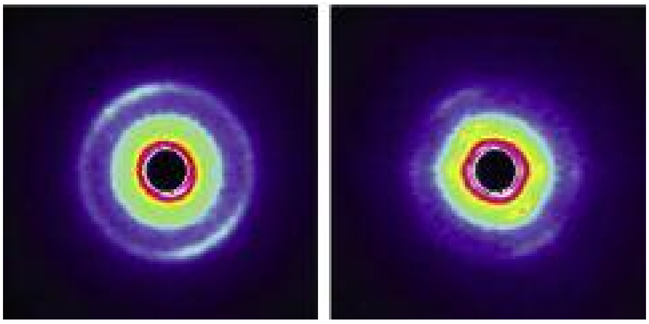
"And you can recreate high pressure, high temperature mineral processing and track the reactions. Material scientists are also looking to study surface chemistry. The beamline can look at just the top few molecules or look deep into the material.

"We achieved first light on 13 August," Kirby says. "Now we're running pilot experiments and hope to have the first users in by November."

A Closer Look at the Beating Heart

One of the first researchers through the door will be using the unique properties of SAXS/WAXS to explore the miracle of the heart beat and detect the early indications of heart disease.

"There's only so much you can tell about the heart out of the body," says James Pearson, a physiology researcher at Monash University. "Using the new beamline, we'll be able to study the biochemistry of the beating heart *in situ*.



A SAXS image of heart tissue. Each pattern shows reflections as coloured rings or spots around the central black hole, which is a filter to stop the main X-ray beam. The intensity and position of the ring-like reflections show that that the protein movements in the damaged part of the heart are abnormal. Being able to discriminate whether cardiac muscle is living or not has only been possible until now by taking a biopsy. With the SAXS we can now evaluate the health of the muscle in the intact heart.

Photo: James Pearson, Monash University

"We hope to learn more about the cascade of events that triggers each and every heart beat. Which proteins are the 'heart controllers'? What causes the heart beat to weaken in chronic heart disease?"

"We're following two muscle proteins – actin and myosin. Using transgenic animals we can see how things change when other proteins are inactivated.

"Our results have challenged current theories on how the heart functions. We hope to go on to look at which therapies are best for people recovering from heart failure and diabetes."

To date Pearson has used the giant SPring8 synchrotron in Japan. It's required him to have two sets of experimental animals – one in Melbourne, one in Japan. He's looking forward to a simpler life when the SAXS/WAXS beamline opens.

He's also looking forward to using another new beamline – the medical imaging line that will open in 2009. It will allow him to see blood flow in the heart, lung, brain and kidney.

"The high intensity beams can show us the small vessels which just aren't visible using conventional techniques," he says. "But these small vessels are the ones that actually determine how much blood gets to an organ. They're the ones that are central to cardiovascular disease."

It's been an interesting journey for Pearson, who came to take an interest in the human heart following studies of pelicans. "A pelican lays a small egg – about 100 grams," he says. "The chick rapidly grows to 4–5 kg in a couple of months. Then it has to adjust to the huge demands of flight. How do the bird's blood vessels, airways and organs grow to make it ready for flight?"

The performance of the human heart is no less remarkable. And, with the help of synchrotron light, the secrets of a broken heart may soon be revealed.

Visit www.synchrotron.org.au for more information.