



PERSONAL PERSPECTIVES

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During the celebration of the International Year of Crystallography, IYCr2014, three important summits were organized in widely separated parts of the world: Karachi (Pakistan), Campinas (Brazil) and Bloemfontein (South Africa). These IUCr-UNESCO summit meetings were intended to bring together not only scientists in academia and industry from those countries but also science administrators and policy makers. The objective was to face the neces-

sity for scientists within the crystallography realm to "*think beyond political borders and other distinctions ...*", which is a critical aspect to define and shape the future of crystallography. In this regard, *Arbor* wanted to enquire deeper into this future by asking a group of outstanding scientists, principal actors of key advances in different branches of crystallography, not only about their views on current crystallography but also on its promise to the future.



Prof **Paul D. Adams** focuses his research activity on three main areas: computational methods development, accelerator resources for structural biology and bioenergy research. He is very well known for his role in the development of a new software system called PHENIX, for the automated solution of macromolecular structures using crystallographic methods, which recently includes the analysis of neutron diffraction data. One area of interest at the Advanced Light Source is the structural study of large macromolecular machines. More recently, as part of the Joint Bioenergy Institute, he is developing new technologies to improve the conversion of biomass to fuels.

P.D.A.: *It has been very exciting to be a part of the development of macromolecular crystallography over the last 25 years. Structures that were monumental challenges in the 1980s are now routine and can be solved in minutes. So, is there nothing left to do in X-ray crystallography? Personally, I see a bright future, with many challenges still to be overcome. Over the two decades new computational methods have made it possible to refine atomic models even with very little experimental data. However, a big challenge remains – how to build atomic models into low resolution maps de novo. I predict important developments in the future, where we learn how to make use of diverse sources of information to construct ensembles of models consistent with the experimental data. There are also exciting new developments in X-rays sources. Free electron lasers have opened up new approaches, with the ability to outrun radiation damage and study nanocrystals. This presents many new opportunities in how to best analyze the raw diffraction patterns, how to exploit experimental phasing, and even the possibility of ab initio phasing. Ultimately crystallography's goal is an atomic model that explains biology or chemistry. I anticipate renewed efforts to go beyond structure and instead probe dynamics and correlated motions in molecules, for example by making use of diffuse scatter. Finally, we have a great history of adopting whatever methods enable us to solve difficult problems. Cryo-electron microscopy will therefore undoubtedly play a major role in our future.*

Paul D. Adams

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Prof **G. R. Desiraju** was President of the International Union of Crystallography from 2011 to 2014. His research in crystallography has been directed to the analysis of the factors that determine the crystal structure of a small organic molecule and whether or not one can predict such crystal structures using experimental, computational, or database-related methods. These goals constitute a part of the subject of crystal engineering. This subject today also has come to include an understanding of the process of crystallization. Not surprisingly, he has been very active during the IYCr2014. His main personal goal was “... to reinforce a sense of group identity and to convey their enthusiasm for this remarkable subject to the larger scientific community ...”.

G.R.D.: *The occasion of the International Year of Crystallography (IYCr2014) prompts one to think about the future of this field of science. Crystallography is to some the study of the external and internal structure of crystals, while to others it is an imaging technique par excellence. I can visualize the most promising of scenarios for this evergreen subject. For chemists, crystallography will be used in conjunction with spectroscopy and computation to obtain the structures of systems that are becoming more complex and diverse. As a part of this structural endeavour, space and time resolved crystallography will be used along with synthesis and dynamics to study chemical reactions and processes, the most obvious of them being crystallization itself, the mechanistic elucidation of which is the Holy Grail of the subject of crystal engineering. Biologists will use crystallography as a means of achieving a more quantitative approach to systems biology. Phenomena of the greatest importance will be investigated and will lead to surer methods of drug design and development. I can visualize an enhanced emphasis on the study of smaller, less ordered, lower dimensional crystalline domains, and concomitantly the growing importance of large facilities with ever more intense X-ray sources. It is also likely that we will see a greater and more general use of electron and neutron diffraction. Methods will be developed to handle vast amounts of crystallographic data with scientists from remote locations synergizing experimental and computational data so that one may obtain a composite knowledge of increasingly complex forms of matter.*

G. R. Desiraju

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Prof **S. Larsen** was General Secretary and Treasurer of the International Union of Crystallography from 1995 to 2005 and President from 2008 to 2011. Her scientific research interests are vast and cover biological crystallography, charge density, chemical crystallography, hydrogen bonding, and more specifically the relations between structure and function.

S. L.: *For almost 50 years I have been active in crystallography, and I am pleased to have this opportunity to reflect on the present state and future of crystallography. The development of instrumentation, computers and advanced software has made it possible within hours to obtain structural information on crystalline materials that earlier would have taken months/years, and crystallography has become an integral part of most sciences, e.g. a chemist can now get the most detailed information on a compound a couple of hours after it has been prepared and crystallized. The large research infrastructures, synchrotrons and neutron sources have also had a great impact on crystallographic science to the extent that it is fully justified to say that synchrotron radiation has revolutionized structural biology. Earlier crystallography was mainly associated with diffraction experiments, but the large infrastructures have opened for a wider use of X-rays and neutrons in spectroscopy, small angle scattering and reflectivity measurements significantly enlarging the scope of crystallography to become the science with X-rays, electron and neutrons that provide structural information. The impact of X-ray Free Electron Lasers on crystallography that has happened the last years will surely increase in the future. With all this growth and diversity of crystallography the education and training of young scientists becomes increasingly important.*

The IUCr congress in Madrid 2011, the successful operation of the ALBA synchrotron, and three out of four gold medals in the crystal growing contest held during the IYCr illustrate the strong position of crystallography in Spain. It is my hope that this monograph with contributions from internationally leading Spanish crystallographers will give insight and inspiration to the crystallographic community.

Sine Larsen

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The main research activities of Prof **K. Diederichs** are dedicated to the development of X-ray structure solution methods and their application, analysis of radiation damage, protein structure analysis and prediction (homology modelling, threading and *ab initio*), inverse problems in Biology like phase problem in crystallography and protein folding, among others. For the protein crystallographers, his name is inseparable from XDS, together with W. Kabsch.

K.D.: *Crystallography has come of age: 100 years ago, William and Lawrence Bragg received the Nobel Prize in Physics "for their services in the analysis of crystal structure by means of X-rays". The discipline has influenced almost every branch of Natural Sciences, and its techniques regularly unveil Nature's secrets, as anybody can witness in the weekly issues of Science and Nature. But all that glitters is not gold. Some of the concepts developed decades ago now need revision. For example, analysis of crystallographic data quality is still somewhat fixated on values of R_{merge} (also called R_{sym}), and the distinction between accuracy and precision, as well as indicators of unmerged data precision and those of merged data precision is only now starting to be accepted in the community. But scientists are human beings whose opinions and judgements - although they think they are rational! - also depend on those of their peers. Thus, changes need some time, but are needed and, once accepted, will enable further progress. So, where is the field heading? Producing X-rays ten orders of magnitude stronger than synchrotron beams, X-ray Free Electron Lasers will allow us to do experiments we could never dream of. In the short term, this should allow time resolution at the femtosecond scale; in the long run, we may be able to obtain diffraction images from - ultimately - single molecules. Even the phase problem may be conquered: the development of quantum computers will enormously change our capabilities for computation - not only in Crystallography!*

Kay Diederichs

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Prof **M. Martínez-Ripoll** has a long experience in experimental techniques and methodologies for crystal structure solution, with special interest in structure-function relationships of biological macromolecules. From 2008 to 2015 he has been member of the *IUCr Commission on Biological Macromolecules*. He was pioneer in introducing in Spain the “modern” techniques of computational crystallography and always showed a profuse and enthusiastic participation in the teaching and dissemination of science, being author of a successful website (Cristalografía–Crystallography), offered in two languages (<http://bit.ly/ebUalj>).

M.M.R.: *Crystallography is a vital part of much modern research into the structure and properties of materials ranging across many scientific fields like Chemistry, Biology, Biomedicine, Physics, Materials science, Engineering and Mineralogy. However, although it underpins nearly all of the sciences today, it remains relatively unknown to the general public. The International Year of Crystallography (IYCr2014) has greatly helped to raise awareness of the role that this science plays in our world, and many efforts have been made to spread the message of crystallography in various countries where scientific activity is not as well developed or as well organized as elsewhere.*

However, crystallography still seems to remain an unresolved matter in academic environments of even some developed countries. As an example, the American Crystallographic Association and the US National Committee for Crystallography suggested in 2006 that “perhaps due to rapid technological advances in the field of modern crystallography, there appears to be a declining number of professional crystallographers, as well as a lack of sufficient education and training in crystallography...” Indeed, as it occurs in Spain, this is very probably due to the fact that crystallography is erroneously considered as a minor technical issue, whose application and interpretation is trivial. The author of these paragraphs wants to be optimistic and hopes that the lack of academic attention that, with notable exceptions, crystallography has earned in Spain is properly corrected.

It is worth mentioning the collection of resources listed on the official web site of the IYCr (<http://bit.ly/1BYMGyd>) that will remain as a permanent repository in the website of the International Union of Crystallography (<http://bit.ly/1zCsBOX>), providing material and links of high educational value for both students and teachers.

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