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Oral Abstracts

Direct detection of protons in oxidized and reduced human manganese superoxide dismutase

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Human manganese superoxide dismutase (MnSOD) is a physiologically critical enzyme located in the mitochondria that actively prevents degeneration of the organelle. The enzyme prevents the presence of heavily damaging reactive oxygen species by converting their main precursor, superoxide ($O_2^{\bullet-}$), into either oxygen (O_2) or hydrogen peroxide (H_2O_2), through a redox reaction with the active site Mn (**Scheme 1**).

Scheme 1

$$\boldsymbol{k_1} \quad Mn^{3+} + O_2^{\bullet-} \leftrightarrow Mn^{2+} + O_2$$
$$\boldsymbol{k_2} \quad Mn^{2+} + O_2^{\bullet-} + 2H^+ \leftrightarrow Mn^{3+} + H_2O_2$$

The redox reaction is thought to be achieved using concerted proton and electron transfers, [Mn^{3+} + e^- + H^+] ↔ [$Mn^{2+}(H^+)$], that enables the bypass of high-energy intermediates that otherwise would not be feasible. However, the catalytic mechanism of MnSOD has been largely unknown due to the difficulty in detecting the means in which the catalytically vital protons are delivered from bulk solvent, through a restrictive active site funnel, and to a putative proton acceptor associated with Mn in a confined active site, all in a manner that surpasses thresholds for diffusion-limited catalysis (k_{cat} of ~20,000 s^{-1} and k_{cat}/K_m of ~10^9). The current hypothesis among the literature is the presence of a step-wise, orderly proton relay, though there is a lack of consensus in the identity of the molecules that would participate in this relay.

Detecting hydrogen atoms using X-ray crystallography is difficult, requiring sub-angstrom resolutions to see only the non-exchangeable hydrogen atoms. Furthermore, studying mechanisms of oxidoreductase metalloenzymes using X-ray diffraction is problematic as irradiation reduces the active site metal. Neutron crystallography provides the novel ability to visualize directly hydrogen atoms at moderate resolutions and thereby the protonation states and orientation of molecules that may participate in proton transfers. The low-flux, non-ionizing nature of neutron beams require experimental compensations so that diffraction resolution requirements are met. Strategies include use of a small unit cell, large crystal growth, and perdeuteration; where all the hydrogens in the enzyme are replaced with deuterium to increase the signal-to-noise ratio 40-fold. Our MnSOD crystal system harbors large unit cell dimensions that would normally not be amenable for neutron diffraction. (a = b = 80 Å, c = 240 Å). The recently commissioned Macromolecular Neutron Diffractometer at Oak Ridge National Laboratory enabled us to collect neutron diffraction data to a resolution that hydrogen (deuterium) positions could be visualized - the largest unit cell to date.

To study the mechanism of MnSOD, we utilized the non-ionizing nature of neutrons to obtain room-temperature structures of human MnSOD in its two oxidation states, Mn^{3+}SOD and Mn^{2+}SOD, from the same crystal. Direct detection and comparison of the protons in these structures enabled visualization of unusual protonation states for solvent bound to the active site metal, and the amino acid residues that separate the active site from bulk solvent. A “proton juggling” mechanism was observed.

Investigating reactivity, redox distribution, and magnetism of giant spin clusters

Theodore Betley

Our pursuit of high-spin clusters has led to the discovery of giant spin cluster formation where clusters exhibit well isolated ground states exceeding room temperature. Modification of ligand architectures allows for anodic/cathodic redox shifting of the resultant clusters. The enhanced electrophilicity allows post-synthetic modification of the clusters to manipulate ground spin states. Furthermore, redox shifting of the clusters enables the formation of high-spin charge transfer salts. Our efforts using advanced X-ray absorption and neutron scattering techniques to discern redox delocalization and origins of electronic/magnetic anisotropy will be discussed.

Local orbital degeneracy lifting as a precursor to an orbital-selective Peierls transition

E. S. Bozin, W. G. Yin, R. J. Koch, M. Abeykoon, Y. S. Hor, H. Zheng, H. C. Lei, C. Petrovic, J. F. Mitchell & S. J. L. Billinge

Fundamental electronic principles underlying all transition metal compounds are the symmetry and filling of the *d*-electron orbitals and the influence of this filling on structural configurations and responses. Here we use a sensitive local structural technique, x-ray atomic pair distribution function analysis, to reveal the presence of fluctuating local-structural distortions at high temperature in one such compound, $CuIr_2S_4$ [1]. We show that this hitherto overlooked fluctuating symmetry-lowering is electronic in origin and will modify the energy-level spectrum and electronic and magnetic properties. The explanation is a local, fluctuating, orbital-degeneracy-lifted state. The natural extension of our result would be that this phenomenon is likely to be widespread amongst diverse classes of partially filled nominally degenerate *d*-electron systems, with potentially broad implications for our understanding of their properties.

[1] E. S. Bozin, W. G. Yin, R. J. Koch, M. Abeykoon, Y. S. Hor, H. Zheng, H. C. Lei, C. Petrovic, J. F. Mitchell & S. J. L. Billinge, "Local orbital degeneracy lifting as a precursor to an orbital-selective Peierls transition", Nature Communications **10**, 3638 (2019).

Lockdown – how mutations in penicillin-binding protein 2 confer cephalosporin resistance to *N. gonorrhoeae*

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Increasing resistance of *Neisseria gonorrhoeae*, the causative agent of gonorrhea, against extended spectrum cephalosporins (ESCs) threatens public health and a better understanding of the underlying mechanisms is needed to develop replacement antimicrobials. A major mechanism of cephalosporin resistance ($Ceph^R$) in *N. gonorrhoeae* is mutations in the *penA* allele, which encodes penicillin-binding protein 2 (PBP2). As a first step toward understanding how mutations cause resistance, we have investigated the molecular mechanism of acylation by cephalosporins. Crystal structures of wild-type PBP2 in complex with cefixime and ceftriaxone reveal that acylation elicits several changes, comprising rotation of a threonine side chain (Thr498) to contact the β-lactam carboxylate, with subsequent twisting of the KTG active-site motif to form the oxyanion hole, and rolling of the β3-β4 loop to form a cluster of interactions around the R1 group of the antibiotic. Further crystal structures show that these changes do not occur when a mutated variant of PBP2 from a $Ceph^R$ strain is acylated by ceftriaxone. Among the key mutations, a N512Y mutation may hinder rolling of the β3-β4 loop and a G545S mutation blocks recognition of the β-lactam carboxylate. Overall, these data suggest that the cephalosporin resistance of *N. gonorrhoeae* is the result of an energetic barrier created against acylation by restricting the dynamic behavior of PBP2.

Electrons or photons, diffraction rules them all

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Phase contrast imaging of macromolecules using elastically scattered electrons is based on diffraction as are the Bragg reflected X-ray intensities, the primary data in X-ray crystallography. A fundamental difference is the objective/projector lens system that for electrons performs a second Fourier transform so that the recorded data is in real space and not in Fourier (or reciprocal space). While this eliminates the “phase problem”, well known in crystallography, the problem becomes an orientational one, as the orientations of a very large number of particle projections have to be found. There are a number of other analogies between the two experimental methods beyond these. If one intends to perform de novo structure determination at resolutions hovering around 4 Angstroms, the key challenges are also very similar. In the absence of a homologous model structure, both the establishment of connectivity and - most significantly - the proper register are difficult. For cryoEM maps, the problem is even more vexing as the usual markers such as Selenium positions or heavy atom sites are missing. Using the de novo cryoEM structure determination of a eukaryotic DNA transposase, methods will be discussed that resulted in a reliable de novo structure of a relatively small (~160kD) protein-DNA complex.

Cryo-neutron crystal structure of left-handed Z-DNA d(CGCGCG)

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The hexamer d(CGCGCG) constitutes the first oligonucleotide for which a single crystal X-ray structure was reported.[1] When the publication appeared 40 years ago, Z-DNA caused somewhat of a shock as the two antiparallel strands were wound around each other in a left-handed fashion. Thus, Z-DNA bore little resemblance to the model of the right-handed double helix built by Watson and Crick.[2] Striking features of Z-DNA are the zig-zag (hence Z-DNA) like arrangement of phosphate groups along the backbones, alternating low (-10°, CpG steps) and high helical twists (-50°, GpC steps), different sugar puckers adopted by Cs (C2′-*endo*) and Gs (C3′-*endo*), and a convex surface in place of the major groove. In Z-DNA crystals duplexes are tightly packed, resulting in a small volume per base pair of ca. 1,000 Å^3. Z-DNA crystals diffract X-rays to an exceptionally high resolution of beyond 0.6 Å,[3] permitting visualization of virtually all waters in the asymmetric unit (ca. 85).[4] Therefore, Z-DNA offers an ideal case to test the benefits of low-temperature neutron diffraction data collection to potentially determine donor-acceptor patterns of first- and second-shell water molecules. Nucleic acid fragments pose challenges for neutron crystallography because water molecules are located on the surface rather than inside sequestered spaces such as protein active sites or channels. Water molecules can be expected to display dynamic behavior, particularly in cases where water is not part of an inner shell and directly coordinated to DNA atoms. Thus, nuclear density maps based on room temperature diffraction data with a resolution of 1.6 Å did not allow unequivocal determination of the orientation of water molecules.[5] We will discuss the cryo-neutron crystal structure of Z-DNA based on data collected on the Macromolecular Neutron Diffractometer (MaNDi) at the Oak Ridge National Laboratory Spallation Neutron Source (ORNL SNS).

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The Rigaku Oxford Diffraction XtaLAB Synergy: from Powder Analysis to Electron Density Studies and Protein Structure Solution

Joseph Ferrara, Pierre Le Magueres, Mark Del Campo, Keisuke Saito, Jakub Wojciechowski, Mathias Meyer

Over the course of the last three years, the Rigaku Oxford Diffraction XtaLAB Synergy X-ray diffractometers have been proven to be effective instruments for a wide range of diffraction experiments. The series include a dual wavelength microfocus sealed tube (the XtaLAB Synergy-S), and a microfocus rotating anode (the single wavelength XtaLAB Synergy-R and dual wavelength XtaLAB Synergy-DW).

The combination of a powerful microfocus X-ray beam (with a choice of Cu, Mo or Ag wavelength), with divergence that is user-tunable, to a versatile full 4-circles goniometer and the highly sensitive direct photon counting HyPix detectors allow powder, small molecule and protein crystallographers to cover a wide range of crystallography experiments.

In this work, we present results for the following experiments performed with the microfocus sealed tube Cu/Mo XtaLAB Synergy-S:

- Absolute structure of a tiny crystal of benzophenone
- Analysis of a powder mixture in which a minor phase of 0.8% relative weight of rutile was successfully detected.
- Electron density study of hexamine to 0.37 Å.
- Structure solution of lysozyme by S-SAD phasing from a 1 hour data set collected on the 1st home laboratory curved photon counting detector, the HyPix-Arc150º.

Small-Angle Neutron Scattering as a probe of Nanoscale Magnetic Dynamics

Dustin A. Gilbert

Small angle neutron scattering (SANS) is a neutron diffraction technique sensitive to features on the order of 2 nm - 500 nm. Recently, SANS has played a crucial role in the discovery and subsequent exploration of a chiral magnetic feature called a skyrmion. The magnetic skyrmion consists of magnetic moments assembled in a coplanar looped structure, with an out-of-plane core and perimeter, which gives them a non-zero topological charge. Collections of skyrmions typically form hexagonally ordered arrays due to their mutual interactions, which is seen in characteristic hexagonal SANS patterns. These structures present exciting opportunities for magnetic storage technologies, but also have interesting fundamental qualities. Recently, we have used SANS to in-situ investigate dynamics in skyrmions and skyrmion lattices. In the first of these investigations, we observe the ordering dynamics of skyrmion lattices: by rapidly entering, exiting and crossing the skyrmion stability window and measuring the diffraction pattern with time-resolved SANS, the ordering kinetics is captured. Interestingly, the ordering occurs on the timescale of seconds, as compared to typical magnetic dynamics, which occur on the nanosecond timeframe. The SANS results also show that, even jumping across the skyrmion stability window causes dynamic skyrmion formation and dissolution. In a second set of experiments, we probe the in-situ dynamics of the skyrmion at gigahertz frequencies by utilizing a Doppler-shift measurement scheme. An in-plane RF field is applied to excite a gyration mode in the skyrmions. As the neutron diffracts from the moving skyrmion, which is moving at similar speed as the neutron, an additional momentum is imparted, which distorts the diffraction pattern. At frequencies incommensurate with the gyration frequency, the SANS pattern simply shows a hexagonal feature, reflecting the hexagonal lattice ordering. However, on-resonance, the background increases dramatically and the intensity of the peak amplitudes decreases. These results demonstrate unique uses of diffraction to study dynamics in nanoscale magnetic features.

Modulations in magnetic materials

M. S. Henriques, V. Petricek

In the last five decades neutron scattering techniques have shown that spin arrangements in magnetic materials are often more complicated than the simple ferromagnetic or antiferromagnetic configurations predicted by Néel [1]. Modulated magnetic structures are constantly discovered in a variety of magnetic materials. In such phases, the periodicity of the magnetic structure is different from the parent unit cell.

As predicted by the kinematic theory of diffraction, the different periodicity manifests itself in a neutron diffraction pattern as magnetic satellite reflections, hence the basic three-dimensional translation symmetry is violated. To index all the diffraction spots, one (or more) additional vector(s), or propagation vector(s) have to be added to the reciprocal base. The structure is said to be commensurate if the components of the propagation vector are rational numbers and incommensurate if at least one of the components is irrational.

Commensurate and incommensurate magnetic structures can be described using the superspace approach [2]: the magnetization density can be generalized to higher-dimensional spaces to recover the translation symmetry. Within this formalism, the underlying spin arrangement can be described by a periodic modulation function of the magnetization density. The modulation function may be anharmonic and is parametrized as Fourier series in terms of sine and cosine functions.

The symmetry of modulated magnetic structures can be unambiguously described using magnetic space and superspace groups. The symmetry relations provide a robust description of the symmetry modes for the spin configuration and its constraints consistent with the parent paramagnetic phase and the magnetic propagation vector.

Here we will review the fundamental concepts of superspace formalism and magnetic symmetry, and present the working flow and the capabilities of the magnetic option of Jana2006. In particular, the new magnetic option implemented in Jana2006 is capable of handling different sets of diffraction data to consistently solve and describe commensurate and incommensurate magnetic structures based on symmetry considerations [3]. Several examples of magnetic ordering models will be presented for both commensurate and incommensurate types of magnetic structures.

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The Spallation Neutron Source Second Target Station and Diffraction Instruments

K. W. Herwig

The Second Target Station (STS) at the Spallation Neutron Source (SNS) will provide transformative capabilities for the study of a broad range of materials using neutron scattering. The STS will complement the capabilities of the current two neutron scattering facilities at Oak Ridge National Laboratory, the SNS First Target Station and the High Flux Isotope Reactor. STS will provide world-leading peak cold neutron brightness with a broad range of neutron energies available between source pulses. This talk will provide an overview of the STS project status, its current conceptual design and illustrate the types of science enabled by its unique characteristics. This talk will emphasize the capabilities presented by the current STS diffraction instrument concepts and describe opportunities for research community engagement in selecting the initial STS instrument suite.

Total scattering as a tool for quantifying local structure in iron-based superconductors

R. J. Koch, P. Mangelis, T. Konstantinova, H. Lei, M. Abeykoon, A. Wang, R. B. Neder, M. T. McDonnell, M. Feygenson, C. Petrovic, Y. Zhu, A. Lappas, S. J. L. Billinge, and E. S. Bozin

We report neutron and x-ray total scattering studies of two different iron-based superconductor systems, $FeSe_{1-x}S_x$ and $K_xFe_{2-y}Se_{2-z}S_z$. Through different levels of data analysis and simulation, we uncover a deep structural complexity spanning many length scales. In $FeSe_xS_{1-x}$, we uncover a local symmetry breaking nematic distortion, which exists preformed with a correlation of about 4 nm well above the temperature of the global symmetry breaking transition.[1] Our results suggest that the low-temperature macroscopic nematic state in $FeSe_xS_{1-x}$ forms from an imperfect ordering of orbital-degeneracy-lifted[2] nematic fluctuations which persist up to at least 300 K. Within $K_xFe_{2-y}Se_{2-z}S_z$, our analysis suggests a degree of correlated vacancy order which emerges moving towards the sulfur end of the phase diagram at 5 K,[3] adding nuance to the discussion surrounding phase separations, magnetism, and superconductivity in this system.

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Synthesis, Magnetic Behavior and Neutron Diffraction of Transition Metal Vanadate Single Crystals

Joseph Kolis, L. Duminda Sanjeewa, Ovi Garlea, Michael McGuire, Colin McMillen, Tiffany Pellizzeri,

Single crystals with bridging groups linking first row transition metal ions can lead to exceptionally rich and complex magnetic behavior. A common class of bridging groups is the tetrahedral oxyanions EO_4^{x-}, (E = Si, P, As, S, V, Mo etc.), and these linking groups can lead to an enormous array of new structure types with unusual magnetic behavior. This talk will feature the role of vanadate building blocks (VO_4^{3-}) in magnetically interesting transition metal layered materials. The vanadates display a rich diversity of structural behavior including multiple bridging modes such as corner and edge sharing. In addition the presence of vacant d-orbitals in the bridging center can have a significant effect on the magnetic coupling behavior. Thus they provide an excellent contrasting system to the more common phosphate bridging groups.

In this talk we will examine the magnetic behavior of a range of first row transition metal ions (Fe^{2+}, Fe^{3+}, Mn^{2+}, Mn^{3+}, Co^{2+}) containing bridging vanadates, using neutron diffraction to help determine their magnetic structures. A focus of the talk will be the use of the high temperature hydrothermal synthesis method to prepare large, high quality single crystals of the various materials. The ability to grow crystals at moderate temperatures (500-700˚C) minimizes the presence of lattice defects and site disorders, which considerably improves the quality of the neutron diffraction and magnetic data, especially at low temperatures. Also the growth of the materials in sealed aqueous media allows for good control of chemical factors like stoichiometry, oxidation potential and acidity. These considerations lead to the synthesis of a wide range of new materials in the form of high quality crystals. In many cases the crystals are large enough to enable single crystal neutron diffraction.

In this talk we will discuss the synthesis, magnetism and neutron diffraction of several novel compounds where subtle chemical variations lead to significant changes in the molecular and magnetic structures. For example the series $Na_2BaM(VO_4)_2$ (M = Mn^{2+}, Fe^{2+}, Co^{2+}) all have similar chemical structures and are members of the glaserite family, but each one displays dramatically different magnetic behavior between room temperature and 2K.[1,2] Another interesting system for discussion is the mixed vanadate carbonate material $A_2M_3(VO_4)_2(CO_3)$ where A = K, Rb and M = Mn^{2+}, Co^{2+}. The chemical structure is quite complex and has two unique layers, one built of corner sharing vanadates and one of trigonal planar carbonates. The material also has a complex magnetic behavior and undergoes three magnetic phase transitions between 300-2K. In all cases the full magnetic structures were determine using neutron diffraction.[3,4]

The vanadates make an excellent case study both for the role of hydrothermal synthesis as well as the use of tetrahedral oxyanion building blocks in low dimensional transition metal complexes. The synthesis, chemical structures and magnetic structures of such materials will be discussed with an emphasis on the role of neutron diffraction.

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X-ray and Neutron Diffraction Studies of Negative Thermal Expansion Materials

Cora Lind-Kovacs, La'Nese Lovings

Negative thermal expansion (NTE) materials have attracted significant attention over the past two decades since this behavior was shown to arise from certain structural features in several families of metal oxides [1]. While much progress has been made in elucidating the structural basis of the NTE phenomenon, phase transitions as a function of composition, temperature and pressure are much less understood. This talk will focus on materials in the scandium tungstate ($A_2M_3O_{12}$) family that deviate from behavior expected based on simple models like the rule of mixtures [2, 3]. The M-site generally contains Mo or W, while the A-site can be substituted by trivalent cations ranging in size from Al^{3+} to the smaller lanthanides, or by mixtures of di- and tetravalent cations. In this family, NTE is observed in an orthorhombic structure, but many compositions show a reversible phase transition to a structurally related denser monoclinic polymorph with positive expansion upon cooling. This structure is also commonly observed at very low pressures (<0.6 GPa) upon compression. However, some compositions show a strong suppression of this undesirable transition, or kinetically sluggish behavior during heating/cooling cycles. Combined X-ray and neutron studies are attractive to elucidate the behavior of such compositions.

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NMR-Assisted Crystallography in Tryptophan Synthase: Proton Positions, Stable Intermediates, and Transition States

Viktoriia Liu, Bethany G. Caulkins, Jacob Holmes, Rittik Ghosh, Robert P. Young, Eduardo Hilario, Li Fan, Michael F. Dunn, and Leonard J. Mueller*

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NMR-assisted crystallography – the synergistic combination of solid-state NMR, X-ray crystallography, and first-principles computational chemistry – holds remarkable promise for mechanistic enzymology; by providing atomic-resolution characterization of stable intermediates in the enzyme active site – including hydrogen atom locations and tautomeric equilibria – it offers insight into structure, dynamics, and function. Here, we make use of this combined approach to characterize the aminoacrylate intermediate in tryptophan synthase, a defining species for pyridoxal-5′-phosphate-dependent enzymes on the β-elimination and replacement pathway. By uniquely identifying the protonation states of ionizable sites on the cofactor, substrates, and catalytic side chains, as well as the location and orientation of structural waters in the active site, a remarkably clear picture of structure and reactivity emerges. Most incredibly, this intermediate appears to be mere tenths of angstroms away from the preceding transition state in which the β-hydroxyl of the serine substrate is lost. The position and orientation of the structural water immediately adjacent to the substrate β-carbon suggests not only the fate of that hydroxyl group, but also the pathway back to the transition state and the identity of the active site acid-base catalytic residue. Enabling this analysis is the ability to measure active-site isotropic and anisotropic NMR chemical shifts under conditions of active catalysis, and the development of fully quantum mechanical computational models of the enzyme active site that allow the accurate prediction of NMR spectral parameters.

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Fatty acids, important protons and potent poisons

Jeremy Lohman, Purdue University

Ketosynthase enzymes assemble carbon scaffolds of polyketide natural products and fatty acids. The energy to power the carbon-carbon bond formation comes from ATP used by acyl-CoA carboxylases to make malonyl-CoAs as ketosynthase substrates. These two different enzyme classes have complex biophysical, catalytic and regulatory mechanisms that have been debated for decades and remain unresolved (important protons). We have synthesized analogs of the “hyperreactive” malonyl-CoA intermediate to provide new tools for structural studies. A combination of X-ray/neutron co-crystal structures with our analogs will provide new insights into the structure-function relationships of these enzymes to enable drug design and polyketide synthase enzyme engineering (potent poisons).

Symmetry Breaking Of A Dimeric Iron(II) Hydride Complex

Sean F. McWilliams, K. Cory MacLeod, Maxime Tarrago, Brandon Q. Mercado, Xiaoping Wang, Eckhard Bill, Shengfa Ye, Patrick L. Holland

Iron hydride complexes are important in catalysis, including the active site of nitrogenase enzymes, and transits between different spin states have been postulated to be crucial in some the catalytic mechanisms. In this work, we describe the interplay of spin state changes and geometric changes in a diiron(II) complex with two bridging hydrides. The two iron sites switch between tetrahedral (high-spin) and square-planar (intermediate-spin) geometries in a coupled fashion, such that the overall spin state of the dimer is always S = 3. X-ray crystallography at different temperatures gives only hints of these geometries, but neutron diffraction shows definitive characterization of the iron geometries by locating the hydride positions precisely. The experimental studies on structure, spectroscopy, and magnetism are interpreted using DFT and ab initio computations that show the pathway for the interconversion. The results show how rapid hydride motions can lead to major modulations of the electronic structure, giving insight into the unique low-mass, strong-field nature of the hydride ligand in coordination chemistry.

Structure and dynamics of aminoacrylate intermediates of tyrosine phenol-lyase

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The structures of aminoacrylate intermediates of wild-type, F448A mutant, and perdeuterated tyrosine phenol-lyase (TPL) formed from L-tyrosine, 3-F-L-tyrosine, S-ethyl-L-cysteine, and L-serine, with 4-hydroxpyridine bound, were determined by X-ray crystallography. All the aminoacrylate Schiff's base structures in chain A are identical regardless of the substrate used to form them. The 4-hydroxypyridine is also in an identical location, except for F448A TPL, where it is displaced about 1 Å due to the increased size of the active site. In chain B, we have found different complexes depending on the substrate. With wild-type TPL, L-tyrosine gave no density, 3-F-L-tyrosine gave a *gem*-diamine, and L-serine gave a *gem*-diamine, in chain B. S-Ethyl-L-cysteine formed an aminoacrylate in chain B with both wild-type and F448A TPL, but perdeuterated TPL with S-ethyl-L-cysteine formed a *gem*-diamine of aminoacrylate in chain B. The kinetics of aminoacrylate intermediate formation from L-tyrosine and S-ethyl-L-cysteine were followed by stopped-flow spectrophotometry at temperatures from 281 to 320 K and hydrostatic pressures ranging from 1 to 1.5 kbar. There are large negative values of $\Delta S^{\ddagger}$, $\Delta C_p^{\ddagger}$, $\Delta V^{\ddagger}$, and $\Delta\beta^{\ddagger}$ for aminoacrylate intermediate formation for L-tyrosine, but not for S-ethyl-L-cysteine. Formation of the aminoacrylate intermediates from L-tyrosine and S-ethyl-L-cysteine show heavy enzyme kinetic isotope effects with perdeuterated TPL that are strongly temperature and pressure dependent, and may be normal or inverse depending on conditions. These results suggest that conformational dynamics as well as vibrational coupling play a key role in the mechanism of the elimination reaction of TPL.

Translation inhibition in bacteria through antimicrobial peptides and hibernation factors

Raktim Roy, The Scripps Research Institute

Bacterial resistance to clinically used drugs is becoming a major public health concern. Proline-rich antimicrobial peptides (PrAMPs) have kindled renewed interests due to their targeted inhibitory effect on the bacterial protein synthesis, making them effective therapeutic leads, against human pathogens.

We have reported crystal structures at less than 3 angstroms resolution for a set of PrAMPs, providing insights into their mode of ribosome inactivation and translation inhibition. These ribosome-inactivating peptides sterically interfere with the tRNAs in the A and P sites and also occlude the peptide exit tunnel of the bacterial ribosome. We purified 70S ribosomes from *Thermus thermophilus*, which were then co-crystallized with mRNA, tRNAs and the PrAMPs. Our biochemical experiments show that the ribosome was effectively stalled during translation right after the initiation step, in presence of the RIPs. This inhibition was also equally potent in cellular environment and was reflected in corresponding hindered cell growth and MIC values in very low micro-molar ranges. We also found from the high-resolution structures, that all of these PrAMPs have a common mode of binding and their spatial architecture inside the Ribosome overlaps with the binding sites of three well-known classes of antibiotics, a feature that would markedly reduce the probability of appearance of drug resistance.

A second class of protein molecules was also studied using Cryo-EM techniques to understand the ribosome hibernation phenomenon. The hibernation factor YqjD was mapped to its binding site at the periphery of the ribosome elucidating the mechanism of sequestration during stress. The associated biochemistry also indicates towards the validation of the ribosome granule hypothesis that is observed during stress. In combination, our work provides a paradigm for translation inhibition through sequestration of the ribosomes from the active population.

High-energy x-ray diffraction for chemistry and material science at the APS

Uta Ruett, Olaf Borkiewicz, Saul Lapidus, Wenqian Xu, Andrey Yakovenko, and Yang Ren

The Structural Science group at the Advanced Photon Source (APS) at Argonne National Laboratory is operating a suite of four beamlines for high-energy X-rays (≥ 30 keV) with main emphasis on in situ and operando experiments in the area of chemistry and materials science.

High-energy X-ray diffraction (HEXRD) is a bulk structure characterization technique widely used in materials research taking advantage of the high penetration power into material, large accessible q-range, and small correction factors. *In situ* measurements study structural changes of materials under various conditions including metastable and intermediate phases. *Operando* experiments are essential for the insight of changes in functional devices during operation to improve their performance. There is a strong emphasis on the research of energy storage systems and the synthesis of materials ranging from in situ growth to operando studies of the functionality. Moreover, gas storage system, catalysis processes, engineering materials etc are studied.

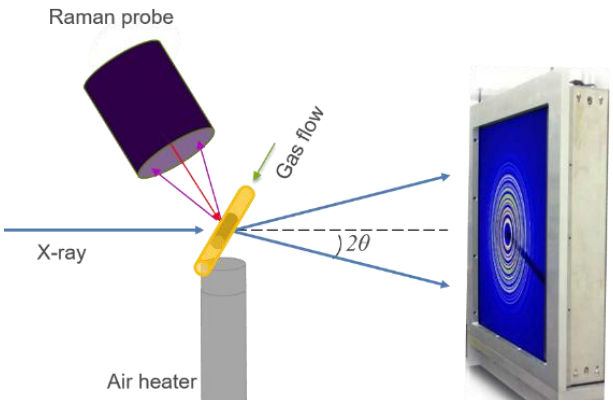

Figure 1Setup in 17-BM for multimodal powder diffraction.

The techniques offered by the beamlines cover high-resolution powder diffraction (11-BM), rapid acquisition powder diffraction (17-BM), total scattering for PDF analysis (11-ID-B), and diffraction under extreme conditions at 106 keV (11-ID-C).

The beamlines operate in x-ray transmission geometry with monochromatic beams and area detectors, and in case of 11-BM with an array of analyzer crystals and scintillators for highest resolution. Most recent developments include an in-line Raman system at 17-BM that allows simultaneous measurement of HEXRD/PDF and Raman spectroscopy data under controlled temperature and gas environment (Fig.1). The station 11-ID-B is now also enabling studies on surfaces and interfaces with an optional line focus of a few micrometer beam height (Fig.2). A hexapod will allow highly accurate control of specimen orientation enabling surface and interface scattering. At 11-ID-C, a heavy-load hexapod stage provides similar capabilities, but for heavy equipment up to 250 kg. The high-resolution beamline 11-BM has got the option to switch to an area detector for rapid checks on the sample status. It is possible to mail in samples to 11-BM, 11-ID-B and 17-BM.

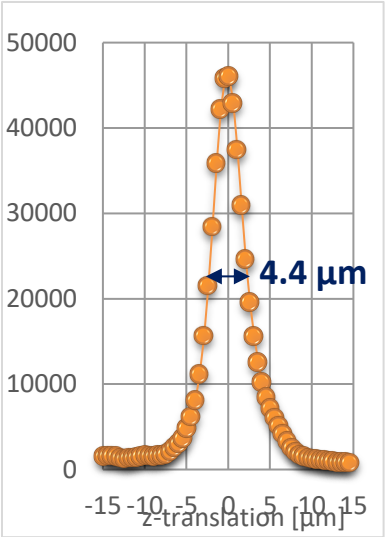

Figure 2Derivative of a knife edge scan showing the shape of the focused beam in the vertical direction

An outlook will be given about the new options becoming available after the upgrade of the APS to a lowest emittance storage ring in a few years. Especially, the upgrade plans converting 11-ID-D into a high-energy X-ray beamline operating between 27 keV to 120 keV photon energy will be discussed.

A disordered superspace approach to understand highly structured diffuse scattering

Ella Mara Schmidt and Reinhard B. Neder

Single crystal diffuse scattering is generally interpreted using correlation parameters, that describe probabilities for certain configurations on a local scale. If the diffuse maxima are at a general position in reciprocal space many parameters are needed to simulate a short range ordered structure in direct space, which reproduces the observed diffuse maxima.

In the field of incommensurate crystallography a (3+d)-dimensional approach is taken to describe satellite reflections in reciprocal space, that cannot be indexed with integer (h,k,l) . A 3-dimensional aperiodic crystal structure is periodic in (3+d)-dimensional superspace and the atomic positions and/or occupancies of the 3D structure are described by modulation functions.

A perfectly periodic superspace gives rise to sharp satellite reflections. In order to describe broadend satellite reflections we introduce disorder into superspace. By introducing phase domains in the superspace structure we can generate structures that give rise to diffuse maxima at any position in reciprocal space with an arbitrary width [1]. The disordered superspace approach also allows for a straight forward computational generation of a disordered structure using only few parameters.

The compound ThAsSe shows highly structured diffuse planes at G±0.14<110>*±Ɛ<110>*±η[001]* with Ɛ and η essentially continuous [2]. The observed extinction conditions and the sharp diffuse rods can be directly interpreted using the disordered superspace approach. The diffuse planes in reciprocal are reproduced from a computational model crystal, that was build using the disordered superspace approach.

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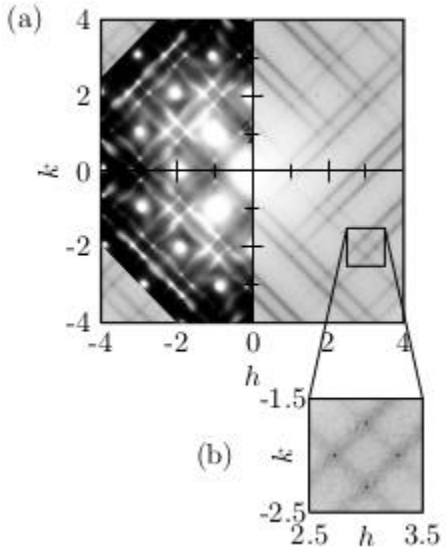

Figure 1: (a) Overly of the experimental hk0-layer of diffuse scattering of ThAsSe taken from [2] and the simulated diffuse scattering pattern from a model crystal generated with the disordered superspace approach. (b) Enlargement of the sharp satellite reflections on top of the diffuse p

MacCHESS after the CHESS-U upgrade

David J. Schuller, Aaron D. Finke, Richard E. Gillilan, D. Marian Szebenyi

Macromolecular X-ray science at the Cornell High Energy Synchrotron Source(**MacCHESS**) is an NIH-funded facility in Ithaca, NY which assists the biomedical research community with structural biology research; in particular X-ray crystallography and Small Angle X-ray Scattering(SAXS). In June 2018, The Cornell Electron Storage Ring (CESR) and Cornell High Energy Synchrotron Source (CHESS) shut down for an upgrade funded by the state of New York. Topics discussed will include progress of the upgrade, benefits including improved flux, revised organization of CHESS including the role of MacCHESS, and how to request beam time as we open to users in October 2019.

Why won't Uracil Form Large Single Crystals? Analysis of the Crystalline Structure of Uracil

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Large X-ray quality crystals have been formed of all the ribonucleic acids except uracil (a cyclic ribonucleic acid, C4H4N2O2). To date, it has proven to be very problematic to form large single crystals of uracil with only low quality crystals being formed near the sublimation temperature (338 oC) [1]. This study will attempt to determine why this is so.

Previous analysis determined that uracil crystallizes in space group P21/a with unit cell parameters: a = 11.938(1) Å, b =12.376(9) Å , c = 3.6552(3) Å, and β = 120.90(4)0. After careful analysis, Stewart et. al. concluded that there were two possible hydrogen bonding patterns that were conceptually feasible. The difference between the two structures lies in the rotation about the C2-C5 axis, swapping a carbon atom, for a nitrogen atom. The first structure contained an oxygen atom with two N-H•••O hydrogen bonds while the other oxygen atom possessed none. The second structure contained one N-H•••O hydrogen bond to each oxygen atom. Stewart determined that his laboratory single crystal data supported the former pattern with no detectable contribution of the second hydrogen bonding pattern (besides some streaking in X-ray photographs).

TOF neutron diffraction data were collected at the Spallation Neutron Source, Oak Ridge National Laboratory to further investigate the possibility of the presence of the alternative hydrogen bonding pattern in crystals of uracil. Neutron scattering length difference between carbon and nitrogen should be sufficient to detect the presence of the alternative hydrogen bonding pattern, if present. If this alternative hydrogen bonding pattern is indeed detected, this could provide an explanation as to why large crystals of uracil are difficult to grow. The neutron diffraction data will be modeled using The GSAS-II program package. Upon refinement (convergence with R(F2) = 5.604 % with wR = 2.75 %) 8.06 % of the alternative H-bonding pattern was discovered. This new model will be described in terms of the stacking layer model encoded into GSAS II. X-ray diffraction data will be simulated based upon this stacking model which will be compared to experimental X-ray data. [1] Stewart, R.F. & Jensen, L.H. (1967). Acta Cryst., 23, 1102

Crucial Insights from Crystallography into Magneto-Structural Phase Transitions in Molecule-Based Systems

Michael Shatruk (Department of Chemistry and Biochemistry, Florida State University)

The development of molecular materials with “switchable” physical properties has attracted considerable attention in recent years. Arguably, the most actively investigated group of materials are spin-crossover (SCO) transition metal complexes, which exhibit switching between the high-spin (HS) and low-spin (LS) electronic configurations. This spin-state conversion is achieved by changes in temperature, pressure, or photoexcitation, which make SCO complexes promising materials for various applications that rely on bistable systems. Besides the SCO complexes, which rely on spin-state switching at the metal center, metal-free radicals are also emerging as a major source of interest. In these latter systems, the spin-change associated with radical-dimer interconversion can be also controlled by heat, light and pressure, often giving rise to hysteretic behavior with wide regions of magnetic bistability wherein the radical and dimer forms are capable of coexistence. In this contribution we will demonstrate the use of small-molecule crystallography to achieve crucial information on the nature of spin-state switching, associated with dramatic structural changes in the underlying material.

Structural consequences on transforming growth factor beta-1 activation from near therapeutic X-ray doses

Timothy R. Stachowskia,d, Thomas D. Granta,c, and Edward H. Snella,b

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Understanding how cells respond to radiation therapy is a major goal in developing effective cancer treatments. Since extracellular signaling proteins orchestrate complicated behaviors between cells that collectively direct the future of tissues, they represent a promising class of targets for therapeutic intervention. Transforming growth factor beta-1 (TGFβ-1) is one such protein that in response to radiation exposure initiates downstream signaling pathways that control a number of cancer related processes such as proliferation, migration, and invasion. Normally, the 25 kDa dimer of TGFβ-1 is secreted with the 55 kDa dimer, latency associated peptide (LAP), that renders TGFβ-1 inactive, and together are known as latent-TGFβ-1 (LTGFβ- 1). Dissociation from this arrangement allows the now “activated” TGFβ-1 to bind cognate receptors that initiate signaling pathways and finally alter gene expression. Ionizing radiation triggers activation and was first observed in the immuno-histochemical staining of irradiated mammary gland cells [1]. In vitro work also showed that in addition to activated TGFβ-1, radiation also generated in-activatable (i.e. damaged) LTGFβ-1, suggesting two separate structural pathways. Chemically generated reactive oxygen species (ROS) can also activate TGFβ-1 through a non-conserved methionine in LAP [2].

Ultimately, the structural pathway underlying radiation driven TGFβ-1 activation is poorly understood because historically it has been probed with only cellular and biochemical assays. Techniques such as X-ray crystallography and small angle solution X-ray scattering (SAXS) are advantageous for this system because the same X-rays used to initiate activation can also be used to directly and simultaneously monitor structural changes. However, because radiation
therapy for cancer treatment uses doses that are far lower than those required to yield structural data, new data collection methods combined with complementary structural solution techniques must be used to study this process. Our recent work using SAXS and complementary techniques aimed to (1) characterize structural changes induced by therapeutic-level radiation exposure, (2) identify protein regions most sensitive to radiation, and (3) investigate the radiation chemistry generated from low-dose X-rays. Our results suggest that the damage pathway results from oxidative stress and that X-ray exposure is not sufficient for activation [3]. SAXS, circular dichroism, and crystallography show that LAP is highly dynamic and conformationally distinct between TGFβ-1 binding states [3, 4]. These studies pave the way for a structural understanding of systems impacted by therapeutic level X-ray doses.

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Probing magnetic interactions in Re-based double perovskites

C. Thompson

Double perovskites, A2B'BO6, have been intensely studied due to their interesting chemical and physical properties. The different B-site cation combinations allow for a wide range of novel materials with unique magnetic behavior, from ferromagnets to spin glasses. These properties are not only dependent on the B-site cations but also on the structure-types. For instance, double perovskites with both 3d and 5d transition-metal ions occupying B-sites adopt a tetragonal (I4/m) or monoclinic (P21/n) cation ordered structure. However, cation disordered structures are obtained with the B-sites having a decreasing difference of the ionic radii or charge state, i.e., orthorhombic Pbnm. Recently, we have synthesized five new rhenium-based double perovskites. We have performed synchrotron X-ray and neutron powder diffraction measurements as well as XANES, magnetic and thermal transport property measurements to understand structure-property relationships in this system. The structural and magnetic properties of the five new rhenium-based double perovskites will be presented and compared to their A-site substituted analogs.

Systematic Determination of magnetic structures driven by space groups in GSAS-ii

Robert Von Dreele

Current development of GSAS-II includes facilities for creating magnetic structures or importing them from mcif files. GSAS-II adopts the BNS (Belov-Neronova & Smirnova) nomenclature for magnetic symmetry, thus allowing description of any magnetic structure with complete translational lattice symmetry and avoiding fractional reflection indices. Magnetic structures in GSAS-II are always split into two components; one for the nuclear ("chemical") structure and the other with only magnetic ions; these are tied together by constraints during refinement. Graphical displays allow easy display of results. Use is made of a special version of the k-SUBGROUPSMAG suite of programs (Gallego, et al.) to create possible magnetic models for testing against the neutron powder diffraction data. This talk will summarize the current status of these developments in GSAS-II.
Acknowledgement: This work was supported by the US DOE under contract No. DE-AC02-06CH11357.

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SER-CAT's Current and Future Challenges in Meeting the $815M APS-Upgrade

Bi-Cheng Wang, John Rose and John Chrzas
SER-CAT, University of Georgia and Advanced Photon Source

The US Department of Energy has finally given the green light to a $815M upgrade of APS synchrotron storage ring that will boost the brightness of the X-ray source by up to 1000 times and the beam size will be reduced by a factor of 70 (https://physicsworld.com/a/advanced-photon-source-set-for-815m-upgrade/). The APS-upgrade project (APS-U) is scheduled to start as soon as the APS' operation moves to a four-year "installation/commissioning/power-up" period that is projected to begin in September 2022. The first year of this period is referred to as a "dark" period in which no X-rays are available for testing or experimentation. Our understanding is that SER-CAT will have access to X-rays comparable to current 22ID intensity in the latter part of 2023 for its Members and Associate Users. Together with the upgrade, an updated APS/DOE regulations and roles regarding to post-upgrade operations of the Collaborative Access Teams (CATs) will also be implemented.

By year 2022, the SER-CAT 22ID beamline will have provided 20 years of service. Thus, the APS shutdown period will be an opportunity to upgrade the 20-year old 22ID, which has in the past contributed so much to the structural biology community (as the second most productive beamline worldwide in terms of PDB deposits) to continue providing a world class research resource for scientists using the intense APS-U microbeams. In addition, the SER-CAT Board has decided to add a second ID beamline to replace beamline 22BM since it will not benefit from the APS-U storage ring upgrade without significant investments from SER-CAT and the APS.

SER-CAT is currently engaged in active planning to meet the various challenges and opportunities presented by the APS-U. Some of our preliminary plans will be shared with the community during the PDC 2019 meeting.

Structural and magnetic properties of R_2TiO_5 (R = Dy and Yb)

Haidong Zhou (University of Tennessee/Physics Department)

The structure and magnetic properties of R_2TiO_5 (R = Dy and Yb) have been investigated using x-ray diffraction, neutron diffraction and scattering, and alternating current (ac)/direct current (dc) magnetic susceptibility measurements. For Dy_2TiO_5, it has an orthorhombic structure. There is a two-dimensional (2D) magnetic ordering appearing below 3.1 K, which is followed by a three-dimensional magnetic transition at 1.7 K. The related spin structure can be indexed with the propagation vector k = [0 1/2 0], corresponding to a coplanar model of interwoven 2D sheet extending in the [0 1 0] direction. On the other hand, for Yb_2TiO_5 with smaller radius Yb^{3+} ions, it has an average disordered fluorite structure with additional diffuse scattering features, which are caused by structural short-range orthorhombic order. The magnetic property measurements show a broad peak at $T_f \approx 0.35$K that displays Arrhenius behavior with an activation energy of 2.51(5) meV, but without long range magnetic ordering down to lowest measured temperatures. Zero-field neutron scattering measurements show broad magnetic diffuse scattering in the elastic channel with an antiferromagnetic-type gapless excitation extending to 1.5 meV. A polarized state with partial spin order is induced with an applied magnetic field which opens a gapped excitation that increases monotonically with field strength.

Poster Abstracts

Structural performance of ribosomal proteins during mRNA unwinding by *E. coli* ribosomes in solution

Emily Armbruster[1,2], Kevin Weiss[2], Loukas Petridis[2], Jose Borreguero Calvo[2], James Byrnes[3], Peter Cornish[1], Sai Venkatesh Pingali[2]

[1]Department of Biochemistry, University of Missouri, Columbia, MO
[2]Oak Ridge National Laboratory, Oak Ridge, TN
[3]Brookhaven National Laboratory, Upton, NY

Proteins, the workhorse of a biological cell, are produced and distributed by a large, flexible, macromolecular machine called the ribosome. Messenger RNA (mRNA) is translated by the ribosome to create a protein in a process that involves molecular movements of the ribosome and determining the various structural conformations involved can provide insight toward understanding ribosomal function. Currently, the field of functionally oriented structural biology emphasizes the importance of mapping conformational space. However, mapping the continuous structural variation of the ribosome is difficult due to low energetic barriers between ribosomal conformational states[1,2].This difficulty has interfered in characterizing the conformational distortions of the ribosome as it unwinds structured mRNA during translation, an important phenomenon that impacts the production and diversity of proteome. This study uses experimental small-angle scattering methods to divulge the structural dimensions of 70S *E. coli* ribosome in solution. We observed structural differences between a ribosome that is bound to structured mRNA and a ribosome that is vacant or bound to linear mRNA. This comparison shows the proteins on a ribosome interacting with an mRNA secondary structure elongate by 27% in the maximum dimension of ribosomal proteins.

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Relating crystal structure to vapochromic responses in polymorphic compounds

Nathaniel M. Barker, Stephen Taylor, Ethan Ferguson, Jeanette Krause, William Connick, Peng Zhang

Department of Chemistry, University of Cincinnati

Vapochromic compounds have been well-known for many years. However, not until the work of Mann and co-workers, studying a mixed Pt…Pd salt, that their sensing ability was recognized.[1] Since then, vapochromic materials, specifically Pt-centered vapochromic complexes, have been widely studied.[2–4]

We have been working with a vapochromic Pt salt that forms different polymorphs dependent on the recrystallization technique. Upon isolation, these types of materials can be used to detect different volatile organic compounds (VOC's) or environmentally-troublesome anions with high selectivity and sensitivity by undergoing a noticeable color change. In addition, the emission and response properties undergo a shift that can be directly related to the intra- and inter-dimer Pt…Pt distances of the respective polymorph. X-ray crystallography has been vital in determining the overall structures of these polymorphic complexes and the details of the Pt…Pt interactions that give rise to the color, luminescence, and response properties of these materials.

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An Update on Current SER-CAT's APS Facilities as well as Near and Long Term Upgrade Plans

John Chrzas, Albert Fu, John Rose and Bi-Cheng Wang
SER-CAT, University of Georgia and Advanced Photon Source

The SER-CAT APS facility currently consists of 2 beamlines (an undulator (22ID) and a bending magnet (22BM)) as well as its network and computer infrastructure. The APS upgrade (APS-U), which is currently planned to start with a 1-year dark period in the Fall of 2022, is a critical event in the life of SER-CAT, and is the focal point for the development and continued success of the facility.

The poster will present the following:

1) Current beamline and computer capabilities
2) Pre APS-U hardware, software and compute upgrades
3) SER-CAT upgrade plans for the APS-U dark period and beyond, which include the development of a second undulator beamline (22ID-E)

In situ Low-temperature Pair Distribution Function (PDF) Analysis and Molecular Dynamics Simulations of CH_4 and CO_2 Hydrates

Bernadette R. Cladek, S. Michelle Everett, Marshall T. McDonnell, Matthew G. Tucker, David J. Keffer, Claudia J. Rawn

Natural gas hydrates (NGH) form in ocean floor and sub-surface permafrost deposits in high-pressure, low temperature environments. Research on these deposits is driven by their potential as a future energy source. Naturally occurring CH_4 hydrates primarily crystallize in the sI clathrate structure. This lattice is composed of hydrogen bonded water cages (the host), each of which occlude one gas molecule (the guest). Though the sI framework can host other molecules, this research focuses on CH_4-CO_2 hydrates to support current explorations in which CH_4 may be harvested from hydrate deposits via exchange with CO_2. CO_2 replacement in the hydrate structure is energetically preferred, facilitating CO_2 byproduct sequestration while obtaining new fuel sources. Equilibrium models predict that a mixed hydrate solid solution in which CO_2 replaces some CH_4 is stable at higher temperature and lower pressure than pure CH_4 hydrate, and thermodynamic stability increases as the CO_2 fraction increases. The impact of varying the type of guest molecules and mixed guest systems is a relevant topic to study due to concerns about the stability of NGH under changing environmental conditions. A detailed understanding of the guest-host interactions in gas hydrates is necessary for the advancement of emerging technologies and processes which will utilize NGH deposits. The gas hydrate crystal has a high degree of disorder at all temperatures due to the motion of the occluded gas molecules and their interactions with the H_2O lattice. Molecular dynamics (MD) simulations show that this disorder is not described by long-range crystallographic models. *In situ* neutron total scattering experiments and pair distribution function (PDF) analysis are used to characterize the short-range order in CH_4-CO_2 hydrates. Extraction of detailed information from PDF data of complex systems requires methods such as MD simulations combined with Reverse Monte Carlo (RMC) fitting. Preliminary MD models of CH_4-CO_2 hydrates demonstrate the benefit of neutron PDF experiments by providing simulated PDFs, visualization of molecular motion, and analysis of thermodynamic interaction energies throughout the CH_4-CO_2 guest composition. *In situ* variable temperature neutron PDF data of CH_4, CO_2, and mixed CH_4-CO_2 hydrate were collected at the NOMAD beamline at the Spallation Neutron Source (SNS), Oak Ridge National Laboratory. RMCProfile is used to fit the data to large box models produced with MD simulations. PDF experiments performed *in situ* provide structural characterization, while the variable temperature measurements lead to inferred dynamics. Dynamics will also be directly observed with complementary inelastic neutron scattering (INS) experiments on the VISION beamline for chemical bond analysis.

Local Structure of Metal-Organic Framework-Derived Carbons as Determined by Neutron Pair Distribution Function Analysis

Gregory S. Day, Matthew Ryder, Katharine Page, Hong-Cai Zhou

Metal-organic frameworks (MOFs) are a class of porous materials constructed through the coordination of organic linkers to inorganic nodes. These structures are highly versatile in terms of design, with nearly infinite variation in the metals and linkers chosen. However, as they are constructed from coordination bonds, MOFs have a tendency to be labile and are often thermally sensitive, oftentimes losing structural cohesion and porosity at temperatures above 300 C. To combat this, researchers have been investigating the controlled carbonization of these MOFs, pyrolyzing them under conditions in which they can still maintain some porosity, to form highly stable and robust frameworks with well dispersed metal or metal oxide subunits. These materials are of great interest in areas such as catalysis and water remediation where the weaknesses of traditional MOFs can be a detriment. However, despite the interest in these materials, there has been little effort focused on their structural characterization. To that end, we have begun investigating the local structure of a number of MOF-derived carbons through controlled calcination under different gas environments and temperatures in order to gain better insight into the formation of these materials and tune them towards specific applications.

Neutron Diffraction Studies of Reaction Intermediates of Aspartate Aminotransferase

Victoria N. Drago, Steven Dajnowicz, Andrey Y. Kovalevsky, and Timothy C. Mueser

Vitamin B_6 derivative, pyridoxal 5'-phosphate (PLP), is a highly versatile cofactor involved in many different chemical reactions. PLP- dependent enzymes catalyze a broad range of chemistry including transamination, racemization, phosphorylation, a-decarboxylation, aldol cleavage, b and g-elimination, and replacement reactions; some of which have no analogues in organic chemistry. PLP-dependent enzymes have important roles in the metabolism of amino acids and glycogen and are found in numerous pathways, including the interconversion of aamino acids and the biosynthesis of antibiotic compounds. As ubiquitous proteins with significant metabolic functions, PLP-dependent enzymes are attractive targets for specific inhibitor design, including novel antibacterial, anti-malarial and anti-cancer agents. Aspartate aminotransferase (AAT) is a model of a fold-type I PLP-dependent enzyme involved in transamination reactions. Our previous work determined the protonation states of the internal and external aldimine in AAT, showing the pyridine nitrogen is protonated and phenolic oxygen is deprotonated in both instances, whereas the Schiff base nitrogen is only protonated in the external aldimine. To understand the complete AAT catalytic mechanism, we have solved two neutron structures capturing the carbinolamine intermediate and the half reaction product pyridoxamine-5'-phosphate (PMP). Together our work provides a better image of the electronic modulation of the PLP cofactor through the study of the protonation states at each of these stages in the reaction mechanism.

A multimodal investigation of bimetallic MOFs and their role in C-C activation for room temperature propylene hydrogenation

Amani M. Ebrahim,1 Deependra M. Shakya,2 Otega Ejegbavwo,2 Rajesh Thayalan,3 Sharfa Farzandh,2 Amy J. Brandt,2 Ning Rui,4 Sanjaya D. Senanyake,4 Anatoly I. Frenkel,1,4 Gregory Tate,5 John R. Monnier,5 Kostas D. Vogiatzis,3 Natalia B. Shustova*2 and Donna A. Chen*

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Olefins, a big component of natural gas, require selective conversion. The selective cleavage of C-C bonds remains an important goal for the preferential formation of necessary commodity materials. The activation of olefins homolytically or heterolytically depends on the feasibility of bond dissociation by assisted pi interactions through the utilization of transition metals. A CuBTC (copper-based benzene tricarboxylic acid-based metal organic framework (MOF)) is prepared with the addition of an active Rh component, resulting in a bimetallic system of Rh-Cu pair sites. Unlike catalysts that contain purely Rh-Rh bonds, we showed that selective Rh sites are catalytic active for room temperature propylene hydrogenation. CuRhBTC represents one of the first bimetallic metal organic framework (MOF) materials which demonstrates remarkable catalytic chemistry for olefin hydrogenation. The hypothesis explaining its catalytic activity relies on the assumption that Cu pairs up with Rh at the paddlewheel structure of this MOF. By combining a multimodal approach, we link the structure and reactivity of this bimetallic system and help establish its mechanism. Our preliminary ex-situ experiments established good spectral contrast between possible oxidation states of rhodium. Here we present information on Rh ion speciation under in situ conditions, using a multimodal approach focusing on the structural changes in the MOF using spectroscopic and scattering methods. The information obtained from such complimentary techniques reveals key understanding of the active sites and establishes its working mechanisms. Understanding the nature of the Rh in its active state and determining the atomic coordination geometry and reactant/catalyst interactions during reaction conditions will advance our understanding of the mechanistic relationship between metal ions and reactivity for olefin hydrogenation and will guide further synthetic design and optimization of room temperature hydrogenation catalysts.

Structural Investigation of Arabidopsis Cellulose Synthase Interactive Protein 1

Yichong Fan, Qiu Zhang, Utsab Shrestha, Sarah Lucas, Samuel Solomon, Ying Gu, Loukas Petridis, Hugh O'Neill

Cellulose biosynthesis is a tightly regulated process that is performed by plasma membrane-localized cellulose synthase (CESA) complexes (CSCs). A recent study identified CESA interactive protein 1 (CSI1) mediates an interaction between microtubules and cellulose synthase. Microtubules are crucial for many aspects of normal plant development. Cortical microtubules were reported to be oriented in parallel to the cellulose microfibrils during cellulose synthesis in many different cell types and organisms, and disruption of cortical microtubules using various microtubule inhibitors disorganizes the pattern of cellulose microfibril deposition. CSI1 directly binds to microtubules as demonstrated by an in vitro microtubule-binding assay. A further study also established a model in which CSI1-dependent small CESA compartments (SmaCCs) and microtubule-associated cellulose synthase compartments (MASCs) are formed through a process that involved endocytosis, which represents an important mechanism for plants to quickly regulate cellulose synthesis abiotic stress. Considering the important role of CSI1 in cellulose synthesis, it is critical to understand the structure and function of CSI1. In our study, we combine computational modeling with experimental approaches, including SAXS, SANS and FRET, to interpret the structure of CSI1, and how it interacts with CSCs and microtubules.

Superstructure formation in the system $Pr_{2-x}Sr_xNiO_{4+\delta}$

Matthias Frontzek, Anna Marsicano, Werner Paulus, Monica Ceretti

$Pr_2NiO_{4+\delta}$ can accommodate extra oxygen atoms on interstitial sites, the non-stoichiometric region being $0 < \delta < 0.25$. The δ can be easily and quantitative reliable varied by electrochemical techniques using an aqueous alkaline electrolyte in a reversible topotactic reaction. Another possibility is to rely on thermal diffusion by heating a sample in vacuum or in oxygen atmosphere. The minimal δ achievable with this is 0.12. The oxygen content can be tracked by the change in the ***c***-lattice constant. Recent work shows that no loss of oxygen occurs when the sample is heated in air [1].

The change of oxygen content does not affect the quality of the single crystals. Moreover, the oxygen content seems to be well defined over the whole volume. The interstitial oxygen forms a well-defined superstructure with resolution limited peak width. The formation of these structures indicates the existence of well-defined diffusion pathways which indicate a novel transport mechanism [1].
In our contribution we will present early results form diffraction experiments on WAND², HFIR and TOPAZ, SNS.

[1] M. Ceretti, O. Wahyudi, A. Cousson, A. Villesuzanne, M. Meven, B. Pedersen, J. M. Bassat, W. Paulus, Journal of Materials Chemistry A, **3** (2015) 21140

Quality Control at SER-CAT

Zheng-Qing Fu, John Chrzas, John Rose and Bi-Cheng Wang

SER-CAT, Sector 22, APS, Argonne National Lab and Department of Biochemistry & Molecular Biology, University of Georgia, Athens, GA 30602, USA

Quality control for experiments conducted at synchrotron beam lines is challenging as it not only involves complicated instruments but also users with different backgrounds and expertise levels. As high-speed detectors are widely used at synchrotron facilities, it has become more dynamic and challenging as users may forget to continue following data collection basics while they push for high speed. Quality control is the highest priority at SER-CAT, and has been closely monitored through its automation development. In this work, some of these developments will be presented, including the recent advances.

Work supported in part by SER-CAT Members and University of Georgia.

Conformational Dynamics of Disordered regions of c-Src Kinase

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Intrinsically disordered proteins traverse a wide range of interconverting conformations because of their flat energy landscape. Therefore, studying intrinsically disordered proteins is a challenge for structural biology. Before molecular dynamics (MD) simulations can be used to gain insight into the conformational dynamics of these systems, structural information is needed to validate models. However, the traditional structural biology techniques like X-ray diffraction or NMR cannot be used to determine structure of IDPs. But low-resolution techniques like small angle scattering become an invaluable means for obtaining ensemble-averaged structural information on these disordered systems [1]. However, acquiring the structural details on disordered regions without truncating the proteins is a technical problem. Hence, we are approaching this challenge using the powerful combination of small angle neutron scattering and small-angle X-ray scattering to obtain structural information guided by molecular dynamics simulations to understand the structural dynamics of the disordered region of a human oncoprotein, c-Src kinase. It is one of the non-receptor tyrosine kinases that phosphorylate many downstream signaling proteins and is abnormally expressed in many cancers [2]. It is composed of 4 domains: the N-terminus intrinsically disordered Src homology 4 (SH4), SH3, SH2 and kinase domains. The N-terminal disordered region has been identified to form intramolecular complex with the other regulatory domains of Src [3]. We will use a bacterial transpeptidation ligase, sortase, to ligate protiated SH4 with the deuterated SH3 and SH2 domains that can be contrast matched with deuterium oxide based buffer as performed for segmental labeling of multi-domain proteins recently [4]. Segmentally labeled c-Src will be studied using Bio-SANS to obtain scattering information only from SH4 in the presence of the SH3 and SH2 domains. We will combine this information with small-angle X-ray scattering information from the holoprotein and all-atom MD simulations to model different sub-states of the SH4 domain to study the conformational dynamics of c-Src.

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Solvothermal intercalation of iron-amine complexes into iron sulfide layered materials

Colin Harmer, Kirill Kovnir

Recent interest in the intercalation chemistry of layered iron chalcogenides has led to the discovery of many new compounds with magnetic properties ranging from simple paramagnetism to antiferromagnetism and superconductivity. The parent superconducting compounds, mackinawite-FeS and β-FeSe, are composed of iron-chalcogen layers stacked via van der Waals forces. These relatively weak interlayer forces make iron chalcogenides suitable candidates for intercalation studies. Numerous reports have shown that drastic changes to magnetic behavior can arise from intercalation by a variety of species, such as, simple cations, metal hydroxides, metal-amine complexes, and neutral organic molecules. Although a wide variety of intercalates are possible, their diversity can pose a challenge when trying to assess direct relationships between the intercalated species and bulk properties. One approach towards a more systematic study is to intercalate iron-chalcogenides with a coordination complex and subsequently tune the complex while assessing structural and property variations. Our study focuses systematically modifying the ligand of the previously reported $[Fe_8S_{10}]Fe(en)_3 \cdot en$ compound, while observing changes to the structure, stability and bulk thermodynamic properties. $[Fe_8S_{10}]Fe(en)_3 \cdot en$ consists of $[Fe_8S_{10}]^{2-}$ layers intercalated by tris(ethylenediamine)iron(II) and a free ethylenediamine. Through solvothermal synthesis, we have made two new compounds intercalated with bidentate amines, 1,2-diaminopropane and 2,2'-bipyridine. We show that the interlayer spacing increases with the size of the coordination Fe-amine complex. This work will focus on the solvothermal synthesis, structure, and properties of the ethylenediamine, 1,2-diaminopropane and 2,2'-bipyride-contaning compounds with an emphasis on findings from recent X-ray pair distribution function and synchrotron powder X-ray diffraction experiments.

Crystal Structures, Optical, and Magnetic Properties of Copper (II) hybrid Ruddlesden-Popper phase Perovskite Derivatives

Noah P. Holzapfel and Patrick M. Woodward

Layered halide perovskite derivatives have recently shown great promise for photovoltaics, luminescence, and spintronics. By reducing the dimensionality of the perovskite structure, new pathways to tune the physical properties can be explored. Herein, we report a comprehensive investigation into the crystal structures, magnetic, and optical properties of a series of hybrid Ruddlesden-Popper LHPDs with the general formula of $(A')_2CuX_4$. The compounds being revisited include A' = $CH_3NH_3^+$, $CH_3CH_2NH_3^+$, and $CH_3CH_2CH_2NH_3^+$. The new structures being reported here include $(CH_3CH_2CH_2CH_2NH_3^+)_2CuCl_{4-x}Br_x$ ($0 < x < 4$). By tuning the length of the organic spacer and halide composition, magnetic and optical structure-property relationships can be elucidated. The entirety of this series exhibits soft ferromagnetic behavior indicated by a narrow hysteresis loop upon magnetization versus field experiments. Effective moments and Weiss constants were also extrapolated from the Curie-Weiss model. It has been shown that increasing the interlayer distance lowers the magnetic transition temperature (T_c). Substituting in Br^- for Cl^- has been shown to increase the Weiss coupling constant. Substitution of chloride with bromide also causes an absorbance shift to lower energy of the ligand to metal charge transfer energy.

Local structure of disordered pyrochlore High-Entropy Oxides (HEOs)

Bo Jiang, De-Ye Lin, Katharine Page

Recent studies have shown that by mixing equivalent multiple cations on a single crystallographic site of a transition metal oxide can form stable single phase material with high configuration entropy. Here, three kinds of high-entropy oxides (HEOs) pyrochlore of $La_2M_2O_7$, $Nd_2M_2O_7$-1 $Nd_2M_2O_7$-2 with five elements on the M-site are produced through conventional solid-state reaction route. The local structure of $La_2M_2O_7$ and $Nd_2M_2O_7$ HEOs were investigated by pair distribution functions (PDFs) from neutron total scattering. The computed PDFs from special quasirandom structures (SQS) method are compared with real space PDFs in this work. We demonstrate that $Nd_2M_2O_7$-1 (M=Ta, Sc, Sn, Hf, Zr) HEOs is successfully synthesized with M-site microscopic region disordered completely, and other two HEOs compounds show local lattice distortions due to the slightly differing bond environment with HEOs.

Understanding stacking faults in nanoscale transition metal borides

Palani Raja Jothi, Boniface Fokwa, and Katharine Page

Recently, transition metal borides have received considerable attention because of their excellent properties in energy related applications. Various transition metal boride nanostructures were synthesized by solid-state method using $SnCl_2$ redox chemistry. The structural characterization of these materials was completed through Rietveld analysis of X-ray dfiffraction data, showing severe intensity mismatch and systematic absences. The intensity mismatch was more severe in the case of metal monoboride nanostructures. Our preliminary refinement results show that the main reason for the intensity mismatch is stacking faults. More understanding on the formation mechanisms of stacking faults in nanoscale metal borides will be studied through Pair Distribution Function (PDF) analysis in future.

Following in the steps of Fieser, Lipscomb, and Hartsuck: the x-ray crystal structure of 5,5,10,10-tetrachlorotricyclo[7.1.0.04,6]decane

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Fifty-five years ago, Louis Fieser and David Sachs published the synthesis of 5,5,10,10tetrachlorotricyclo[7.1.0.04,6]decane (C8H8Cl4) [The Journal of Organic Chemistry 29, no. 5 (1964): 1113-1115]. Two isomers were reportedly synthesized, with the major product melting at 175176°C and a very minor product which melted at 228-230°C. Assuming one product to be a cis addition and the other a trans addition, Sachs and Fieser enlisted the assistance of Fieser's colleagues William Lipscomb and Jean Hartsuck to determine via x-ray crystallography which isomer was the major product. The lower melting major product exhibited a monoclinic space group with a 2-fold axis and a perpendicular mirror plane. The higher melting isomer was orthorhombic. From these data, the lower melting isomer was assigned to be a cis configuration, and the higher melting isomer was assigned to be the trans isomer. Apparently, a complete data set was not collected on either isomer.

This presentation describes the crystal structure of the major (cis) isomer of 5,5,10,10tetrachlorotricyclo[7.1.0.04,6]decane, one of the first crystal structures reported for any tricyclo[7.1.0.04,6]decane. 22381 reflections were collected using Mo Ka (l= 0.71073 Å) from 468.8° 2q at room temperature. Of these, 2554 were independent reflections. An analysis of the data indicated that the space group was C2/m, with a unit cell of a = 14.835(3) Å, b = 7.5789(18) Å, and c = 11.9433(11) Å, and b = 121.509(11)°. The calculated density of the crystal is 1.427 g/cm3. The chlorine atoms and the carbon atoms bonded to them lie along a mirror plane, and the cyclopropane rings are approximately parallel to the other four cyclooctane ring carbon atoms. A lower temperature data collection is planned in order to lower the R factor for this crystal structure.

Structure-centered design of accelerated reactivators to treat organophosphate poisoning

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Nucleophilic oxime reactivators of organophosphate (OP) inhibited acetylcholinesterase (AChE) are the only true antidotes against OP intoxication in nerve agent or OP pesticide exposure. Within the past decade it has become increasingly clear that for effective and complete recovery from an OP intoxication antidotal action is needed in both peripheral and central nervous system tissues. We have used the structure-assisted antidote design approach to create novel oxime reactivators that possess superior *in vitro* properties for reactivation of various OP-conjugates of human AChE (hAChE) compared to the known oximes. Starting with RS194B oxime we have analyzed its molecular interactions with native and VX-inhibited hAChE by resolving X-ray structures of its respective complexes at 2.4 and 2.25Å resolutions. We have used these structures as molecular templates to design and test, first *in silico*, a small library of bis-oximes intended to remedy the oxime orientation problem. Seven of these "smart" bis-oximes, selected by computational docking analysis and synthesized in large quantities, were proven as effective reactivators *in vit*ro. In reactivation of sarin, cyclosarin, VX and paraoxon inhibited hAChE our piperidine, piperazine and homopiperazine derivatives exceeded efficacy of RS194B. For one of the representative bis-oximes, LG-703, we also confirmed productive binding orientation of the bis-oxime in hAChE directly by solving the X-ray structure of the binary complex. Our library of uncharged heterocyclic bis-oxime antidotes is thus a conceptually novel, effective scaffold of nucleophilic reactivators and a promising new resource for creation of adjustable, accelerated centrally active antidotes against OP intoxication.

Visualizing an oxyanion tetrahedral intermediate in HIV-1 protease: Insights for catalysis and drug design

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HIV-1 protease is indispensable for virus propagation and an important therapeutic target for antiviral inhibitors to treat AIDS. As such inhibitors mimic transition state analogues, a detailed understanding of the enzyme mechanism is crucial for the development of better anti-HIV drugs. Here we used room temperature joint X-ray/neutron (XN) crystallography to directly visualize hydrogen atoms and map hydrogen bonding interactions in a protease complex with peptidomimetic inhibitor KVS-1 containing a reactive nonhydrolyzable ketomethylene isostere, which, upon reacting with the catalytic water molecule, is converted into a tetrahedral intermediate state, KVS-1_{TI}. We unambiguously determined that the resultant tetrahedral intermediate is an oxyanion, rather than the *gem*-diol, and both catalytic aspartic acid residues are protonated. The oxyanion tetrahedral intermediate appears to be unstable, even though the negative charge on the oxyanion is delocalized through a strong $n \rightarrow \pi^*$ hyperconjugative interaction into the nearby peptidic carbonyl group of the inhibitor. Keto-darunavir (keto-DRV), which has a similar modification introduced into the clinical drug DRV to possess the ketomethylene isostere, is a significantly less potent protease inhibitor than DRV in solution. These findings shed light on the reaction mechanism of peptide hydrolysis catalysed by HIV-1 protease and provide valuable insights for further improvements in the design of protease inhibitors.

Total scattering analysis of poorly-crystalline nanosheet aggregates

Peter C. Metz, Jue Liu, and Katharine Page

Since the advent of the Graphene Era, synthesis approaches producing isolated and aggregated nanosheet materials with broad arrays of physical and chemical properties have been developed. Excitement in this field is rooted in the promise of scalable synthesis and self-assembly of nanoscale ordered structures, but robust atomic structure characterization has remained a significant challenge. Fundamental questions persist, including the role of water/solvents in apparent properties, and the structural similarity of nanosheets to bulk analogs. From a diffractionist's viewpoint, the trouble in addressing these structure characterization problems is two-fold: the inverse nanostructure problem is ill-posed due to the collapse of resolved Bragg features in the scattering signal, and the *de facto* standard for structure analysis (X-ray diffraction) is often poorly matched to key structure features like light elements and structural or surface-bound waters. We have employed X-ray and neutron total scattering methods to probe the local order in nanosheet materials, including layer-layer correlations difficult to ascertain by diffraction methods alone. Progress in data analysis methods is presented, including application to layer-disordered δ-MnO_2 and Mo_2C MXene cases.

Mechanical Bending and Spin-Orbital Coupling in 2D Hybrid Perovskite Films

Sreya Paladugu, Xixiang Zhu, Bin Hu, Kate Page

Hybrid organic-inorganic perovskites are promising materials for flexible electronic devices due to their solution processability. Spin-orbital coupling (SOC) is a fundamental parameter that affects the optoelectronic performance of perovskite devices. This work investigates the use of mechanical bending to introduce compressive strain in perovskite films ((PEA)2 (MA)n–1 Pbn Br3n+1, n=5), as a mechanism to control SOC strength. Linear/circular photoexcitation modulated photoluminescence (PL) studies show that increasing compressive mechanical strain gives rise to weaker orbit-orbit interaction, decreasing SOC in the films. Furthermore, the PL lifetime is found to decrease from 329ns to 204ns due to the compressive strain in the thin film. Future efforts will focus on determining structure-property relationships, through X-ray pair distribution function studies (PDF) on the thin films.

IRON-PILLARED MONTMORILLONITE

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Swelling clay minerals – smectites are commonly used in many industries as fillers or absorbers. Their stability is limited and usually low, due to the collapsing of their layered structure by the aggressive surrounding environment of extreme pH. The pillaring process can enhance their stability against such strong conditions. This study presents the structural changes upon the "pillaring" process by Fe characterized by X-ray Diffraction analysis (XRD) and other additional techniques, like X-ray Fluorescence analysis (XRF), and Mössbauer spectroscopy.

Sodium saturated montmorillonite, Upton was used in this study. The pillaring solution (PS) consists of sodium carbonate and ferric nitrate. Three pillared montmorillonites PS1-Upton, PS2-Upton, and PS3-Upton were prepared by addition of PS (100 mL, 200 mL, and 300 mL) to the montmorillonite suspension (20 g/L). All three pillared montmorillonites were aged at 60ºC for 24 hours in the oven. The resulting suspensions were centrifuged, and four times washed by DI water. The final solid cakes were decanted and dried at 80ºC in the oven overnight.

The pillaring process caused a significant color change of the particles from white to brown-red. The XRD patterns of the oriented air-dried (AD) unaltered Na-Upton, and pillared PS1-Upton, PS2-Upton, and PS3-Upton confirmed the successful pillaring treatment. The intercalation of PS into the interlayer space of Na-Upton montmorillonite caused expansion of the interlayer space by shifting of the basal diffraction (*001*) from 13 Å to 15.2 Å (PS1-Upton). Interestingly, the increasing PS content caused a slight collapse of the pillaring process and decreasing of the basal spacing to 15.0 Å and 14.8 Å for PS2-Upton and PS3-Upton, respectively. The XRF results showed that the Fe content increased from 1.1 wt. % (Na-Upton) up to 35.5 wt. % (PS3-Upton). It was in agreement with the Mössbauer data. The room temperature Mössbauer spectra of Na-Upton provided a low quality noisy spectrum with a lack of iron in the montmorillonite fitted with one doublet of the isomer shift (IS) 0.29 mm/s and the quadrupole splitting (QS) 0.57 mm/s typical for Al-rich smectites. On the other hand, the pillaring process enhanced the iron content in PS1-Upton, PS2-Upton and PS3-Upton, which is confirmed by well-developed Mössbauer spectra fitted with two doublets of similar ISs 0.3 mm/s and QSs 0.5 and 0.8 mm/s, respectively. Iron was successfully intercalated to the interlayer space. The 4K Mössbauer spectra reveal the magnetic ordering in all three pillared montmorillonites with two hyperfine magnetic splittings (B) at 45 T and 49 T, typical for ferrihydrite and goethite, respectively. The relaxed magnetic field was also observed in the 4K Mössbauer spectra of Upton. It can be concluded that all methods confirmed successfully prepared Fe-pillared montmorillonite.

Grazing-angle neutron diffraction for 3D structure of water distribution in fusogenic lipid membrane complex

Shuo Qian, Durgesh Rai

Grazing-angle neutron diffraction is a valuable technique to study large unit cell structure such as lipid membranes and their morphology under the influence of other molecules. The relatively large scale of the lipidic structure, in orders of several nanometers, necessitates a diffractometer covering small angular range for the application. The film-like sample geometry further requires the neutron beam to be grazing-incident at the sample surface. In the lack of dedicating neutron membrane diffractometer, we have developed two small-angle neutron scattering instruments, namely the Bio-SANS and the EQ-SANS, to perform this type of experiments.

With this technique, we obtained the first direct imaging of water distribution between lipid bilayers transiting from a lamellar structure to non-lamellar rhombohedral phase, which depicts the water layer change during the first step of membrane fusion process. The D2O used in hydrating the sample stands out of the structure with much higher neutron scattering length density. The results show the planar water was significantly reduced and was squeezed into pockets around the hemifusion stalk.

The configuration we have implemented expands the application of a regular small-angle neutron scattering instrument, and it can be adopted by other similar instruments. The experiment also demonstrated the recently developed the time-of-flight small-angle neutron beam line is suitable for Grazing-angle neutron diffraction that provides detailed structure of lipid membrane complex.

The SER-CAT Program: Meeting the Challenges of APS Upgrade

John P. Rose, John Chrzas and Bi-Cheng Wang
SER-CAT, University of Georgia and Advanced Photon Source

The undulator X-rays provided by the Advanced Photon Source (APS) and its extensive user base currently account for over 55% of all Protein Data Bank (PDB) publications coming from the United States (data taken from biosync.sbkb.org). Thus, the APS "dark period" scheduled for September 2022 will have a significant impact on the nation's structural biology community. This will also be the first time that a light source producing a majority of the nation's PDB entries has gone dark leaving hundreds of APS user groups looking for alternate beamlines to support their research needs. Finding beam time during the "dark period" will be challenging since few facilities in the US can provide undulator A intensity.

SER-CAT, Sector 22 is a member funded research resource for scientists in the southeastern and other regions of the US, including ~170 NIH funded research group. SER-CAT's virtual beamline 22ID ranks second in the world for PDB deposits with over 98% of all SER-CAT data currently being collected from the researcher's home institution.

In addition, the SER-CAT program provides user support, SER-symposium activities including annual SER-CAT Awards, staff research efforts, and assists in fundraising for the SER-CAT project. With respect to the APS-U, the highest priority will be in (1) securing beam time at other synchrotron facilities for its Member and Associate Users during the APS "dark period" and (2) working with John Chrzas for equipment purchases for upgrading 22ID-D, and building a new ID beamline (22ID-E).

The presentation will provide an overview of SER-CAT plans for member support during the APS-U "dark period" and the post APS-U operations.

An accompanying poster by John Chrzas will present SER-CAT facility upgrade plans.

Diffraction Quality Optimization and Data Collection at Ambient Temperatures under Humidity Controlled Conditions

Silvia Russi[a] & Aina Cohen[a], representing the entire SMB Team

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The Structural Molecular Biology (SMB) group of the Stanford Synchrotron Radiation Lightsource (SSRL) is developing a program for remote access crystallography data collection at near physiological temperatures and controlled humidity. The utility of controlled hydration to change the properties of protein crystals is well documented, beginning with the pioneering dehydrated hemoglobin and myoglobin studies of Perutz, Kendrew and Huxley (1940's-1950's). Crystal dehydration increases the protein/solvent ratio and may trigger changes in crystal packing, unit cell dimensions and space group, which can change the internal order of the crystal lattice (mosaicity, diffraction power) and crystal/cryo-solution dynamics. Integrating controlled hydration within the pipeline of room temperature data collection will enable optimization per protein crystal sample. This capability also opens the door to new investigations on protein dynamics. To this end, a novel plate has been developed for crystallization, sample transport and automated sample mounting for diffraction data collection at ambient temperatures. Future automation at SSRL-SMB and LCLS-MFX will support diffraction data collection and crystal screening at ambient temperatures or 100K using a rapid nozzle switcher.

Toward Elucidating the mechanism of lytic polysaccharide monooxygenases: Chemical insights from X-ray and neutron crystallography

Gabriela C. Schröder, W.B. O'Dell and Flora Meilleur

Lytic polysaccharide monooxygenases (LPMOs) are mononuclear copper oxidases that disrupt saccharide chains by oxidizing carbons involved in glycosidic bonds.[1] LPMOs are abundant in both bacteria and fungi and have been shown to be catalytically active on cellulose, chitin, hemicellulose, amylopectin and amylose.[2] LPMOs are responsible for the oxidative cleavage of crystalline cellulose, which makes them essential in biorefinery processes. Chain disruption of crystalline cellulose by LPMO increases the accessibility of the substrate to hydrolytic enzymes and cellulose-active LPMOs are already in use industrially. Fungal lytic polysaccharide monooxygenases (LPMOs) have been intensely studied since their first characterization in 2010 as a unique class of copper enzymes capable of oxidizing carbohydrates. The LPMO active site consists of a single copper ion coordinated in a conserved 'histidine-brace' motif. The amino and N_δ nitrogens of the N-terminal histidine along with N_ε of His84 provide three equatorial ligands in T-shaped coordination. Tyr168 provides one axial ligand to the copper ion. LPMOs require the input of two electrons and of one oxygen molecule (O_2 or H_2O_2) to achieve hydroxylation of one carbon in the glycosidic bond. To further understand the mechanism by which LPMOs oxidize the glycosidic bond, we combine high resolution X-ray and neutron protein crystallography to deliver precise, all atom structures of key reaction intermediates that can reveal i) the positions and interactions of all hydrogen atoms in the enzyme, ii) atomistic details of the active site without perturbing the metal oxidation state, and iii) the chemical nature of the activated dioxygen species coordinated to the active site copper. Previous work in our group has shown provided insight into the binding of oxygen at the LPMO active site as well as the role of His 157 protonation in catalysis. Oxygen pre-binds in an active site pocket containing His157 and it has been computationally shown that low pH conditions where His157 is doubly protonated, make oxygen binding energetically favorable. We have sought to gain further insight into the catalytic mechanism of LPMO using X-ray and neutron crystallographic structures. We have heterologously expressed *Nc*PMO-2 and grown crystals sufficiently large for neutron protein diffraction. To investigate the effect of His 157 protonation on oxygen binding and catalysis, crystals were soaked in low pH conditions and a complete neutron dataset at 2.1 Å was collected on MaNDi at the Spallation Neutron Source (SNS) at Oak Ridge National Laboratory. Additionally, to complement previous X-ray data collected on the reduced active form of LPMO at cryo-conditions, we collected a 2.5 Å cryo-neutron dataset at MaNDi at SNS on an ascorbate reduced LPMO crystal to determine the nature of the activated oxygen species at the LPMO active site.

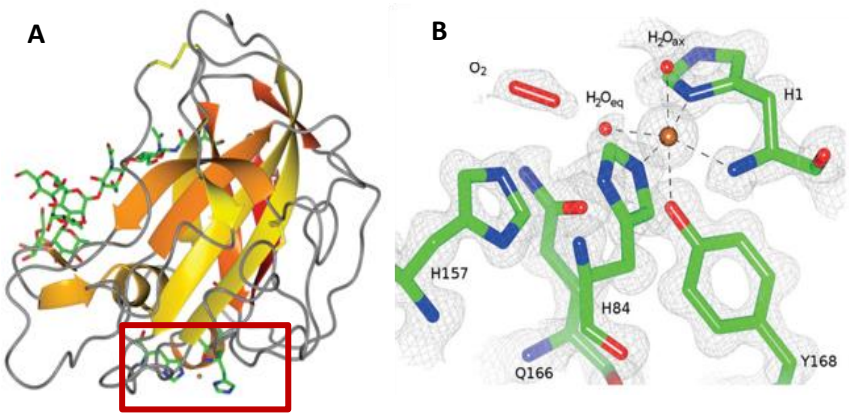

Figure 3 (A) The structure of LPMO showing the location of the active site. (B) LPMO active site illustrating the classic "histidine brace" coordinating the active site copper. *Figure from O'Dell et al.*[1]

1. O'Dell W.B., Agarwal P.K. & Meilleur F. (2017) Oxygen Activation at the Active Site of a Fungal Lytic Polysaccharide Monooxygenase. *Angew. Chemie - Int. Ed.* **56**, 767–770
2. Frandsen K.E.H., Simmons T.J., Dupree P., *et al.* (2016) The molecular basis of polysaccharide cleavage by lytic polysaccharide monooxygenases. *Nat. Chem. Biol.* **12**, 298–303

Why won't Uracil Form Large Single Crystals? Analysis of the Crystalline Structure of Uracil

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Large X-ray quality crystals have been formed of all the ribonucleic acids except uracil (a cyclic ribonucleic acid, C4H4N2O2). To date, it has proven to be very problematic to form large single crystals of uracil with only low quality crystals being formed near the sublimation temperature (338 oC) [1]. This study will attempt to determine why this is so.

Previous analysis determined that uracil crystallizes in space group P21/a with unit cell parameters: a = 11.938(1) Å, b =12.376(9) Å, c = 3.6552(3) Å, and β = 120.90(4)0. After careful analysis, Stewart et. al. concluded that there were two possible hydrogen bonding patterns that were conceptually feasible. The difference between the two structures lies in the rotation about the C2-C5 axis, swapping a carbon atom, for a nitrogen atom. The first structure contained an oxygen atom with two N-H•••O hydrogen bonds while the other oxygen atom possessed none. The second structure contained one N-H•••O hydrogen bond to each oxygen atom. Stewart determined that his laboratory single crystal data supported the former pattern with no detectable contribution of the second hydrogen bonding pattern (besides some streaking in X-ray photographs).

TOF neutron diffraction data were collected at the Spallation Neutron Source, Oak Ridge National Laboratory to further investigate the possibility of the presence of the alternative hydrogen bonding pattern in crystals of uracil. Neutron scattering length difference between carbon and nitrogen should be sufficient to detect the presence of the alternative hydrogen bonding pattern, if present. If this alternative hydrogen bonding pattern is indeed detected, this could provide an explanation as to why large crystals of uracil are difficult to grow. The neutron diffraction data will be modeled using The GSAS-II program package. Upon refinement (convergence with R(F2) = 5.604 % with wR = 2.75 %) 8.06 % of the alternative H-bonding pattern was discovered. This new model will be described in terms of the stacking layer model encoded into GSAS II. X-ray diffraction data will be simulated based upon this stacking model which will be compared to experimental X-ray data. [1] Stewart, R.F. & Jensen, L.H. (1967). Acta Cryst., 23, 1102

Accessing ligand-induced dynamics in maltose binding proteins using diffraction, scattering and computational methods

Shantanu Shukla, Laura Stingaciu, Jose Borreguero Calvo, Christopher Stanley, Pratul Agarwal, Matthew Cuneo, Dean Myles

ATP-dependent transport is energetically expensive, and its evolutionary cost likely shapes the specificity and affinity profiles of ABC transporter systems, especially of their periplasmic binding proteins (PBPs). PBPs have a conserved αβ-fold in which two hinged globular domains provide a binding pocket that undergoes large ligand induced conformational changes. To characterize differential ligand binding in structurally related isoforms, we determined the atomistic structures of three maltose binding protein (MBP) isoforms from *Thermotoga maritima* (tmMBP1, tmMBP2 and tmMBP3) using X-ray crystallography. We then used small-angle X-ray scattering to quantify the conformational ensembles sampled by the three isoforms in solution, both in the presence and absence of their cognate ligands. The scattering data was fitted against the trajectories generated by computational molecular dynamics (MD) simulations. These studies show that the three MBP isoforms exhibit a strong size-selective preference for substrates, with tmMBP1 and tmMBP2 binding tri- and tetra-saccharides and tmMBP3 binding only the disaccharide. In addition, the MD simulations revealed motions in surface loops remote from the binding pocket that were suppressed upon substrate binding, suggesting possible correlated motions and/or conformational substates that may help regulate substrate binding. We have used neutron spin echo spectroscopy and small angle neutron scattering to examine the total internal dynamics of these proteins, independent of either diffusion or tumbling motions in solution. We will present our results and discuss how this may help decipher possible allosteric control of the ABC transporters by the associated PBPs.

Reconstruction of lipid nanodisc structure using small-angle scattering profiles

Jacob Sumner, Benjamin Smith, Swati Pant, Hugh O'Neill, Shuo Qian, Qiu Zhang

Lipid nanodiscs effectively mimic a small section of phospholipid bilayer membrane while being water soluble due to encircling amphipathic membrane scaffolding proteins (MSP). MSPs provide structure to the nanodisc by surrounding the alkyl groups of the phospholipids. Membrane proteins can then be reconstituted into the lipid nanodisc, which results in soluble membrane proteins in a near-native membrane environment without using detergents.

The goal of this study is to reconstruct the 3D structure of lipid nanodisc structural components, such as the lipid bilayer and MSPs. Identifying the sub-component structure of lipid nanodiscs is possible through contrast matching the neutron scattering length densities of the sub-components. Data is collected using small-angle x-ray scattering (SAXS) and small-angle neutron scattering (SANS) in varying D_2O concentrations for neutron contrast variation series. With proper contrast matching, the entire structure of the lipid nanodisc as well as its individual components of can be identified, which allows one to discern the structure of an integrated membrane protein separately from the surrounding nanodisc.

The scattering data were used to reconstruct the 3D morphology of the lipid nanodisc with the DENSS electron density profile and the DAMMIF bead model. The SANS and SAXS data generated provide accurate structural information for the lipids and MSPs, respectively, using DENSS.

We hope to expand upon these results and conduct future experiments with membrane proteins integrated in lipid nanodiscs with the approach reported here.

Superconductivity and short-range magnetic order in quasi-one-dimensional materials

K.M. Taddei, L.D. Sanjeewa, B.H. Lei, Y. Fu, Q. Zheng, D.J. Singh, A.S. Sefat, C. dela Cruz

Even in the absence of a microscopic theory, a generalized recipe has emerged for unconventional superconductivity. In the common scenario, some ordered phase in a strongly-ish correlated material is suppressed giving rise to quantum fluctuations which can act as a possible pairing mechanism. The nature of these fluctuations – whether they are of the ordered phase, resultant of a quantum critical point or some more exotic pair density wave – is still hotly debated. Therefore, it is useful to find new unconventional superconductors which can provide further insight into the most relevant components of this recipe. The recently discovered family of $A_xTM_3As_3$ (A = Alkali, x = 1,2 and TM = Cr, Mo) superconductors provides such an opportunity in a system with a novel quasi-one-dimensional structure. Here we present results of joint ab initio and neutron scattering studies which reveal spin-fluctuations, a frustrated structural instability and a potential path to tuning the Fermi level in in KCr_3As_3 and related materials. These results suggest a path to uncover a rich phase diagram for this system analogous to the traditional unconventional superconductors.

Active-Site Protonation States in an Acyl-Enzyme Intermediate of a Class A β-Lactamase with a Monobactam Substrate

Venu Gopal Vandavasi[1], Patricia Langan[1], Kevin L. Weiss[1], Jerry M. Parks[2], Jonathan B. Cooper[3], Stephan L. Ginell[4], and Leighton Coates[1]

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Expression of a variety of β-lactamases to combat antibiotics is a major defensive mechanism in pathogenic bacteria. β-lactamases specifically hydrolyze the β-lactam ring of the β-lactam-antibiotics via a general base hydrolysis mechanism and make them ineffective before they could inhibit penicillin binding proteins and halt cell wall synthesis. The precise mechanism of hydrolysis of different antibiotics depends both on the antibiotic and the β-lactamases in the context. Several key residues from β-lactamase have been shown to be involved in the process. In contrast to most of the β-lactam antibiotics where at least two rings are present, in monobactams the β-lactam ring is not fused to another ring. Aztreonam is a monobactam that has a large R group attached its the β-lactam ring and is used to treat severe infections caused by *Pseudomonas aeruginosa* in patients with chronic cystic fibrosis.. The protonation states of key active site residues have been determined previously for the apo form of a CTX-M β-lactamase. However, they have not yet been determined for a monobactam acyl-enzyme intermediate. Here we present data on direct visualization of protonation states in an acyl-enzyme intermediate of a class A β-Lactamase with a Aztreonam using neutron and high resolution X-ray crystallography. Our data provides new insights on the hydrogen bonding pattern in the active site and subtle mechanistic aspects of hydrolysis of monobactam antibiotics.

Chemical short-range order in oxynitride perovskites

Xin Wang, Ram Seshadri, Patrick Woodward, and Katharine Page

Anion ordering of transition metal oxynitrides is emergingly playing a crucial role for controlling and tuning physical and chemical properties, for example, combining the merits of oxides and nitrides. Total scattering is a powerful way to determine O/N local or long-range order, since it covers both Bragg peaks and diffuse scattering signal. For analyzing total scattering data, there are mainly two approaches, i.e. unit-cell based Rietveld-like refinement (e.g. with PDFgui) and supercell-based Reverse Monte Carlo (RMC) approach. Here, in this project, we will combine such unit-cell and supercell- based approaches to investigate the multiple-anion order in $MTaO_2N$ (M=Ca, Sr, Ba) oxynitride perovskites. The objective of this project is to understand the fundamental link between anion ordering and physical properties (e.g. nature and extent of chemical short-range order and its impact on electronic properties). This will benefit the control over those properties for practical application.

The Bio-Deuteration Laboratory at Oak Ridge National Laboratory

Kevin L. Weiss[1], Viswanathan Gurumoorthy[1], Sarah L. Lucas[1], Gwyndalyn Phillips[1], Swati Pant[1], Shuo Qian[1], Qiu Zhang[2], and Hugh O'Neill[1]

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Neutron scattering is a powerful, non-destructive method for obtaining unique information about the structure and dynamics of complex biological systems. The power of this method originates primarily from a sensitivity for hydrogen, which is one of the most abundant elements found in biology. Furthermore, the large neutron scattering length difference between hydrogen and deuterium can be exploited to selectively highlight different components of systems to obtain unique information regarding structure and dynamics. This makes the production of deuterium-labeled materials crucial for maximizing the utility of neutron scattering experiments for the biological sciences. To satisfy this critical need, the Center for Structural Molecular Biology operates the Bio-Deuteration Laboratory (BDL) as a centralized resource and training ground for the preparation of deuterium-labeled biomaterials in support of ORNL's neutron scattering facilities. Technical capabilities and recent developments of the BDL will be presented.

Reverse Monte Carlo modeling for low-dimensional systems

Yuanpeng Zhang, Marshall McDonnell, Wei Liu, Matthew Tucker

Reverse Monte Carlo (RMC) is one of the commonly used approaches for modeling total scattering data. However, to extend the capability of the RMC method for refining the structure of nanomaterials, the dimensionality and finite size need to be considered when calculating the pair distribution function (PDF). To achieve this, the simulation box must be set up to remove the periodic boundary condition in one, two or three of the dimensions. This then requires a correction to be applied for the difference in number density between the real system and the simulation box. In certain circumstances an analytical correction for the uncorrelated pairings of atoms is also applied. The validity and applicability of our methodology is demonstrated by applying the algorithms to simulate the PDF patterns of carbon systems with various dimensions, and also by using them to fit experimental data of CuO nanoparticles. This alternative approach for characterizing the local structure of nano-systems with the total scattering technique will be made available via the RMCProfile package. The theoretical formulation and detailed explanation of the analytical corrections for low-dimensional systems – 2D nanosheets, 1D nanowires and 0D nanoparticles – is also given.

Extending the Concept of Visible-Light Color Photography to Synchrotron Crystallography: Adding Spectroscopic Information to Structural Coordinates by X-ray Diffraction

Dayong Zhou, Lirong Chen, Palani Kandavelu, Unmesh Chinte, Zheng-Qing Fu, Zhongmin Jin, James Fait, Gerold Rosenbaum, Dennis Mills*, John Chrzas, John Rose and Bi-Cheng Wang

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Diffraction from the soft X-ray region (wavelengths > 1.5Å) has played an important role in recent success for macromolecular structure determinations by Native-SAD phasing (reviewed by Rose, Wang & Weiss, 2015; Rose & Wang, 2016). Other unique applications of soft X-rays for structural biology research, which may not be well recognized, are also becoming possible due to recent advances in both experimental design and data collection technology.

In this presentation, we are focusing on the use of wavelength-dependent data for polychromatic X-ray analyses. In layman's terms, the concept is equivalent to that of using color photography (recording the components of light according to wavelength) to aid in the positive identification & differentiation of visible objects. Polychromatic X-ray analysis can improve the accuracy in the identification & differentiation of atoms in both macromolecules and small molecules by combining atomic spectral information with structural coordinates, similar to the power of color photography for visible objects.

Examples will be given for the exploration of biophysical/biochemical aspects of metals/ions in protein crystals, including the positive identification of atoms (e.g. Fe vs. Zn) and the valence states (and redox-states) of individual atoms in a molecule containing more than one atom of the same metal. The theoretical basis and test results will be presented.