Crystallography meeting showcases advances in biomedical research

By Raj Gosavi

Structural biologists from NIEHS were on hand as the annual Mid-Atlantic Macromolecular Crystallography (MAMC) Meeting marked its 43rd year May 30-June 1 at Duke University.

Starting in 1970 as a small group gathering at a professor’s home in Charlottesville, Va., the meeting has flourished over the years. Head of the organizing committee and chair of Duke Department of Biochemistry Richard Brennan, Ph.D., (http://www.biochem.duke.edu/modules/biochem_brennan_lab/index.php?id=1) said that this year’s meeting attracted a record number of attendees — more than 180 — traveling from as far away as Connecticut.

As one of the powerful structural biology techniques, crystallography offers a unique perspective into the world of proteins, enzymes, and nucleic acids (see text box). The annual MAMC meeting provides attendees with an opportunity to share the latest developments in structural biology, and to exchange the most current techniques in the field of macromolecular crystallography.

As the meeting’s keynote speaker, Los Alamos National Laboratory structural genomics researcher Thomas Terwilliger, Ph.D., (https://solve.lanl.gov/terwilliger/) said afterwards, “The Mid-Atlantic Macromolecular Crystallography Meeting was a wonderful success. It was a great opportunity to see exciting structural biology results, and new methods for X-ray crystal structure determination and analysis.”

A grand group meeting

The posters and talks provided three-dimensional snapshots of macromolecules involved in cell signaling, cellular disruption and defense, nucleic acid biology, and cell division. One of the speakers, Bret Freudenthal, Ph.D., a postdoctoral fellow in the NIEHS Laboratory of Structural Biology (LSB) DNA Repair and Nucleic Acid Enzymology Group headed by Samuel Wilson, M.D., utilized time-resolved crystallography to capture an additional metal binding site transiently formed in the polymerase active site following catalysis, which has been undetectable using other approaches.

The meeting had a perfect mix of scientists from universities, research institutes, and industry. One of the attendees, NIEHS visiting fellow Sara Andres, Ph.D., of the LSB Genome Stability Structural Biology Group headed by Scott Williams, Ph.D., remarked, “Most of the speakers are graduate students and postdoctoral fellows, which provides a valuable career development opportunity.” Other NIEHS attendees, including LSB biologist Andrea Moon, remarked on the camaraderie among attendees that created a comfortable setting for interpersonal interaction.

Technological advances in the field of crystallography

Among the sponsors for the meetings were vendors who exhibited improved tools for crystallographers. Vendors attending this meeting each year benefit from interactions with the scientific community, as much as the scientists do from the representatives. Mike Murray, Ph.D., currently with Rigaku and formerly a member of the NIEHS Laboratory of Molecular Genetics group headed by Thomas Kunkel, Ph.D., said, “This meeting is one of the best crystallography meetings I get to attend. Knowing the cutting-edge science being presented helps us push the developments [in supplies and equipment] even further.”

Program developers and users

The final step in obtaining a crystal structure of a macromolecule consists of utilizing computer programs available for the purpose. Presentations and workshops from the program developers provide opportunities to learn, for both beginners and advanced users. This cross talk between the users and developers makes the programs more efficient and accommodating.

The crystallography community in the Research Triangle Park, N.C., area, including scientists at NIEHS, continues to enjoy...
outstanding success in the field. The number of scientists utilizing crystallography in their work is constantly growing and currently includes NIEHS researchers with interests in structural biology, molecular genetics, signal transduction, reproductive and developmental toxicology, and neurobiology. The crystallography facility at NIEHS continues to expand and become more efficient, as it provides core support for the growing number of users.

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The power of macromolecular crystallography

Macromolecular X-ray crystallography is a technique used to determine the atomic resolution structures of macromolecules, such as proteins and enzymes, nucleic acids, ribosomes, and viruses. The diffraction of X-rays from macromolecules in a crystal is used to obtain information in the form of electron density around the atoms in a molecule. The chemical structure is then determined by fitting a model to the electron density.

While much can be learned from amino acid or nucleic acid sequences, the strength of crystallography is in its ability to provide the important third dimension. Due to its powerful nature, biochemists have been applying crystallography to address questions ranging in size from small chemicals to large intermolecular protein interactions.

In the 100 years following the discovery of X-ray diffraction, X-ray crystallography has found applications in many areas, including biology and biotechnology. Starting from small molecule structure determination, the interdisciplinary field progressed in the early days with research by inorganic chemists, material scientists, and mineralogists. Physicists were instrumental in the birth of X-ray crystallography, and even now crystallography continues to contribute to, and gain from, the efforts of physicists.

The application of crystallography to macromolecules has enabled its valuable contributions to biomedical research. Crystallography also continues to advance the environmental health sciences, by providing insights into the effect of environmental agents on human health.

The versatile nature of the X-ray crystallography is evidenced from its wide application in multiple disciplines. Because of the power and wide application, the General Assembly of the United Nations is recognizing 2014 as the International Year of Crystallography.