Design of a High Resolution Macromolecular Neutron Diffractometer (MaNDi) for Structural Biology Research at the SNS

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With the advent of third-generation synchrotron X-ray sources, it was envisioned that ultra-high resolution macromolecular crystallography (UHRXMC) at resolutions of 0.5 Å to 1.0 Å would provide detailed information on the positions of critical hydrogen atoms within the active sites of enzymes. To date, in about 82 structures in the PDB in this resolution range, significant numbers of hydrogen atoms including those in the active sites could not be identified. Furthermore, only about 0.5% of all macromolecular structures in the PDB are amenable to UHRXMC and hence other complementary techniques are needed for the identification of critical hydrogen atoms involved in the catalytic mechanisms in a majority of enzyme systems.

Neutron Macromolecular Crystallography (NMC) has been shown to provide accurate proton positions, protonation states and hydration states, as well as hydrogen/deuterium exchange, in macromolecular crystals even at moderate 2 Å to 2.5 Å resolution. One major bottleneck that severely constrains the productivity of NMC is the limited flux at the current sources and the requirement of large crystals. The advent of the Spallation Neutron Source (SNS), with over an order of magnitude increase in neutron flux, the advances in neutron optics and detectors, as well as advances in structure genomics and deuteration. provide an exciting opportunity to push the NMC field to new horizons. Hence we propose to develop a dedicated world-class high resolution time-of-flight single crystal macromolecular neutron diffractometer (MaNDi) for structural biology research at the SNS. MaNDi has been designed to be able to collect a full hemisphere of Bragg data with a resolution of 1.5 to 2 Å on a crystal with a lattice constant up to 150 Å in 1 to 7 days. The higher throughput and resolution are accomplished by the use of a wide wavelength bandwidth of cold neutrons (1.8 Å < λ < 4.5 Å) sorted into a large number of high resolution wavelength channels by time-of-flight and by an array of high resolution position-sensitive area detectors covering a large solid angle. We envision that the unprecedented high data rates and resolution with MaNDi will open up new avenues and greatly advance the field of structural biology, enzymology and protein dynamics.

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