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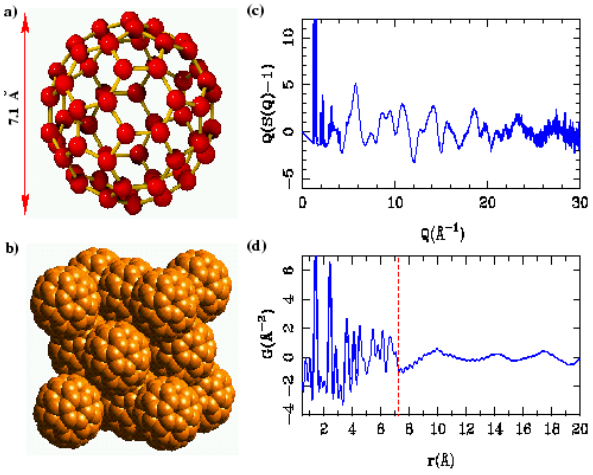
Local Structure of Folded Proteins

Presenter: S.J.L. Billinge

Recently, great advances have been made in our ability to study the local atomic structure of materials using the atomic pair distribution function (PDF) technique. We are now able to extract short-range atomic correlations with unprecedented resolution using high-energy x-ray synchrotron radiation and computer modeling techniques. Modern third-generation sources such as the APS at Argonne National Laboratory provide large fluxes of high-energy x-rays making measurements possible on smaller and more dilute samples opening the door to the study of protein structures using this technique. The advantage of such an approach in principle is that the molecules under investigation need not be spatially or orientationally ordered. This means that it is, in principle, possible to study proteins in solution.

We illustrate the PDF approach using a particular example, which happens to be a very favorable case that is relevant to the protein problem. The example we will use is that of a solid made up of bucky-balls (C_{60} molecules). At room temperature these balls rotate rapidly and there is no orientational relationship between them; atoms on one ball are essentially uncorrelated with atoms on neighboring balls. Crystallographic approaches can reveal the spatial arrangement of the balls if they are long-range ordered, but not reveal any information about the structure of the balls themselves. The PDF measurement does, however, give the local atomic structure of the molecules themselves. This is shown in the figure. Neutron scattering data are shown in the upper right panel and the atomic PDF in the lower panel. Sharp peaks appear in the PDF at distances corresponding to the separation of pairs of atoms. Using computer modeling we can reconstruct the 3-dimensional structure of the C_{60} molecule, even though they were rotating at high speed.



The protein problem is significantly harder because of the size of the proteins and their relative flexibility. However, we expect that limited information, such as the coordination environment of a binding site for example, can be extracted using differential techniques. We have carried out a feasibility study by calculating the theoretical PDF for HIV protease with heavy ions substituted in the main flaps. This simulates the scattering we would be observed experimentally.

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