PCS Protein Crystallography Station

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The PCS at LANSCE is a high performance beam line that forms the core of a capability for neutron macromolecular structure and function determination.

Neutron crystallography is a powerful technique for locating H atoms which can be hard to detect using X-rays. The PCS therefore provides unique information about how H is involved in the function of biological macromolecules. Most PCS Users require this information in order to understand the details of enzyme mechanism, drug binding, or protein hydration and dynamics. Overleaf are some highlights from the User program.

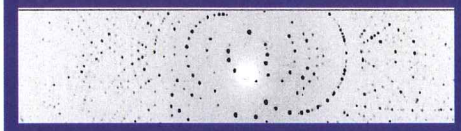
Users of the PCS have free access to an integrated capability unique to Los Alamos that includes neutron beam-time, deuteration facilities, the expression of proteins and the synthesis of substrates with stable isotopes, and also support for data reduction and structure analysis. The PCS accommodates around 20-40 users per year and beam time is allocated through a peer review process. The call for proposals for 2010 is given overleaf.

The PCS is the first protein crystallography beam line to be built at a spallation neutron source and is the only resource of its kind in North America. The beam-line exploits the pulsed nature of spallation neutrons and a large electronic detector in order to efficiently collect wavelength resolved Laue patterns using all available neutrons in the white beam.

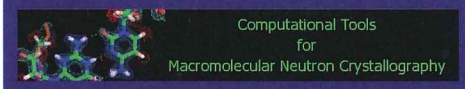
User Support & Capabilities

Deuteration Laboratory for protein expression, protein deuteration, and synthesis of substrates with stable isotopes.

Robotic Purification and Crystallization Laboratory, including support with crystal mounting and H_2O /D_2O exchange.



Mail-in data collection option; data processing with d*TREK customized for Time-of-Flight Laue data..



Computational Tools for Macromolecular Neutron Crystallography (MNC) is an NIH funded consortium between LANL and LBL to develop and distribute ***PHENIX*** and ***nCNS*** structure determination software :

http://mnc.lanl.gov

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LANSCE

CALL FOR PROPOSALS
for Run Cycle Beginning the June 2010

You are invited to apply for beam time on the PCS. **The deadline for submitting proposals is 6:00 p.m. MST Monday, March 22, 2010.** Rapid access proposals may be submitted at any time, but require compelling evidence of sufficient scientific urgency to justify special scheduling. Users of the PCS have access to free neutron beam-time, free perdeuration services and also support for data reduction and structure analysis.

For technical information about the **PCS** and experimental requirements, contact Paul Langan (505) 665 8125, langan_paul@lanl.gov or Zoë Fisher (505) 665-4105 zfisher@lanl.gov.

Proposal Submission: Proposals must be submitted using the process on the LANSCE website. To access the proposal submission site, go to the LANSCE home page, http://lansce.lanl.gov/. On this page click the tab "Lujan Center' and then the link 'Submit a Proposal.This will take you to the on-line submission system. Detailed instructions for preparing the proposals can be found on the proposal submission sites under "Step-by-Step Guide to Submitting an Online Proposal."

User Highlights

The innovative strategies being used at the unique neutron PCS facility at Los Alamos are producing insights into biological systems that could not have been obtained using any other technique. Using information on the location of H in the active site of **Diisopropyl Florophosphatase**, Users from the Goethe University of Frankfurt have reengineered the enzyme to perform better in detoxifying nerve agents (Blum et al. *Proc. Nat. Acad. Sci.* 2009, 106:713). Several enzymes that are involved in bioenergy and renewable fuels are being studied, including biomass hydrolyzing and sugar metabolizing enzymes. By collecting neutron data sets from a series of complexes of **D-Xylose Isomerase** with various cofactors and substrates bound, Users from Fox Chase Cancer Center and Toledo University have been able to locate H and its movement at different stages of the sugar isomerization reaction. New insights into the catalytic mechanism are being used to improve enzyme performance (Katz et al *Proc. Nat. Acad. Sci.* 2006, 103:8342; Kovalevsky et al. *Biochem* 2008, 47: 7595). By determining the protonation state of the catalytic residues in **Endothiapepsin** Users from Oak Ridge National Laboratory and the University of Southampton have been able to determine the mechanism of an important **Aspartic Proteinase** drug target (Coates et al. *J. Am. Chem. Soc.* 2008, 130:7235). User from Florida University have elucidated key H features in the active site of **Carbonic Anhydrase** that support proton transfer and lead to a new proposed enzyme mechanism. This information is being used to re-engineer the enzyme to be pH-insensitive and thermally stable for carbon sequestration or biodiesel production (Fisher et al. *Biochem.* 2010, 49:415). By directly revealing induced protonation during drug binding of the anticancer drug MTX Users from Case Western Reserve University have revealed the mechanism for enhanced drug binding to the enzyme **Dihydrofolate Reductase** (Bennett et al. *Proc. Nat. Acad. Sci.* 2006, 103:18493).