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Complex Protein Structures by Neutron Scattering[1]

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Neutron scattering by an atom, unlike X-ray scattering, does not depend on the atomic number of that atom. Deuterium atoms scatter neutrons to the same extent as carbon or oxygen atoms and give positive peaks in a nuclear density map, while its isotope, hydrogen, gives a negative peak. Therefore neutron diffraction provides two results that are difficult to obtain from macromolecular X-ray diffraction studies: (1) the locations of hydrogen atoms, including the more mobile ones, and (2) the extent to which a hydrogen atom can be replaced by deuterium. The method shows whether an amino acid side chain (at a given pH value) is ionized or not. For example, one can ascertain whether histidine residues are singly or doubly protonated at the pH of study. Neutron diffraction studies can also be used to determine the absolute configuration of the course of a biochemical reaction by anomalous scattering and enzymatic deuteration of the substrate. Neutron diffraction experiments, however, require large crystals and these are often impossible to obtain for many macromolecules. Examples of reports of the use of neutron diffraction to provide information on enzymatic mechanism will be presented. This includes descriptions of our work on the enzyme D-xylose isomerase for which the orientation of a metal ion-bound water molecule in the active site was found. This water, thought to be involved in the isomerization step, was shown to be water (rather than hydroxyl) at pH 8.0. This analysis also revealed that one lysine has two rather than three attached hydrogen atoms and therefore lacks a positive charge. High-resolution X-ray studies (at 0.94 Å) indicate how some side chains might move during catalysis. This combination of neutron and X-ray diffraction can contribute greatly to the elucidation of enzyme mechanisms. I thank Amy Katz, Xinmin Li, H. L. Carrell, Leighton Coates, Leif Hanson, Joel Harp, Paul Langan, and Benno Schoenborn who were involved in many of the described studies, and particularly Gerard Bunick. We honor his contributions and regret that he is no longer with us.

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