Neutron Structure Determination via Macromolecular H/D Derivatives

David A. Langs, Herbert A. Hauptman, Hongliang Xu, *Hauptman-Woodward Medical Research Institute, Inc., 700 Ellicott St., Buffalo, NY 14203 USA*. E-mail: langs@hwi.buffalo.edu

The principle of H_2O/D_2O solvent variation (Schoenborn, 1976) in neutron diffraction has long been used as a tool for structural phasing. The first crystal structure application of this procedure gave a 5Å map for the peptide antibiotic gramicidin A that was originally crystallized from ethanol (Koeppe & Schoenborn, 1984). A gramicidin derivative was synthesized for which the two methyl groups of Val^1 had been deuterated, to be contrasted with the native wild-type hydrogenated structure. Unfortunately crystals of sufficient size could not be obtained to help extend the initial 5Å model to the 2.5Å limit of the native data.

A problem arises when multiple H/D replacement sites are covalently bound to the same atom, in that these atoms will be only 1.7Å apart: the substructure can not be easily determined by conventional ΔE direct methods unless data are measured to better than 1.2Å. This is highly unlikely due to the weak flux rates at most neutron scattering facilities.

We have devised a new structure determination method for such H/D derivative applications which allows one to obtain the macromolecular phases directly without first having to solve the substructure, such that lower resolution neutron data sets can be successfully utilized.

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[1] Schoenborn B. P., *Biochim. Biophys. Acta*, 1976, **457**, 41-55. [2] Koeppe R. E. , Schoenborn B. P., *Biophys. J.*, 1984, **45**, 503-507.

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