## introduction

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## International Conference on Neutrons in Biology

This issue contains articles based on talks presented at the International Conference on Neutrons in Biology, held in Santa Fe, New Mexico, in October 2009. The conference highlighted the most current advances achieved in the field of neutron scattering analysis of biological systems and examined the prospects for using neutrons to address some of the greatest scientific challenges that we face in the 21st century, including renewable energy, the environment and human health. In addition to scientific sessions on protein crystallography, small-angle neutron scattering (SANS), reflectometry, inelastic scattering, fiber diffraction, instrumentation and deuteration and crystallization, the conference included a workshop on 'Computational Tools for Crystallography' and a special focus session on 'Neutrons for Renewable Energy and the Environment'. This conference was also an opportunity to celebrate Benno Schoenborn's many contributions to the field. Following a distinguished career in national research laboratories and universities around the world, Benno formally retired in May 2009.

After welcoming addresses from Al Hurd, Director of the Lujan Center of Los Alamos Neutron Science Center (LANSCE), and Jose Olivares, then acting Director of the Bioscience Division at Los Alamos National Laboratory (LANL) and now Executive Director of the National Alliance for Advanced Biofuels and Bioproducts, the first session on neutron crystallography opened with a keynote address by Ryota Kuroki in which two examples of drug binding to receptors were presented: porcine pancreatic elastase with the potent inhibitor FR13080 and human immunodeficiency virus type 1 protease with the potent inhibitor KNI-272. Julian Chen described how mechanistic insights from the structure of diisopropyl fluorophosphatase, a calcium-dependent phosphotriesterase, are being used to redesign the enzyme to better detoxify a wide range of organophosphorus nerve agents. Investigations into the molecular mechanism(s) of sweet taste were presented by Susana Teixeira, with structure determination of the artificial sweetener thaumatin. Andrey Kovalevsky presented the findings of a very elegant study led by Yukio Morimoto on the Bohr effect in the allosteric binding and release of oxygen in Hb. Pavel Afonine gave an overview the state-of-the-art computational methods being developed in the PHENIX (Python-based Hierarchical ENvironment for Integrated Xtallography) software package, focusing on tools for structure determination using neutron crystallographic data. New computational methods for neutron crystallography were also the topic of Dritan Siliqi's talk, in which he demonstrated that the Freelunch, Difference Electron Modification and Electron Density Modification techniques could be used to increase the visibility of hydrogen in the neutron structures of proteins.

There followed a mini-symposium on 'Neutrons for Renewable Energy and the Environment' organized by Mike Kent. Yoshiharu Nishiyama presented a keynote address on how neutron fiber diffraction is being used to understand the hydrogen-bonding network in cellulose, which is widely regarded as a major contributor to the recalcitrance of lignocellulosic biomass to conversion into fermentable sugars. Venki Pingali explored the structural effects of acid pretreating biomass in order to improve its breakdown into sugars using the SANS technique. SANS was also used by Mike Kent to study the enzymatic hydrolysis of biomass to sugars. Paul Langan described a broad range of efforts at LANL to use neutron crystallography to better understand the enzymes involved in the conversion of biomass into sugars and the metabolism of these sugars during their conversion to biofuels and other added products. Carbonic anhydrase is a ubiquitous metalloenzyme that reversibly converts carbon dioxide to carbonic acid and bicarbonate ions in the mammalian respiratory system and has great potential for enhancing the growth of algae for renewable fuels and also for carbon capture. Zoe Fisher described the latest results of studies on the hydrated proton-transfer wire implicated in the enzymatic process. The structural information from these different techniques and length scales is being used by S. Gnanakaran to build a predictive multi-scale model of biomass and its conversion.

Recent developments in instrumentation for neutron crystallography were presented at a session that included descriptions of the capabilities of the PCS at LANSCE (Andrey Kovalevsky), LADI-III at the Institute Laue– Langevin (ILL; Matthew Blakeley), iBIX at J-PARC (Ichiro Tanaka) and TOPAZ at the Spallation Neutron Source (SNS; Xiaoping Wang). This session was a rare gathering of all of the scientists directing operational macromolecular neutron crystallography beamlines across the world and this opportunity was used to discuss strategies for collaborating to best address future opportunities and challenges.

Sessions on SANS, inelastic neutron scattering, neutron reflectometry and fiber diffraction illustrated the diversity of information that is provided by neutrons in biology. William Heller described the dedicated Bio-SANS instrument at HFIR and Cameron Nylon described the new SANS2d instrument at ISIS, which is an example of the next generation of SANS instruments with two tandem two-dimensional detectors. Rex Hjelm presented the findings of a fascinating study using SANS to unravel the complex dynamic process of moving cellular organelles along the microtubule network. Studies of phase transitions, hydration, folding/unfolding and drug binding in DNA using complementary X-ray and neutron scattering and diffraction techniques were presented by Trevor Forsyth. Progress towards developing a unified model for protein dynamics was presented by Hans Frauenfelder. Neutron reflectivity is used extensively to study the structure of biological membranes. Jarek Majewski used a thermoresponsive polymer to tailor the local curvature of a fully hydrated tethered bilayer, thus forming an excellent model for an intact biological membrane. Luke Clifton explored the interaction of puroindolines (seed defense proteins in wheat) with lipid bilayers to better understand wheat endosperm texture and also to provide valuable insight into protein–lipid interactions.

The second session on neutron crystallography opened with a keynote address from Alberto Podjarny in which he described the neutron structures of aldose reductase and a type III antifreeze protein. This work highlights recent advances in the capability of neutron crystallography to study biological systems at the protonation level with radically small perdeuterated crystals. Jenny Glusker illustrated recent work on the movement of H atoms involved in sugar conversion by D-xylose isomerase, an important enzyme for biofuel production. Hemoglobin was again the subject of Tim Mueser's studies of erythrocyte senescence and Taro Yamada presented neutron crystallographic analyses of T<sub>6</sub> insulin and the complex of trypsin with the inhibitor BPTI.

The *PHENIX* (http://www.phenix-online.org) and *nCNS* (http://mnc.lanl.gov) software packages are being developed for the international neutron macromolecular crystallography community by an National Institutes of Health-funded consortium of scientists led by Paul Langan and Paul Adams. These packages now include a generalized X-ray and neutron crystallographic analysis approach that provides more accurate and complete structures for biological macromolecules. Pavel Afonine presented an excellent overview and then together with Marat Mustyakimov led a workshop on 'Computational Tools in Neutron Crystallography' in which hands-on tutorials demonstrated the many features of both packages.

Benno Schoenborn gave a colourful narrative of the development of the unique contribution of neutron scattering applied to biological structures. Benno first discussed the possibility of using neutron diffraction to investigate hydrogen bonding in proteins with Herman Watson, Uli Arndt, John Kendrew and Christopher Nobbs in the MRC tearoom in 1965. Two years later, with support from Christophe Hirs and using Walter Hamilton's single-detector diffraction peaks from a rather large (by today's standards) myoglobin crystal. Benno's career is a kaleidoscope of people, places and achievements always pushing the limit in knowledge, theory, instrumentation and software, the impact of which will be substantial well into the future.

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Organizing Committee: Paul Langan (LANL; Chair), Matthew Blakeley (ILL), Trevor Forsyth (Keele, ILL), Mike Kent (SNL), Robert Knott (ANSTO), Jarek Majewski (LANL), Nobuo Niimura (J-PARC), Volker Urban (ORNL).