The ARC Centre of Excellence for Coherent X-ray Science: Physics, Chemistry and Biology Working Together.

Keith A Nugent

ARC Centre of Excellence for Coherent X-ray Science, School of Physics, The University of Melbourne, Vic., 3010

Abstract — **The ARC Centre of Excellence for Coherent X-Ray Science will develop or use novel x-ray sources, such as the Australian Synchrotron, High Harmonic Generation Lasers and X-ray Free Electron Lasers, to solve problems in structural biology.**

I. Developments in coherent x-ray science

The development of x-ray crystallography has had an enormous impact on science, with possibly the most profound impact being in the field of structural biology and the discovery of the structure of DNA. The use of x-rays in structural biology, with its impact in biotechnology, is a major motivator for the construction of synchrotron sources around the world, including the new Australian Synchrotron.

The application of x-ray crystallography naturally requires that the molecule to be investigated can be formed into a crystal. Indeed, if this step can be achieved, the recovery of the structure from diffraction data is relatively routine. Attention is now being turned to the very large and important class of molecules that cannot be crystallized, the most famous of these being the membrane proteins. The aim of the ARC Centre of Excellence for Coherent X-ray Science (CXS) is to evolve strategies for obtaining structure from non-crystalline samples.

X-ray sources are themselves developing at an enormous rate. Historically the rate of increase of brightness of x-ray sources exceeds that predicted by Moore's law. Over the next few years, x-ray free-electron lasers will become operational, and UV free-electron lasers are operating now. These are true lasers with an essentially fully coherent output. The resulting beams will have a brightness some ten orders of magnitude brighter than that of a current synchrotron, in pulses that are tens to hundreds of femtoseconds in duration. These sources will be more specialized, and more expensive, than current synchrotron sources but the extreme brightness will the make the observation the scattering of x-rays from a *single* molecule a realistic possibility.

In parallel with the development of free-electron lasers, the development of high harmonic generation (HHG) lasers has been proceeding extremely quickly. In these systems, a very short pulse of visible, or IR, laser light is shone into a gas jet. The interaction of the intense fields act to generate the harmonics of the incident field out to high order, including the production of coherent soft x-rays. This is an emerging area and the reported brightness of the sources being created is increasing monthly. The potential applications of these sources in biology and biophysics have yet to be properly identified and explored.

II. The structure of CXS

The Centre has four university partners – The University of Melbourne Schools of Physics and Chemistry; La Trobe University Schools of Physics and Biochemistry; Monash University Centre for Synchrotron Science and the Swinburne Optics & Laser Laboratory at Swinburne University of Technology. We also have an alignment with a related Emerging Science Initiative within CSIRO and we have five international partner organizations.

The Centre has been funded for five years and has $9M of ARC funding, $1.8M from the Victorian State Government through its STI initiative and about $4M support from the partner universities. The CSIRO ESI funding is about $1.5M per year for two years in the first instance.

III. The scientific program

The long-term goal for CXS is to evolve techniques that will facilitate the structural determination of protein structures that cannot be crystallized. However this is an acknowledged major international goal for 21st century science and there are many approaches being taken to address this problem. However, with that overarching theme, we intend to build on our expertise in x-ray image formation, x-ray sources and biology to develop biophysical applications of non-crystalline diffraction.

The idea of trying to reconstruct an object from its x-ray scattering has a long history. The first experimental demonstration was published in 1999 by Miao and co-workers at Stony Brook University and the Brookhaven National Laboratory. Since that time, many groups have been developing the method both theoretically and experimentally, and the method is now at the heart of the international free-electron laser program and its quest to image a single biomolecule.

CXS has significant expertise in non-crystalline diffraction and related techniques and will use them with HHG lasers, the Australian Synchrotron and free-electron lasers to solve problems in cellular architecture, two-dimensional crystal diffraction, structural biology and materials science. We aim to maintain a focus on important biological problems, which will require a deep-seated collaboration across scientific disciplines. We will create an internationally leading interdisciplinary program working at the interface of physics, chemistry and biology.

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