

Keynote Lectures

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Keywords:

KN28

Acta Cryst. (2011) **A67**, C16

Structural Basis of Cell Regulatory Processes

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KN29

Acta Cryst. (2011) **A67**, C16

High-pressure studies of molecular crystals

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During a long time high-pressure crystallography was dealing more with minerals, metals, and inorganic solids, which were interesting for physics, mineralogy, geochemistry, or materials sciences. Diffraction studies of the organic solids and coordination compounds were limited, although the pioneering work by Bridgeman, Vereschagin, Kabalkina, Fourme, Katrusiak, Allan and some other researchers can be referred to. An enormous progress in the instrumentation and software development for high-pressure research was achieved in the last one-two decades, and this has made diffraction studies possible even for low-symmetry organic crystals. Together with an increased interest in molecular crystals with respect to their applications as materials, devices and pharmaceuticals, this has resulted in a noticeable increase in the number of research groups involved in high-pressure diffraction studies of organic and coordination compounds. This lecture aims to give a general overview of the research in this field, in retrospect and prospect. Attention will be paid, in particular, to the following aspects of research: i) crystallization at high pressure; the crystal structures of high-pressure phases as a tool to study intermolecular interactions; ii) studies of the anisotropic structural strain within the limits of stability of the same phase; understanding the intermolecular interactions; iii) phase transitions at high pressure, thermodynamics and kinetics; iv) pressure-induced chemical reactions; v) effect of pressure on thermal / photochemical reactions.

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Keywords: high pressure, molecular crystals, intermolecular interactions

KN30

Acta Cryst. (2011) **A67**, C16-C17

Powder diffraction at the nanoscale: structure and defects

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Powder diffraction pattern of nanostructured materials are characterized by broad maxima that overlap widely. This is accentuated if additional defects are present, which destroy the remaining periodicity of the object. Thus the information content that appears to be present is reduced and standard structure determination and refinement procedures do not work any longer. The shape and continuous intensity distribution of these maxima do hold, however, a lot of information on the particle size and defects, which can quantitatively be interpreted by appropriate whole pattern matching.

If the diffraction pattern is measured to very high values of Q , above some 20 \AA^{-1} , a lot of further information about the sample is collected, despite the fact that the diffraction pattern at high Q does not contain any sharp features but broad oscillations at best. With this high Q range, the powder pattern can be transformed via a sine Fourier

transformation into the pair distribution function (PDF) [1]. The PDF, in analogy to the Patterson function, shows maxima at interatomic distances. Their heights correspond to the number of neighboring atoms, their positions and their widths are a direct measure of the interatomic distance and distance distribution. Thus the PDF can be interpreted likewise for crystalline, nanocrystalline and highly disordered materials.

To model the diffraction pattern and the PDF quantitatively, two different approaches are used and will be presented in this contribution. In the first, which closely related to a Rietveld approach, the structure is modeled as (super)cell and the diffraction pattern respectively the PDF is calculated by applying appropriate periodic boundary conditions. As this approach relies on the periodic boundary conditions, the disordered structure has to maintain an average lattice.

The alternative approach models the nanostructured system atom by atom into the required size shape with the intended defect composition [2]. The resulting nanoparticle need not to be of any strict periodicity nor of any simple shape and may contain any kind of defects. Thus core-shell particles, multiple twins or inorganic-organic hybrid nanoparticles [3] can be described. The powder pattern of such an object is calculated via the Debye equation, thereby automatically taking into account its final size. The PDF is calculated straightforwardly as well.

A very small nanoparticle that contains defects is just one of the many possible conformations with equivalent defects at different positions within the particles. Thus the powder diffraction pattern/PDF must be calculated from an ensemble modeling of many individual particles whose average diffraction pattern/PDF is matched to the experimental one. A population based evolutionary algorithm allows to refine quantitatively the structure, defect structure, size, shape and size and shape distribution of these nanoparticles [2,4]. Several examples will be presented.

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Keywords: defect, nanoparticle, pair distribution function

KN31

Acta Cryst. (2011) **A67**, C17

Molecular basis of antihistamine specificity against Human Histamine H1 receptor

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H1 blockers are very effective drugs inhibiting the action of

histamine H1 receptor (H1R) and alleviating the symptoms of the allergic reactions. These compounds, particularly the first generation antihistamines, can also bind to other aminergic G protein coupled receptors and cardiac ion channels and cause considerable side reactions. The crystal structure of H1R in complex with doxepin, a first generation antihistamine, allows us to characterize its ligand-binding pocket in detail. The site is associated with an anion-binding region, which is occupied by a phosphate molecule in the crystal structure. Docking of various second-generation antihistamines reveals the unique carboxyl group present in this class of antihistamines interacts with Lys1915.39 and/or Lys179 (ECL2), both of which form part of the anion-binding pocket and are not conserved in other aminergic receptors. This study explains the specificity improvements of second-generation antihistamines and outlines the future direction for development of more specific and safer antihistamines.

Keywords: Membrane proteins, G-protein coupled receptors, histamine

KN32

Acta Cryst. (2011) **A67**, C17

Structure of quasicrystalline surfaces

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Quasicrystals are a type of intermetallic alloy with an atomic structure having long range order but without translational periodicity. Their surfaces have been studied extensively in the past decade [1]. There now exists an extensive database of clean surface studies of Al-based icosahedral and decagonal quasicrystals, and investigations have begun recently on icosahedral quasicrystal surfaces with Ag-In-Yb composition, isostructural to the binary Cd-Yb family [2].

These studies have been challenging because new techniques for surface preparation, as well as new methods of data analysis, have been required. The challenge of the absence of periodic boundary conditions has generated a number of different approaches to tackling surface structure determination: the analysis of long-range structure in a non-periodic fashion; a focus on local structure, in a way that makes boundary conditions unnecessary; and the use of periodic approximants as substitutes for quasicrystals.

Successes achieved in understanding quasicrystal surface structure have led to a number of important spin-off activities. The surfaces themselves have been used as templates for epitaxial growth and several new phenomena has been discovered. Molecular adsorption on quasicrystal surfaces and epitaxial layers has led to increased understanding of the factors influencing surface reactivity. Expertise accumulated in the study of quasicrystals has paved the way for studies of the surfaces of other period complex metallic alloys, typically large unit cell materials but with a cluster sub-structure.

This lecture will discuss the advances outlined above illustrated with examples from the authors' own work and that of other workers in the field.

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Keywords: quasicrystal, surface, scanning tunnelling microscopy