28. Hai-fu Fan

Professor of crystallography,
Member of the Chinese Academy of Sciences,
Institute of Physics, Chinese Academy
of Sciences, Beijing 100080, P. R. China
fan@aphy.iphy.ac.cn
http://cryst.iphy.ac.cn

Methods of solving protein structures / Solution of incommensurate modulated structures / Electron crystallography / Methods for powder diffraction analysis / Crystallographic programming

About fifteen years ago when the crystallographic community was celebrating the Nobel Prize for direct methods, the program *Multan* was dominating the field of crystal-structure analysis of small molecules. Thanks to direct methods people can routinely solve a crystal structure containing one hundred independent non-hydrogen atoms in a few days. This provides one of the most important experimental basics of small-molecule based drug design. Most of the huge number of direct-method users might not realize what is behind the well-optimized automatic programs: there are discoveries in theory and innovations on algorithms contributed by the pioneers of direct methods with two decades of efforts. The scientific activity on studying direct methods could not have been conducted within either pharmacy or chemistry. It could only be done inside crystallography.

During the last decade the application of direct methods has expanded into a much wider area. It has expanded from small molecules to proteins. When diffraction data at atomic resolution are available, direct methods can solve proteins containing more than one thousand independent non-hydrogen atoms, which is 10 times more complicated than what could be called 'complex structure' in the 1980's. For protein data at $2 \sim 3$ Å resolution, direct methods have been successfully combined with traditional protein crystallographic techniques to make the phasing procedure more efficient and flexible. Direct methods have expanded from dealing with single crystal diffraction to phasing of powder patterns, and become a major technique for *ab-initio* structure determination using power diffraction data.

Direct methods have been expanded from solving conventional crystal structures to incommensurate modulated structures. Finally direct methods have been expanded from X-ray crystallography to electron microscopy as a tool of both diffraction analysis and image processing. All these have strongly impacted structural biology, material science and other relevant disciplines. However all these could not have been achieved within either structural biology or material science. They could only be achieved in crystallography. That is the reason why crystallography could not be a part of the related disciplines. Looking forward to the future of crystallographic methods and of crystallography itself, I would say, we have our own way to go.