

Keynote Lectures

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Many crystalline solids can be prepared only as microcrystalline powders and are not suitable for structural characterization by single-crystal X-ray diffraction methods. For such materials, it is necessary instead to tackle structure determination using powder X-ray diffraction data. Although there have been several successful reports of the structure determination of organic molecular solids using traditional strategies for structure solution from powder X-ray diffraction data, the majority of recent work on such materials has exploited the direct-space strategy for structure solution, followed by Rietveld refinement. Indeed, the recent upsurge of activity in this field (in both academic and industrial sectors) has taken place closely in parallel with the development of the direct-space strategy for structure solution, for which a range of different computational implementations are now available. In the direct-space strategy, a hypersurface defined by an appropriate R-factor (in our case the powder profile R-factor) is searched using an appropriate global optimization technique (such as Monte Carlo, simulated annealing or Genetic Algorithm techniques). Our recent research is focused on the development, optimization and implementation of Genetic Algorithm techniques in this field, as well as the application of these techniques to solve the crystal structures of a wide range of different types of molecular materials from different areas of the solid state and materials sciences. The lecture will describe fundamental aspects of the direct-space strategy for structure solution from powder X-ray diffraction data, and will be illustrated by examples selected to highlight the current scope and potential for the application of techniques in this field.

Keywords: structure solution, powder diffraction, molecular solids

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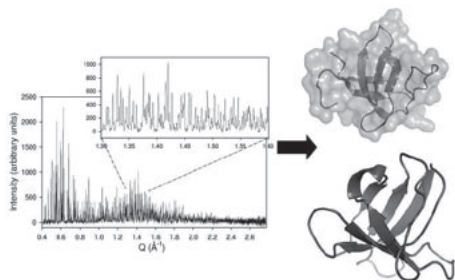
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Powder diffraction studies of proteins

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Studying biological macromolecules in the absence of good quality single crystals is a challenging field attracting considerable scientific interest. Modern developments of X-ray powder diffraction have allowed the structural investigation of a range of proteins establishing the method as a useful complementary tool to traditional approaches [1]. Protein powder specimens consist of a large number of randomly oriented diffracting micro-crystals which are usually formed rapidly by batch crystallization under a variety of conditions. An overview of the most recent developments in this field will be presented including: (a) application of the molecular replacement technique and structure refinements of selected proteins (b) methods for successful cryocooling (c) experimental phasing and extraction of molecular envelopes (d) high throughput automated data collection allowing systematic investigations such as screening



and phase diagram mapping and (e) application of the method on biologically interesting proteins. Practical applications of the methods will be illustrated by recent examples.

[1] Margiolaki, I. & Wright, J. P. *Acta Cryst.* (2008). A64, 169-180

Keywords: protein crystallography structures, powder crystallography, synchrotron structural biology research

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Structural biology studies of the avian influenza H5N1 virus

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Highly pathogenic avian influenza A virus strains with H5N1 subtype are entrenched in poultry worldwide and pose a growing threat to human health. Of the 382 reported human cases of avian influenza since 2003, 241 have been fatal. The development of novel anti-influenza therapeutics is vital in order to increase preparedness against a global influenza pandemic. To this end, we initiated a structural biology program in China to systematically study the proteins from the avian H5N1 influenza A virus (A/goose/Guangdong/1/96). Our aims are to understand the underlying mechanisms of viral replication and the interaction of the virus with host cell factors. Here I will report some exciting recent progress in our efforts.

Keywords: avian influenza H5N1, crystal structure, drug target

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The crystallochemical basis of synthetic mineral immobilisation technologies

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The selection of synthetic mineral immobilisation matrices for the treatment of inorganic pollutants is governed by several considerations. First, toxic metals should be incorporated in their least harmful chemical states. For example, As^{3+} and Cr^{6+} are less poisonous than As^{5+} and Cr^{3+} . Second, as it may be necessary to simultaneously accommodate the oxidized and reduced species of different metals, the suite of mutually compatible minerals that can be selected is restricted. Third, structures with multiple cation and/or anion acceptor sites minimize the number of phases required to crystallise simultaneously, and allows greater flexibility to respond to variations in waste stream composition. This, in turn, limits the chance of undesirable compounds forming. Finally, phases with the highest proportions of appropriate cation acceptor sites are advantageous, to achieve high waste loadings with less 'bulking' through the introduction of inert additives. Within these constraints, a subset of structural families - perovskite, spinel, apatite, zirconolite, zeolites, clays - form the basis of many synthetic mineral immobilisation technologies. The crystallochemical properties of these waste forms are complex and remain the subject wide investigation. The final products are usually far from thermodynamic

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equilibrium leading to a range of interesting and decisive crystal chemical features including nanometric domains, polytypism and miscibility gaps. Such features must be investigated using a combination of crystallographic probes - neutron, X-ray, electron - that can examine the waste forms at different scales to give a complete understanding of the distribution and chemical state of waste metals

Keywords: mineral wasteforms, wasteform design, crystallochemical modification

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Imaging of nanostructures at diffraction-limited resolution from electron diffraction patterns

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Elucidation of the atomic order of complex nanostructures requires a local probe and sub-Å resolution. High resolution structural information can be obtained from diffraction patterns, in principle, which is not subjected to the resolution limitation of imaging lenses and their aberrations. But the use of diffraction patterns for imaging requires the solution of the phase problem without the 3-D periodicity of crystals. Here we report the coherent electron nanoarea electron diffraction technique and diffractive imaging of individual nanostructures using iterative phase retrieval and phase extension techniques. We demonstrate this technique using examples of nanometer-sized CdS quantum dots and Au nanoparticles imaged at sub-Å resolution with an electron microscope of nominal resolution of 2.4 Å and information limit of 1.1 Å. We show that in the diffractive images atoms at sub-angstrom distances are clearly resolved. Significant contrast improvement is also obtained compared to high resolution electron micrographs. The issues critical to the image reconstruction will be discussed in the talk. The high sensitivity of electron diffractive imaging promises a general imaging technique for ultrafine particles and nanocrystals. The contributors to the work reported here include Weijie Huang, B. Jiang, K.W. Kwon, M. Shim. The work is supported by DOE BES and NSF DMR.

Keywords: high resolution electron imaging, nanocrystals, phase determination

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Structure and function of multifunctional channels

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Water permeation through biomembranes should be strictly separated from the movement of ions in biological cells. The water channels must therefore be highly specific for water to prevent any ions. Aquaporin-1 can permeate 2 billion or more water molecules in a second without proton permeation. For accomplishing the function, structure analyzed at a resolution of 3.8 Å by electron crystallography showed peculiar structural determinants including an unusual fold for which we named aquaporin fold [1]. After finding of aquaporin-1,

thirteen water channels, aquaporin-0 to 12, were identified in human body. By analyzing structure of aquaporin-0 at a resolution of 1.9 Å, we discriminated water molecules [2]. Aquaporin-4 is the predominant water channel in brain. By the two-dimensional crystals, showing the same molecular packing *in vivo*, its structure was analysed to 3.2 Å resolution and revealed weak but specific interactions suggesting a structural role for the water channel in the adhesion of membrane layers in glial lamellae. The aquaporin-4 molecule acquired cell adhesive and channel functions. We named this type channels as “Adhennel” family [3]. Structure of another Adhennel family protein, a Gap Junction channel, connexin 26 was analyzed by electron crystallography and we proposed a plug gating model [4]. By focusing on multifunctional channels, I would like to introduce recent results in structural biology of membrane proteins by utilizing our cryo-electron microscope with helium cooled specimen stage [5].

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- [5] Fujiyoshi Y., *Adv. Biophys.* 35 (1998) 25-80.

Keywords: channel proteins, electron microscopy, membrane protein crystallization

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Experimental charge density modeling: Some frontier examples

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Experimental charge density research is now a very mature field which attracts many crystallographers and other scientists: hence, one can now handle difficult problems with success like interesting materials, proteins (1), host guest compounds, large molecules, which may contain transition metals or rare earths. It contributes to better a understanding of electronic structures, reactivity, inter or intra molecular interactions (2). The interplay between X-ray charge density results and complementary ab initio or DFT calculations also allows both experimental and theoretical fields to progress. These studies may be performed at home, on synchrotron facilities, coupled or not to other experiments like diffraction of polarized neutron, Compton scattering, NMR, and NQR to provide a thorough model of the electronic structure. Recent experiments also show the possibility to model the charge and spin density of long living metastable states (3) This lecture will illustrate these new results and draw some lines for the future.

(1) First charge density study of a subatomic resolution protein structure: the human Aldose Reductase case Benoit .Guillot, Christian Jelsch, Alberto Podjarn y and Claude Lecomte, *Acta Cryst* D64,2008 567-588

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(3) Sebastien Pillet, Vincent Legrand , Mohamed Souhassou, Claude Lecomte et Al Out-of-equilibrium charge density distribution of spin crossover complexes from steady-state photocrystallographic measurements: experimental methodology and results *Z. Fur Kristallographie* 2008,000