

analysis, metabolome analysis, gene disruption experiments, and other methods as necessary.

Keywords: structural genomics, functional genomics, model organism

MS15.25.5

Acta Cryst. (2005). A61, C26

Structural Proteomics : a Rich Source of Purified Proteins for Functional Assays

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Structural proteomics efforts generate 2-3 times more purified proteins than structures. We have developed general enzymatic assays to screen individually purified proteins for enzymatic activity. The assays have relaxed substrate specificity and are intended to identify sub-subclasses of enzymes (phosphatase, phosphodiesterase, esterase, protease, dehydrogenase, and oxidase) to which the unknown protein belongs. Further biochemical characterization of proteins is facilitated by the application of secondary screens with natural substrates (substrate profiling). We demonstrated the feasibility and merits of this approach for hydrolases and oxidoreductases, two very broad and important classes of enzymes and identified over 40 new enzymes (phosphatases, phosphodiesterases, esterases). The screens were also applied to quickly characterize the large family of unknown proteins in *E. coli*, the haloacid dehalogenase (HAD)-like hydrolases.

Keywords: structural proteomics, enzyme screens, phosphatases

MS16 HIGH RESOLUTION X-RAY INELASTIC SCATTERING

Chairpersons: Gian Carlo Ruocco, Alfred Baron

MS16.25.1

Acta Cryst. (2005). A61, C26

Dynamics of Glassy Materials by High Resolution Inelastic X-ray Scattering

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The nature of short wavelength excitations in glassy materials is highly debated in the physics of disordered materials. What is the length scale beyond which the continuous homogeneous medium approximation breaks down in glasses? What is the microscopic origin of sound attenuation in strong and in fragile glasses? Is there any relationship between propagating acoustic modes and the boson peak?

The development of high resolution inelastic x-ray scattering technique allowed us to experimentally address these problems by measuring the dynamical structure factor $S(Q,E)$ of glassy materials in the mesoscopic region between 1 and some tens nm^{-1} , both varying the energy (E) at fixed exchanged wave vector (Q) and varying Q at fixed E [1]. A review is here reported, together with a comparison with results obtained by complementary techniques like Brillouin light scattering [2] and inelastic ultra-violet scattering [3].

[1] Sette F., Krisch M.H., Masciovecchio C., Ruocco G., Monaco G., *Science*, 1998, **280**, 1550. [2] Fioretto D., Mattarelli M., Masciovecchio C., Monaco G., Ruocco G., Sette F., *Phys. Rev. B*, 2002, **65**, 224205. [3] Masciovecchio C., Gessini A., Di Fonzo S., Comez L., Santucci S.C., Fioretto D., *Phys. Rev. Lett.*, 2004, **92**, 247401.

Keywords: glasses, X-ray scattering, light scattering

MS16.25.2

Acta Cryst. (2005). A61, C26

Collective Dynamics of Liquid Metals: from Simple to Extremely Non-Simple

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Recent developments in high-resolution inelastic X-ray scattering

using third-generation synchrotron radiation facilities allow one to investigate the collective dynamics of a wide variety of liquid metals. The IXS studies have started from simple liquid metals such as the first experiment of liquid Li [1], Na, and Mg, and encompassed to several non-simple metals such as liquid Ga, Ge, and Si [2]. The experimental results revealed characteristic common features in the collective dynamics: 1) A clear indication for propagating modes, and 2) a positive deviation of the collective excitations by about 20 % from the hydrodynamic value. In addition, an indication of a short time (sub-picosecond) retaining of the nearest-neighbour correlation is visualized from the quasielastic line of some non-simple liquid metals [2]. A generalized Langevin formalism with a memory function containing two viscoelastic decay channels [3] is commonly used for analyzing the above IXS data.

In this paper, we review the experimental technique of IXS for liquid metals, and then the common feature of the collective dynamics of liquid metals in detail. Some of them are discussed in connection with results of ab initio molecular dynamic simulations.

[1] Sinn H., et al., *Phys. Rev. Lett.*, 1997, **78**, 1715. [2] Scopigno T., et al., *J. Phys.: Condens. Matter*, 2000, **12**, 8009. [3] Hosokawa S., et al., *J. Phys.: Condens. Matter*, 2003, **15**, L623. [4] Levesque D., et al., *Phys. Rev. A*, 1973, **7**, 1690.

Keywords: X-ray inelastic scattering, phonons, liquid metals

MS16.25.3

Acta Cryst. (2005). A61, C26

Vibrational Dynamics of Iron in Proteins

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High-resolution x-ray measurements near the nuclear resonance reveal the complete vibrational spectrum of a Mössbauer nucleus. I will illustrate novel opportunities that this site-selective method provides for characterizing the vibrational dynamics of ^{57}Fe at the active sites of heme proteins, iron-sulfur proteins, and related model compounds. (1) Quantitative data on the frequency, the amplitude, and in some cases, the direction of all iron vibrations provide a uniquely detailed benchmark for modern quantum chemical vibrational predictions, with which they can be directly compared on an absolute scale. (2) Measurements on oriented single crystals of iron porphyrins reveal low-frequency out-of-plane vibrations that we identify with the long-sought heme “doming” mode, similar to the motion that takes place on oxygen binding to heme proteins. Moreover, the experimental data provide a direct experimental estimate of the force constant for Fe displacement normal to the heme plane and suggest that this Fe motion is an important element in protein control of biological reaction energetics. (3) Comparisons with calculations and with independent Raman isotope shift measurements probes the extent to which active site vibrations couple to global protein motions.

Keywords: heme proteins, Mössbauer spectroscopy, vibrational spectroscopy

MS16.25.4

Acta Cryst. (2005). A61, C26-C27

High-Resolution Inelastic X-ray Scattering of Materials of Geophysical Interest

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Inelastic X-ray scattering (IXS) has progressively arisen as one of the major spectroscopic tools with the advent of bright X-ray sources of 3rd generation. It offers the unique opportunity to investigate the phonon or electronic properties *in situ*, at various conditions of pressure and temperatures, and is thus very well suited to the study of the composition and dynamics of the Earth and planetary interiors.

The elasticity and the sound wave anisotropy of hcp-metals, namely iron and cobalt have been investigated at high-pressure by very high resolution (meV) IXS. I will address the case of hcp-iron, the main constituent of the Earth's inner core, and report the direct experimental determination of the anisotropy in the propagation of longitudinal acoustic waves in textured sample above 100 GPa. Hcp-cobalt, here chosen a proxy for iron, has also been studied with the advantage to be

available as single crystals, thus making the determination of the full elastic tensor possible at high pressure.

The electronic and magnetic properties of minerals under extreme conditions of pressure or temperature can also be studied through X-ray emission spectroscopy (XES) in the fluorescence regime. We measured the spin state of iron in the main constituent of the Earth's lower mantle, *i.e.* the iron-bearing magnesium silicate perovskite (Mg,Fe)SiO₃, by studying the K β emission line to pressures exceeding 140 GPa. Geophysical implications for both the anisotropy of propagation of acoustic waves in the Earth's core and the physical properties of the lowermost mantle will be discussed.

Keywords: geophysics, inelastic X-ray scattering, high-pressure

MS16.25.5

Acta Cryst. (2005). A61, C27

Phonon Dispersions in fcc δ -Pu-Ga by High Resolution Inelastic X-ray Scattering

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The phonon spectra of plutonium and its alloys have been sought after in the past few decades following the discovery of this actinide element in 1941, but with no success. This was due to a combination of the high neutron absorption cross section of ²³⁹Pu, the common isotope, and non-availability of large single crystals of any Pu-bearing materials. We have recently designed a high resolution inelastic x-ray scattering experiment using a bright synchrotron x-ray beam at the ESRF, Grenoble and mapped the full phonon dispersion curves of an fcc δ -phase polycrystalline Pu-Ga alloy[1]. Several unusual features including, a large elastic anisotropy, a small shear elastic modulus C', a Kohn-like anomaly in the T₁[011] branch, and a pronounced softening of the [111] transverse modes are found. These features can be related to the phase transitions of plutonium and to strong coupling between the lattice structure and the 5f valence instabilities. Our results also provide a critical test for theoretical treatments of highly correlated 5f electron systems as exemplified by recent dynamical mean field theory (DMFT) calculations for δ -plutonium[2]. Recent work on imaging phonons in Pu-Ga alloys with thermal diffuse scattering[3] will also be discussed.

This work was performed under the auspices of the U.S. Department of Energy by the University of California, Lawrence Livermore National Laboratory under contract No. W-7405-Eng-48.

[1] Wong J., et al., *Science*, 2003, **301**, 1078. [2] Dai X., et al., *Science*, 2003, **300**, 953. [3] Wong J., et al., *Appl. Phys. Lett.*, 2004, **84**, 3747.

Keywords: lattice dynamics, inelastic X-ray scattering, phonon softening

MS17 NON-COVALENT INTERACTIONS IN CRYSTALS OF SMALL MOLECULES AND MACROMOLECULES

Chairpersons: Gautam R. Desiraju, Mariusz Jaskolski

MS17.25.1

Acta Cryst. (2005). A61, C27

Multipolar Interactions in Structural Chemistry and Biology

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The past decades of molecular recognition studies have greatly enhanced our knowledge on apolar, ion-dipole, and H-bonding interactions. However, much less attention has been given to the role that multipolar interactions, in particular those with orthogonal dipolar alignment, adopt in organizing a crystal lattice or stabilizing complexes involving biological receptors.

In a recent fluorine scan of thrombin inhibitors to map the fluorophilicity/fluorophobicity of an enzyme active site, we discovered favorable C–F_(ligand)...C=O_(protein) interactions, with the F-atom approaching the electrophilic C-atom in a nearly orthogonal way, along the pseudotrigonal axis of the carbonyl unit. The attractive nature of such contacts was subsequently established in model studies.

Using Cambridge structural database (CSD) and protein database (PDB) mining tools, we now have established the generality of these previously rather overlooked interactions. A number of illustrative examples of these interactions found in X-ray crystal structures of small molecules and protein-ligand complexes will be shown to demonstrate their propensity and thus potential importance for both, chemical and biological molecular recognition processes. [1]

[1] Paulini R., Müller K., Diederich F., *Angew. Chem. Int. Ed.*, 2005, *in press*.

Keywords: nonbonded interactions, databases, X-ray crystal structure analysis

MS17.25.2

Acta Cryst. (2005). A61, C27

Carbonyl...Carbonyl Interactions are Structurally Ubiquitous and Important

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Recent years have seen an increasing interest in intermolecular interactions that are *not* mediated by hydrogen. An early analysis [1] of the Cambridge Structural Database (CSD) identified the isosteric nature of nitro and carbonyl groups in molecular design applications. This prompted further work on dipolar carbonyl-carbonyl interactions that will be reviewed and extended in this talk. In *small organic molecules* it has been shown that CO groups in simple ketones and trans-amides form three main interaction motifs, and that the most frequent sheared-antiparallel arrangement has an attractive interaction energy of ca. -22kJ mol⁻¹, competitive with medium-strength H-bonds. In *proteins*, PDB analyses show that CO...CO interactions stabilise α -helices, β -sheets and β -strands, including the stabilization of the partially allowed Ramachandran conformations of asparagine and aspartic acid. In *organometallics*, we are now studying CO...CO interactions using the CSD. Although compromised by steric hindrance, very significant numbers of CO...CO interactions are observed in M–C=O systems. The antiparallel motif again predominates, and C...O distances are usually shorter than in organic systems, indicative of the stronger dipole in the M–C=O case. Preliminary DFT calculations indicate attractive energies of -20 to -30 kJ mol⁻¹ for the predominant motif, similar to or stronger than the attractive energies in organic systems.

[1] Taylor R., Mullaley A., Mullier G.W., *Pestic. Sci.*, 1990, **29**, 197-213.

Keywords: intermolecular interactions, crystallographic databases, ab initio energy calculations

MS17.25.3

Acta Cryst. (2005). A61, C27-C28

Small Molecules and Macromolecules make Contact: Messages from Protein Structures to Atomic Resolution

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Atomic and ultra-high resolution macromolecular crystal structure determination and *ab initio* quantum chemical calculations have become indispensable tools for comprehensive structure interpretation, as they permit acquiring snapshots along the reaction pathway and the assignment of function to the residues involved in catalysis. Fine electronic detail can be visualised and yield valuable information on protein function. The assessment and description of intra- and intermolecular contacts reaches a degree of accuracy which in the past was considered impossible for macromolecules.

The release of geometric restraints and the low coordinate error in atomic resolution protein structures allow the identification of deviations from standard stereochemistry which, at lower resolution, might not have been accounted for. These deviations may occur in intramolecular interactions as well as in intermolecular (protein-ligand) contacts. Quantum chemical calculations, or direct multipole refinement, on these accurate model templates complement the structural data with information beyond the analysis of contact distances. The charge distribution which one can obtain determines the chemical properties and hence characteristics such as substrate