

6M detector is a two-dimensional hybrid pixel array detector, which operates in single-photon counting mode (Broennimann et al., 2006). It consists of 2527 x 2463 pixels with a pixel size of 0.172 mm. This detector features several advantages compared to current state-of-the-art CCD and imaging plate detectors. The main features include: no readout noise, superior signal-to-noise ratio, a point spread function of one pixel, readout time of 5 ms, framing time of 100 ms, a dynamic range of 20bit, high detective quantum efficiency (100% at 8 keV, 80% at 12 keV, 50% at 16 keV) and the possibility to suppress fluorescence by an energy threshold. The short readout and fast framing time allow to take diffraction data in fine-phi-slicing mode with continuous rotation of the sample without opening and closing the shutter for each frame. Because of the specified properties, this detector is especially suited for the study of weak diffraction phenomena, time-resolved experiments and accurate measurements of Bragg intensities. Results from various x-ray experiments are presented, including crystallographic diffraction data, as well as results from diffuse scattering and x-ray absorption experiments. All data have been collected with the PILATUS 6M detector at the X06SA and X05LA beamline of the SLS. Broennimann, Ch., Eikenberry E. F., Henrich B., Horisberger R., Huelsen G., Pohl E., Schnitt B., Schulze-Briese C., Suzuka M., Tomizaki T., Toyokawa H., Wagner A. (2006). *J. Synchrotron Rad.* 13, 120-130. Kraft, P., Henrich B., Eikenberry E. F., Schlepuetz C. M., Kobas M., Graafsma H., Broennimann Ch. (2008). *J. Synchrotron Rad.*, submitted.

Keywords: macromolecular crystallography, area detectors, detector development

## MS.65.2

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### Remote access to the SSRL protein crystallography beam lines

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Protein crystallography users of the Stanford Synchrotron Radiation Laboratory (SSRL) have the option to conduct diffraction experiments from their home institutions by means of advanced software tools that enable network-based control of highly automated beam lines. Remote experimenters have access to the same tools as local users, and have the ability to mount, center, and screen pre-frozen samples, and to collect, analyze and backup diffraction data. Central to this remote access capability is the Stanford Auto Mounting (SAM) system which transports samples directly from a cassette or uni-puck storage container in a liquid nitrogen-filled dewar, to the beam line goniometer. SAM is seamlessly integrated into the Blu-Ice/DCS beam line control system. This efficient and reliable system gives researchers the ability to screen up to 288 crystals without human intervention and remount the best quality crystals for data collection. The technical details of the beam line automation and remote access developments and the impact on macromolecular crystallography experiments will be presented.

Keywords: remote access, macromolecular crystallography, automation

## MS.65.3

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### Exploiting the anisotropy of anomalous scattering boosts the phasing power of SAD/MAD experiments

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The anisotropy of anomalous scattering (AAS) in crystals of brominated nucleic acids and selenated proteins is shown to have significant effects on the diffraction data collected at an absorption edge. For conventionally collected single- or multi-wavelength anomalous diffraction data, the main manifestation of AAS is the breaking of the equivalence between symmetry-related reflections, inducing intensity differences that can be exploited to yield extra phase information. We present a new formalism for describing AAS which allows these effects to be incorporated into the general scheme of experimental phasing methods, using an extended Harker construction. This requires a paradigm shift in the data processing strategy, since the usual separation of the data merging and phasing steps is abandoned. The data are kept unmerged, down to the Harker construction where the symmetry-breaking is explicitly modelled and refined and becomes a source of supplementary phase information. These ideas have been implemented in the phasing program SHARP. Refinements on actual data show that the exploitation of anisotropy of anomalous scattering can deliver substantial extra phasing power compared to conventional approaches using the same raw data. Examples are given that show improvements in the phases which are typically of the same order of magnitude as those obtained in a conventional approach by adding a second wavelength data set to a SAD experiment. Such gains - which come without collecting new data - are highly significant, since radiation damage will frequently preclude the collection of a second wavelength data set. Finally, we outline further developments in synchrotron instrumentation and in the design of data collection strategies that could help to maximise those gains.

Keywords: anisotropy of anomalous scattering, SAD/MAD phasing, polarised dispersion

## MS.65.4

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### Microcrystal manipulation with laser tweezers

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Over the last years huge investments in several structural genomics initiatives have been undertaken to automate all steps from protein expression to structure solution. Robotic systems are used in almost all steps from protein expression to sample changers on synchrotron beamlines. The last purely manual step is the transfer of the crystal from the crystallization drop onto a support for the subsequent X-ray diffraction experiment. Crystal "fishing" is relatively easy for crystals with dimensions >25 microns, however difficult for smaller crystals. As microfocus synchrotron beamlines allow data collection of crystals with dimensions of only a few microns, new approaches have to be found to facilitate and automate this last manual step. Laser tweezers which are routinely used for cell sorting offer the

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means to manipulate micron sized objects in solution. A laser is focused by a high NA objective lens to produce an optical trap. Trapped crystals can be manipulated within the crystallization drop to both sort and mount them on standard crystal supports used in cryo macromolecular crystallography. The talk will demonstrate several successful examples of this new mounting technique and discuss the limitations like laser beam induced radiation damage.

Keywords: optical trapping, laser tweezers, microcrystals

### MS.65.5

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#### Serial crystallography using protein beams

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By spraying aligned molecules continuously across a synchrotron beam, we hope to develop a new method for solving protein structures which cannot be crystallized (Starodub et al *J. Synch Res* 15, 62 (2008)). We have developed a particle injector which provides a single-file beam of hydrated proteins or cells either continuously or on-demand (for synchronization with a free-electron X-ray laser). We are also developing methods for aligning molecules in a beam, including flow alignment, laser alignment and magnetic field alignment. First results will be presented showing ring diffraction patterns from Photosystem I protein crystallites consisting of just 19 x 19 x 21 unit cells, obtained using the coherent undulator beamline 9.0.1 at the Advanced Light Source at 2nm wavelength (Shapiro et al, *J. Synch Rad.* (2008) submitted). Design details of the aerojet gas-focussing droplet beam generator will be given (DePonte et al (2008), Weierstall et al *Expts in Fluids.* (2008)). Radiation damage aspects of diffractive imaging using femtosecond hard X-ray pulses will also be discussed. A solution to the inversion problem of multiple scattering for soft X-rays will be presented. This group effort (see papers for the many contributors) is supported by NSF, CBST, and ARO awards.

Keywords: femtosecond X-rays, serial crystallography, diffractive imaging

### MS.66.1

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#### Multi-component solids in crystal engineering

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Multi-component solids have always been studied as an integral part of structural chemistry. The earliest of these substances is perhaps the quinone-hydroquinone donor-acceptor complexes which were identified more than 150 years ago. In the context of recent developments in crystal engineering, the central issue seems to be whether or not there are any fundamental differences between single-component crystals and multi-component crystals with regard to matters such as crystallisation, design principles, structural specificity, propensity towards polymorphism, crystal structure prediction and property tuning. Kitaigorodskii stated that studies of binary crystals of organic substances are a key for studying intermolecular interactions. We have stated that the very isolation of a two-component solid is evidence of the fact that some intermolecular interactions between the different molecules in the solid are more

significant, stronger or more specific than the interactions that are possible between molecules of the same type. Multi-component crystals can have fixed stoichiometries and well-defined structures, or they can be of the substitutional solid solution type. Both varieties are useful in crystal engineering. These themes will be illustrated with examples taken from our research over the years.

Keywords: mixed crystal, co-crystal, hydrogen bond

### MS.66.2

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#### From a molecular dating agency to successful co-crystal synthesis

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The crystal structure of a compound, the 3-D orientation and organization of molecules in a highly regular manner, ultimately determines most of the fundamental physical properties of that particular material, e.g. thermal stability, hygroscopicity, conductivity, and mechanical strength. Consequently, an ability to control and change the crystalline environment of both known and unknown compounds (without altering the individual molecular properties) would be of enormous significance to both manufacturers and consumers of solid specialty chemicals such as pharmaceuticals, pigments, energetic materials, toxins, foodstuff, and detergents. The deceptively simple act of molecular recognition, which eventually leads to crystallization, is achieved by balancing a range of relatively weak non-covalent forces, and this presentation will highlight some of our attempts at establishing practical and versatile supramolecular design strategies based on tunable site-specific intermolecular interactions.

Aakeroy, C.B.; Desper, J.; Smith, M.M., *Chem. Commun.* 2007, 3936-3938.

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Aakeroy, C.B.; Salmon, D.J. *CrystEngComm*, 2005, 7, 439-448.

Keywords: co-crystal, hydrogen bonding, halogen bonding

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#### Multicomponent crystals; Their formation, characterisation and application

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My talk will focus on the role that multicomponent crystals (e.g. solvates, hydrates, cocrystals, salts) play in the design of new organic solids. I will cover mainly applications in the pharmaceutical area, illustrating the various methods of preparing such solids as well as demonstrating some of the resulting benefits. The xanthenes (caffeine, theophylline and theobromine) have been extensively studied within my group and they illustrate many of the important aspects of this area. In addition to describing our experimental