

Notes of a Protein Crystallographer-Cold Spring Harbor Meeting in 1971 revisited: A commemoration of the birth of the Protein Data Bank (PDB40).

I began writing these notes at Blackford Hall within the grounds of Cold Spring Harbor Laboratory, Friday, October 28, 2011; a diaphanous morning. Looking through the window, a beautiful view of the Long Island Sound is in the horizon. For me this is a pilgrimage to the origins of the Protein Data Bank and also an occasion to experience from the inside what in 1971 was referred to as the ‘Coming of Age’ of Protein Crystallography (1).

How many times had I seen the volume of the proceedings of that momentous meeting on the bookshelf of my Ph. D. mentor, Marvin L. Hackert, in his office in Patterson Laboratories at the University of Texas at Austin. I had landed at UT Austin in the fall of 1972 (just as the volume had been published) as a graduate student sponsored by a Fullbright Scholarship from the Spanish-American Binational Committee. How many times had I browsed through the black and white photographs of the icons of the field: Max Perutz, W.C. Love, D. Hodgkin, Lyle Jensen, M. G. Rossmann and so many others, then unknown and now full-fledged Nobel Prize Laureates (e.g., Tom Steitz)? How many times had I looked with envy at the roster of participants in such a remarkable gathering? Sadly, may have passed away: Aaron Klug, Paul Sigler, Don Wiley, and Carl-Ivar Brändén among others but many were present this time also.

As soon as the commemorative meeting was called by the currently World Wide PDB (wwPDB), I could not resist signing up to go to commemorate four events: i) the celebration of the spectacular trajectory of our field during these past four decades; ii) the 40th anniversary of the birth of the PDB; iii) my personal satisfaction of having been a ‘real’ protein crystallographer for forty-years; and iv) the pleasure of stepping on the ‘sacred grounds’ where so many pioneers of macromolecular crystallography and molecular biology had previously been, met and discussed the insights and advances of the field. Incidentally, after more than twenty two years at Abbott laboratories as a protein crystallographer and drug-designer, Jonathan Greer, my manager at Abbott labs and a participant in the 1971 symposium gave me his personal copy of the CSH volume that I am now treasure and that I consulted as an inspiration to write these notes.

It was indeed a momentous meeting planned with loving care by the entire Protein Data Bank team to commemorate the birth of the PDB. It was a unique opportunity to see old friends and enjoy ourselves. The mood was celebratory as many of the old participants in the meeting were there to present reminiscences, anecdotes, historical vignettes and sociological insights on the events and forces that made the birth of what is now the Protein Data Bank a reality. But there was also a ‘show’ of the novel structures, methods and combined approaches that will maintain the macromolecular structural community as a vibrant area of research for many years to come and the PDB as a critical resource for the structural and biomedical community at large. It was refreshing to see so many young and eager crystallographers in the audience mingling and discussing their latest results with the old timers.

I have selected a few highlights to convey the excitement of the meeting. The complete details are available from the official meeting site at CSH (meetings.cshl.edu/meetings/pdb40.shtml), including also the full book of abstracts. Michael Rossmann opened the meeting with an excellent historical perspective of the early work on hemoglobin and myoglobin at Cambridge, UK, in the late fifties and early sixties and the events leading to the community effort to create a central depository of macromolecular structures. He then went on, emphatically saying that ‘he was not a fossil’, to present the latest results of his work on the structures of the multiple components of the T4 phage.

Jane Richardson described her journey from being the master illustrator of the first protein structures with ribbons and helices to her efforts to improve the quality of new structures. Axel Brunger presented his latest efforts to enhance the structure determination and refinement of low resolution structures, using a novel refinement term based on the interatomic distances D_{ij} . Richard Henderson, one of the pioneers of the structure determination of Rhodopsin by electron diffraction using low doses, reviewed the challenges still facing the high resolution determination of structures by electron microscopy. After a hilarious introduction by Gerard Kleywegt (PDBe), a few gentle remarks by Hans Deisenhofer reminded the audience that not everybody in the community of protein crystallographers of the seventies and eighties accepted the notion of depositing the efforts of their many years of hard labor in a common depository.



PDB40 Speakers: Back row: Soichi Wakatusi, Johann Deisenhofer, Michael Rossmann, Janet Thornton, Andrej Sali, Richard Henderson, Stephen Burley, Wayne Hendrickson. Front row: Susan Taylor, Jane Richardson, Ad Bax, Axel Brunger, Mei Hong, Cheryl Arrowsmith, Wah Chiu, Angela Gronenborn. Not shown: Kurt Wüthrich and David Searls. Photo from RCSBPDB

John Markley (Chair) and Kurt Wüthrich reviewed the contributions of the methods related to NMR and Mei Hong kept the audience spellbound with her latest results using solid state NMR to study the detailed structure of proteins embedded in membranes. Wayne Hendrickson retold the story of the breakthrough of the Crambin structure at atomic resolution and described his latest work on SLAC1 and related proteins. I was particularly intrigued by the ideas and concepts expressed by David Searls reviewing the language of molecular and structural biology in relation to linguistics and the possibility of expressing the molecular biological processes in the future in a 'linguistic framework' to facilitate their description. Appropriately, Helen Berman closed the meeting describing the spirit of assembly with the following words: collegiality, community and collaboration, passion and persistence.

Where will the PDB be ten years from now? This might not be as difficult to guess, but how about predictions for the PDB at the next 40th anniversary? Very shrewdly, the organizers prepared a white board in the main hallway of the meeting where attendees could put their comments, guesses and predictions for the next celebration of the PDB at fifty and eighty years old. Prompted by the white board, I intently looked at the crystal ball a few times. Within the next ten years: Will we have a sizeable number of structures obtained by single molecule diffraction? Will the promise of these methods be realized helping us to populate the PDB with structures of macromolecules obtained 'without crystals'? or with micro (nano?) crystals? I also made a guess at the longer projections: Would there be an entry (or a section) at the PDB of 'far tomorrow' for cell organelles such as mitochondria, chloroplast? You, the reader, can make your own predictions.

A more detailed account of the meeting will be presented elsewhere by the organizers of the meeting. This brief note was threaded with personal notes, reminiscences, and jotted comments, combined with some scientific details of the talks presented by the prominent speakers. It is not meant to be a full report or not even a professional meeting summary. These are just the 'notes of a protein crystallographer' at the celebration of his 40th anniversary in the profession.

In closing, I do wish that the new generations of macromolecular crystallographers have the opportunity to browse the website of the meeting with the corresponding photos (meetings.cshl.edu/galleries/pdb40/). More importantly, I also wish that those images of the old and new protein crystallographers, together with the proceedings of the meeting, copies of the presentations and discussions, inspire them as the volume published in 1972 inspired me forty years ago. Anniversaries are to be celebrated but they are also supposed to inspire the new generations to seize the torch and continue the path of discovery: different tools but the same spirit.

[1] D.C. Phillips, pg. 589. Structure and Function of Proteins at the Three-Dimensional Level. *Cold Spring Harbor Symposia on Quantitative Biology. Volume XXXVI*. Cold Spring Harbor Laboratory, 1972.

Cele Abad-Zapatero