Advanced Photon Source

79th Pittsburgh Diffraction Conference

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October 2-4, 2022, 79th Pittsburgh Diffraction Conference hosted at the Advanced Photon Source (APS) at Argonne National Laboratory (ANL)

Booklet
Agenda and Abstracts

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Agenda for Pittsburgh Diffraction Conference hosted at the Advanced Photon Source (APS)

Time	E1100/E1200 Bldg 402	Lower Gallery Bldg 402
Sun, Oct 2, 1 pm	Registration	
Sun, Oct 2, 2 pm	Opening / welcome	
Sun, Oct 2, 2:30 pm	**"Welcome to APS" Laurent Chapon, Director of APS Lower Gallery, Bldg 402**	
Sun, Oct 2, 3:30 pm	**Break**	
Sun, Oct 2, 4 pm	**Session 1A Upgrade plans for biology / MX beamlines Chair: Zhongmin Jin**	**Session 1B Upgrade plans for diffraction beamlines for chemistry and material science" Chair: Angus Wilkinson**
Sun, Oct 2, 4:00 pm	Dean Haeffner (ANL)	Peter Kenesei (ANL)
Sun, Oct 2, 4:25 pm	Robert Fischetti (ANL)	Uta Ruett (ANL)
Sun, Oct 2, 4:50 pm	Karolina Michalska (ANL)	Jason Benedict (Buffalo)
Sun, Oct 2, 5:15 pm	Thomas Irving (IIT)	Zulu Maddury Somayazulu (ANL)
Sun, Oct 2, 5:40 pm	**Poster Session / Vendors / Reception**	
Sun, Oct 2, 7 pm	End of 1st Day	

Mon, Oct 3, 8:30 am	**Session 2 A "CryoEM microcrystal electron diffraction: a new tool for the structural biologist"** **Chair: Brent Nannenga**	**Session 2B,** **"New opportunities: coherent x-ray beam"** **Chair: Stephan Hruszkewycz**
Mon, Oct 3, 8:30 am	Tamir Gonen (UCLA)	Yanwen Sun (SLAC)
Mon, Oct 3, 8:55 am	Emma Danelius (UCLA)	Ross Harder (ANL)
Mon, Oct 3, 9:20 am	Brent Nannenga (ASU)	Dina Sheyfer (ANL)
Mon, Oct 3, 9:45 am		Stephan Hruszkewycz (ANL)
Mon, Oct 3, 10:10 am	**Collaboration break / Vendors**	
Mon, Oct 3, 10:30 am	**Session 3A** **"AI and crystallography"** **Chair: James Holton**	**Session 3B** **"Automation & autonomous experiments"** **Chair: Kevin Stone**
Mon, Oct 3, 10:30 am	Sabine Hollatz (SLAC)	Daniel Olds (BNL)
Mon, Oct 3, 10:55 am	Stephanie Wankowicz (UCSF)	Suchismita Sarker (CHESS)
Mon, Oct 3, 11:20 am	Zheng-Qing Fu (UGA/SER-CAT)	Chris Tassone (SLAC)
Mon, Oct 3, 11:45 pm	Scott Classen (LBL)	Joe Strzalka (ANL)
Mon, Oct 3, 12:10 pm	**Lunch / APS tour / Vendors / Poster**	
	Chair: Wenqian Xu, E1100/1200	Chair: Tiffany Kinnibrugh. Lower Gallery
Mon, Oct 3, 12:15 pm	Joe Ferrara (Rigaku)	Alex Prendergast (Formulatrix)
Mon, Oct 3, 12:35 pm		Joern Lange (X-spectrum)
Mon, Oct 3, 12:55 pm	Joyce Frank "MiTeGen Tools for CryoEM"	Pascal Hofer (DECTRIS)
Mon, Oct 3, 1:30 pm	**Session 4 A** **"MX and Room Temperature Crystallography Studies"** **Chair: Aina Cohen&Leighton Coates**	**Session 4B** **"PDF in bulk and thin films"** **Chair: Olaf Borkiewicz**
Mon, Oct 3, 1:30 pm	Simone Brixius-Anderko (Pitt)	Karena Chapman (SBU)
Mon, Oct 3, 1:55 pm	Marcus Fischer (StJude)	Yaohua Liu (ORNL)
Mon, Oct 3, 2:20 pm	Silvia Russi (SLAC)	Ann-Christin Dippel (DESY)
Mon, Oct 3, 2:45 pm	Crissy Tarver (Stanford)	Marc Michel (VT)
Mon, Oct 3, 3:10 pm	**Collaboration break / Vendors**	
Mon, Oct 3, 3:30 pm	**Session 5 A** **Time-Resolved Structural Biology at the XFEL and Synchrotron** **Chair: Aina Cohen and Crissy Tarver**	**Session 5B** **"Synergies TEM, X-rays, Neutrons"** **Chair: Cora Lind-Kovacs**
Mon, Oct 3, 3:30 pm	Kevin Dalton (Harvard)	Efrain Rodriguez (UMD)
Mon, Oct 3, 3:55 pm	Mark Wilson (UNL)	Nestor Zaluzec (ANL)
Mon, Oct 3, 4:20 pm	Guillermo Calero (Pitt)	Keith Taddei (ORNL)
Mon, Oct 3, 4:45 pm	Joyce Frank (MiTeGen)	Ashfia Huq (SNL)
Mon, Oct 3, 5:10 pm	**Poster / Vendor**	
Mon, Oct 3, 6:30 pm	**Banquet and Sidhu Award Presentation** **Michael Martynowycz** **TCS building** Determining membrane protein structures using microcrystal electron diffraction	
Mon, Oct 3, 8:30 pm	End of 2nd Day	

Tue, Oct 4, 8:30 am	**Session 6 A** **"The role of the APS in understanding Covid structure-function"** **Chair: Bob Fischetti**	**Session 6B** **"In situ and operando structural science for clean energy"** **Chair: Andrey Yakovenko**
Tue, Oct 4, 8:30 am	Andrzej Joachimiak (ANL)	Julia Oktawiec (NU)
Tue, Oct 4, 8:55 am	Meng Yuan (TRSI)	Stephan Rosenkranz (ANL)
Tue, Oct 4, 9:20 am	Karen Anderson (Yale)	Tom Runcevski (SMU)
Tue, Oct 4, 9:45 am	Roy Mariuzza (UMD)	Tim Fister (ANL)
Tue, Oct 4, 10:10 am	**Collaboration break / Vendors**	
Tue, Oct 4, 10:30 am	**Awards and Business Meeting** **Poster awards** **Next conference** **Lower Gallery**	
Tue, Oct 4, 11:30 am	**Lunch / ALCF Tour/ Vendor/ Poster**	
	Chair: Andrey Yakovenko / Tyra Douglas E1100/E1200	
Tue, Oct 4, 11:45 am		
Tue, Oct 4, 12:05 pm		
Tue, Oct 4, 12:25 am		Leticia Rosa (PiTec)
Tue, Oct 4, 1:30 pm	**Outlook into the Future** James Holton (LBNL) "The Last Angstrom: a Second Golden Age for Structural Biology" Rajeev Assary (ANL) "AI- Assisted Materials Discovery" **Lower Gallery**	
Tue, Oct 4, 3:00 pm	**End of Conference**	

School on XPD and PDF Analysis on Wednesday, October 5

8:30 – 9:30 am	Introductory Talks	
9:30 – 12:00 pm	Hands on Training XPD	Hands on Training PDF
12:00 pm – 1:00 pm	Lunch Break	
1:00 pm – 3:00 pm	Hands on Training XRD	Hands on Training PDF

Session	Speaker	Title
1A	Dean Haeffner (ANL)	“Overview of the APS-U Upgrade from a Beamline Perspective“
1A	Robert Fischetti (ANL)	“Structural Biology with the APS-U”
1A	Karolina Michalska (ANL)	“eBERlight – a virtual facility for biological and environmental science”
1A	Thomas Irving (IIT)	“Current Capabilities and Planned Upgrades to the BioCAT Beamline 18ID”
1B	Peter Kenesei (ANL)	“Engineering Materials Science”
1B	Uta Ruett (ANL)	“Capabilities of the “Structural Science (SRS)” beamlines after the upgrade of the APS”
1B	Jason Benedict (Buffalo)	“Advanced Crystallography at NSF’s ChemMatCARS”
1B	Maddury Somayazulu (ANL)	“HPCAT upgrade plans“
2A	Tamir Gonen (UCLA)	“Quo Vadis MicroED “
2A	Emma Danelius (UCLA)	“Structural investigation of protoglobins using MicroED “
2A	Brent Nannenga (ASU)	“Small molecule structure determination and analysis by MicroED”
2B	Yanwen Sun (SLAC)	“Ultrafast x-ray photon correlation spectroscopy at the Linac Coherent Light Source”
2B	Dina Sheyfer (ANL)	“Coherent X-ray methods and recent advantages in 3D Laue microscopy”
2B	Ross Harder (ANL)	“Bragg Coherent Diffraction Imaging at the Advanced Photon Source”
2B	Stephan Hruszkewycz (ANL)	“New opportunities for materials science with coherent x-rays”
3A	Sabine Hollatz (SLAC)	“Machine Learning for Scoring Diffraction Patterns”
3A	Stephanie Wankowicz (UCSF)	“Leveraging machine learning to detect heterogeneous features from diffraction data“
3A	Zheng-Qing Fu (UGA/SER-CAT)	“How Alphafold2 can help in structure and function research?”
3A	Scott Classen (LBL)	“MX Sample Centering with Google Cloud Platform AutoML”
3B	Daniel Olds (BNL)	“Teaching Robots Beamline Science–How Automation and AI is Accelerating Research at Light Sources”
3B	Suchismita Sarker (CHESS)	“ML-guided high-throughput experimentation for material design and discovery”
3B	Chris Tassone (SLAC)	“SMASH-ML: Solving Materials and Structures through Simple Heuristics and Machine Learning”
3B	Joe Strzalka (ANL)	“Automating Sample Handling for Grazing-Incidence X-ray Scattering Experiments”
4A	Simone Brixius-Anderko (Pitt)	“Targeting aldosterone biosynthesis for the treatment of resistant hypertension”
4A	Marcus Fischer (StJude)	“Impact of temperature on ligand binding and discovery”
4A	Silvia Russi (SLAC)	“New Remote Access Program for Elevated-Temperature and Humidity-Controlled Experiments at SSRL”

4A	Crissy Tarver (Stanford)	“Crystal Structures of Angiopoietin-like 4’s Carboxy-Terminal Domain (cANGPTL4) Reveal A Fatty Acid Binding Pocket”
4B	Karena Chapman (SBU)	
4B	Yaohua Liu (ORNL)	“PIONEER: single-crystal neutron diffractometer for small samples at the Second Target Station”
4B	Ann-Christin Dippel (DESY)	“PDF of thin film systems: new insights from advanced x-ray total scattering techniques”
4B	Marc Michel (VT)	“New Approaches for Unraveling Crystallization Pathways in Geochemical Systems”
5A	Kevin Dalton (Harvard)	“Variational inference to estimate structure factors from inconventional diffraction exeriments”
5A	Mark Wilson (UNL)	“Serial Crystallographic Approaches to Understanding Enzyme Mechanism”
5A	Guillermo Calero (Pitt)	“Towards Molecular Movies of Enzyme Catalysis”
5A	Joyce Frank (MiTeGen)	“Improved sample preparation and mounting for fixed target serial synchrotron crystallography”
5B	Efrain Rodriguez (UMD)	“Solid state reactions on the beamline, what we gain by peering into the 'black box'”
5B	Nestor Zaluzec (ANL)	“Computationally Mediated Diffraction and Imaging in the Argonne PicoProbe Electron Optical Beam Line”
5B	Keith Taddei (ORNL)	“Hydrogenas superconductivity’s ‘hidden variable’in a quasi-1-D candidate spin tripletsuperconductor”
5B	Ashfia Huq (SNL)	“X-ray and Neutron Diffraction: Which One, When and Why?”
6A	Andrzej Joachimiak (ANL)	“Structural studies of SARS-CoV-2 proteins and their complexes”
6A	Meng Juan (TRSI)	“A comprehensive epitope map of the SARS-CoV-2 spike protein“
6A	Karen Anderson (Yale)	“Structure-based and Comp. Design of Novel SARS-CoV-2 Protease Inhibitors as Promising Preclinical Candidates”
6A	Roy Mariuzza (UMD)	“Structural Basis for T Cell Recognition of SARS-CoV-2”
6B	Julia Oktawiec (NU)	“Cooperative Gas Binding and Structural Transformations in Redox-Active Metal–Organic Frameworks”
6B	Stephan Rosenkranz (ANL)	“Structural, Magnetic, and nematic correlations in iron based superconductors”
6B	Tom Runcevski (SMU)	“In situ Crystallization of Model Minerals on Titan, Saturn's Moon”
6B	Tim Fister (ANL)	“Multiscale characterization of lead acid batteries using x-ray diffraction”

Structure-based and Computational Design of Novel SARS-CoV-2 Protease Inhibitors as Promising Preclinical Candidates

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While major advances have been made in vaccinations and treatment of COVID-19, SARS-CoV-2 remains a significant problem, particularly in vulnerable patient populations with weakened immune systems. The development of novel antiviral drugs for treatment has been of critical importance. Previous drug development efforts focused on the SARS-CoV-2 main protease have resulted in the approval of a combination therapy, Paxlovid. While the antiviral component, nirmatrelvir, is a highly potent protease inhibitor, it is also metabolized rapidly and requires the addition of a metabolic inhibitor. This can cause major issues with drug-drug interactions, particularly in immunocompromised patients, and so it is critical to continue antiviral development efforts and produce safe alternatives. A collaborative effort using structure-guided drug design and computational chemistry targeting the essential SARS-CoV-2 main protease have identified several novel classes of inhibitors. Lead optimization using computational chemistry, biochemistry, and structural biology coupled with cellular studies of potential inhibitors identified a lead compound, Mpro61, as a potent inhibitor with no significant off-target effects. Initial pharmacokinetic studies suggested a more favorable profile for Mpro61 than nirmatrelvir, making it an ideal candidate for further study. Preliminary in vivo efficacy studies in mouse models of COVID infection have shown encouraging results, and more comprehensive studies currently underway. This presentation will cover this multidisciplinary and collaborative research effort, spanning the drug development process from compound design to animal testing.

AI-driven Materials Discovery

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key words: *Molecules and Materials for Energy Storage, Optimal Properties, Active Learning, Deep Learning for Properties Prediction, Machine Learning for Diffusion, Deep Learning for Catalysis, Towards Autonomous Experiments for Optimization and Synthesis*

1 Abstract

New and improved materials are essential for decarbonization. Innovative energy solutions and selected chemical transformation can enable decarbonization. In energy storage, optimal electrolytes, electrodes, membranes with low-carbon footprints are critical. In chemical conversion, improved catalysts and optimized processes are needed. Challenging and important part of this is society demands these progresses in an **economically viable** and and **accelerated fashion**. Accurate and predictive simulations coupled with Artificial Intelligence (AI) methods is capable of leading this challenge of *Materials Discovery* [1]. These simulations can predict properties with high fidelity. These predictions can be used to screen materials that satisfy multiple properties via optimization [2]. In this presentation, I will describe some of our recent efforts [2, 3, 4, 5, 6, 7] in active learning coupled with large scale first principles simulations to down select/optimize desired *molecules* for non-aqueous redox flow battery molecules. Additionally, I will present some of the recent efforts to compute accurate properties of molecules with the use of data-driven and deep learning approaches. In terms of *materials*, I will describe application of machine learned force fields enable us to simulate the hoping processes in *nano* second resolutions at relatively high temperature to estimate the activation barriers of ionic carrier diffusion relevant to multivalent ion storage for next generation Mg-based battery and how this enable the discovery of new layered materials for anode protection [6]. Relevant to chemical transformation and catalytic materials discovery, I will present our recent research of using graph neural networks based on data-driven materials for identifying most active catalysts towards selected chemical processes [8]. With these accurate property predictions using intelligent techniques, we are in the age of achieving autonomous materials discovery for variety of research areas and I will introduce a future looking pathway for autonomous electrochemistry.

References

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Targeting aldosterone biosynthesis for the treatment of resistant hypertension

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Primary aldosteronism is the most common form of resistant hypertension which is associated with a high mortality due to an increased risk for cardiac disease. It develops from an overproduction of the steroid hormone aldosterone by the cytochrome P450 enzyme 11B2 (CYP11B2, aldosterone synthase). CYP11B2 is 93% identical to cortisol producing CYP11B1 which impedes the design of drugs specifically targeting CYP11B2. LCI699 (Isturisa©) was initially developed as hypertension drug inhibiting CYP11B2, but due to poor selectivity then became the first FDA approved drug for CYP11B1-mediated Cushing's disease. Thus, targeting CYP11B2 is an attractive, yet unrealized option for treating primary aldosteronism.

To promote directed targeting of CYP11B2 we pursued two strategies using functional and structural techniques. First, we aimed to elucidate key features of the CYP11B2 interaction with the drug LCI699 to enhance the design of more selective compounds for primary aldosteronism. Using recombinant human CYP11B2, we determined the inhibitory potency of LCI699 on CYP11B2 catalysis to be 36 nM. To examine the structural basis for the high inhibitory potency, we solved the X-ray crystal structure of the CYP11B2/LCI699 complex and identified a tight coordination of LCI699 to the heme iron. Compared to the CYP11B1 structure, we could identify crucial differences in the active site architecture between both proteins. Second, we investigated the structural basis of CYP11B2 interaction with the small iron-sulfur cluster protein adrenodoxin. Adrenodoxin transfers electrons for CYP11B2 catalysis and is mandatory for aldosterone biosynthesis. Surprisingly, we observed that adrenodoxin binding increases the inhibitory potency of LCI699 more than 4-fold. Furthermore, we could solve a structure of an adrenodoxin/CYP11B2 complex using X-ray protein crystallography and identify key residues which are involved in the interaction.

Obtained structural and functional information can be used to enhance the design of more selective drugs targeting CYP11B2 for the treatment of primary aldosteronism. Moreover, targeting the interaction between adrenodoxin and CYP11B2 could be used as future orthogonal treatment option for primary aldosteronism.

Towards Molecular Movies of Enzyme Catalysis

Guowu Lin[1], Sandra Vergara[1], Paola Zinser[1], Brisa Chagas[1], Xiaohong Zhu[1], Silvia Russi[3], Nicolas Sluis-Cremer[2], Aina Cohen[3] and Guillermo Calero[1]

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Amino acid residues in their binding pockets *undergo transient ultra-fast (pico- to milli-seconds) vibrational, rotational and translational motions to allow substrate binding* in active sites. These transient-state intermediates are critical for enzymatic activity, drug action and drug resistance. Moreover, contemporary structural biology approaches, such as X-ray crystallography and single particle cryo-electron microscopy (cryoEM) only have the ability to resolve the structures of thermodynamically stable species, and cannot inform of kinetic intermediates. One of the next challenges in structural biology is advancing from a static picture to the observation of enzymes in action. Time-resolved (TR) structural studies can uncover conformational changes occurring in the nano-to milli-second timescale (real time) revealing hidden transition-state intermediates and hence increasing the "druggable landscape" available for molecular modelling and inhibitor testing and development. *Albeit its significance, TR structural studies have been scarce as they present technical challenges.* Recently my laboratory has embarked in performing TR studies of RNA polymerase II and the small GTPases, NRAS and KRAS using X-ray crystallography; and HIV-1 reverse transcriptase (RT) using single particle cryoEM. We have designed novel techniques such as UV photolysis of caged substrates followed by data collection at 140 and 170 Kelvin, creating, for the first time, molecular movies of the mechanism of nucleotide addition by Pol II and RT, and GTP hydrolysis by NRAS and KRAS.

MX Sample Centering with Google Cloud Platform AutoML.

Scott Classen[1], Shawfeng Dong[2], Feng Chen Liu[2], Giles Mullen[3], and James Holton[1]

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Fully automated and unattended Macromolecular Crystallographic (MX) data collection relies on robust alignment of crystal samples within the X-ray beam. Loop centering is often performed through a manual click-to-center operation or traditional machine vision strategies based on edge detection and other procedural techniques. Artificial Intelligence, Machine Learning, and Convolutional Neural Networks have also been used to achieve sample recognition steps, but often involve tools that are not readily accessible for non-experts. In this talk I will outline our recent use of the AutoML Vision tool available from Google Cloud Platform (GCP). AutoML Vision is one of a number of AI/ML tools offered by GCP via an intuitive web-based user interface designed for non-experts to take advantage of the immense potential of AI/ML tools. With AutoML you can train custom models for object classification and detection. The trained models can be downloaded and deployed on local GPU hardware. This presentation details of the development and deployment of our AutoML-based loopDHS sample centering software at beamline 8.3.1 at the Advanced Light Source.

VARIATIONAL INFERENCE TO ESTIMATE STRUCTURE FACTORS FROM UNCONVENTIONAL DIFFRACTION EXPERIMENTS

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ABSTRACT

In order to obtain electron density, integrated reflection intensities must be averaged and converted to structure factors. Intensities cannot be merged directly because they are contaminated with systematic errors. These errors originate from a variety of sources including the volume of crystal in the X-ray beam, the mosaic properties of the crystal, and fluctuations in beam intensity. In the conventional setting, it is straightforward to correct these errors through an algorithm known as scaling. In the case of serial and time-resolved experiments, scaling is complicated by the experimental design. Unlike conventional rotation-method crystallography, reflections originating from short X-ray pulses are partial; they do not reflect the full intensity of the corresponding Bragg peak. Partiality may either be corrected using a model of the Bragg peaks' shape or by averaging over a large number of images. I will present a third alternative which is agnostic to the lineshape of Bragg peaks and works with a small number of images. This method uses a statistical technique known as variational inference combined with deep learning to jointly learn structure factors along with a scaling model. In this way, the model chooses the optimal corrections for a particular experiment. Though it is applicable to conventional data as well, I anticipate this technique will be most valuable for time-resolved and serial experiments with both mono and polychromatic X-rays.

Structural investigation of protoglobins using MicroED

Emma Danelius

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The electron cryo-microscopy (cryo-EM) method Microcrystal Electron Diffraction (MicroED) allows the collection of high-resolution structural data from vanishingly small crystals, typically with a thickness in the nanometer range. Since its initial demonstration in 2013, data collection and analysis schemes have been fine-tuned, and MicroED has been successfully used to determine over 100 molecular structures.

By circumventing the crystal size limitations, MicroED has the potential to enable structural studies of new and important targets. Several novel structures of small molecules, natural products and peptides have been determined by MicroED using ab initio methods. However, there are so far only a couple of novel protein structures derived by MicroED. For protein crystallography, molecular replacement is the most commonly used method to solve new structures, using phase information of a homology model.

Taking advantage of recent technological advances including higher acceleration voltage and using a highly sensitive camera in counting mode, we have determined the first structure of a Aeropyrum pernix protoglobin (ApePgb), as well as ligand bound complexes. The variant ApePgb GLVRSQL is an engineered ApePgb that was obtained through directed evolution, selected for biocatalytic cyclopropanation, N–H insertion, and Si–H insertion reactions. The structure reveals a reorientation of an alpha helix into a dynamic loop, as well as a ruffled distortion of the heme group. Since this is the first structure of an ApePgb, no wild-type structure was available as search model. Instead, the structure was phased by molecular replacement using a predicted model. This shows that MicroED now enables investigation of structures that were previously beyond technological reach.

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Pair distribution functions of thin film systems: new insights from advanced x-ray total scattering techniques

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Pair distribution function (PDF) analysis has become a most powerful tool to study the local structure of materials that comprise some degree of disorder, in bulk systems and more and more in thin films. The particular difficulty to obtain high quality total scattering data and derive PDFs from thin films lies in the small amount of sample being spread out in two dimensions but confined to typically below 1 μm in the third dimension. In addition, this layer is deposited on a substrate that is usually thicker by a factor of at least 1000. Different approaches to obtain PDFs from thin films range from the dedicated (high-energy) surface diffraction technique at grazing incidence [1-3] to powder-diffraction type measurements in transmission geometry at normal incidence [4], through a cross-section or on an exfoliated layer [5]. Each of these methods is applicable and effective for varying kinds of layers with respect to e.g. their thickness, substrate and anisotropy effects. In addition, the technical boundary conditions for carrying out *in situ* and *operando* experiments largely depend on the measurement geometry. This presentation will showcase a variety of PDF studies on thin films with different structures from amorphous to highly-textured [6] across the methodology spectrum, including recent developments at beamline P07 at PETRA III enabling temperature-dependent grazing incidence x-ray total scattering experiments at variable high and low temperatures.

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Impact of temperature on ligand binding and discovery

Marcus Fischer, PhD

St. Jude Children's Research Hospital

Shifting crystallographic data collection temperature repopulates the protein conformational landscape and can reveal high-energy states that may be invisible at cryogenic temperature. While the effect of temperature on the protein conformational ensemble has been shown in several studies, the impact on ligand binding and ligand discovery is less understood. To address this question, we compared paired datasets collected both at cryogenic and room temperature. Our analysis focuses on how temperature differences impact ligand binding sites locally and globally, how these differences can misinform the validation of computational methods that use experimental data as a gold standard and how this can mislead the discovery of new chemical matter. Our results also indicate that water networks in ligand binding sites get reshuffled with temperature and we introduce a new algorithm, Flipper, to identify temperature-sensitive regions in electron density maps. Overall, the work suggests that high-temperature crystallographic data can provide useful alternative structural templates for ligand discovery.

Pittsburg Diffraction Conference 2022

Structural Biology with the APS-U

Robert F. Fischetti[1], Nagarajan Venugopalan[1], Vukica Srajer[2], Robert Henning[2], Lisa Keefe[3], Andrzej Joachimiak[4], Karolina Michalska[4], Spencer Anderson[5], Joseph Brunzelle[5], Bi-Cheng Wang[6], John P. Rose[6], John Chrzas[6], Malcolm Capel[7], Jordi Benach[8], Anton J. Frommelt[8]
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After 25 years in operation, the Advanced Photon Source (APS) is undergoing a massive upgrade (APS-U). The current electron storage ring will be replaced with state-of-the-art technology that will increase the brightness of the X-ray beams up to 500 times. Replacing the storage ring will require a year-long shutdown period, currently scheduled to begin in April 2023, during which the APS will not be accessible to users.

I will present an update on structural biology at the APS, the impact of the dark period on the user community, and information about accessing other light sources during the dark period. The APS-U will be a high-brightness, high-energy source, enabling game-changing structure determination capabilities. Looking forward, I will briefly summarize the new capabilities of each APS structural biology CATs.

Multiscale characterization of lead acid batteries using x-ray diffraction

Tim Fister,[1] Tiffany Kinnibrugh,[2] Mark Wolfman,[1,2]

1. Chemical Sciences and Engineering Division, Argonne National Laboratory
2. X-ray Science Division, Argonne National Laboratory

Lead acid batteries continue to be a significant portion of the secondary battery market, but the transition to vehicle electrification has shifted an emphasis from power density and dynamic charge acceptance to cycle and calendar life. Unlike most lithium-ion materials, lead acid batteries involve the growth and dissolution of crystals within the electrode active material during each cycle, which can be affected by changes in local acid concentration, electronic and ionic conductivity gradients, and pore-clogging. This can lead to chemical heterogeneity, both at the cell and particle level. Failure in lead acid batteries involve two interconnected processes: negative sulfation and positive active material softening and grid corrosion. The analysis of these processes has largely been driven by electrochemical analysis and postmortem tear-down studies of failed batteries. Here, we use high energy synchrotron diffraction to analyze these processes in operating batteries. Maps of the entire battery volume are compared to the overall electrochemical response and the escalation of cell-level gradients over repeated cycles. These data show lead sulfate crystal ripening on the negative that can lead to cell imbalance, especially during cycling at partial state of charge or at deep discharge. This imbalance also leads to excessive overcharging on the positive electrode, which drives the conversion of interfacial 'alkaline' species to rutile lead dioxide which has poor chemical and electronic connectivity to the underlying positive grid. Using these reactions as an example of dynamic, electrochemically driven crystal growth and dissolution, we discuss routes for characterizing these processes using novel x-ray scattering approaches to analyze particle size distribution and speciation of electrolyte phases. We will also outline future work that could take advantage of the smaller beams and coherence after completion of the APS upgrade.

Improved sample preparation and mounting for fixed target serial synchrotron crystallography

Authors and affiliations -> Gabrielle Illava,[a] Richard Jayne,[b] Aaron D. Finke,[c] David Closs,[b] Wenjie Zeng,[d] Shawn K. Milano,[a] Qingqiu Huang,[c] Irina Kriksunov,[c] Pavel Sidorenko,[e] Frank W. Wise,[e] Warren R. Zipfel,[f] Benjamin A. Apker,[b] Joyce Frank,[b] and Robert E. Thorne,[b]*

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In the last decade, a wide array of sample preparation and delivery technologies have been demonstrated for XFEL- and synchrotron-based serial crystallography. Drawing upon this work, we have developed an integrated system that addresses key issues in serial crystallography in a robust way while maintaining flexibility required to address diverse real-world crystal handling challenges [1]. The key elements of this system are: (1) sample supports incorporating microfabricated thin films that are fully compatible with existing infrastructure for high-throughput cryo-crystallography including SSRL-developed in-situ crystallization plates [2], allow efficient removal of excess surrounding solvent and positioning of microcrystals at particular locations, generate ultra-low-background scatter while allowing easy optical imaging, and allow both room-temperature data collection and rapid cooling for cryogenic data collection; (2) a sample loading station that allows easy dispensing and subsequent removal of liquid (e.g., ligand- and/or cryoprotectant-containing solutions, buffer to facilitate dispersing or positioning crystals) from the sample supports via precisely controllable time-varying suction; and (3) a humid "gloveless" glovebox for crystallization tray manipulations, crystal soaking, and sample support loading and sealing that, unlike commercial humidity chambers, can generate and maintain the near saturating humidities (>95% r.h.) required to maintain microcrystals at their as-grown hydration and maximize crystal isomorphism while maximizing allowable working times. This system's ease of use, flexibility, and optimized performance make it attractive not just for serial microcrystal crystallography but also for routine single- and few-crystal data collection.

[1] G. Illava et al. Integrated sample-handling and mounting system for fixed-target serial synchrotron crystallography. Acta Cryst. D77, 628-644 (2021).

[2] E. L. Baxter et al. High density grids for efficient data collection from multiple crystals. Acta Cryst. D72, 2-11 (2016).

How Alphafold2 can help in structure and function research?

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Abstract

Recent advances in structure prediction by Alphafold2 improves model accuracy significantly to such a level (Jumper J. *et al*., Nature 596:583-589, July 15, 2021) that it could potentially provide a simple way to phase X-ray diffraction data via Molecular Replacement in cases where a homologous X-ray structure is unavailable. In addition, since the Alphafold2 model is based on the target protein's sequence, the approach addresses model bias error associated with the molecular replacement method. The approach will also significantly increase the efficiency of structure production since it is not dependent on isomorphous heavy atom derivatives or anomalous scatterers (e.g. selenomethionine labeling). In this talk, a server program developed at SER-CAT to use Alphafold2 for this purpose will be discussed.

Quo Vadis MicroED

Tamir Gonen

University of California, Los Angeles

In 2013 the method of microcrystal electron diffraction began to gain momentum with the demonstration that protein structures could be determined from three dimensional crystals using electron diffraction. Over the past decade several technological milestones were developed, optimized and described. Several laboratories and facilities regularly collect MicroED data and solve important structures from materials, small molecules, natural products to peptides, soluble proteins and importantly membrane proteins. Here I will describe MicroED from its beginnings to todays practice and discuss where the method is going in the coming years and where we could see its biggest impact in the coming years.

Associate Division Director in the APS X-ray Science Division (XSD)

Dean Haeffner

APS X-ray Science Division (XSD), Argonne National Laboratory

The APS-U is a major upgrade of the current APS that is currently underway. During a one-year shutdown of the APS (currently scheduled to begin April 17, 2023), the entire existing APS storage ring will be replaced with a new multi-bend achromat (MBA) storage ring. All beamline front ends and insertion devices will be upgraded and tailored to optimally operate with the new ring, resulting in an increase in hard x-ray brightness of at least two orders of magnitude. The increase in brightness greatly improves the ability to perform experiments that exploit the coherence of the photon beam and also allows much more efficient operation of x-ray optics to enable experiments using focal spots of < 25 nm. Nine beamlines ("Feature Beamlines") that are either completely new or are major renovations of existing APS beamlines are part of the project, and another 15 beamlines are receiving significant enhancements. The talk will focus on a technical description of the improved x-ray performance provided by the APS-U and discuss some of the new beamline capabilities that are part of the project.

Dr. Ross Harder
Advanced Photon Source, Argonne National Laboratory

Bragg Coherent Diffraction Imaging at the Advanced Photon Source

X-ray Bragg coherent diffraction imaging has evolved into a powerful tool for local structure and strain characterization at the nanoscale. Unencumbered by high resolution x-ray optics, or stringent sample preparation requirements, the technique has enabled imaging of strain in nano-scale materials at operando conditions. By measuring the coherent scattering in the vicinity of a Bragg peak of a crystal lattice and computationally inverting to an image, the technique has demonstrated quantitative strain resolution at the 10^-4 level with sub 10nm spatial resolution. This talk will introduce the method and describe details of the coherent diffraction measurements and image retrieval process. I will also present a handful of recent studies performed at the Advanced Photon Source at Argonne National Laboratory where strain imaging was used.

Machine Learning for Scoring Diffraction Patterns

Sabine Hollatz, James Holton and Aina Cohen

Structural Molecular Biology (SMB) team, Stanford Synchrotron Radiation Lightsource (SSRL), SLAC National Accelerator Laboratory, Stanford University, Stanford, CA 94503.

When applied to diffraction images can deep neural networks predict the presence of diffraction, its resolution, its spot shapes, ice contamination, and distinguish between different unit cells? If so, machine learning could provide resolution and contamination feedback during an experiment as well as dramatically reduce time, storage, and effort required to aptly process challenging datasets.

We trained deep learning image classifiers and random forest regression models on simulated diffraction images using James Holton's simulator. Therefore, training and testing datasets could be labeled precisely. Prediction results were evaluated using confusion matrices, ROC curves, and prediction error analysis.

Predicting the presence of diffraction succeeded with 95% accuracy on simulated test data and 80% accuracy on a real dataset collected during a crystallographic experiment and labeled by hand. Elongated spots were predicted with an accuracy of 76%, ice contamination at 23%, and two different unit cells at 50%. A random forest regression model could reach a 92% accuracy in predicting resolution of 2Å or better but did not generalize to a real dataset.

These results indicate that training images might have been downsampled too much in order to keep the image size feasible for training deep neural networks and might have lost too much information about the spots themselves. The random forest regression model memorized the dataset. These conclusions led to the simulation of an improved training dataset of cropped instead of downsampled diffraction images that was simulated from 117 different unit cells and integrated all desired traits.

The Last Angstrom: a Second Golden Age for Structural Biology

James M Holton[a,b,c]

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A hundred years ago, when crystallography was born, the world was going through a tumultuous time. But humanity emerged from that pandemic with a keen interest in attaining better command of our destiny. Landmark discoveries in physics, chemistry and biology transformed our understanding of the natural world and created previously unimaginable tools. For example, studies of the “natural predators of bacteria” brought us molecular biology as we know it. Insulin, penicillin, modern genetics and the electron microscope all appeared within ten years.

I predict an analogous explosion of scientific progress in the 2020s. We have already seen ground-breaking achievements in crystallographic productivity, cryoEM, and structure prediction. There is no danger that measurement and observation will go out of style, and the future of crystallography in particular I believe lies in those “fine details” that connect biology to chemistry. Much as the “last mile” in shipping logistics can be the most challenging, the “last Angstrom” between predicted and actual atomic positions will be hard-won, but worth it. So, what do we do after breaking ground? We build.

I predict the next structural biology revolution will require a change in the nature of the models we use. Current representations of “the structure” do not lend themselves to describing motion, which is key to function, nor can they explain observed structural data to within experimental error. I predict this hidden information will become unlocked by improved models. I will show how distortion models developed for cryoEM can capture and correct non-isomorphism between crystals. I will show how the effectiveness of multi-copy refinement is limited by topological traps. These can be eliminated, possibly revealing large-scale correlated motions. And finally, radiation damage effects may be rendered correctable using fine-grained sampling in space and time during data collection, provided the proper statistical treatment of ultra-weak images can be worked out. These problems are by no means solved, but I show that the solutions do exist, and effort is all that is needed to realize them.

Title: New opportunities for materials science with coherent x-rays

Stephan Hruszkewycz (ANL)

Abstract: Recent progress in 3D coherent x-ray diffraction imaging methods can enable high resolution structural imaging of nano-structured crystalline materials as well as unique in-situ observations of crystal dynamics. In this talk, I discuss developments in Bragg coherent diffraction imaging (BCDI) and x-ray photon correlation spectroscopy developed by our group that aim to broaden the envelope of materials science problems that can be addressed with this family of techniques.

Title: X-ray and Neutron Diffraction: Which One, When and Why?

Ashfia Huq
Materials Physics, Sandia National Laboratories

Abstract: X-ray diffraction is a technique that has been around for over a century and is used for structural characterization of materials ubiquitously. While sources available in laboratories generally provide ready access to X-rays, no such facility is available for neutron diffraction and hence the access to a reactor or spallation source becomes critical for these studies. The advent of the user facilities based around synchrotron and neutron sources has expanded the horizon of what is available to a structural scientist. In this presentation I will show a few examples of how these two complementary techniques can be used for deeper understanding of structure property relationship of crystalline materials with an emphasis on powder diffraction.

Current Capabilities and Planned Upgrades to the BioCAT Beamline 18ID at the Advanced Photon Source

Jesse Hopkins, Weikang Ma, Maxwell Watkins, Richard Heurich, Mark Vukonich, and Thomas C. Irving
CSRRI and Dept. of Biology, Illinois Institute of Technology, Chicago IL 60616.

The BioCAT facility is a NIH supported Mature Synchrotron Facility for Structural Biology that has operated since 1998 to provide programmatic access to the APS for X-ray scattering and diffraction studies of the structure and dynamics of non-crystalline biological systems. About 65 percent of the time goes to static and time-resolved macromolecular solutions scattering with an emphasis on combined techniques for increased information content. the other 35% devoted to macromolecular fiber diffraction with an emphasis on static and time-resolved studies of muscle systems. In this presentation I will give an overview of current capabilities and discuss the expected benefits of APS-U for all our programs on 18ID.

Structural studies of SARS-CoV-2 proteins and their complexes

Andrzej Joachimiak[1,2,3], Jerzy Osipiuk[1,2], Mateusz Wilamowski[1,3], Natalia Maltseva[1,2], Christine Tesar[1,2], Changsoo Chang[1,2], Michael Endres[1,2], Robert Jedrzejczak[1,2], Lucy Stols[1,2], Kemin Tan[1,2], Karolina Michalska[1,2] and Youngchang Kim[1,2],

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The coronavirus SARS-CoV-2 is an agent causing COVID-19 disease and world-wide pandemic affecting millions. Although this virus is similar to both, human and animal SARS- and MERS-CoVs, the detailed information about SARS-CoV-2 proteins structures and functions is urgently needed to rapidly develop effective therapeutics. We applied the high-throughput protein production and structure determination pipeline at the Center for Structural Genomics of Infectious Diseases and Structural Biology Center to produce SARS-CoV-2 proteins and determine high resolution crystals structures. We focused on nonstructural proteins (Nsps) expressed as polyproteins 1a and 1ab that are processed and assemble into a large membrane-bound replicase-transcriptase complex and exhibit multiple enzymatic and binding activities. Thus far, we have determined 65 structures for 10 CoV-2 proteins and their complexes. These structures include Nsp3 ADP-ribose phosphatase domain (ADRP, also known as macrodomain) and PLpro papain-like protease, Nsp5 main protease Mpro, Nsp7/Nsp8 primase complex, Nsp9 RNA-binding protein, Nsp10/Nsp16 a 2'-O-ribose methyltransferase complex and Nsp15 a uridylate-specific endoribonuclease. We compare these structures with previously reported homologs from SARS and MERS coronaviruses and point to similarities and differences. We also determined structures of complexes with ligands and inhibitors, including FDA approved drugs. We deposit all structures to the Protein Data Bank and release the coordinates to scientific community prior publication. We also share all reagents and protocols. These structures provide a basis for structure-based drug development.

Engineering Materials Science

Peter Kenesei*, Jonathan Almer, Sarvjit Shastri, Jun-Sang Park, Andrew Chuang, John Okasinski, Ali Mashayekhi

X-ray Science Division, Argonne National Laboratory

The APS-Upgrade brings a great opportunity to review past years demands from the User Community, and to address these needs with the new beam properties, and state-of-the-art instrumentation along with recently developed and emerging new measurement techniques. High-energy x-rays (above 40 keV) provide sufficient transmission through experimentally relevant size of samples in applied sciences and engineering with a focus on overall performance, response and failure or lifetime modeling. This requires to capture and locate rare events in bulk materials, then a sophisticated 3D tracking and investigation process of the microstructural reasons of such special events. The observations and the results of analysis can be directly used to evaluate, develop or validate material models or extend understanding of microstructure related mechanisms on performance which are crucial steps for engineering final products.

In this presentation the scientific mission of the future 20-ID High-Energy X-ray Microscopy beamline will be shown based on experiences and technique developments at the current 1-ID beamline. A quick virtual tour will be presented of the present stage of the instrument design which will serve mainly energy sciences (nuclear, battery, solar) and materials physics and engineering (aerospace, automotive, medical and civil engineering, functional materials) related research. The planned measurement techniques will be discussed with example use cases.

PIONEER: a single-crystal neutron diffractometer for small samples at the Second Target Station, ORNL

Yaohua Liu and Peter Torres
Second Target Station Project, Oak Ridge National Laboratory

PIONEER is a single-crystal neutron diffractometer currently being designed for the Second Target Station (STS) at the Spallation Neutron Source, Oak Ridge National Laboratory. Because of the high cold-neutron flux enabled by the compact STS moderator and advanced neutron optics, PIONEER will allow scientists to study tiny crystals (0.001 mm^3) and ultra-thin films (10 nm), which are comparable to those typically used for x-ray studies but not feasible at existing neutron diffractometers. Here, we will present an update on the instrument development and show the neutron optics design that allows high-flux, high-uniformity beam transportation and reduces background. To achieve this, PIONEER will take a kinked beamline geometry with two sets of Montel mirrors (also known as nested KB mirrors) and a virtual source in between. This design helps reduce the background by moving the sample out of the direct line of sight to the moderator and provides a method to tune the beam size at the sample position. We will present Monte Carlo ray-tracing simulation results to show the beam transport performance and demonstrate PIONEER's capabilities for measuring small-volume samples.

In addition to measuring small-volume samples, PIONEER will enable a high-resolution mode to study large unit-cell crystals and a polarized incident beam option for measuring weak magnetic signals and complex magnetism. A variety of sample environments will be enabled, including high/low temperatures, high magnetic fields, and high pressures, which will assist researchers in accelerating materials discovery to address energy and environmental challenges.

Structural Basis for T Cell Recognition of SARS-CoV-2

Daichao Wu[1], Grigory A. Efimov[2], Brian G. Pierce[1] and Roy A. Mariuzza[1]*
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T cells play a vital role in combatting SARS-CoV-2 and forming long-term memory responses. Whereas extensive structural information is available on neutralizing antibodies against SARS-CoV-2, such information on SARS-CoV-2-specific T cell receptors (TCRs) bound to their peptide–MHC targets is lacking. We determined crystal structures of public and private TCRs from COVID-19 convalescent patients in complex with HLA-A2 and two SARS-CoV-2 spike protein epitopes (YLQ and RLQ). The structures revealed the basis for selection of particular TRAV and TRBV germline genes by the public but not the private TCRs, and for the ability of private TCRs to recognize natural variants of RLQ. The structures also explain the inability of public TCRs to recognize a natural variant of YLQ (P272L) that has been implicated in SARS-CoV-2 escape from vaccine-induced T cell responses. By elucidating the mechanism for TCR targeting of an immunodominant yet variable epitope (YLQ) and a conserved but less commonly targeted epitope (RLQ), this study provides information for prospective efforts to rationally design vaccines to elicit pan-coronavirus immunity.

Determining membrane protein structures using microcrystal electron diffraction

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The cryogenic electron microscopy (cryoEM) method microcrystal electron diffraction (MicroED) is a powerful tool for determining atomic-resolution structures from tiny crystals. MicroED has been demonstrated on many difficult samples. However, membrane proteins remain a challenge for MicroED. The intrinsic properties of membrane proteins require sample handling and data collection techniques to be developed and optimized. Here, the milestones leading to adapting MicroED to nanocrystals of membrane proteins are discussed and future opportunities are laid out.

eBERlight – a virtual facility for biological and environmental science

Zou Finfrock[1], Alex Lavens[1], Krzysztof Lazarski[1], Changsoo Chang[1], Gyorgy Babnigg[1], Kenneth Kemner[2], Andrzej Joachimiak[1], **Karolina Michalska[1]**

[1]X-ray Science Division/[2]Biosceinces Division, Argonne National Laboratory

The use of synchrotron-based x-ray techniques over the past 25 years has revolutionized many scientific disciplines, including biology, medicine, material engineering, and environmental research, among others. In parallel with scientific advances, progress has been made in accelerator technology and x-ray methods, paving the way for an undergoing generational upgrade of the Advanced Photon Source (APS) facility. After completion in 2024, the so-called APS-U will become the nation's brightest high-energy, storage-ring based x-ray source, delivering x-rays that will be between 100 and 1,000 times brighter than they are today. The new design of the storage ring, the beamline improvement program and new feature beamlines will offer transformative opportunities, allowing researchers to study samples unprecedented spatial and temporal scales. To facilitate and coordinate access to these resources to the community supported by DOE Office of Biological and Environmental Research community, a new program, eBERlight, is being developed. eBERlight, a virtual entity, will serve as a liaison between BER researchers and the APS-U, offering an integrated platform enhancing user science through focused communication with users and coordinated activities among the relevant APS beamlines, while at the same time leveraging additional Argonne resources to provide a comprehensive environment for the BER users.

79th Pittsburgh Diffraction Conference - 2022

Title: New Approaches for Unraveling Crystallization Pathways in Geochemical Systems

Abstract:

Recent advances in crystallization science have expanded our understanding of how certain minerals grow in nature and the laboratory. Studies of nonclassical crystallization processes show how oligomers, clusters, and nanoparticles can be the building blocks for larger and more crystalline solids. Such pathways are important for explaining certain complex structures observed in natural (a)biotic systems and can be used for the controlled synthesis of solids with desirable physical and chemical characteristics. Key to understanding nonclassical processes and unlocking their potential for making technological materials is observing and measuring the structures formed at each stage of a reaction. We have developed a new approach that uses *in situ* synchrotron total scattering and pair distribution function (PDF) analysis to probe the physical and chemical characteristics of the intermediate solids formed at the early stages of chemical reactions. One example will show how the structural characteristics of amorphous calcium phosphate precursors precipitated in water control phase selection during crystallization of hydroxylapatite and brushite, which has relevance to bone mineralization. A second will show the effects of synthesis pH on the structure of ~1 nm ferric hydroxide clusters that are precursors to ferrihydrite. Due to the limited extent of structural order and the extreme small sizes of these particles, the data obtained from these experiments can not be analyzed using standard approaches that assume periodicity and are based on a unit cell. New approaches are needed to develop and test competing structural models.

F. Marc Michel, Associate Professor, Department of Geosciences, Virginia Tech, Blacksburg, VA 24061 USA (presenting)
Olaf Borkiewcz, Lead Beamline Scientist, X-ray Science Division, Advanced Photon Source, Argonne National Laboratory, Argonne, IL 60439 USA
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Small molecule structure determination and analysis by MicroED

Brent Nannenga
Arizona State University

Microcrystal Electron Diffraction (MicroED) can be used to determine the high-resolution structures of small molecules from extremely small crystals. Often, MicroED can be applied on samples without the need for additional crystallization experiments, which allows rapid structure determination. In this presentation we will describe the application of MicroED for small molecule structure determination and how MicroED can be combined with other analytical techniques to shed new light on the structure and function of organic compounds and materials.

Cooperative Gas Binding and Structural Transformations in Redox-Active Metal–Organic Frameworks

Julia Oktawiec, Henry ZH Jiang, Ari Turkiewicz, Jenny G Vitillo, Douglas A Reed, Lucy E Darago, Benjamin A Trump, Varinia Bernales, Harriet Li, Kristen A Colwell, Hiroyasu Furukawa, Craig M Brown, Laura Gagliardi, Jeffrey R Long

Adsorption-based processes are generally more energetically efficient than distillation-based separations.[1] Metal–organic frameworks have shown considerable promise as highly selective adsorbents, with powder X-ray diffraction (PXRD) studies providing key insight into the mechanism of selectivity. In particular, the ability to replicate gas dosing conditions in our laboratory while measuring *in situ* at Beamline 17-BM at APS has allowed us to gain an unparalleled understanding of the structural underpinnings of framework behavior. For example, these experiments allowed us to demonstrate that strong and reversible oxygen adsorption in the redox-active material $Co_2(OH)_2$(bbta) (H_2bbta = 1*H*,5*H*-benzo(1,2-*d*:4,5-*d*′)bistriazole) relies on metal-based electron transfer with secondary coordination sphere effects.[2] Notably, O_2-binding in this material weakens as a function of loading, as a result of negative cooperativity arising from electronic effects within the extended framework lattice. Structural studies further elucidated the structural and electronic changes that arise upon nitric oxide (NO) adsorption in $Co_2(OH)_2$(bbta) and the analogous material Co_2Cl_2(bbta).[3] At room temperature, NO adsorbs reversibly in Co_2Cl_2(bbta) without electron transfer. In contrast, adsorption of low pressures of NO in $Co_2(OH)_2$(bbta) is accompanied by charge transfer from the cobalt(II) centers to form a cobalt(III)–NO^- adduct, and disproportionation occurs at higher pressures of NO to generate cobalt(III)–nitro (NO_2^-) species and N_2O gas. As with O_2 adsorption, the adducts formed by nitric oxide adsorption are likely facilitated by secondary sphere hydrogen bonding interactions with framework hydroxo groups, demonstrating that both O_2 and NO uptake can be tuned by changing the primary and secondary coordination environment of the framework metal centers. More generally, the differences in adsorption behavior of Co_2Cl_2(bbta) and $Co_2(OH)_2$(bbta) were confidently established by analysis of powder X-ray diffraction studies. The structural insight from this work allows us to extend the tunable properties that can be used to design metal–organic frameworks for adsorption-based applications.

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Teaching Robots Beamline Science – How Automation and AI is Accelerating Research at Light Sources

Daniel Olds

National Synchrotron Light Source II

Brookhaven National Laboratory

With many new and upgraded x-ray light source facilities coming online, as well as advances in detector technology, the data generation rates of worldwide synchrotron user facilities are skyrocketing. For example, in 2021 the National Synchrotron Light Source II (NSLS-II) produced over 1 petabyte of raw experimental data. At the same time, the changes brought about by the COVID-19 pandemic often limited on-site staffing and user access, precipitating a need for improvements and expansion of remote operations at these facilities. These two things have made many of the conventional human-driven approaches to operation and data analysis challenging and limited our capability to fully leverage and efficiently utilize the capabilities of these facilities. New methods employing artificial intelligence for both operations and data analysis have demonstrated great promise at x-ray light sources, particularly when integrated directly with the beamlines.

In this contribution, recent work developing and deploying AI methods at the NSLS-II will be presented with examples that span operations to data analysis. Examples include determination of crystal structure from powder diffraction data via ensembles of trained classifiers, automated insights during in situ material studies via constrained matrix factorization, automation of high-throughput data collection via reinforcement learning, and automated data quality monitoring via supervised learning methods. Finally, we will demonstrate a fully AI-driven, multimodal measurement spanning beamlines and techniques made possible through the culmination of these technologies.

Solid state reactions on the beamline, what we gain by peering into the 'black box'

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Abstract: *In situ* powder diffraction experiments allow solid state chemists to 'peer' into relevant reactions at high temperatures and gain useful information on a material's thermal stability and phase transitions driven by their chemistry. In this talk, I will present our work on two coupled reactions in complex metal oxides at high temperatures under different atmospheres such as hydrogen, methane, air, and inert gas. Known as *chemical looping*, these cyclic reactions employ a metal oxide to combust fuels or produce hydrogen thermally; both the oxygen reduction reaction and oxygen evolution reaction are also key for chemical looping. At the Advanced Photon Source (Argonne National Laboratory) and the Spallation Neutron Source (Oak Ridge National Laboratory), we have carried out such chemical looping reactions on perovskite oxides such as $La_{1-x}Sr_xFeO_{3-\delta}$, and LnB_2O_4-type oxides such as $LuFe_2O_4$. I will focus on the LnB_2O_4-type oxides, which are layered structures with the transition metal *B* in a undercoordinated environment. These materials have some advantages over perovskite oxides in that their phase transitions began at relatively lower temperatures. We also present electron microscopy work to understand how oxygen incorporates into the lattice to develop incommensurate charge density waves in the crystal structures. We compare the mix-valence multiferroic $LnFe^{2+}Fe^{3+}O_4$ ($LnFe_2O_4$ where Ln = Y, Lu, and Yb) to the Mn-substituted versions *Ln*FeMnO4. While both compounds display reversible oxygen uptake and release, they display some key differences in their mechanisms for doing so. We provide crystal-field arguments to explain the mechanisms for oxygen uptake. Overall, these high-temperature, variable atmosphere experiments on the beam lines help us pursue materials design for chemical looping cycles.

Structural, magnetic, and nematic correlations in iron based superconductors

Stephan Rosenkranz

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Obtaining a microscopic theory of unconventional superconductivity remains a major challenge of condensed matter physics. In the iron pnictides and chalcogenides, superconductivity emerges from a normal state that is in the vicinity of a structural phase transition as well as antiferromagnetic and nematic orders. While a detailed understanding of the role of these orders and associated fluctuations remains unclear, neutron and synchrotron x-ray powder diffraction has played a crucial role in elucidating the extent and competition, coexistence, and coupling of these order over large phase space of doping, temperature, and families of compounds and discovered new states that help solve some of the questions and are crucial to guide theoretical studies.

Here, I will discuss powder diffraction investigations in particular on hole doped and phosphor substituted '122' and '1111' iron arsenide compounds. These studies revealed a strong coupling of magnetic and lattice correlations, the presence of an unusual double Q magnetic state, which establishes an itinerant nature of the magnetism in these systems, the presence of strong nematic fluctuations over a large region in temperature-composition space, enabled the derivation of a universal phase diagram, and uncovered a universality of the various magnetic orders encountered in these systems that provides a unified model to describe the electronic and magnetic phases across different families of iron pnictides.

Work supported by U.S. DOE BES DMSE

"Capabilities of the “Structural Science (SRS)” beamlines after the upgrade of the APS"

Uta Ruett and SRS group

X-ray Science Division (XSD) at Argonne National Laboratory

Today the Structural Science group (SRS) operates 11-BM (high-resolution power diffraction), 11-ID-B (Total scattering for Pair Distribution Function (PDF) analysis), 11-ID-C (Diffraction under extreme conditions), and 17-BM (rapid data acquisition powder diffraction) serving research in materials synthesis, electrochemistry, applied materials science, correlated electron systems, geology, catalysis, pharmaceuticals, etc.

After the upgrade, the beamline 11-ID-D will become enhanced for high-energy diffraction, which includes new canted superconducting undulators as insertion devices at sector 11 for highest flux. The station 11-ID-D will enable a combination of total scattering with small angle scattering and focusing into the submicrometer range, which allows us to close the gap between the resolution in reciprocal and real space to provide a complete picture of the structure of materials.

An overview will be given for the new and continued experimental capabilities for powder diffraction and total scattering at the upgraded APS.

In situ Crystallization of Model Minerals on Titan, Saturn's Moon

Tomče Runčevski, SMU

Earlier this year, NASA announced the new New Frontiers mission – Dragonfly – to be launched in 2026 on the course to Titan, Saturn's moon, to explore the surface. Chemically speaking, Titan features an exceptionally interesting environment. It has dense atmosphere and active photochemistry. The former NASA mission – Cassini – has detected over 30 different organic molecules. These molecules precipitate on the surface and solidify as molecular solids, cocrystals and/or clathrate hydrates, or Titanean minerals. Surprisingly, the crystal and local structure, as well as many physicochemical properties of many of these simple molecules remain unknown. For example, the crystal structure of propionitrile has not been reported, or the structure of many cocrystals. To get a glimpse of the how the surface of Titan could look like, we performed experiments in the laboratory and at synchrotron and neutron sources, mimicking the conditions on the moon (93 K, 1.45 atm, nitrogen atmosphere, ice surface). We have characterized a number of solids, such as molecular crystals and cocrystal, using various diffraction and total scattering techniques, as well as thermoanalytical methods. These results can help inform the Dragonfly endeavors, but also shine light of the physical chemistry of very simple molecules at cryogenic conditions.

New Remote Access Program for Elevated-Temperature and Humidity-Controlled Experiments at SSRL

Silvia Russi

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Expanding on its mature cryo-crystallography program, the Structural Molecular Biology (SMB) group at the Stanford Synchrotron Radiation Lightsource (SSRL) now supports a fully remote user-access program for diffraction experiments at controlled humidity conditions. During data collection at SSRL BL12-1, crystals can be maintained in a controlled temperature environment or at controlled humidity (and ambient temperature conditions) including stepwise crystal dehydration experiments. To enable robotic sample exchange at the beam line, 10 samples on standard magnetic bases fit into a new SSRL in-situ plate. The plate is a combination of a crystallization plate and a uni-puck, serving as a one-spot crystallization and sample storage and shipping container. For shock-free transport to the beam line, six SSRL in-situ plates fit inside an insulated thermal shipper, which contains a phase-changing liquid to maintain the temperature for up to 7 days during transport using a standard courier service like FedEx. At the beam line, in-situ plates are loaded into a humidity-controlled bay accessible to the sample exchange robot. To initiate an experiment, the Blu-Ice control software incorporates a new user interface to mount samples from inside the in-situ plates.

These novel tools and automation offer SSRL users a seamless home-lab to remote-lab experience, opening the door to more advanced remote access diffraction studies. Exciting opportunities enabled by this technology include exploring phase transitions, controlled dehydration to achieve higher resolution data, and studying protein structure and dynamics at near physiological temperatures. For example, the possibility to trigger chemical reactions within enzyme crystals during serial diffraction experiments can provide detailed mechanistic information. To support and accelerate these goals, a number of advanced options are available to the SSRL user community that build upon this new remote-access program.

ML-guided high-throughput experimentation for material design and discovery

Suchismita Sarker (CHESS)

The rapidly emerging fields of Artificial Intelligence (AI) and Machine Learning (ML) have become dominant problem-solving approaches for many traditional industries and promise to alter many aspects of material discoveries. Material discovery in compositionally complex space expands the probability of finding desired alloy systems. However, materials with targeted properties in higher dimensional space are expensive, complex, and time-consuming. In addition, physio-chemical understanding to design a material with desired properties is sometimes insufficient. Therefore, data-driven machine learning (ML) approaches are promising to guide the search. However, the limitation is the availability of a large dataset. In this talk, I will show that combining both physics and data allows the construction of robust machine learning models with sparse data and takes advantage of existing domain knowledge and data-informed science and assist high-throughput experimentations to understand the synthesis-structure-property relationship shown in **Figure 1**. In addition, I will discuss two separate studies: (a) the real-time closed-loop, autonomous phase mapping at the synchrotron x-ray diffraction, (b) discovery of metallic glasses and understanding of their properties. The strategy proposed here could be easily adapted to efficiently exploring various complex design spaces where a physio-chemical understanding is insufficient, moreover experimental observations are sparse and expensive to obtain.

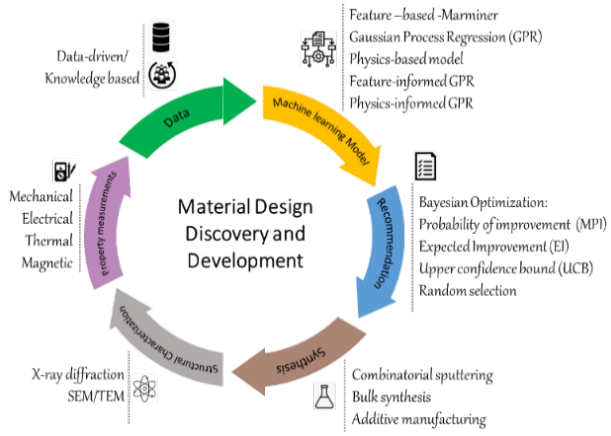

Figure 1: **Material design, discovery, and developments**: Steps towards data-driven machine learning, integrated physics and physiochemical theories, Bayesian optimization strategies for recommendation and high-throughput material design, discovery, and developments process

Coherent X-ray methods and recent advantages in 3D Laue microscopy

Dina Sheyfer (Argonne National Laboratory)

The nanoscale heterogeneities alter the structural, magnetic, electronic, and electrochemical behavior; they govern the physical processes and macroscopic properties in matter. Despite significant efforts in discovering and characterizing macroscopic states of matter, progress in understanding the fundamental mechanisms behind these phenomena often encounters challenges in probing structure and dynamics of matter at the nano- (sub)microscale. Recent developments in coherent x-ray sources and methods significantly advance the capabilities of nano and sub-microscale measurements, offering superb spatial and temporal resolution (ultrasmall and ultrafast). In this seminar, I will present studies utilizing X-ray Photon Correlation Spectroscopy, Bragg Coherent Diffractive Imaging. I will show recent development in Laue microdiffraction which allow rapid data acquisition and 3D reconstruction method to image the internal structure of crystalline materials.

HPCAT upgrade plans

Maddury Somayazulu[1], Nenad Velisavjlevic[2], Eric Rod[1] and Kevin D'Amico[3]

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Concurrent with the upgrade of the MBA lattice of the storage ring at APS in 2023, HPCAT has been planning several upgrades. HPCAT at sector 16 of the APS is dedicated for synchrotron x-ray based high pressure research. With four simultaneously operating beamlines, HPCAT covers a plethora of techniques ranging from powder diffraction to inelastic x-ray scattering. Apart from diamond anvil cells of various kinds, HPCAT also offers large volume capabilities with the robust Paris Edinburgh cell as high-pressure platforms. Temperatures from 2 K to 3000 K are achievable with cryostats and in-situ laser heating. Smaller beam size translates directly into being able to achieve higher pressures while higher brightness and spatial coherence translates into probing higher strain rates and effects of non-hydrostatic stresses. The extreme conditions research community worldwide has therefore been awaiting capabilities to surpass existing synchrotron-based probes and the APS-U offers that next quantum leap.

While most existing techniques (except for nuclear forward scattering) are planned to be refined and improved leveraging better detectors, focusing optics and better sample positioning, HPCAT will also add several new techniques. This talk will detail the planned and on-going upgrades which will be completed in synch with the return of the stored beam in 2024.

Acknowledgements: The staff of HPCAT have been actively involved in all the discussions, plans and town hall meetings that has formed the crucial input for the formulation of this plan. HPCAT is funded by DOE-NNSA office of experimental sciences whose funding for operations and HPCAT upgrade is gratefully acknowledged. The contributions from various groups in XSD and APS in general, was very timely and crucial and helped us evaluate various possibilities as well as incorporate their suggestions.

Automating Sample Handling for Grazing-Incidence X-ray Scattering Experiments at the APS

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Synchrotron experiments offer many opportunities for automation in the areas of data analysis workflows, data collection, sample alignment and sample handling, especially in a relatively mature technique such as Grazing Incidence X-ray Scattering (GIXS) frequently employed for screening large numbers of materials. Here we focus on one aspect of automating the experimental cycle, namely sample handling, for the dedicated GIXS instrument hosted by the nanoscale morphology and kinetics program at Beamline 8-ID-E, and migrating to the APS-U feature beamline 9-ID CSSI. We have developed a system based on a commercial robotic arm that leverages our existing infrastructure and addresses some of the distinct challenges posed by thin film samples in grazing-incidence geometry, as compared to samples for transmission studies. The control system combines both vendor-supplied and third-party software for programming the robot, and uses an EPICS IOC to integrate the robot into beamline controls. We have successfully implemented two different strategies for transferring either multi-sample cassettes or individual samples to and from the instrument. In-house 3D printing capabilities greatly facilitated the development and suggest a strategy for a pilot-scale program for mail-in remote experimental access. Prospects for automating other aspects of the experimental cycle are also discussed. These efforts are increasingly important to take full advantage of the higher brilliance from next-generation synchrotron sources, such as the APS-U.

This research used resources of the Advanced Photon Source, a U.S. Department of Energy (DOE) Office of Science User Facility at Argonne National Laboratory and is based on research supported by the U.S. DOE Office of Science-Basic Energy Sciences, under Contract No. DE-AC02-06CH11357.

Ultrafast x-ray photon correlation spectroscopy at the Linac Coherent Light Source

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Nearly fully transversely coherent femtosecond x-ray pulses produced by x-ray free electron laser sources opened up the possibilities of direct measurement of nano/atomic scale dynamics of complex systems at their native time scales via x-ray photon correlation spectroscopy (XPCS). Central to the experimental concept are the capabilities of generating two identical x-ray pulses in rapid succession. The two pulses then produce two coherent scattering patterns of the sample systems with the dynamics information encoded in the intensity autocorrelation functions. While area detectors capable of independently measuring the scattering patterns from two subsequent x-ray pulses with a femto- to picosecond separation will not be available in the foreseeable future, it was proposed that the correlations between the two scattering patterns can nevertheless be obtained from the summed scattering pattern, by analyzing the speckle visibility. In this talk, I will present such a methodology with a demonstration experiment that probes the nanoscale nonuniform flow dynamics within a free flowing jet. Following this, I will summarize our decade-long developments of x-ray optical instrumentation, i.e., x-ray split-delay optics at the Linac Coherent Light Source towards delivering the highly desired picosecond-separated x-ray twin-pulses.

Hydrogen as superconductivity's 'hidden variable' in a quasi-one-dimensional candidate spin-triplet superconductor

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In the race to find new topological materials, superconductivity has found renewed interest as a potential host of the Majorana Fermion. This exotic solution to the relativistic wave-equation is predicted to arise as a quasiparticle in superconductors with either spin-triplet pairing or with topological Dirac-like dispersions in their band structure. Recently, a new family of quasi-1D superconductors $A_{1,2}M_3As_3$ (with A= Alkali metal and M = Cr or Mo) was discovered which is proposed to exhibit both of these rather rare properties. Of this family, several members are predicted to be spin-triplet superconductors which, given the quasi-1D structure, directly invokes the original toy-model built by Kitaev for realizing localized Majorana modes. Additionally, first principles calculations have suggested the entire family of compounds to exhibit numerous Dirac-like crossings near the Fermi energy. Excitingly, this gives multiple potential routes to Majorana modes in a single family of materials – even in a single compound. However, despite this promise, the study of these materials has been somewhat hampered due to their extreme air sensitivity, an inability to charge dope and an enduring ambiguity as to the nature of their superconducting state. Here, we report the results of neutron and x-ray scattering studies together with first principles calculations which help resolve these impediments. We show the presence of both short-ranged magnetic and structural instabilities in the '233' compounds which allow for us to infer a spin-triplet pairing and draw similarities to the broader family of unconventional superconductors. Using the complementarity of x-ray and neutron diffraction we report a hidden effect of a widely reported synthesis technique whereby H is accidentally and unknowingly doped into the system. In doing so, we resolve a long-standing inconsistency in the reported materials properties and provide an unconventional mechanism to charge dope the '133' stoichiometry between a spin-glass and a superconducting state. Together, these results suggest that the $A_{1,2}M_3As_3$ superconductors are a potential playground of topological physics and provide some of the tools necessary to access these highly sought states.

Crystal Structures of Angiopoietin-like 4's Carboxy-Terminal Domain (cANGPTL4) Reveal a Fatty Acid Binding Pocket

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Angiopoietin-like 4 (ANGPTL4) is a secreted protein that plays a role in cardiovascular disease and progression of several aggressive cancers, including pancreatic ductal adenocarcinoma (PDAC). ANGPTL4 is natively present in two fragments: an amino-terminus coiled-coil domain (nANGPTL4) and a carboxy-terminus fibrinogen-like domain (cANGPTL4), which have demonstrated diverse biological functions. We have investigated cANGPTL4's molecular role in PDAC progression through biochemical and structure-function studies. Binding studies show that cANGPTL4 can bind to myristic and palmitic acids. Crystal structures of this protein in complex with glycerol, myristic acid, and palmitic acid reveal a binding pocket for saturated fatty acids (PDB 6U0A, 6U73, and 6U1U respectively). Our cell culture experiments show that these protein complexes are internalized by facilitated endocytosis, which also leads to attenuation of Wnt/β-catenin signaling. Overall, these data suggest that cANGPTL4 aids in the progression of PDAC by providing energy and biological materials necessary for cellular growth, proliferation, and metastasis by binding to fatty acids.

Furthermore, crystallization of cANGPTL4 along with recombinant inorganic pyrophosphatases from pathogenic bacteria (as well as several other proteins) were tested for optimization by 23 ionic liquids (ILs). The ILs were used as additives at concentrations of 0.1, 0.2, and 0.4 M. All proteins were crystallized in the absence and presence of an IL. For 9 of the 11 proteins, precipitation conditions were converted to crystals with at least one IL. The ILs could be ranked in order of effectiveness, and it was found that ~83% of the precipitation-derived crystallization conditions could be obtained with a suite of just eight ILs, with the top two ILs accounting for ~50% of the hits. Structural trends were found in the effectiveness of the ILs, with shorter-alkyl-chain ILs being more effective. The two top ILs, accounting for ~50% of the unique crystallization results, were choline dihydrogen phosphate and 1-butyl-3-methylimidazolium tetrafluoroborate.

Title: SMASH-ML: Solving Materials and Structures through Simple Heuristics and Machine Learning

Abstract

In this talk, we will discuss how we take couple high throughput synchrotron x-ray scattering experiments, machine learning, and robotics in order to develop autonomous SMART data collection systems. With particular focus on the foundational tools which are required in order to fully automate materials discovery including: automated data interpretation tools, machine controlled DAQ, and decision algorithms which automate the design of experiment and instrument optimization. We are able to demonstrate that in as few as 30 unsupervised in-situ experiments characterizing a synthesis pathway active learning algorithms are able to determine how to synthesize a class of nanocrystals of varied sizes, inform researchers about what syntheses are improbable, and provide a model which can be queried to perform virtual syntheses without running subsequent experiments. These developments provide a roadmap as to how to build AI driven R&D to both predict catalytic targets as well as how to make them, and illustrate a pathway to creating digital twins of user facilities, while improving the user experience.

Leveraging machine learning to detect heterogeneous features from diffraction data

Stephanie A. Wankowicz[1], Blake Riley[2], Ashraya Ravikumar[1], Shivani Sharma[2], Saulo de Oliveira[3], Gydo C. P. van Zundert[4], Henry van den Bedem[3], Daniel Keedy[2], James S. Fraser[1]

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4) Schrödinger, New York, New York

Biomolecules adopt a dynamic ensemble of conformations, each with the potential to interact with binding partners or perform the chemical reactions required for many cellular functions. Crystal structures obtained from high-resolution X-ray diffraction data reflect this heterogeneity as a spatial and temporal conformational average; however, reliably extracting heterogeneous features from diffraction data has remained a challenge. We have developed qFit, a software package for modeling the flexibility of protein and ligand molecules based on experimental data from X-ray crystallography or cryo-electron microscopy. qFit uses mixed integer quadratic programming (MIQP) to evaluate an extremely large number of combinations of sidechain conformers and backbone fragments to explain the electron density locally. Here, we show qFit's ability to detect new conformations of proteins in single proteins and across thousands of structures. Our results demonstrate the power of computational machine learning computational techniques to provide new insights into conformational heterogeneity. Overall, improved modeling of high-resolution X-ray data will connect dynamics to the structure-function relationship and help drive new design strategies for inhibitors of biomedically important systems.

Serial Crystallographic Approaches to Understanding Enzyme Mechanism

Mark A. Wilson

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Serial crystallography allows time-resolved structural studies of enzyme catalysis at room temperature. I will describe our work using time-resolved crystallography to elucidate the catalytic mechanism of isocyanide hydratase (ICH), an enzyme involved in degrading antimicrobial isocyanide natural products. Recent mix-and-inject serial crystallography experiments at both LCLS and SSRL illustrate how catalysis activates enzyme motions in ICH and possibly in other systems.

A comprehensive epitope map of the SARS-CoV-2 spike protein

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Variants of SARS-CoV-2 have largely reduced neutralization to antibodies elicited by prior infection and vaccination. Universal vaccines and broadly neutralizing antibodies with high potency are urgently needed to overcome the rapid evolution and extensive antigenic variation of SARS-CoV-2. Here by analyzing the extensive functional and structural information generated by us and others on SARS-CoV-2 neutralizing antibodies, we present an in-depth antigenic map of the SARS-CoV-2 spike protein. We found that neutralizing potency and breadth for antibodies to SARS-CoV-2 are often somewhat mutually exclusive. We also found some common sites of vulnerability that are targeted by rare, broadly neutralizing antibodies, which generally retain activity to SARS-CoV-2 variants and other sarbecoviruses. These sites, which so far seem to be less prone to escape, provide insights into design of next-generation vaccines and therapeutic antibodies that provide more universal protection.

Computationally Mediated Diffraction and Imaging in the Argonne PicoProbe Electron Optical Beam Line.

Nestor J. Zaluzec
Argonne National Laboratory
Photon Science Directorate

Capabilities for ultra high spatial resolution electron scattering studies in hard and soft matter has continuously evolved with advances in electron optical instruments.
The most advanced of these instruments, should in reality no longer be termed electron microscopes but rather "electron optical beam lines". They allow us to routinely create and manipulate electron probes ranging in dimension from millimeters to below 100 picometers. Concomitant with advances in electron optics are the corresponding developments in ancillary detectors from spectrometers to direct electron and pixel array sensors. Together with computationally mediated control these resources facilitate a range of capabilities for advanced characterization of materials and complement the scattering experiments conducted in neutron, x-ray instruments.

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First Name	Last Name	Poster Catagory	Poster Nummer
Yao	Abusa	physical, chemical, and materials science - method development	27
Andrew	Bond	life sciences and biochemistry - small molecules	11
Zhihengyu	Chen	physical, chemical, and materials science - fundamental science	20
Maria	Curria	physical, chemical, and materials science - applied science	13
Tyra	Douglas	physical, chemical, and materials science - method development	28
Tyler	Eastmond	physical, chemical, and materials science - method development	29
Joe	Ferrara	physical, chemical, and materials science - method development	38
Justin	Hoffman	physical, chemical, and materials science - fundamental science	21
Stephanie	Hong	physical, chemical, and materials science - fundamental science	22
Benjamin	Hulbert	physical, chemical, and materials science - method development	30
Thomas	Irving	life sciences and biochemistry - macromolecules	1
Joonas	Jamsen	life sciences and biochemistry - macromolecules	2
Zhongmin	Jin	life sciences and biochemistry - method development	7
James	Kaduk	life sciences and biochemistry - small molecules	12
Saugat	Kandel	physical, chemical, and materials science - method development	31
Eun Byoel	Kim	physical, chemical, and materials science - applied science	14
Charles	Lake	physical, chemical, and materials science - applied science	15
Yaohua	Liu	physical, chemical, and materials science - method development	32
Yasukazu	Nakaye	physical, chemical, and materials science - method development	33
Abiodun	Oshinowo	physical, chemical, and materials science - fundamental science	23
Florian	Quis	physical, chemical, and materials science - applied science	16
Joseph	Race	physical, chemical, and materials science - fundamental science	24
Ben	Redemann	physical, chemical, and materials science - applied science	17
Lynn	Ribaud	physical, chemical, and materials science - method development	34
Simon	Roemig	physical, chemical, and materials science - applied science	18
Uta	Ruett	physical, chemical, and materials science - method development	35
Silvia	Russi	life sciences and biochemistry - method development	8
Silvia	Russi	life sciences and biochemistry - method development	9
David	Schuller	life sciences and biochemistry - macromolecules	3
Edward	Snell	life sciences and biochemistry - macromolecules	4
Santhoshkumar	Sundaramoorthy	physical, chemical, and materials science - fundamental science	25
Tim	Sweeney	life sciences and biochemistry - method development	10
Niklas	Thompson	physical, chemical, and materials science - method development	36
Davis	Unruh	physical, chemical, and materials science - fundamental science	26
Stephanie	Wankowicz	life sciences and biochemistry - macromolecules	5
James	Weng	physical, chemical, and materials science - method development	37
Shenglan	Xu	life sciences and biochemistry - macromolecules	6
Andrey	Yakovenko	physical, chemical, and materials science - applied science	19

79th Pittsburgh Diffraction Conference's Abstract

Non-Hydrolytic Sol-gel Synthesis and Characterization of Mixed A-Site $Al_{2-x}In_xW_3O_{12}$ Negative Thermal Expansion Materials

Abiodun Oshinowo and Cora Lind-Kovacs

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Negative Thermal Expansion (NTE) materials contract upon heating. These materials may find applications in composite materials, in high precision optical mirrors, in the aerospace industry, in dental fillings and in electronics. Of all the families of NTE materials, the $A_2M_3O_{12}$ (A = trivalent cation, M = tungsten, molybdenum) family has attracted special attention because of the wide range of cations that can be incorporated into the structure due to the chemical flexibility of the A and M sites. The substitution at the A site in the $A_2M_3O_{12}$ compounds is being investigated by synthesizing and characterizing several $Al_{2-x}In_xW_3O_{12}$ compounds of different compositions. Materials of this family tend to adopt an orthorhombic structure at high temperature where they exhibit NTE, but for many compositions an "undesirable" phase transition to a monoclinic phase with positive expansion can occur at low temperature. The identity of the A site cations determines the crystal structure and affects the phase transition temperature. The goal of this research is to stabilize the orthorhombic phase of the NTE structure of different compositions within a wider range of temperatures and probe their phase transition and expansion behavior as a function of composition. The substituted metal cations are Al^{3+} and In^{3+}. The "non-hydrolytic" sol gel (NHSG) method was used to synthesize "raw samples" of these compounds, which were subsequently calcined for crystallization and further analysis by XRD, TGA, SEM and EDX.

Enhancing Protein Crystallization Successes in Droplet-Based Microfluidics Using a Surface Science Approach

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Protein structure determination continues to be an important aspect of advancing the understanding of cellular function and it is foundational to structure-based drug design efforts. Macromolecular X-ray crystallography remains the benchmark technique for determining protein structures at (or near) atomic resolution, yet high throughput protein crystallization continues to suffer from time- and sample-consuming bottlenecks that result in an approximately 85% failure rate in producing diffraction quality crystals. DeNovX takes a surface science approach to improving crystallization outcomes for proteins and small molecule active pharmaceutical ingredients, primarily using engineered nucleation features to reduce the energetic barriers to nucleation to improve crystallization outcomes while preserving diffraction quality. Replicate, controlled batch vapor diffusion crystallization studies using engineered nucleation features show 1.1-9.0-fold increases in crystallization hit percentages while reducing the crystallization onset times by an average of 40% for select known crystallizers and challenge proteins. The use of engineered nucleation features also produces an average of 2.5-fold more crystalline material, which is beneficial for serial crystallography data collection using fixed target or flowing sample injection techniques. This poster will discuss batch protein crystallization results and preliminary studies of protein crystallization in microliter droplet-based microfluidics that incorporate engineered nucleation features.

High Throughput Mechanocrystallization and Synchrotron X-ray Powder Diffraction of Pharmaceutical Cocrystals

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Over 70% of active pharmaceutical ingredients (APIs) exhibit poor water solubility and/or bioavailability, which are leading causes of drug failures. Cocrystallization mates an API with a heterosynthon and is a crystal engineering approach to creating water soluble API compositions, but it is not yet efficient and reproducible in high throughput screening (HTS) workflows. Mechanocrystallization can produce shear forces that facilitate API cocrystal formation, and a high confidence proof of concept using a cocrystal of the API acetaminophen with the coformer 2,4-pyridinedicarboxylic acid as a benchmark in a 48 well format gave excellent reproducibility across six continuous variation studies. The prototyping activities and data collected by our interdisciplinary team include a subset of 324 samples showing 100% agreement in forming known cocrystalline phases while identifying numerous new phases yet to appear in the literature. This poster will present the results of these method qualification studies for a variety of API cocrystalline systems and will highlight the key benefits of this workflow that include superior reproducibility and 2x the analytical data (diffraction + spectroscopic) on the same sample form factor at a rate 10x faster and requiring 10x less material than competing approaches (e.g., solvent drop grinding, ball milling, etc.).

Sample Displacement Correction for X-ray Diffraction in Debye-Scherrer Geometry with a Flat Area Detector

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The effect of small changes in sample-to-detector distance on unit-cell parameters is examined for synchrotron powder diffraction in Debye-Scherrer (transmission) geometry with a flat area detector. An analytical correction equation is proposed to fix the shift in 2θ values due to sample capillary displacement. This equation, which is applied during the Rietveld refinement step, does not require the use of an internal standard reference material, and is analogous to the sample displacement correction equation for Bragg-Brentano experiments. The Δ2θ correction equation is compared to another sample displacement correction based on the use of an internal standard reference material in which new integration and calibration parameters of area detector images are determined. Example datasets showing the effect of a 4 mm sample displacement on unit-cell parameters for 25 °C CeO_2 and a temperature series of ZrW_2O_8 including both types of displacement corrections are described. These experiments were performed at powder XRD beamlines at the National Synchrotron Light Source II at Brookhaven National Laboratory and the Advanced Photon Source at Argonne National Laboratory.

Processing and Short-Range Order in Multiple Principal Element Alloys and their Suboxides

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The formation of a nanometer-thick protective oxide film on the surface of an alloy, termed passivation, protects a metal from corrosion processes. The passivation behavior in an aqueous solution is determined by its crystal structure, composition, degree of chemical short-range order (SRO) and the composition/pH of the electrolyte. Our previous research revealed that for binary Fe-Cr and Ni-Cr alloys, the initial stages of passive-film formation can be understood within the context of SRO. However, the effect of SRO on passivation of emerging compositional complex alloys is lacking. In this research, we are interested in determining how SRO affects the passivation behavior of a series of multi-principal elemental, $(FeCoNi)_{1-x}Cr_xAl_y$, alloys. The specific aim of this work is to examine if the presence of Al affects Cr-Cr neighbor identities in alloys with constant chromium content. Alloy compositions were designed so that we could determine the SRO in non-Al containing, "control", alloy samples (x = 0.10, y = 0 at%) and corresponding alloys with a fixed amount of Cr containing various Al concentrations (x = 0.10, y = 0.03, 0.06, 0.09). Samples were measured at Oak Ridge on the POWGEN beamline to study their total scattering and determine the SRO in the alloy system. PDF refinement fittings on the collected diffraction data are being performed to determine the ordering of the various elements in the phases, primarily the Cr-Cr ordering. This should provide an atomic scale understanding of the structure and reveal how tuning the Al content varies the Cr ordering within each alloy. These alloys are vital towards understanding the role of ordering as it pertains to the corrosion and oxidation resistance of complex concentrated alloys.

Mcgovernite, How Powder Diffraction Revealed New Information and Improved a Single Crystal Study.

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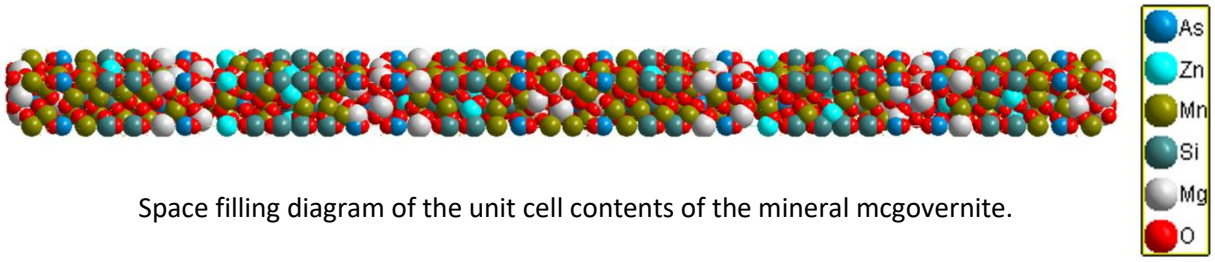
Mcgovernite is a rare enigmatic mineral discovered in 1927 which has an extraordinary rhombohedral unit cell (a=8.206 Å, b = 8.206 Å, c=204.118 Å, V = 11903.8 Å^3). Even the formula unit of this mineral has been elusive for 50-years until it was determined as $M^{2+}_{19}Zn_3(OH)_{21}(AsO_3)(AsO_4)_3(SiO_4)_3$ (M = Mn, Mg, Zn). Hawthorne (2018) recently reported a single crystal study that used a centrosymmetric model ($R\bar{3}c$) which contained disorder at three cationic sites. This study will demonstrate how APS synchrotron powder diffraction data, could supplement a single crystal study and provide information leading to a model that better describes the crystal structure.

Powder diffraction data have a unique advantage over single crystal data in that it is not influenced by twinning. The structure solution by charge flipping, generated from the synchrotron powder diffraction data clearly indicated that the noncentrosymmetric space group $R3c$ was favored over the centrosymmetric space group $R\bar{3}c$. Using this observation and reexamining the data collected by Hawthorne, an alternative model emerged in which the "single" crystals used in Hawthorne's study were, in reality merohedral inverse twins. This could not be easily determined without the powder diffraction data, for the only evidence for twinning in the single crystal data were in the Wilson statistics. The E^2-1 result of 1.054 indicated a "super centro" result. This could be due to nonequivalence of the Friedel's pairs due to resonant scattering. Ultimately, the inversion symmetry in the noncentrosymmetric model was broken by only 5 % of the atoms in mcgovernite. Using Hawthorne's single crystal data set, the noncentrosymmetric $R3c$ model generated improved statistics (R_F = 2.179 % for 8707 unique reflections) over the published centrosymmetric $R\bar{3}c$ model (R_F = 5.02 % for 3772 unique reflections).



Space filling diagram of the unit cell contents of the mineral mcgovernite.

Macromolecular diffraction at CHESS 2022 and beyond

David J. Schuller, Richard E. Gillilan, Qingqiu Huang, Zhongwu Wang, Steve Meisburger, D. Marian Szebenyi, Jeney Wierman

CHESS, Cornell University, 161 Synchrotron Drive, Ithaca, NY

The Cornell High Energy Synchrotron Source hosts a variety of X-ray science in fields ranging from materials science to chemistry to quantum physics to biology. A new building is currently under construction to house a High Magnetic Field beamline.

CHESS has two beamlines dedicated to structural biology. The BioSAXS beamline offers a number of solution scattering techniques including SEC-SAXS, High Pressure SAXS and Time-Resolved SAXS. The FLEXX beamline offers standard macromolecular crystallography, serial crystallography and high pressure crystallography.

79th Pittsburgh Diffraction Conference: Poster Abstract

Title: Fully Automated Nanoscale to Atomistic Structure from Theory and Diffraction Experiments

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Abstract:

Prior to computational investigation into the structural and electronic properties of materials, precise knowledge of their atomistic structure is required. Diffraction techniques are commonly used to probe and characterize the structure of a material, but unless the material is crystalline and has been previously studied, inverting diffraction spectra to fully determine the atomistic structure is a significant challenge. Theoretical insight requires searching a vast structural space where it is critical to not only match the experimental diffraction data but also minimize other quantities such as the energy to ensure that the structures are both physically plausible and realizable. In response, we have developed the FANTASTX (Fully Automated Nanoscale to Atomistic Structure from Theory and eXperiment) code, a multi-objective evolutionary algorithm which performs machine-learning informed data-driven structure search using genetic algorithm and basin hopping methods. It includes full support for X-ray diffraction (XRD) and pair distribution function (PDF) analysis. The FANTASTX code has demonstrated significant speed-ups in the inversion of spectra which previously required manual inversion and we have also produced novel insights into the structures of blue-layer amorphous IrO_2 and gold nanoclusters.

Hauptman-Woodward Research Services – Structural Solutions

Edward Snell

The Hauptman-Woodward Medical Research Institute Research Services Group

For over two decades the Hauptman-Woodward Medical Research Institute (HWI) has operated a high-throughput crystallization screening laboratory. This provides an efficient and effective method to identify initial conditions for crystallization and has recently been named the National Crystallization Center. Capabilities at HWI have expanded to include synchrotron services at one of the premier industrial beamlines, and most recently access to cryo-electron microscopy for single particle studies. The Institute is an independent not-for-profit research institution and developments in the laboratory are adopted rapidly to the research services provided. Industry and academia are supported.

The National Crystallization Center runs the equivalent of sixteen 96 well plates simultaneously with 200 nl of protein in each drop. Experiments are monitored using brightfield, UV-two photon excited fluorescence and second harmonic generation imaging, typically over a six-week duration. The images can be automatically classified with high reliability and precision and optimization services are available for industry. The combination of imaging modalities allows for the detection of initial crystallization conditions otherwise missed by visible only methods. Synchrotron services are offered by subscriptions to the Industrial Macromolecular Crystallography Association Collaborative Access Team (IMCA-CAT) beamline at the Advanced Photon Source and multiple other sources worldwide. Cryo-electron microscopy studies are carried out in-house on a Glacios 200 kV system with the latest Falcon IV detector. A dedicated sample handling and preparation facility is available, together with internal computing, in a purpose-built facility optimized for cryo-electron microscopy purposes. The HWI Research Services Group provides expert support to develop studies, implement experimental campaigns, and analyze data. Priority in the Cryo-EM Center and IMCA-CAT is given to industry, and industry practices are made available to academia in all Centers. Details can be found at https://hwi.buffalo.edu/research-services.

Whole Specimen Analysis of Lead Chalcogenide Nanostructure Morphologies: Implications for Alternative Energy Generation

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Abstract

Characterization of semiconductor nanoparticle (NP) morphologies is demonstrated using the Warren–Averbach (WA) method of powder X-ray diffraction. WA analysis provides crystallographic direction-dependent size distributions. It is as information-rich as electron microscopy, with the benefit of being applicable to a whole specimen. Lead chalcogenide NPs are characterized to demonstrate the analysis. The WA method reflects the homogeneity of quantum dots, differentiates the spheres and cubes from anisotropic morphologies, and distinguishes nanowires via the oriented attachment mechanism versus the solution–liquid–solid method.

CRYSTAL STRUCTURES OF LARGE-VOLUME COMMERCIAL PHARMACEUTICALS

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As part of a continuing project, the challenging room-temperature crystal structures of six commercial pharmaceutical APIs have been solved by Monte Carlo simulated annealing techniques using synchrotron X-ray powder diffraction data (11-BM at APS), and optimized using density functional techniques. **Merimepodib**, $C_{23}H_{24}N_4O_6$, crystallizes in $P2_12_12_1$ with a = 4.60827(2), b = 12.30400(14), c = 37.9583(4) Å, V = 2152.241(20) Å^3, and Z = 4. A new polymorph of **germacrone**, $C_{15}H_{22}O$, crystallizes in $C2/c$ with a = 26.0073(4), b = 9.84381(11), c = 10.53725(13) Å, β = 95.7525(11)°, V = 2684.06(4) Å^3, and Z = 8. **Baricitinib (Olumiant)**, $C_{16}H_{17}N_7O_2S$, crystallizes in $I2/a$ with a = 11.81128(11), b = 7.06724(6), c = 42.5293(3) Å, β = 91.9280(4)°, V = 3548.05(5), and Z = 8. **Cynarine monohydrate**, $C_{25}H_{24}O_{12}(H_2O)$, crystallizes in $P2_1$ with a = 13.88124(12), b = 15.36081(4), c = 5.59335(2) Å, β = 94.9763(4)°, V = 1188.158(6) Å^3, and Z = 2. **Fulvestrant (Faslodex) hydrate (ethyl acetate)**, $C_{32}H_{47}F_5O_3S(H_2O)_{0.16}(C_4H_8O_2)_{0.025}$, crystallizes in $R3$, with a = 23.39188(16), c = 16.50885(13) Å, V = 7823.08(7) Å^3, and Z = 9. **Omadacycline (Nuzyra)**, $C_{29}H_{40}N_4O_7$, crystallizes in $R3$ with a = 24.34424(9), c = 14.55217(5) Å, V = 7468.80(3) Å^3, and Z = 9. Other new structures may be discussed as they become available.

Structural study of two new hybrid layered double perovskites: $(C_6H_5CH_2NH_3)_2Ag_{0.5}In_{0.5}Cl_4$ and $(C_6H_5(CH_2)_2NH_3)_2Ag_{0.5}In_{0.5}Cl_4$

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Hybrid layered perovskites have been demonstrated to have a wide variety of interesting properties including ferroelectricity. Hybrid layered perovskites like those of the Ruddlesden-Popper (RP) homologous series ($A'_2A_{n-1}M_nX_{3n+1}$) are susceptible to structural distortions such as octahedral tilting, out-of-center displacement of metal cations, and ordering of dynamically disordered organic cations which can lead the polar structures needed for ferroelectricity. Many hybrid *n* = 1 RP phases containing Pb^{2+} or Cd^{2+} have been shown to be ferroelectric but when M^{II} is replaced with a 1:1 ratio of M^{I} and M^{III} (i.e., Ag^{+}/In^{3+}), compounds with otherwise identical compositions adopt centrosymmetric space groups.

We aim to understand this difference in affinity for polar structures by studying the crystal structures of $(C_6H_5CH_2NH_3)_2Ag_{0.5}In_{0.5}Cl_4$ and $(C_6H_5(CH_2)_2NH_3)_2Ag_{0.5}In_{0.5}Cl_4$ using laboratory powder x-ray diffraction, synchrotron powder x-ray diffraction, and single crystal x-ray diffraction. We make comparisons between the structures of these newly reported double perovskites and their single perovskite Pb^{2+} and Cd^{2+} derivatives focusing on: 1) the bonding environment of the metal cations and halide anions, 2) the octahedral tilting, 3) the hydrogen bonding between the organic cations and halide anions, and 4) the packing of organic cations.

Development of Operando Grazing-Incidence Pair Distribution Function for Analysis of Cobalt Oxide Water-Splitting Catalysts Under Electrochemical Bias

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Operando grazing-incidence pair distribution function (GIPDF) of molecular-domain water-splitting catalysts under electrochemical bias has great potential to give key insights on the mechanism of oxygen and hydrogen production. Of particular interest is amorphous cobalt phosphate formed through electrolytic deposition ("CoPi") which has shown respectable efficiency and self-healing properties at catalytic oxidative potentials. The structure of CoPi has previously been deduced using pair distribution function of a scraped-off film; however, the ability to understand the structure of the native film under electrochemical bias remains a challenge. To do so requires analysis of native ultrathin (<100 nm) films which can be fully biased without the significant impedance present in thick films. GIPDF offers excellent sensitivity for ultrathin films and fast acquisition times needed for operando experiments. Here is demonstrated a custom electrochemical cell design which allows for GIPDF to be performed on ultrathin CoPi films. The results presented show the ability of GIPDF to study CoPi films down to 30 nm thick, the thinnest first-row transition metal oxide film studied by GIPDF to date. Orientational analysis is also possible from a single GIPDF scan. Additionally, depth-dependence of CoPi films was accomplished by simply varying the incident angle of the incoming X-rays to distinguish the structure of the surface versus the bulk. Finally, a CoPi film under a layer of electrolyte solution can be resolved, allowing for future operando experiments under water-splitting electrocatalytic biases.

Synchrotron powder diffraction simplified: the high-resolution diffractometer 11-BM at the Advanced Photon Source

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Synchrotrons have revolutionized powder diffraction. They enable the rapid collection of high quality powder diffraction patterns with tremendous resolution and superb signal to noise. In addition, the high penetration and exceptional data sensitivity possible at high-energy light sources, like the Advanced Photon Source (APS), allow exploration of trace containment levels, in-situ sample environments and crystallographic site occupancies which previously demanded neutron sources. Despite all these advantages, relatively few scientists today consider using a synchrotron for their powder diffraction studies.

To address this, the high resolution synchrotron powder diffractometer beamline 11-BM at the APS offers rapid and easy mail-in access for routine structural analyses with truly world-class quality data[1]. This instrument offers world-class resolution and sensitivity and is a free service for non-proprietary users[2]. The instrument can collect a superb pattern suitable for Rietveld analysis in less than an hour, is equipped with a robotic arm for automated sample changes, and features variable temperature sample environments. Users of the mail-in program typically receive their high-resolution data within two weeks of sample receipt. The diffractometer is also available for on-site experiments requiring more specialized measurements.

This presentation will describe this instrument, highlight its capabilities, explain the types of measurements currently available, as well as recent significant improvements to the instrument's performance. We will discuss plans to improve access and the available sample environments and collection protocols. We are particularly interested in seeking input from potential users within the powder diffraction community.

More information about the 11-BM diffractometer and its associated mail-in program can be found at our website: http://11bm.xray.aps.anl.gov.

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Uncovering the adsorption mechanism of CO_2 on Ca-based layered double hydroxides using total scattering

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Abstract

Layered double hydroxides (LDHs) are bimetallic hydroxides arranged in a layered fashion where the difference in the oxidation states of the metallic cations creates a positive charge that is counteracted by the presence of hydrated anions in the interlayer space. LDHs are known for their high catalytic activity, density of exposed basic adsorption sites and potential for anion exchange. In addition, the identity of the metallic cations and anions determines the properties of each member of this family of materials, hence their relevance in several different industries, such as drug delivery, environmental remediation and waste water treatment, among others. Mg-based LDHs have been studied for decades as CO_2 sorbents for low-temperature carbon capture (CC) applications due mainly to their low cost and high surface area, however, the basicity of their adsorption sites has been deemed insufficient to achieve high selectivity and working capacity. Recent studies suggest that substituting Mg(II) for Ca(II) could enhance the basicity of the adsorption site without significantly increasing the energy penalty of the CO_2 desorption operation. This study aims at investigating the interaction mechanisms between CO_2 and Ca-LDHs under different environments, as a first assessment of their potential as efficient sorbents for CC. Here we present our preliminary results, where *ex situ* and *in situ* total scattering has been combined with thermogravimetric analysis (TGA) to assess the working capacity of $Ca_2Fe(OH)_6Cl.2H_2O$ and $Ca_2Al(OH)_6Cl.2H_2O$ as a function of relative humidity.

Data-Driven Extraction of Pair Distribution Functions from Complex Environments

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High-energy X-ray scattering, complemented by real-space analysis via the pair distribution function (PDF), is an indispensable tool in determining the local atomic structure of amorphous and nanoscale materials. While the application of PDF analysis to bulk systems is a mature field, there is burgeoning interest in extending its domain of application to more complex sample environments, such as thin films and dilute solutions, with an eye toward *in operando* measurements under realistic operating conditions. A central challenge to any such measurement is that the diffraction signal originating from the component of interest is typically buried beneath signal originating from the sample environment, which itself may be due to multiple, independent background components. Establishing robust and reproducible methods for reducing raw diffraction data from such measurements is critical to push the boundary of PDF analysis.

We present one approach toward achieving this goal, which exploits statistical information inherently encoded in the raw, azimuthally-integrated diffraction images, and extends the ad-hoc PDF data reduction algorithm utilized in the popular program PDFGetX3 [1]. By posing the (multi-component) background subtraction task as a rank minimization problem [2], we demonstrate, through simulations, that accurate PDFs can be reconstructed in a semi-automated fashion from noisy measurements, in which the desired scattering represents a small fraction of the total scattered intensity. Application to (i) studying the solvation structure of solutes in dilute solution and (ii) the *in situ* growth of nanoparticle thin films are presented.

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Anion redox in $Li_{5-x}Cu_xGaS_4$ triggered through Cu^+ cation in Li-ion battery cathode

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Abstract

To mee the increasing demand of Li-ion batteries (LIBs) for higher capacity and energy density, researchers are looking into combining both cation and anion redox in the new generation cathode materials. In this regard, for the first time, we have developed a Cu^+ containing quaternary chalcogenide cathode, $Li_{5-x}Cu_xGaS_4$, through a facile solid-state metathesis reaction and explored its potential as cathode material for LIBs. The cathode material showed reversible capacity of 200 mAh/g at a current density of 10mA/g. The spectroscopic studies (XANES and XPS) showed that the redox contribution for such huge capacity was provided by cation triggered anion redox process. The *insitu* diffraction studies show excellent structural stability through the electrochemical cycle. Further, the material was tested for fast charging applications and the results showed 75% of its initial capacity retention at a current density of 200 mA/g. In this presentation the details of synthesis, crystal structure analysis and spectroscopic investigation as a function of electrochemistry will be discussed.

The Structural Molecular Biology Program at the Stanford Synchrotron Radiation Lightsource

Silvia Russi and Aina Cohen representing the entire SSRL-SMB team
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The Structural Molecular Biology (SMB) program at the Stanford Synchrotron Radiation Lightsource (SSRL) provides an integrated suite of macromolecular crystallography (MC) and small angle X-ray scattering (SAXS) beam lines enabling studies on the most challenging problems in structural biology. Two state-of-the-art microfocus MC beamlines with exceptional brightness (BL12-1 and BL12-2) are equipped with high-frame-rate (100+ Hz) EIGER-16M pixel array detectors for rapid shutterless data collection using very small crystals and rapid shutterless-helical collection with longer crystals. All SSRL MC beam lines offer the option to collect data remotely using cryo-cooled crystals, including fully autonomous crystal screening, data collection and data processing. More recently, *in situ* crystallization and remote data collection schemes under humidity controlled conditions have been released that simplify crystal handling and transport at near-physiological temperatures. These tools avoid direct manipulation of crystals, support robotic sample exchange, and allow full rotational access of the sample in a controlled humidity environment. All MC beam lines support MAD and SAD data collection, including automated X-ray fluorescence scans around the metal absorption edges and software to optimize the data collection strategy. To monitor radiation damage and further support the study of metalloenzyme structure, BL9-2 includes a remote accessible single crystal UV-visible microspectrophotometer. Advanced data analysis tools provide rapid feedback during fast-paced experiments including support of serial diffraction techniques. We offer many options for training new users to our facility or to macromolecular crystallography. This includes our annual Rapidata hands-on training course: https://www-ssrl.slac.stanford.edu/rapidata/rapidata-2023/ Please visit our poster to learn more about training options and on how to become an SSRL user, or visit this webpage: https://smb.slac.stanford.edu/forms/becominguser/.

Similarities in instrumentation and software environments form the foundation of a synergistic relationship between the SSRL BL12-1 and the Macromolecular Femtosecond crystallography instrument (MFX) at LCLS, through a Gateway approach. The MFX instrument includes a highly automated goniometer setup for diffraction experiments, developed and supported by the SMB group. The experimental front-end is based on developments at SSRL and LCLS XPP to provide an efficient framework to carry out goniometer-based experiments using automated strategies tailored to handle a variety of sample requirements, crystal sizes and experimental goals. These developments coupled with improvements in data processing algorithms make it possible to derive high-resolution crystal structures at the LCLS XFEL using only 100 to 1000 still diffraction images.

Lattice Flexibility and Regeneration of Cu-Based Porous Coordination Pillared Layered Frameworks during CO_2 Adsorption

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Coordination pillared-layer (CPLs) metal-organic frameworks are highly porous compounds with functionalized ligands and flexible lattices that promote CO_2 adsorption. The functional units consist of pillar-ligands and layered sheets with the general formula $[Cu_2(pzdc)_2(P)]_n$ (pzdc = pyrazine-2,3 dicarboxylate, P = pillar ligands). These components create axially aligned pore-galleries along which gas transport and adsorption occurs. Novel CPLs can be synthesized by modifying the pillar structure, particularly by introducing a metallic cation to increase the electrostatic interaction between the pillar-ligands and quadrupole moment of CO_2 molecules. The chemical alteration can affect the flexibility of the crystalline lattice during cyclic gas absorption and regeneration. The evolution of lattice parameters in gas environments is particularly important in understanding the adsorption behavior of the CPL. We have used *in-situ* x-ray diffraction during CO_2 adsorption to probe the structure of the CPL variants $[Cu_2(pzdc)_2(Cu(pyac)_2)]_n$ ($Cu(pyac)_2$ = bis[3-(4-pyridyl)pentane-2,4-dionato]copper(II)), and $[Cu_2(pzdc)_2(bpy)]_n$ (bpy = 4,4'-bipyridine) with and without metals at the pillar ligands, respectively. Experiments were conducted using a laboratory x-ray diffractometer incorporating a specifically designed gas cell. The gas environment for these measurements was varied from ambient conditions to 50 atm of CO_2. The experiments measured the powder diffraction during initial activation, in the dehydrated structure under an inert environment of nitrogen or vacuum, and at 1 atm steps along the CO_2 gas pressurization ramp. The maximum lattice flexing is observed at 1-5atm CO_2 pressure. The initial results indicate that, up to 50 atm CO_2 pressure, there are structural changes that occur with minimal apparent structural hysteresis on desorption of CO_2 molecules. Further research is focused on enhancing diffraction data quality through effective dehydration and structural refinement of CPL compounds. The investigation of lattice flexibility of CPLs has the potential to provide industrial solutions to CO_2 capture and preventing greenhouse gas emission.

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Investigation of the Oxygen Uptake Behavior of $LnM^{2+}M'^{3+}O_4$

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Hexagonal layered $LnM^{2+}M'^{3+}O_4$ (Ln is a rare earth element, M and M' are transition metals) has been attracting great interest in materials chemistry and physics due to its unique crystal structure and high tunability in compositions. The oxidized form of $LnFe_2O_4$ was recently studied and synthesized at a low temperature (200 °C) to form $LuFe_2O_{4.5}$ (Fe^{2+} is oxidized into Fe^{3+}) and the oxygen uptake behavior suggested its potential as an oxygen storage material. Oxygen storage materials are interesting due to their numerous applications in chemical looping technologies. We previously synthesized Mn substituted version $LnMnFeO_4$ (Ln=Yb, Y, Lu) and found that they can also be readily oxidized into $LnMnFeO_{4.5}$. We performed synchrotron and neutron diffraction measurements and found that the structural transition from $LnMnFeO_4$ to $LnMnFeO_{4.5}$ are similar to the $LnFe_2O_4$ case. To further explore these types of materials, we newly synthesized a series of $LnM^{2+}M'^{3+}O_4$ and their oxidized phase $LnM^{2+}M'^{3+}O_{4.5}$ with different Ln, M, and M' elements ($ErMnFeO_4$, $LuMnFeO_4$, $LuMnGaO_4$, and $LuFeGaO_4$). The oxidation of synthesized $LnM^{2+}M'^{3+}O_4$ all led to a phase transition from *R-3m* to *P-3*. TGA measurements showed that the materials absorb oxygen by 1.7 – 2.5% at around 200 °C. We aim to gain deeper understanding on how Ln, M^{2+}, and M'^{3+} site elements impact the phase and structural transitions upon oxidation of $LnM^{2+}M'^{3+}O_4$ and their capability as oxygen storage materials by performing 11 BM synchrotron X-ray diffraction and neutron diffraction measurements.

Ligand binding remodels protein side chain conformational heterogeneity

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While protein conformational heterogeneity plays an important role in many aspects of biological function, including ligand binding, its impact has been difficult to quantify. Macromolecular X-ray diffraction is commonly interpreted with a static structure, but it can provide information on both the anharmonic and harmonic contributions to conformational heterogeneity. Here, through multiconformer modeling of time- and space-averaged electron density, we measure conformational heterogeneity of 743 stringently matched pairs of crystallographic datasets that reflect unbound/apo and ligand-bound/holo states. When comparing the conformational heterogeneity of side chains, we observe that when binding site residues become more rigid upon ligand binding, distant residues tend to become more flexible, especially in non-solvent exposed regions. Among ligand properties, we observe increased protein flexibility as the number of hydrogen bonds decreases and relative hydrophobicity increases. Across a series of 13 inhibitor-bound structures of CDK2, we find that conformational heterogeneity is correlated with inhibitor features and identify how conformational changes propagate differences in conformational heterogeneity away from the binding site. Our findings agree with models emerging from NMR studies suggesting that residual side chain entropy can modulate affinity and point to the need to integrate both static conformational changes and conformational heterogeneity in ligand binding models.

Title: Sub-50 Microsecond Time Resolved SAXS at BioCAT

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Abstract: Time resolved SAXS (TR-SAXS) allows the measurement of kinetic intermediates after an initiating event. The BioCAT beamline (Sector 18) at the Advanced Photon Source uses chaotic and laminar flow microfluidic mixers to measure time ranges from ~45 us to 1.5 s. Recent advances include: new mixer designs to optimize accessible time ranges and sample consumption; improved microbeam focusing and mixer fabrication techniques to reduce parasitic scattering; improved positioning and exposure triggering for optimal reliability; and a new, easy to use GUI for controlling all aspects of the experiments. These advances have significantly improved data quality and ease of use. Time resolved experiments can now be done with as little as ~200 uL of sample at modest concentrations for slow (>1 ms) reactions, whereas ultra-fast time resolved measurements can be done with as little as ~1 mL of sample. The TR-SAXS program at BioCAT is open to general users. Supported by NIH: P30 GM138395.

Improved sample preparation and mounting for fixed target serial synchrotron crystallography

Tim Sweeney, MiTeGen

In the last decade, a wide array of sample preparation and delivery technologies have been demonstrated for XFEL- and synchrotron-based serial crystallography. Drawing upon this work, we have developed an integrated system that addresses key issues in serial crystallography in a robust way while maintaining flexibility required to address diverse real-world crystal handling challenges [1]. The key elements of this system are: (1) sample supports incorporating microfabricated thin films that are fully compatible with existing infrastructure for high-throughput cryo-crystallography including SSRL-developed in-situ crystallization plates [2], allow efficient removal of excess surrounding solvent and positioning of microcrystals at particular locations, generate ultra-low-background scatter while allowing easy optical imaging, and allow both room-temperature data collection and rapid cooling for cryogenic data collection; (2) a sample loading station that allows easy dispensing and subsequent removal of liquid (e.g., ligand- and/or cryoprotectant-containing solutions, buffer to facilitate dispersing or positioning crystals) from the sample supports via precisely controllable time-varying suction; and (3) a humid "gloveless" glovebox for crystallization tray manipulations, crystal soaking, and sample support loading and sealing that, unlike commercial humidity chambers, can generate and maintain the near saturating humidities (>95% r.h.) required to maintain microcrystals at their as-grown hydration and maximize crystal isomorphism while maximizing allowable working times. This system's ease of use, flexibility, and optimized performance make it attractive not just for serial microcrystal crystallography but also for routine single- and few-crystal data collection.

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Development of a Monte Carlo Algorithm for Improved Analysis of Multi-Angle EDXD Measurements

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The analysis of amorphous structural data collected with multi-angle energy dispersive X-ray diffraction (EDXD) requires an estimation of the primary beam energy spectrum to normalize diffraction collected at different 2θ angles. At sector 16-BM-B of the Advanced Photon Source, the primary beam is estimated from the highest 2θ angle under the assumption that the associated data is devoid of structural features, which is not always the case. To improve the accuracy of structural data collected at 16-BM-B, a Monte Carlo algorithm was developed that optimizes the primary beam estimation based on an initial guess from the spectrum at the highest 2θ diffraction angle. The initial guess is then refined through statistical and physics-based constraints. The algorithm was validated using molten iron at 3.3 GPa as well as SiO_2 at ambient state and demonstrated minimal invasiveness for properly normalized data as well as the ability to optimize poor initial primary beam estimations. Future development includes investigating additional physics-based constraints to improve the compatibility of the algorithm with lower-Z materials such as amorphous polymers. The implementation of the algorithm at 16-BM-B will allow users to analyze amorphous scattering data with higher levels of accuracy, reducing the need for excessive data corrections.

Time-Resolved X-ray Diffraction Studies of Al-Ni Combustion Synthesis Reactions

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The self-propagating high-temperature synthesis (SHS) of intermetallic compounds is promising for the production of high-temperature structural materials for industrial applications. Typically, SHS reaction products are the result of multi-step processes. The initial combustion reaction, which is usually complete after sub-seconds, is followed by a slower precipitation reaction. The rapid reaction rates challenge the characterization of the phase transformations and kinetics through direct methods like in-situ X-ray diffraction. The observation of the reaction has the following requirements:

1. High-energy x-rays for penetration into the bulk of materials, which are typically pellets >5 mm in diameter.
2. Total scattering captured by an area detector to allow for pair distribution function (PDF) analysis of highly disordered intermediate states.
3. Single photon counting detector for high-energy x-rays to capture all the phase transformations during the fast-kinetical processes.
4. The high flux of a synchrotron dedicated to high-energy x-rays.

A method for studying the phase transformation kinetics of in-situ SHS reactions at beamline 11-ID-C at Argonne National Laboratory's Advanced Photon Source was developed, using the PILATUS 2M CdTe detector to achieve the necessary time resolution. The new experimental setup was tested using Al-Ni as a model system. The preliminary analysis of the first results will be presented here.

Make selenium reactive again: Activating elemental selenium for synthetic optimization of various selenium containing compounds

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The relatively low reactivity of selenium has been an obstacle in the synthesis of selenium-containing materials at low reaction temperatures. Over the years, several recipes have been developed to overcome this hurdle, however, most of the developed methods have been associated with the use of highly toxic, expensive, and environmentally unfriendly reagents. As such, there has been an increasing quest for the design of cheap, stable, and non-toxic reactive selenium precursors usable in the synthesis of low-temperature transition-metal selenides with vast applications in semiconductor nanocrystals, thermoelectrics, and superconductors. Herein, a novel synthetic route has been developed for activating elemental selenium using a low-temperature solvothermal approach and characterized by 1-D and 2-D ^{77}Se NMR, Raman spectroscopy, infrared (IR) spectroscopy, and gas chromatography-mass spectrometry (GCMS). Temperature-dependent selenium dissolution rate and the activation energy of the resultant solution are experimentally assessed. The activated Se solution contained coexisting HSe^- and Se^{2-} ions, as well as dialkyl selenide (R_2Se) and dialkyl diselenide (R-Se-Se-R) species in the dynamic equilibrium to each other. The as-synthesized selenium solution was used to demonstrate the successful synthesis of (i) CdSe nanocrystals with different particle sizes; (ii) polycrystalline room-temperature modification of thermoelectric material, β-Ag_2Se; and (iii) the single crystals of superconducting β-FeSe. The latter ones were for the first time grown from solution. The properties of the produced transition-metal selenides were assessed by combining different spectroscopic, microscopic, and diffraction techniques.

PIONEER: a single-crystal neutron diffractometer for small samples at the Second Target Station, ORNL

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PIONEER is a single-crystal neutron diffractometer currently being designed for the Second Target Station (STS) at the Spallation Neutron Source, Oak Ridge National Laboratory. Because of the high cold-neutron flux enabled by the compact STS moderator and advanced neutron optics, PIONEER will allow scientists to study tiny crystals (0.001 mm^3) and ultra-thin films (10 nm), which are comparable to those typically used for x-ray studies but not feasible at existing neutron diffractometers. Here, we will present an update on the instrument development and show the neutron optics design that allows high-flux, high-uniformity beam transportation and reduces background. To achieve this, PIONEER will take a kinked beamline geometry with two sets of Montel mirrors (also known as nested KB mirrors) and a virtual source in between. This design helps reduce the background by moving the sample out of the direct line of sight to the moderator and provides a method to tune the beam size at the sample position. We will present Monte Carlo ray-tracing simulation results to show the beam transport performance and demonstrate PIONEER's capabilities for measuring small-volume samples.

In addition to measuring small-volume samples, PIONEER will enable a high-resolution mode to study large unit-cell crystals and a polarized incident beam option for measuring weak magnetic signals and complex magnetism. A variety of sample environments will be enabled, including high/low temperatures, high magnetic fields, and high pressures, which will assist researchers in accelerating materials discovery to address energy and environmental challenges.

Hybrid Pixel Array Detector for Time-resolved and Fine Slice Measurements with 56,000 fps Sustainable Frame Rate

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It has been more than ten years since HPAD (Hybrid Pixel Array Detectors) had been widely utilized as X-ray diffraction and imaging detectors. Thanks to its single photon counting capability, HPAD shows images without background noise and wide dynamic range. Due to limitations of the fabrication process, most HPADs are made with monolithic sensor and tiled readout ICs. In conventional HPAD, there were so-called “inter-chip pixels” on the edges of readout ICs. These inter-chip pixels have 1.5 times or wider width and/or height than non-inter-chip pixels. This means, we are losing position information of a hit of photons on those pixels.

We have successfully dealt with this inter-chip pixel problem by use of re-distribution layer on the Silicon sensor. So, in our new detector, non-uniformity in a single sensor module is eliminated.

This new detector is designed based on UFXC32k IC [1] designed by AGH University of Science and Technology and named XSPA-500k [2]. XSPA-500k detector consists of 16 UHXC chips tiled and 1024 x 512 76 um sq. pixels per module. No inter-chip pixels in between ROICs which terribly suffer the image quality.

XSPA-500k is aiming not only for X-ray imaging but also for time-resolved X-ray measurements. Dealing with “inter-chip pixels” is our main feature for imaging, and for time-resolved measurements we understand that frame rate is as important as the size of the pixels and the area of the detector. Thanks to UFXC32k IC’s high count-rate and fast operation capability, combined with our high data throughput backend circuits, XSPA-500k is capable of up to 56,000 fps with full-frame readout and 100,000 fps with 100 lines ROI in the center of the modules with continuous exposure (zero-deadtime mode operation with 2-bit counter/pixel.) If the non-continuous exposure (burst-mode operation [3]) is allowed, it can achieve over 970,000 fps with approximately 2 % duty ratio.

Index Terms— Hybrid Pixel Array Detector, Inter-chip Pixel, Time-resolved X-ray Measurement

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Negative thermal expansion in metal-organic frameworks tuned by node distortion

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Negative thermal expansion (NTE) behavior, or shrinking under heating, is an unusual property found in some metal-organic frameworks (MOFs). The mechanism of NTE in MOF has been described as an analogue to the mechanism for some simpler systems as the low-energy vibration of the framework. Using in situ X-ray total scattering, by powder x-ray diffraction and pair-distribution function analysis, we investigated the structure evolution of a series of Zr based MOFs, NU-1000, with various capping ligands (H_2O/OH, Cl^-, formate, acetylacetonate, and hexafluoroacetylacetonate) on the Zr_6O_8 node. The distortion of the node in these NU-1000 depends on the capping ligands and contributes to the NTE of the MOFs. The multivariate analysis further confirms the high correlation between the node distortion and NTE. These results suggest that the node distortion can be a different mechanism in the NTE of MOFs, and propose a new method to control the long- and short-range order of MOFs by local structure modification.