

## 02-Methods for Structure Determination and Analysis, Computing and Graphics

written (in Fortran) to be easily portable to other computer platforms. This program has begun to play a major role in our studies by providing a tool with which measured diffraction data can be compared to 3D computer simulations. The wide applicability of this program will be demonstrated by showing example diffraction patterns from simulated size-effect displacements in metallic alloys, mineral systems exhibiting oxygen vacancy order and cation relaxations, and conformational disorder in organic crystals. The program and a manual describing its use will be made freely available.

**MS-02.05.03** DIFFUSE SCATTERING AND INTRA-MOLECULAR FLEXIBILITY IN PROTEINS by J-P. Benoit, P.Faure and J.Doucet\*, LURE and Laboratoire de Physique des Solides, Université Paris-Sud, F91405 Orsay, France

The growing interest in the dynamical behaviour of proteins is motivated by the fact that in many cases the functional roles of these biological molecules do not only depend on their rigid three-dimensional structure but also on their deformability or flexibility. The atomic motions implicated in the macromolecular deformations cover indeed an extremely large range in amplitudes (sub-Ångströms to a few tenths of angstroms) and in duration from femto-s when only a few atoms are concerned up to seconds when thousands atoms move in a concerted (or correlated) way. Due to this enormous variety of motions, the experimental approach of the large panoply of techniques used. In order to overcome this difficulty calculation and simulation approaches have been developed. Nevertheless, up to now the likelihood and the efficiency of these theoretical approaches had only been indirectly tested through their ability to facilitate protein structure determination and refinement by NMR or X-ray diffraction methods, or by comparisons of crystallographic B-factors with the mean square fluctuations of atoms.

We evidence here for the first time, direct correspondance between the intramolecular motions predicted by numerical simulations and X-ray diffuse scattering experimental observations.

**MS-02.05.04** STUDIES OF DIFFUSE SCATTERING REVEAL LIQUID-LIKE DISORDER IN PROTEIN CRYSTALS, by Y. Li\*, D.L.D. Caspar, B. Yu, Rosenstiel Basic Medical Sciences Research Center, Brandeis University, Waltham, MA 02254-9110, U.S.A., and J. B. Clarage, Department of Biochemistry and Cell Biology, Rice University, Houston, TX 77251,

Diffuse scattering from protein crystals, notably haloes surrounding Bragg reflections, contain information about both the amplitude and correlation of atomic movements in the protein molecules. We have developed an analytical model for simulating diffuse scattering from protein crystals by representing the averaged Patterson function as the convolution of the peaks in the ideally ordered Patterson with a Gaussian whose variance is a function of the mean square atomic displacement and a correlation function which describes coupling between the movements. Based on this model we have simulated diffuse scattering data collected from lysozyme and insulin crystals in terms of an exponentially decaying correlation function which has

two components separating short range and long range coupling. The results show that the coupling of atomic movements in these highly ordered protein crystals is mostly short-ranged, similar to that in liquid rather than that in elastic solids. The total mean square atomic displacements for tetragonal lysozyme, triclinic lysozyme and 2 Zn rhombohedral insulin are  $0.25 \text{ \AA}^2$ ,  $0.13 \text{ \AA}^2$  and  $0.2 \text{ \AA}^2$ , respectively. About 90% of the total mean square displacements in these crystals are correlated over distances the size of one amino acid residue ( $\sim 6 \text{ \AA}$ ). Movements that are correlated over the distance the order of size of the protein molecule ( $\sim 50 \text{ \AA}$ ) account for about 10% of the total displacements. Experiments are under way to measure diffuse scattering data from cubic insulin crystals at different pH and ionic strength, and to analyze these data in terms of the analytical model described above and empirical models about switching between conformational states that are evident in high resolution structures.

**MS-02.05.05** MODELS FOR DIFFUSE SCATTERING FROM PROTEIN CRYSTALS by Nobuhiro Go<sup>\*1</sup>, Kenji Mizuguchi<sup>1</sup> and Akinori Kidera<sup>2</sup>, <sup>1</sup>Department of Chemistry, Faculty of Science, Kyoto University, Sakyo-ku, Kyoto 606, Japan and <sup>2</sup>Protein Engineering Research Institute, 6-2-3 Furuedai, Suita, Osaka 565, Japan

We have developed a new theoretical framework for the study of X-ray diffuse scattering from protein crystals, in which we start from a general equation and introduce a series of approximate models, appropriate for analyses of experimental data obtainable with different degrees of precision. When a high precision data are available, we can employ essentially the same model used for the recently developed method, NM-REF (Kidera, A.&Go, N.(1992) *J. Mol. Biol.* 225, 457-475), of refinement of protein structure from the usual Bragg diffraction. Further approximation is based on the assumption that the covariance matrix of atomic displacements can be expressed by using a relatively simple empirical correlation function. The formalism using the correlation function retains information about atomic details and allows us to introduce a variety of models, in which (1) the effect of higher order scattering is included, (2) intra- and intermolecular correlations can be distinguished, and (3) amplitudes of fluctuations can be atom-dependent. By calculating diffuse-scattering patterns from a human lysozyme crystal, we have examined the assumptions used in these models and discussed important factors that determine the general feature of the scattering patterns. The higher order scattering is shown to make a significant contribution at high resolutions. It is also shown that the resulting patterns are sensitive to changes in correlation lengths of about 1Å, but they are also affected sensitively by the form of the correlation function. Only the 'average' value of the intra- and intermolecular correlation lengths seems to determine the gross feature of the pattern.

**MS-02.05.06** DIFFUSE SCATTERING IN ELECTRON DIFFRACTION FROM MOLECULAR ORGANIC- AND PROTEIN-CRYSTALS; ANALYSIS OF CRYSTAL-CRYSTAL PHASE TRANSITIONS. By Douglas L. Dorset\*, Electron Diffraction Dept., Medical Fndn. of Buffalo, Inc., 73 High St., Buffalo, NY 14203 USA

Electron diffraction patterns from molecular organic crystals often contain a pronounced directional diffuse component