



The **SER-CAT SPECTRUM**

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Director's Message

Bi-Cheng Wang

Welcome to the July 2009 issue of *The SER-CAT Spectrum*. This issue reports relevant news on SER-CAT's recent advances, developments and activities.

An important milestone on SER-CAT's beam time allocation scheme will take place soon. Following the SER-CAT Board's desire to further advance remote access capabilities, the staff will soon begin implementing beam time allocations in optional 12-hour shifts in the fall run on 22ID upon request. The 22BM line will begin the optional scheduling in the winter run. New staff will be hired to assist with remote data collections during the evening hours.

The harmonic contamination problem on 22ID is now resolved for X-ray wavelengths up to at least 2.3Å. The SER-CAT staff will be happy to help with your data collection using longer wavelength X-rays. Please encourage your colleagues to try Sulfur-SAD data collections on SER-CAT 22ID.

The MD2 microdiffractometer has been ordered and is scheduled for installation during APS' 2009 winter shutdown period if the equipment's software tests out satisfactorily. We look forward to having this new hardware in place soon.

There are other developments/advances at SER-CAT reported in this issue. Thanks to Gary Newton, *Spectrum* Editor, this issue of the *SER-CAT Spectrum* introduces a modified format that focuses on particular areas of achievement and/or expertise. The major category (in addition to the normal titles) includes SER-CAT SPOTLIGHT, USER OPINION, SER-CAT ADVANCES and GOOD TO KNOW... for example.

My wish is that you are all having a wonderful summer and that you enjoy reading this issue of *The SER-CAT Spectrum*. If you have any questions or suggestions on how we may facilitate your research efforts at SER-CAT, please feel free to send comments to kmorris@BCL4.bmb.uga.edu.

SER-CAT Meeting at ORNL

SER-CAT's next research symposium and board meeting is scheduled for March 19-20, 2010 at ORNL and will be hosted by Dr. Leighton Coates. Please mark your calendars with these important dates. More information will be provided as it becomes available.

Longer Wavelength on 22ID

John Chrzas

The vertical focusing mirrors on both 22ID and 22BM provide harmonic rejection for the delivered x-ray beam. The monochromator crystals allow higher energy harmonics to pass through, as well as the desired energy. These higher order harmonics are then rejected by critical angle reflection from the mirrors which is related to the square root of the density of the mirror coating material. For a given mirror angle (nominally 3.5 mrad) this rejection energy can be changed by translating the mirror to a different coating material; each mirror has 3 coatings: platinum, palladium and glass. Recently, a problem with the mechanical system that provides this lane selection on the 22ID mirror was discovered and repaired. The experimental envelope for 22ID can now be extended to a wavelength limit of 2.3Å. Crystallographic data collection has shown no harmonic contamination for experiments using 2.3Å x-rays. Studies have indicated that the monochromator requires ~ 1 hour to thermally stabilize below 2.0Å. The thermal problem is caused by scattered power from the first monochromator crystal. When the monochromator is optimized for low energy work, the second crystal assembly is more-or-less directly under the first crystal, which maximizes the scattered power absorbed by the second crystal assembly. The system also needs time to recover from low energy work, so a new policy will be implemented to require users performing low energy studies to move the monochromator back to 1Å one hour before their beam time ends to restabilize the system for the next user.

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Sixth Annual SER-CAT Symposium at UAH

Gary Newton

The 6th Annual SER-CAT Symposium was hosted by the University of Alabama in Huntsville (UAH) and held at the Shelby Center for Science and Technology on the UAH Campus. Prof. Joseph Ng (UAH) was the primary organizer and coordinator for this symposium; we are very grateful for his efforts for this meeting. Similar to previous meetings, the overall theme was “Interesting structures, methods and advances in SER-CAT facilities” and it attracted over 50 participants (see group photograph) mostly from the southeastern US. This symposium showcases the diverse and often outstanding science emanating from the use of the SER-CAT facility, and this year’s meeting was no exception.

After welcoming remarks by Prof. Joseph Ng and UAH President David Williams, the morning program began with a talk by Prof. B. C. Wang (University of Georgia) who emphasized developments at SER-CAT in sulfur-SAD phase determination. In particular, SER-CAT has embarked on a program of longer wavelength ($\lambda > 1.5\text{\AA}$) beamline optimization, as well as software development for data collection with enhanced signal-to-noise ratio. B. C.’s presentation was followed by a talk by Prof. Liqing Chen (UAH) who spoke about a successful S-SAD phasing of *Penicillium expansum* lipase using 1.9\AA wavelength data collected at SER-CAT 22ID beamline. The next presentation by Stephen Tomanicek (Neutron Scattering Sciences Division, ORNL) presented structural insights into the substrate recognition by the FEN-1 family of enzymes. The final talk in this session was presented by Ying Zhang (Georgia State University) on the structural perspectives on HIV-1 protease drug resistance, a major problem in development of HIV/AIDS treatments.

The keynote speaker, Dr. Richard Myers (Director and President, Hudson-Alpha Institute for Biotechnology, Huntsville, AL), provided a very interesting discussion of his Institute’s efforts directed towards a global genomic approach to human biology and disease. The next talk by Prof. Zhi-Jie Liu (Institute of Biophysics, Chinese Academy of Sciences, Beijing, China) discussed methylation-assisted crystallization of protein molecules. Methylation of lysine residues in a nuclease protein resulted in successful production of crystals which diffracted to 1.2\AA resolution. The last speaker in the morning session, Dr. Marc Pusey (Extremozyme Inc., Huntsville, AL), discussed protein crystallization screening using fluorescence anisotropy. An instrument has been assembled to test the “Fluorescence-based Analytical Crystallization Technologies” (FACT); a high success rate was reported from studies thus far.

Following lunch, eight poster presentations, primarily by students, were held in the lunch room lobby. These posters were judged, and two poster prize winners were announced at the dinner reception held that evening. The winners were Miranda L. Byrne-Steele (UAH) and Rosanna Robertson (MUSC).

The afternoon session began with the presentation of the Young Investigator Award to Guoxing Fu (Georgia State University) from Prof. Irene Weber’s laboratory. Mr. Fu’s award presentation described his work on the structural basis for substrate specificity of executioner caspases. The Outstanding Science Award was presented to Dr. James Hurley (Laboratory of Molecular Biology, NIDDK). Dr. Hurley was unable to attend the symposium, but fortunately his associate at NIDDK, Dr. Hyung Ho Lee, attended and accepted the award on his behalf and presented a talk on the selected work. The lecture discussed mid-body targeting of the ESCRT machinery by a non-canonical coiled coil in CEP55.

Next, Prof. Alena Fedarovich (MUSC) discussed the challenges in the structure determination of the penicillin binding protein A from *Mycobacterium Tuberculosis*. Then, Dr. Zhi-Qing (Albert) Fu (University of Georgia / SER-CAT) described the results of some control tests that were run on data collected at random times at SER-CAT 22ID to search for a diagnosis of higher-than-expected HKL2000 spatial χ^2 ’s. Dr. John Chrzas (University of Georgia / SER-CAT) then described efforts to provide “Light When YOU Need It” to the SER-CAT membership by designing and implementing a virtual synchrotron. Over the last two years or so, the goal of providing a completely automated remote access beamline is very near realization. Next, Dr. Richard Walter (Shamrock Structures LLC) addressed beamline efficiency. In his opinion, based on his experiences, SER-CAT automated crystal mounting and screening implementations are the best that he has encountered. Lastly, Dr. Mark Beno (APS) described new opportunities for macromolecular research from the planned APS renewal. Innovations at APS in instrumentation, X-ray optics, and X-ray sources could generate orders-of-magnitude improvements in sensitivity and precision, as well as deliver new capabilities for enabling experiments that may not be performed today.

In the evening, a Dinner Reception, held inside the U.S. Space and Science Rocket Center, provided an excellent dinner that was enjoyed by all. In addition, we could wander throughout the Rocket Center to view the various excellent rocket and space exhibits. After dinner, former astronaut, Dr. Owen Garriott, gave us a very entertaining and informative talk about his (and his son’s) adventures in space. Dr. Garriott was one of six scientist-astronauts selected by NASA in 1965. He set a world record for duration of 60 days aboard Skylab in 1973 and later was aboard Spacelab-1 in 1983. Dr. Garriott held several positions at the Johnson Space Center. In 1986, after leaving NASA, he has held various important consulting and space industry positions and has received many honors and awards.

EDITOR’S NOTE: SER-CAT thanks the University of Alabama in Huntsville, Laboratory for Structural Biology, Student Volunteers, Department of Biological Sciences, US Space Rocket Center, the Beville Center Catering Service, Marriott Huntsville and GARLIC expressions® for their sponsorship and Prof. Joe Ng and his Organization Committee, Diana Toh and Sheila Fore-Williams, for another outstanding meeting! SER-CAT also thanks all the speakers and attendants for their strong participation and support.



The SER-CAT Outstanding Research award was won by Dr. James Hurley (NIDDK). Receiving the award in Dr. Hurley's absence is an associate from NIDDK Dr. Hyung Ho Lee who also presented a talk on the scientific work which led to this award.



The SER-CAT Young Investigator Award is presented to Mr. Guoxing Fu (GSU) by Prof. B.-C. Wang. Mr. Fu is a student in Irene Weber's lab at GSU.

Pictured below:
Participants in the Sixth Annual
SER-CAT Symposium at UAH



SER-CAT SPOTLIGHT



Studies on IS200/ IS605 Family DNA Transposases

Fred Dyda, NIDDK

Using X-ray diffraction data collected in part at the SER-CAT beamline ID22, we have shown that members of this family of DNA transposons move from one genomic location to another by an unusual asymmetric mechanism that relies only on single stranded DNA. The transposase enzyme, encoded by the transposon, is a member of the HUH nuclease superfamily that uses an active site tyrosine to cleave DNA and to form a 5' phosphotyrosine intermediate. The key to the recombination reaction is a large scale movement of a helix that carries with it this covalent intermediate formed as a result of the cleavage of one end of the transposon DNA so that it can be resolved by a 3'OH DNA end that was generated by a similar cleavage reaction at the other transposon end. Another key feature of the system is that it selects its target, the genomic location where the transposon is integrated at the end of the transposition event, site specifically. This clearly distinguishes the IS200/IS605 family from many other well-studied DNA transposition systems that tend to integrate randomly or with only slight target sequence preferences. A major surprise of our work is the realization that target site selection is achieved by base pairing interactions between the target site sequence and an internal sequence of the transposon. As the only role of this internal segment appears to be in target site selection, the possibility arises that by mutating this internal segment, the transposon could be redirected to a new pre-selected target site. Preliminary data both in vitro and in vivo indicates that this is indeed the case, suggesting that these systems may find very important applications in biotechnology and also in medicine.

Editor's Note: For additional information, go to:

<http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pubmed&pubmedid=18243097>

USER OPINION

My Second Most Favorite Beam Line in the World

Richard L. Walter, Shamrock Structures

I was originally going to call this piece, “The Second Most Powerful Beam Line in the World”. However, I quickly realized that those persons who are more exacting, quantitative, and pure in their use of scientific language than I would call upon such physical concepts as brilliance and calculated flux densities to prove this statement incorrect and would write me to this end (or corner me at some meeting) to discuss the optics of other beam lines. So, at least “favorite” is an opinion, and, outside of the kind of dictatorial worlds to which I am accustomed, an opinion can’t be wrong, right?

So why is 22BM my “second most favorite” beam line in the world? In short, efficiency, reliability, and ease of use. It is true that I too prefer the 0.5 – 1 second/degree maximum exposure times that we routinely use on 22ID over the 4 – 10 second/degree exposures that we typically use to achieve similar results on 22BM. However, competing with the obvious benefits of such beam line muscle for my affections are the new and improved methods and protocols available each time I use 22BM that speed up that time between collecting data sets. Muscle is good, but stamina has its place too!

Beam line efficiency these days is truly defined by things other than the time spent collecting the actual diffraction data. With short detector read out times, efficient data flow management, etc. if you cannot get your actual data set in 10 - 15 minutes then you are either not working on a truly “modern” beam line or you have a really challenging project and not the kind of “rote” that is our typical fare. So, in the end, to me, living a life where I need to collect a lot of data but also need to screen a lot of crystals, the true measure of beam line efficiency is how the dead time between collecting the actual data sets is spent.

Handling this overhead or “dead” time is where 22BM excels. In truth, we could think about putting 22BM and 22ID into the same category here because, as many of you know, I believe that SER-CAT has the luxury of the fastest, most-reliable automounters found anywhere on the planet, and both lines have essentially the same automounters. However, this is old news at SER-CAT and the staff makes automounters seem so easy (which they are not).

What I want to focus on, instead, is the brilliant and creative, yet so elegantly simple thinking that has gone into generating and continually improving the software controls that handle this efficient hardware. The beam line controls at SER-CAT in general are among the best in the world. I know. We all have our stories about when SER-GUI hung up and the impact that it had on our experiments. However, overall, over the long haul, this

software gives SER-CAT users more flexibility and real control of their experiments at a level of intuitive ease of operation that simply is not available elsewhere. And it is a vibrant and ever growing and improving entity.

The continual stream of new and improved SER-GUI versions that roll out routinely on 22BM push the envelope with each incarnation. I never cease to be amazed when I walk into the area and John [Chrzas] says, “you got a second, Rick?” and he walks me over and sits me down to some new way that he has implemented automation and stream-lining of those dead time activities.

True, I do worry that I continue to discuss issues that really are not all that important to the average academic scientist. Not to perpetuate the stereotype, but I realize that many of the readers of this are not seeking to collect the 50th – 60th complex data sets on tired old kinase Y. However, at least some of you are. But, even if that is not your “shtick”, and you are instead working on the structure of the entire cell in crystalline form, you at least will probably have need to look at a lot of crystals in order to achieve your goals (because we all know how variable those samples of crystalline cell are!).

Efficiency of sample handling is as important in these cases of truly challenging, cutting-edge projects as it is to the “molecular replacement crystallography”. This is where I would challenge you to open your minds to the possibility of the impact of automated methods even to your highest science. Not only are sample changing, centering, and even initial indexing (and “strategizing”) being reduced to their most efficient form at 22BM but also even the philosophies of how we collect data are being challenged by the new software developments that are being implemented and tested by John on the line. Efficiency means more samples examined, and this can impact anybody’s work.

And, for the most part, these new implementations are not going to result in your wasting significant amounts of your still precious and limited beam time. John’s upgrades don’t get implemented until they truly work. Sometimes they are not as efficient or intuitive to your way of thinking as you would like (I mean, he is a physicist, so you can’t expect him to think the way that we do ALL the time!). However, they always work, or they don’t get implemented (or quickly get “de-implemented”)...and he does listen to feedback. Plus, there is a failsafe. If you don’t like or feel comfortable with the fully automated methods, if they are not resonating with you, you can always switch back to doing everything “the old-fashioned way”. Though, I have been around long enough to know that the base beam line controls and sample management at SER-CAT are about as old-fashioned as I am an eighty pound ballerina.

The point of all this: if you have not tried 22BM lately, do so. I mean REALLY try it, including using the automation that is being developed. Your feedback will help the CAT continue to develop in a way that gets your home institutions the most for your annual dues. Plus, it will keep the facility where it belongs...as one of the cutting edge, most innovative and vibrant

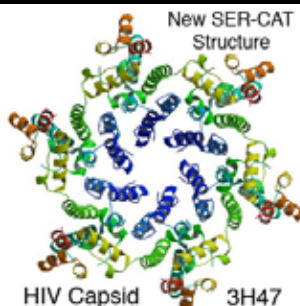
beam lines available on the planet...and this leads to what we all are most interested in, leading on the forefront of cutting edge science and results generation. SER-CAT is a wonderful tool and 22BM is a linchpin in the development of the coming generations of that tool.

In truth, I do struggle a bit with classifying 22BM as my "second favorite". In fact, owing to its higher efficiency in handling those onerous "dead time" functions whose imposed delays do truly frustrate me because I fancy them to be the true limiting factor in how much data I can collect during my assigned slots, it may be my favorite. However, like many of you, it is hard to argue against the merits of a line like 22ID where we HAVE to throw X-ray flux away and, therefore, are never "losing time" in data collection. So, I guess until I take the time to do the actual efficiency analysis, I will continue to go with my gut and call 22BM my second favorite...though it is a nice problem to have, trying to decide which of your two most commonly used beam lines is your favorite and which is your second favorite in the world!



Pictured in the photo above (taken at 22ID) are (on left) Steven J. Schiltz (CEO), (center) Gina M. Ranieri (X-ray data collection Team Leader), and (on right) Richard L. Walter (CSO).

Rick Walter is the CSO of Shamrock Structures LLC. Shamrock is a small, privately owned gene-to-structure CRO based just outside of the Argonne National Lab with significant experience in high volume X-ray data collection for the pharmaceutical industry. More detailed information may be found at www.shamrockstructures.com.



GOOD TO KNOW... Silver Bullets Can Generate Protein Crystals



Bob Cudney
Hampton Research

Structural biology has experienced an accelerating rate of progress in the crystallographic analysis of biological macromolecules. Breakthrough discoveries, together with subtle yet very significant refinements in established methodologies in molecular biology, protein chemistry and crystallography, have ushered structural biology into a golden age. At the crystallographic cornerstone rests crystallization. Often crystallization is referred to as the linchpin and bottleneck, since only about 20% of purified proteins on average do crystallize and produce a structure. Perhaps, due in part to the fantastic diversity of the biological macromolecular population, a global solution or home run has not yet been achieved that will win the crystallization game for all proteins. Presently, swinging-for-the-fence methods are proving incapable of addressing the more intractable crystallization problems. More games have been won on singles than home runs. Similarly, the crystallization game can often be won by employing a portfolio of innovative alternative strategies.

One such alternative strategy, which we have been developing for a number of years now, is based on the idea of identifying conventional and biologically active small molecules that promote crystallization. For decades, the crystallographic community has observed mysterious small molecules in the crystal structures solved by X-ray diffraction methods. Obviously, additives that have a rational biochemical basis are explainable, but there are numerous reports of buffers, precipitants, cryogens, ions, lipids and unexpected small molecules appearing bound and unbound in structures. Our working hypothesis is that various small molecules might establish a positive influence on crystallization by perhaps altering the relationship between the surfaces of the macromolecules as well as perturb or stabilize solvent interactions. Or they may stabilize macromolecular structure or conformation and even play an active role in the crystal lattice.

To simplify screening through the vast array of small molecules for the silver bullet additive essential for crystallization, we formulated combinatorial cocktails of small molecules and evaluated them in simple polymeric and salt-based crystallization reagents at various levels of pH. In addition, including every component in two or more cocktails largely overcomes the risk that any one component might have a deleterious effect

Continued on page 7 right...

SER-CAT ADVANCE

Automated DENZO/SCALEPACK-based data reduction

John Rose

During the past year, Zheng-Qing (Albert) Fu has developed a simple, command line driven, fully automated data reduction pipeline based on the popular DENZO/SCALEPACK program package (HKL Research, Inc.), the CMDDENZO program. The program is aimed at providing a tool to quickly process and characterize a data set providing such parameters as space group, Rmerge, completeness, redundancy, I/ σ I. It is intended for the novice or infrequent user and is not intended to match the expert use of HKL2000, DENZO or SCALEPACK or for the processing of challenging data sets.

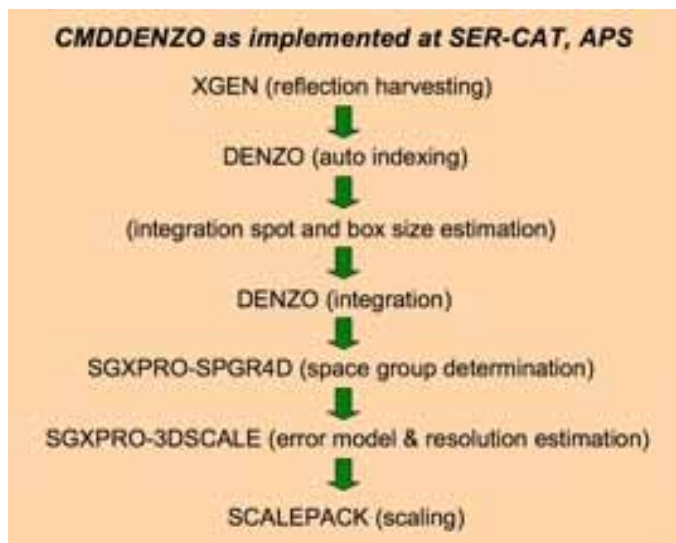


Figure 1. The CMDDENZO workflow.

The CMDDENZO workflow is shown in Figure 1. Reflection harvesting can be carried out by either XGEN (default) or d*TREK (using the -g cmdtproc.py flag). The harvested reflections are used to index the crystal and estimate crystal mosaicity using DENZO. The profiles of the harvested reflections are also used by CMDDENZO to estimate and refine the DENZO integration box and spot size parameters. The data set is then integrated using DENZO. Based on the distribution of integrated intensities, the space group(s) is determined using the program SPGR4D running within the SGXPro workflow. Prior to scaling an error model and an estimate of 'real' resolution of the data set is generated using 3DSCALE running within the SGXPro workflow. The data set is then scaled using SCALEPACK.

CMDDENZO, developed in C++, exploits functions of various programs used in data reduction. It carries out inter program communication, collects needed parameters and calculates required program input (e.g. the DENZO integration box parameters).

To index, integrate and scale a data set the following command is used:

```
>>> cmdddenzo mar300 u u scalesad image_1.0001 900
```

Here 'mar300' indicates the data was collected on 22ID, the first 'u' indicates that the lattice type is unknown, the second 'u' indicates that the space group is unknown, 'scalesad' indicates that a SAD data set containing Bijvoet pairs will be produced, 'image_1.0001' indicated that this is the first image to be processed and '900' is the number of images to be included in the processing run. The CMDDENZO output summary is shown in Figure 2 below.

```

Lattice  Distortion  Symmetrized UnitCell
P23      27.73%      88.53 88.53 88.53 90.00 90.00 90.00
I23      40.65%      134.40 134.40 134.40 90.00 90.00 90.00
F23      42.13%      170.83 170.83 170.83 90.00 90.00 90.00
R3       14.39%      157.19 157.19 157.19 23.85 23.85 23.85
P3       13.60%      57.77 57.77 150.03 90.00 90.00 120.00
P4       0.03%      57.77 57.77 150.03 90.00 90.00 90.00
I4       6.41%      57.77 57.77 310.97 90.00 90.00 90.00
P222    0.01%      57.74 57.80 150.03 90.00 90.00 90.00
C222    0.03%      81.69 81.72 150.03 90.00 90.00 90.00
I222    6.41%      57.74 57.80 310.97 90.00 90.00 90.00
F222    6.41%      81.69 81.72 310.97 90.00 90.00 90.00
P2       0.00%      57.74 150.03 57.80 90.00 90.02 90.00
C2       0.02%      81.69 81.72 150.03 90.00 90.01 90.00
P1       0.00%      57.74 57.80 150.03 90.01 90.00 90.02

<<< Cmd DENZO AutoIndexing Solution >>>
ImageFile: thaun_01030_1_1.0001
PossibleSolution: P4
IndexDistortion: 0.03%
UnitCellABC: 57.770 57.770 150.030
UnitCellAngles: 90.00 90.00 90.00
Mosaicity: 0.129
Estimated Lowest Highest Resolutions: 50.0000 1.4524

<<< Cmd DENZO Integration >>>
ImageFile: image_1.0001  NumberOfFrames= 900
Lattice ID: P4
Number of consecutive frames: 900
... SPGR4D Spacegroup Determination ... Please wait ...
... LogFile = /home/image_1_0001_s.log ...

... SPGR4D spacegroup determination done ...

Under the lattice type used at the auto-indexing and integration,
SpaceGroup 'P43212' will be used in scaling.

<<< SCALEPACK Scaling >>>
ImageFile: image_1.0001  NumberOfFrames= 900
--- 1st pass done ---
--- 2nd pass done ---
--- 3rd pass done ---
--- all done ---

Effective Resolution Range in Reduced Data: 50.0000 1.4500
Rmerge: 0.0390 [ 0.0280, 0.0890]
Redund: 6.00 [ 6.50, 2.60]
Complt: 96.90 [ 99.20, 74.60]
I/SigI: 89.91 [ 190.34, 13.96]
Chi^2: 1.67 [ 1.31, 1.84]

```

Figure 2. The Output summary for the above CMDDENZO data processing run.

CMDDENZO can also be used to quickly (under a minute) to see if the crystal is indexable.

>> **cmdddenzo mar300 u u index image_1.0001 1**

Here 'index' indicates that the only indexing will be carried out using reflections harvested from a single image. The output is the DENZO indexing table, possible lattice, index distortion, unit cell parameters and an estimate of the data resolution as shown in Figure 2. If three or more images are used, an estimate of the crystals mosaicity is also given.

In addition to CMDDENZO, Dr Fu has also developed the automated data reduction pipeline CMDXDS that uses a multi-processor version XDS (xds.mpimf-heidelberg.mpg.de). Users collecting data at SER-CAT are encouraged to test out these tools. For more information about CMDDENZO and CMDXDS at SER-CAT please contact Dr. Fu (fuzq@anl.gov).

PDC at UGA

John Rose

The 67th Annual Pittsburgh Diffraction Conference will be held from October 29-31, 2009 at the University of Georgia Center for Continuing Education.

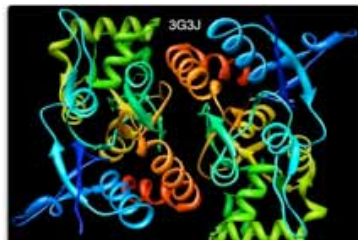
Program topics this year include: RNA Crystallography, Protein Small Angle X-ray Diffraction, Crystallization of Protein-Protein Complexes, Small Molecule Neutron Diffraction, X-ray diffraction in Material Science

In addition, a new feature of the conference is the Pittsburgh Diffraction Society Future Leaders Symposium, which will highlight outstanding research carried out by graduate and undergraduate students.

The conference will be preceded by a hands-on workshop on sulfur-SAD phasing organized by B.C. Wang on October 28th. For more information please see <http://www.pittdifsoc.org/> (2009 PDC information will be available shortly).

SER-CAT's 1000th Structure

In February 2009, the 1000th SER-CAT structure was deposited to the PDB (3G3J): Crystal structure of the GluR6 ligand binding domain dimer I442H K494E K665R I749L Q753K mutant with glutamate and NaCl at 1.32 Angstrom resolution.



See: Chaudhry, C., Weston, M.C., Schuck, P., Rosenmund, C., Mayer, M.L. "Stability of ligand-binding domain dimer assembly controls kainate receptor desensitization" (2009) EMBO J. 28: 1518-1530

Congratulations to Dr. Mark L. Mayer and his staff at the Laboratory of Cellular and Molecular Neurophysiology, NICHD, Bethesda, MD

Currently there are 1036 SER-CAT structures in the PDB.

Continued from page 5 right...

on crystal growth and mask the positive contribution of another component. Experimental results found that the use of silver bullet cocktails more than doubled the number of proteins that could be crystallized compared to similar set ups that are free of the small molecule additives. The crystallization and structural data provided persuasive evidence that incorporation of one or more small molecules in the reagent could be crucial for obtaining crystals. More recent experiments have demonstrated the usefulness of this approach in nucleic acids, viruses and membrane proteins.

X-ray analysis of a subset of the biological macromolecules tested with the silver bullets strongly supports the idea of conventional and biological small molecules mediating crystallization. One simple example is illustrated in Figure 3 below where mellitic acid maintains the lattice of trypsin crystals, serving as a principal link between two protein molecules in the lattice.

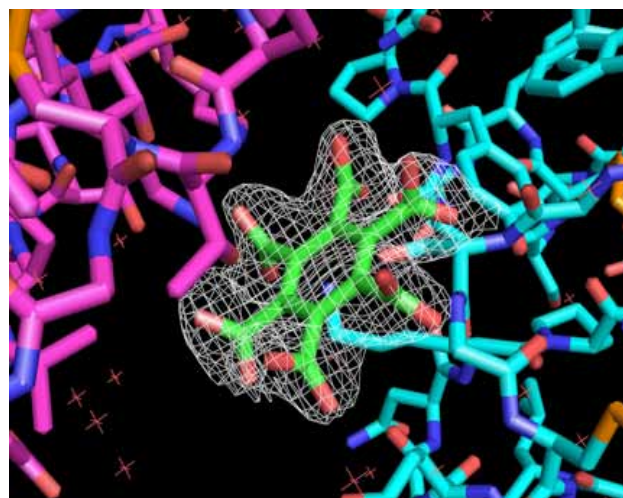
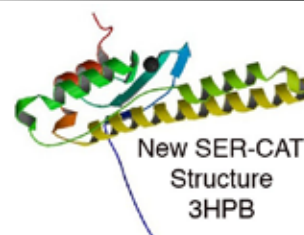


Figure 3. Mellitic Acid maintains the lattice of trypsin crystals

Screening of small molecule libraries under a variety of or even a few select reagent formulations provides a novel and often effective approach to crystallization. Further acquisition of crystallization results involving small molecules may ultimately lead us to a better understanding of the relevant mechanisms involved and perhaps allow us to refine the cocktails of small molecules that serve our interests.

For additional information, go to:

http://hamptonresearch.com/product_detail.aspx?cid=1&sid=179&pid=562



The SER-CAT Spectrum

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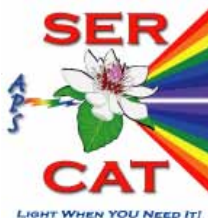
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