

Neutron Scattering in the Biological Sciences: Techniques And Applications

Flora Meilleur^{1,2}

¹ Department of Molecular and Structural Biochemistry, North Carolina State University ² Neutron Scattering Division, Oak Ridge National Laboratory

Corresponding Author	Meilleur, F. Neutron Scattering in the Biological Sciences: Techniques And Applications. <i>J. Vis. Exp.</i> (191), e64806, doi:10.3791/64806 (2023).	
Flora Meilleur		
meilleurf@ornl.gov		
Date Published	DOI	URL
January 20, 2023	10.3791/64806	jove.com/video/64806

Editorial

Neutron scattering and diffraction techniques are uniquely sensitive to the position and dynamics of hydrogen atoms in materials and are powerful tools for the characterization of structure-dynamics-function relationships in biological systems. The sensitivity of neutrons to hydrogen atoms, and to its isotope deuterium, arises from the strong interaction of neutrons with the nuclei of these atoms. This property makes the information available from neutron scattering unique and a valuable complement to data obtained from structural characterization techniques more typically used in biological sciences. Neutrons also have the advantage of not causing any measurable radiation damage to biological samples.

This collection brings together a wide range of neutron techniques that have been developed in order to study biological systems and examples of their applications. Neutron research facilities offer access to advanced, non-destructive suites of instruments for biophysical characterization, which provides structure and dynamic information, spanning from Ångströms to microns and beyond, and from picoseconds to microseconds, respectively. Neutron applications in biology range from the analysis

of individual hydrogen atoms in enzymes to the macroscale analysis of biological complexes, membranes, and assemblies.

At the atomic length scale, neutron macromolecular crystallography is a technique that enables researchers to understand the chemistry catalyzed by enzymes through experimentally identifying hydrogen atoms that are essential to catalysis. Neutron macromolecular crystallography requires large crystals to compensate for the relatively low fluxes of the neutron beams available to conduct experiments. Vahdatahar et al. 1 demonstrate a protocol to grow large, high-quality crystals using the OptiCrys crystallization bench. OptiCrys controls and monitors the temperature and concentration of a crystallization agent of a microdialysis experiment, allowing the experimenter to efficiently survey the protein phase diagram to identify and modulate optimal crystal growth conditions. Schröder and Meilleur² demonstrate how large crystals are handled to collect neutron crystallographic data at ambient and cryogenic temperatures. These authors also demonstrate how to perform crystallographic refinement of a protein model



against neutron data only, or joint refinement against neutron and X-ray data.

Small angle neutron scattering (SANS) is a low-resolution technique used to gain structural information from biological complexes at the molecular level. Time-resolved SANS allows following the structural evolution of complexes over time when conditions are changed. Kelley et al.³ describe a stopped-flow SANS sample environment that supports the fast mixing of biological liquid samples, studying their structural evolution on time scales of seconds to minutes.

Neutron radiography and computed tomography resolve structural features in biological samples on the order of tens of micrometers. This technique is suited to structural characterization of biological materials at the organ level. Bilheux et al.⁴ describe the application of neutron radiography in plant physiology and biomedical applications. The authors describe sample preparation, data acquisition strategy, and data analysis.

Neutrons not only characterize where atoms are (structures) but also how atoms move (dynamics). Neutron spin echo (NSE) is a powerful technique to study the dynamics of biological systems on the time scale of several tens of nanoseconds. Stingaciu⁵ describes the application of NSE to study the dynamics of a human antibody protein and of an intrinsically disordered protein. Each step, from sample preparation to data collection and analysis and computer-aided dynamics simulations are introduced. NSE can also probe the dynamics of biological membranes, as Kumarage et al.⁶ demonstrate a protocol for the measurement of the dynamics of a model lipid membrane.

Neutron scattering is a powerful tool to investigate the structure-dynamics-function relationship in biological material. Recent developments in sample preparation, instrumentation, and data analysis are allowing more complex biological questions to be addressed. This Methods Collections provides researchers with techniques that provide unique insight on the behavior of biological systems.

Disclosures

The authors have nothing to disclose.

Acknowledgments

The authors have no acknowledgements.

References

- Vahdatahar, E., Junius, N., Budayova-Spano,
 M. Optimization of crystal growth for neutron macromolecular crystallography. *Journal of Visualized Experiments*. (169), e61685 (2021).
- Schröder, G. C., Meilleur, F. Neutron crystallography data collection and processing for modelling hydrogen atoms in protein structures. *Journal of Visualized Experiments*. (166), e61903 (2020).
- Kelley, E. G., Nguyen, M. H. L., Marquardt, D., Maranville, B. B., Murphy, R. P. Measuring the timeevolution of nanoscale materials with stopped-flow and small-angle neutron scattering. *Journal of Visualized Experiments*. (174), e62873 (2021).
- Bilheux, H. Z. et al. Neutron radiography and computed tomography of biological systems at the Oak Ridge National Laboratory's high flux isotope reactor. *Journal* of Visualized Experiments. (171), e61688 (2021).



- Stingaciu, L.-R. Study of protein dynamics via neutron spin echo spectroscopy. *Journal of Visualized Experiments*. (182), e61862 (2022).
- Kumarage, T., Nguyen, J., Ashkar, R. Neutron spin echo spectroscopy as a unique probe for lipid membrane dynamics and membrane-protein interactions. *Journal of Visualized Experiments*. (171), e62396 (2021).