

APS Renewal Workshop

- Macromolecular crystallography subgroup
 - Tony Kossiakoff (Uof C, chair)
 - David Eisenberg (UCLA)
 - Keith Brister (LS-CAT/Northwestern)
 - Keith Moffat (UofC)
 - Janet Smith (Michigan)
 - Ward Smith (NIGMS/NIH)

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- Two main areas singled out in the report:
 - micro X-ray crystallography
 - probing reaction dynamics by time-resolved crystallography

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- Micro X-ray crystallography:
- Applied to small crystals in the <1 to $10\ \mu\text{m}$ range of typical dimension, or to small well-ordered volumes within larger crystals
- Must match X-ray beam size to crystal size
- Small X-ray beams raise issues of X-ray stability at the crystal (and hence depend on stability of the source, optics components, goniometer), of crystal mounting, changing and environment, and of detectors
- Limiting issues are radiation damage to the crystal, and signal-to-noise in the diffraction patterns; mono vs. Laue?
- Success would open up a wider range of crystals whose structures can be explored
- Small crystals are more readily penetrated by light; may be suited to time-resolved crystallography

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- Probing reaction dynamics by time-resolved crystallography: what are the technical limitations?
- Triggering the reaction by light – but not all systems are light-sensitive!
 - trapping approaches (excellent review by Bourgeois & Weik on “kinetic protein crystallography” in press in Crystallography Reviews, 2008)
 - chemical approaches including bond cleavage and isomerization (review in Gorostiza & Isacoff, Science 322, 395-99 (2008))
 - genetically-encoded caging (first application to trpR: Strickland, Moffat & Sosnick, PNAS 105, 10709-14 (2008); four other successful applications known)
- Triggering by e.g. pressure jump, T jump, electric field jump
- Detection of intermediates
- Ultrafast X-ray pulses: the duration of the synchrotron X-ray pulse currently limits the time resolution to ~100ps
- Next generation detectors e.g. pixel array detectors that would enable “pump once, probe many” data collection

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- Other aspects:
- SAXS/WAXS and their relation to crystallography
- Combination of techniques e.g. absorption/fluorescence spectroscopy on crystals in situ
- Stronger links to theory and computation e.g. molecular dynamics