Membrane protein structure can be seen using new X-ray free-electron lasers

December 20 2010

Australian researchers have identified a way to measure the structure of membrane proteins despite being damaged when using X-ray Free-Electron Lasers (XFELs), a discovery that will help fast track the development of targeted drugs using emerging XFELs technology.

About 70% of drugs on the market today depend on the activity of membrane proteins, which are complex molecules that form the membranes of the cells in our body.

A major problem for the design of new pharmaceuticals, often known as the “membrane protein problem”, is that they do not form the crystals needed to enable further investigation of the structure to design better drugs.

A major international effort is being mounted to determine the structures of membrane proteins using XFELs - large facilities that create such a bright beam of X-rays it is possible to see the X-ray light bouncing off a single molecule without forming a crystal.

Professor Keith Nugent, Laureate Professor and ARC Federation Fellow and Director of the Australian Research Council Centre of Excellence for Coherent X-ray Science (CXS) at the University of Melbourne said a key problem was that the light from an XFEL was so bright a molecule would start to disintegrate in less than one thousandth of a millionth of a millionth of a second.

In a paper published today in the journal *Nature Physics*, Professor Nugent and Associate Professor Harry Quiney from the ARC Centre of Excellence for Coherent X-ray Science (CXS) have developed a method by which the damage from the XFEL pulse may be included in the data analysis.

Associate Professor Quiney, also of the School of Physics at the University of Melbourne, said results showed that high-resolution molecular structures may be obtained from X-ray scattering data using a few-femtosecond pulse from an XFEL, even if the interaction resulted in significant electronic damage to the target.

“This result has far-reaching implications for the future development of structural biology, because it removes a significant obstacle to the practical realisation of the molecular microscope using XFEL sources,” he said.

It also provides important insights into the complex, turbulent and poorly-understood interactions that are driven by the interaction of an XFEL pulse with an atom, molecule or solid.

Their approach uses sophisticated molecular physics and careful data analysis to determine a new approach to measuring molecular structure.

Although still at the theoretical and computation level when put into practice this discovery will remove a major road-block in the path to solving the membrane protein problem.

This year, CXS signed an agreement with Japanese colleagues and will host the 4th Asia-Oceania Workshop on Science with X-ray Free Electron Lasers in 2011.

Professor Nugent said this was an extremely exciting time for X-ray

science.

“My colleagues and I are convinced that our recent work is a critically important step forward,” he said.

“We are very much looking forward to working with our Japanese colleagues in the coming years”.

Provided by University of Melbourne