KN09

The charge flipping method: a new approach to solve periodic and aperiodic structures Gábor Oszlányi, András Sütő, *Research Institute for Solid State Physics and Optics, Hungarian Academy of Sciences, H-1525 Budapest, POB. 49, Hungary.*E-mail: go@szfki.hu

Keywords: ab-initio structure determination, direct methods, algorithms

The talk summarizes the current state of charge flipping, a recently developed and deceptively simple algorithm of ab initio structure determination [1,2]. This algorithm is iterative and works in dual spaces. Its operation is based on the presence and perturbation of large plateaus of low electron density, but not directly on atomicity or statistical phase relations. Such a working principle radically differs from that of classical direct methods, and offers complementary applications. Charge flipping can be used at different stages of the structure solution process. It can either operate in a truly ab inito manner, without utilizing any preliminary structural information (atom types, chemical composition or space group symmetry), or can be applied to complete a partially known structure or phase set, it can check the stability of a solution, but it can also be adapted to work as an ingredient of other dual-space schemes.
The list of already successful structure solution cases includes periodic and aperiodic crystals using single crystal and powder diffraction data measured with X-ray and neutron radiation [3-12]. Apart from counting applications, the talk mainly deals with algorithmic issues: it describes the basic algorithm and its properties, introduces and compares new improvements of the iteration scheme in real and reciprocal space, helps to identify convergence by new figures of merit, defines the computational cost of a single solution and helps to find parameters that maximize the efficiency of the algorithm. It also discusses the present limitations of structure size, data completeness and of utilizing known information. Finally, we try to foretell what is the future of such an alternative among well-established direct methods.
□This research was supported by OTKA 67980K.

[1] Oszlányi G., Sütő A., *Acta Cryst. A*, 2004, 60, 134
[2] Oszlányi G., Sütő A., *Acta Cryst. A*, 2005, 61, 147.
[3] Wu J.S. *et al.*, *Acta Cryst. A*, 2004, 60, 326.
[4] Palatinus L., *Acta Cryst. A*, 2004, 60, 604.
[5] Palatinus L. *et al, Acta Cryst. B*, 2006, 62, 556.
[6] Zuniga F.J. *et al, Z. Kristallogr*, 2006, 221, 281.
[7] Katrych S. *et al.*, *J. of Alloys and Compounds*, 2007, 428, 164.
[8] Wu J.S. *et al.*, *Nature Materials*, 2006, 5, 647.
[9] Baerlocher Ch. *et al.*, *Z. Kristallogr*, 2007, 222, 47.
[10] Baerlocher Ch. *et al.*, *Science*, 2007, 315, 1113.
[11] Oszlányi G. *et al.*, *J. Am. Chem. Soc.*, 2006, 128, 8392.
[12] Oszlányi G., Sütő A., *Acta Cryst. A*, 2007, 63, 156.

KN10

Combining Electron Microscopy and X-Ray techniques Jorge Navaza, Laboratoire de Microscopie Electronique Structurale.IBS, Grenoble, France.

Transmission Electron Microscopy (TEM) and X-Ray crystallography are two complementary techniques used in structural biology. TEM fascinates by its apparent simplicity to visualize isolated biological systems in almost "in vitro" conditions. The observed systems are, in general, large assemblies of macromolecular structures, for example virus and viral particles. The main limitation of the technique is the rather low resolution of the produced images, usually in the nanometer range.
On the other hand, X-Ray crystallography routinely determines the structures at atomic resolution of individual proteins or complexes involving a limited number of proteins. In most cases the phase problem is solved either experimentally (isomorphous replacement and related techniques) or by numerical methods where the information coming from previously determined molecular structures is efficiently used (molecular replacement). However, in the case of the very large complexes that are now crystallized, phasing by isomorphous replacement is often difficult and atomic models do not exist, in general. In this cases, EM and X-Ray data may be combined to start the process of crystal structure determination. Indeed, an initial phasing model may be a low resolution EM reconstruction of the complex used as a probe in the molecular replacement method. Phases are then extended by density modification, i.e. solvent flattening and non-crystallographic symmetry averaging.
This has been done in the case of big icosahedral particles(virus) where the high symmetry is a guarantee of success in the phase extension process. Moreover, the model is usually obtained by cryo-TEM, a technique that already provides a good representation of the particle in the crystal.
More recently we have applied the technique to multimeric proteins, a classic protein crystallography problem. The particles sizes were too small to use cryo-TEM so that the 3D reconstructions were performed using negatively stained samples. The main problems to solve are linked to the solvent contribution to the observed structure factors at low resolution, which is the range of resolution at which EM and X-Ray data overlap.
But EM and X-Ray data may also be combined the other way: very often X-Ray crystallography determines the structures of the individual proteins that constitute the assemblies whose low resolution reconstructions were determined by TEM. It is then possible to interpret the EM image in terms of atomic models, which brings considerable complementary information to molecular biologists.
This is achieved by docking individual molecules into the EM image, a technique related to molecular replacement, though a simpler one, as the role of observed structure factors is now played by the Fourier coefficients of the EM map, which provides both moduli and phases.
The combined use of EM and X-Ray data will be illustrated with some applications to viral and sub-viral particles, and some multimeric proteins.

KN11

Pressure Induced Phase Transition: The Local Point of View Jean-Paul Itié *Synchrotron SOLEIL, Gif-sur-Yvette France.* E-mail: Jean-paul.itie@synchrotron-soleil.fr

Keywords: P.08.06.18, MS09.24.5, MS12.24.1

Most of materials exhibits pressure induced phase transformations which can induce strong modification of their properties (electronic, magnetic…). These properties are often related to the interaction between the neighboring atoms and therefore the knowledge of the

local order in the new phases is required to understand what happens to the material. In the majority of the cases, x-ray diffraction can provide such knowledge of the local environment of the atoms. But in some cases the long range order does not exist (amorphous material, glasses or liquid) or is only an average of the local order. Therefore more local investigations, like X-ray Absorption Spectroscopy (XAS) are needed to follow the modifications of the short range order. Moreover, in case of dilute specie in a matrix, the local probes become unique tools to determine the effect of the phase transformation on the impurity.
After a short introduction to XAS and to high pressure technology, I will summarize the limitations due to the pressure set-up. Then I will illustrate the possibilities of XAS with few examples:
- Coordination change in glasses (GeO_2, Ge_{1-x} Si_xO_2) under pressure
- Pressure induced phase transformation on perovskites $PbTiO_3$, $BaTiO_3$ [1] and $KNbO_3$ [2]. For the last two samples, both XAS and diffuse scattering experiments have been performed under high pressure in order to check the relation between the off centre position of the Ti (Nb) atoms with respect to the oxygen octahedron and the observation of diffuse scattering lines in the diffraction pattern. For the Ti perovskite, XAS demonstrate that Ti atoms go to the centre of the oxygen octahedron, but at pressures well above the tetragonal-cubic transition. In the case of $KNbO_3$, Nb atoms remain off centre in the whole pressure range studied.
- Phase transformation on $Zn_{1-x}Mn_xO$ [3] for x =0.25 and x=0.05. The effect of pressure on the Mn local environment is determined by the evolution of the XAS spectra. In particular the Mn is in substitution of Zn in both low pressure (zinc blend) and high pressure (rocksalt) phases and the local compressibility is identical to the bulk one although the Mn-O distances differ from the Zn-O ones. The transition is shown to be reversible for x=0.05 and irreversible for x=0.25.

[1] Itié J .P., Couzinet B., Polian A., Flank A.M., Lagarde P., *Europhys. Lett.*, 2006, 74, 706.
[2] Frenkel A.I., Wang F.M., Kelly S., Ingalls R., Haskel D., Stern E.A., Yacoby Y., *Phys. Rev. B*, 1997, 56, 10869.
[3] Pellicer-Porres J., Segura A., Sanchez-Royo J.F., Sans J.A., Itié J.P., Flank A.M., Lagarde P., Polian A., *Appl. Phys.Lett.*, 2006, 89, 231904

KN12

Molecular mechanisms of RNA degradation Elena Conti. EMBL, Heidelberg (Germany) and Max Planck Institute of Biochemistry, Martinsried, (Germany)

The life span of RNAs in the cell depends on the balance between the rate with which they are synthesized and the rate with which they are degraded. Degradation is fast in the case of messenger RNAs (mRNAs) coding for gene products that need to be active only transiently in the cell (cell cycle regulators, transcription factors, circadian regulators etc.), as well as in the case of aberrant mRNAs that need to be rapidly destroyed before being translated into aberrant proteins. Nonsense-mediated mRNA decay (NMD) is a surveillance pathway that detects and degrades mRNA with premature stop codons (PTCs). PTCs can arise from alternative splicing, from defects in mRNA processing, and are also present in an estimated 30% of inherited genetic disorders. The talk will focus on our current understanding of the molecular mechanisms of NMD: how the PTC-containing mRNA is recognized, how it is targeted for rapid degradation and how it is degraded.

[1] ono, F., Ebert, J., Lorentzen, E. and Conti, E. (2006). The structure of the exon junction complex reveals how it maintains a stable grip on mRNA. Cell, 126, 713-725
[2] Glavan F., Behm-Ansmant I., Izaurralde E. and Conti E. (2006). Structures of the PIN domains of SMG6 and SMG5 reveal a nuclease within the mRNA surveillance complex. EMBO J. 25, 5117-5125.
[3] Lorentzen, E and Conti, E. (2005). Structural basis of 3'-end RNA recognition and exoribonucleolytic cleavage by an exosome RNase PH core. Mol Cell 20, 473-481.
[4] Fukuhara, N., Ebert, J., Unterholzner, L., Lindner, D., Izaurralde, E. and Conti, E. (2005). SMG7 is a 14-3-3-like adaptor in the nonsense mediated mRNA decay pathway. Mol Cell 17, 537-547

Reviews:
[1] Lorentzen, E. and Conti, E. (2006). The exosome and proteasome: nano-compartments for degradation. Cell 125, 651-654
[2] Conti, E. and Izaurralde, E. (2005). Nonsense-mediated mRNA decay: molecular insights and mechanistic variations across species. Curr. Op. Cell Biol., 17, 316-325.

KN13

The future potential of neutron diffraction studies in small molecule crystallography. Chick C Wilson, *Department of Chemistry and WestCHEM Research School, University of Glasgow, Glasgow G12 8QQ, UK.*
E-mail: c.c.wilson@chem.gla.ac.uk

Keywords: Neutron Diffraction, Small-Molecule Crystallography, Instrument Development

There has been a recent quiet but substantial revolution in the applications of neutron diffraction in the area of chemical crystallography and molecular materials; many of these exploit the power of neutron diffraction in determining accurately the hydrogen atom parameters in materials. As a result of continuing instrument development at the facilities, along with an appreciation of the developing needs of the chemistry user community, neutron chemical crystallography has responded in a highly successful fashion to modern trends in structural molecular science.
The relevant instrumentation developments include improved single crystal facilities at ILL, Grenoble (notably LADI, VIVALDI and the upgraded D19) and at ISIS, UK (the upgraded SXD), with further instrumentation planned at both sources (notably at the ISIS Second Target Station). Exciting developments in single crystal neutron instrumentation for molecular structure are also taking place at new high power neutron sources in the US and Japan (for example the TOPAS instrument at the 1 MW SNS at Oak Ridge) and the possibilities of powder diffraction are also being explored.
Some of the areas recently advanced in neutron studies of molecular materials include:

- studying structures on a shorter timescale, either to examine a series of samples or to study a single sample under a range of conditions;
- providing a rapid tool for defining the geometry of hydrogen bonds, including weaker hydrogen bonded interactions;
- studying smaller single crystals;
- studying materials under conditions of variable temperature and variable pressure.