Perutz Prize

A path paved with crystals

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My lifelong adventure with crystallography is a journey on a path paved with crystals, in superb company of fantastic people, both senior mentors and young mentees. I will review the multiple projects, all revolving around the molecules of life, with focus on health and disease. The original interest in nucleoside salts and biogenic polyamines was abruptly diverted in 1988 to protein crystallography through the influence of Alex Wlodawer. With his team at the NCI we were able to solve the structure of retroviral protease and provide its correct model for the frantic race to develop AIDS drugs. In another joint project, the structure of antileukemic bacterial asparaginase was solved through a combination of crystallographic tricks. This project, continued with my team in Poznan, has led to the discovery of the structure of two new classes of asparaginases. In collaboration with Anders Grubb in Lund, we obtained the protease inhibitor human cystatin C, which with a hereditary point mutation causes fatal amyloidosis on Iceland. Through the ingenuity (and lucky mistakes) of my team in Poznan, we discovered that the protein oligomerizes through the mechanism of 3D domain swapping. A great deal of research effort has been spent on plant structural biology, in particular on PR-10 pathogenesis-related proteins, which we showed to be capable of binding of several phytohormones, such as cytokinins, gibberellins and also melatonin. When experimenting with the complexes, we discovered that the PR-10 protein from St John's wort, Hyp-1, when incubated with the fluorescent dye ANS, forms crystals with fiendishly modulated superstructures. Interpreted in the supercell, they contain 28 and 36 protein molecules in the asymmetric unit. Both structures were successfully solved and refined. My early interest in methods resulted in the application of the principle of structural correlations, development of parameters for the description of H-bonds in crystals, or innovative calculation of pseudorotation parameters. More recently, with my excellent coworkers, we developed a new, conformation-dependent restraint library for nucleic acids. As a legacy of my small-molecule roots, I have keen interest in macromolecular crystallography at ultimate resolution. We hold the PDB record for DNA (0.55 Å), have several ultrahigh-resolution protein structures, and are now working on a record-breaking crambin structure. With the motto that highest quality should always be sought, also with macromolecular structures, together with several old friends we formed a self-appointed taskforce to detect, and if possible - correct or eliminate the errors that are still lurking in the PDB.