Transitioning from a crystallographer to a structural biologist: Lessons learned

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Although I had determined a number of small molecule crystal structures as a graduate student at Rutgers University making the transition to structural biology was a learning experience. I joined Bi-Cheng (B.C.) Wang's lab at the V.A. Medical Center (VA) in Pittsburgh in 1980. Note at this time the PDB contained only 69 total entries. I began my career by isolating and purifying the oxytocin/vasopressin carrier protein neurophysin (NP) from ovine posterior pituitaries; learning how to grow and mount protein crystals; mastering data collection on the Picker FACS diffractometer; and modifying the space group specific (P21212) data reduction programs in use at the VA to make them space group general and more efficient. I also adapted the LN2-based low temperature system to use chilled isopropanol (- 40° C) to maintain the crystal at 4°C during data collection. The next five years saw dramatic strides in data collection with low power tube-based generators replaced by rotating anodes and point detector systems replaced by 2D area detectors (film and multiwire) increasing data collection efficiency, data quality and data resolution.

Much of my time during these early years was spent searching for one heavy atom derivative. B.C. Wang was working on his ISIR/ISAS phasing package so one good heavy atom derivative was all I needed. I scanned over 100 heavy atom compounds with no luck. The NP structure was eventually solved by iodine-SAD, the first protein structure phased by Wang's Iterative Single Anomalous Scattering method, (B.C. Wang, Methods Enzymol. 115: 90-112, 1985) using inhouse data and crystals grown with p-iodo-Phe-Tyr amide. Today, neurophysin could be readily solved using sulfur-SAD.

The poster will present lessons learned during this time including Rule 1 - Never put your best crystal on first!