Crystallography Education Policies for the Physical and Life Sciences: Sustaining Crystallography in the 21st Century

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BOARD ON INTERNATIONAL SCIENTIFIC ORGANIZATIONS

Abstract

Background: In 2001 and 2003, the United States National Committee for Crystallography (USNC/Cr) Education Subcommittee conducted two surveys to determine the content and extent of coverage of crystallography in university curricula, as well as the views of the broader crystallographic community on the status of crystallography education and training in the US, in both the physical and the life sciences. These surveys suggested that, perhaps as a result of rapid technological advances in the field of modern crystallography, there appears to be a declining number of master practitioner crystallographers, as well as a lack of sufficient education and training in crystallography for individuals who wish to understand and/or use crystallography as a tool in their hypothesis-driven research.

Methods: Recognizing the opportunity to communicate to the broader scientific community the research opportunities afforded by crystallography, as well as the value of crystallographic information, the education committees of the American Crystallographic Association (ACA) and USNC/Cr organized an education summit, which took place June 1-2, 2005 at the conclusion of the ACA national meeting in Orlando, FL. Individuals known for their experience and contributions in crystallography education and training participated in this summit, the outcome of which is a consensus policy statement on crystallography education and training.

Results: Organized in a reverse hierarchal fashion, beginning with post-baccalaureate education and working back to the K-12 level, the policy document makes recommendations for a comprehensive re-evaluation of crystallography education, and it suggests ways to develop in the broader scientific community an appreciation for the value of crystallographic information. Moreover, the visual, aesthetic and quantitative nature of crystallography provides an excellent path to introduce science and scientific methods to the general population. These policies are directed towards our scientific colleagues, who may also be practicing crystallographers, as well as all education policy makers of major scientific societies.

Conclusions: The ACA and the USNC/Cr intend that the document, which stands as the white paper on crystallography education and training, provides guidelines to professional societies and academic departments for crafting future crystallography curricula that adequately address the needs of the scientific community. The education committees of the ACA and the USNC/Cr will provide guidance and support to interested colleagues and policy makers who wish to put these recommendations into practice.

Acknowledgements: The education summit was funded by the USNC/Cr, ACA, CSUPERB and the National Science Foundation. The USNC/Cr and the ACA thank Elaine McClanahan, who facilitated the summit, Dr. Jerry Bell of the ACS for his keynote address, the ACA Continuing Education Committee, the USNC/Cr Education Subcommittee, and the summit participants: Robert Bau(USC), Simon Billinge(Michigan State U), Gloria Borgsdahl(Eppley Institute, U Nebraska), Charles Campana(Bruker-Nonius), Jon Clardy(Harvard Medical School), Frank Fronczek(LSU), Andy Howard(IIT), Allen Hunter(Youngstown State U), Francis Jurnak(UC Irvine), James Kaduk(Innovene), Katherine Kantardjieff(CSUF), Margaret Kastner(Bucknell U), Cheryl Klein Stevens(Xavier U), Marilyn Olmstead(UC Davis), James Pflugrath(Rigaku MSC), Kent Ratajeski(U Montana), Miriam Rossi(Vassar College), Bernhard Rupp(LLNL), Robert Sweet(NSLS), Iris Torriani(U Campinas Brazil), and Victor Young(U Minnesota).

Background

In 2001 and 2003, the United States National Committee for Crystallography (USNC/Cr) Education Subcommittee conducted two surveys (Appendix B) to determine the content and extent of coverage of crystallography in university curricula, as well as the views of the broader crystallographic community on the status of crystallography education and training in the US, in both the physical and the life sciences. These surveys suggested that, perhaps as a result of rapid technological advances in the field of modern crystallography, there appears to be a declining number of master practitioner crystallographers, as well as a lack of sufficient education and training in crystallography for individuals who wish to understand and/or use crystallography as a tool in their hypothesis-driven research. Recognizing the opportunity to communicate to the broader scientific community the research opportunities afforded by crystallography, as well as the value of crystallographic information, the education committees of the American Crystallographic Association (ACA) and USNC/Cr organized an education summit, which took place June 1-2, 2005 at the conclusion of the ACA national meeting in Orlando, FL. Individuals known for their experience and contributions in crystallography education and training participated in this summit (Appendix A), the outcome of which is this consensus policy statement on crystallography education. Moved up front

The ACA is a non-profit, scientific organization of almost 2200 members, which represents the Americas as the regional affiliate to the International Union of Crystallography (IUCr), a member union of the International Council for Science. Founded in 1949 as a merger of the American Society for X-ray and Electron Diffraction and the Crystallographic Society of America, the ACA aims to promote interactions among scientists who study the structure of matter at atomic or near atomic resolution. Such interactions among scientists advance experimental and computational aspects of crystallography and diffraction, as well as support the study of the arrangements of atoms and molecules in matter and the nature of the forces that both control and result from these arrangements. Standing committees of the ACA Council include Communications, Data Standards and Computing, and Continuing Education.

The USNC/Cr represents US crystallographers in the IUCr through the National Academies' National Research Council. The USNC/Cr promotes the advancement of the science of crystallography in the United States and throughout the world. Crystallography is a key tool for a variety of fields in biological and physical sciences. By representing the broad US crystallographic community, the USNC/Cr also serves a unique role in bringing together crystallographers with a wide range of perspectives. This role is increasingly important for maintaining a high level of professionalism in a community that spans several disciplines and professional societies, and that needs international communication and coordination. The USNC/Cr represents the crystallographic leaders in the areas of biochemistry, structural biology, pharmaceuticals, materials research (including crystalline and non-crystalline materials), surface studies, mineralogy, inorganic chemistry, powder diffraction, and crystal growth. It supports activities and issues in interdisciplinary research, research resources and facilities, education and travel support, crystallographic databases, and publication standards and ethics.

Executive Summary

Practically all information about the molecular structure of matter at atomic resolution is the result of crystallographic analysis, using data obtained by X-ray, neutron and electron diffraction methods. Diffraction methods have contributed to our fundamental understanding of chemical bonds, chemical reactions and biochemical pathways, the composition and properties of minerals and ceramics, and to the design of material properties, pharmaceuticals, engineered crystals and engineered enzymes. Methodological advances in the past 30 years provide opportunities for individuals with diverse backgrounds and preparation to use crystallography as an important tool to answer structural problems in their hypothesis-driven research. These same advances now enable users with little or no training (or deeper understanding) to often (but not always) produce quality results

The rich and interdisciplinary science of crystallography has been described eloquently by Paul Ewald in 1948 (see insert). This statement is still true today, and it is with this philosophy that this document is written. Modern crystallography provides enabling technology, methodology and information, and *the bounty of knowledge gained from analysis of its structures is a key underpinning of modern science and technology*. There is common ground in the fundamental physics of crystallography between those in the life sciences and those in the physical sciences, but the objectives of these communities in applying crystallography to their particular research problems are not necessarily the same. Life scientists are generally interested in overcoming the modern-day bottlenecks of crystallization and protein production, and in learning the basic requirements to use the technique, namely data collection and running various software applications that get the job of determining molecular structure done. Physical scientists, particularly those from the fields of inorganic chemistry and materials science, are often concerned about symmetry, space groups and unit cells, which give rise to the material and reactive properties of the crystalline state. These topics naturally require greater depth of understanding of the underlying principles. Each community can be further divided into ***master practitioners*** who require depth of knowledge and hands-on experience, and ***user/consumers***, who require a sufficient working knowledge of the field that enables them to answer specific research questions and to collaborate with those having greater expertise.

Organization and Content This document summarizes the crystallography education and training policies endorsed by the ACA and the USNC/Cr. Organized in a reverse hierarchal fashion, beginning with post-baccalaureate education and working back to the K-12 level, this policy document makes recommendations for a comprehensive re-evaluation of crystallography education, and it suggests ways to develop in the broader scientific community an appreciation for the value of crystallographic information. Moreover, the visual, aesthetic and quantitative nature of crystallography provides an excellent path to introduce science and scientific methods to the general population. The conclusions and recommendations in this document are based on input from the education summit participants: biologists, biochemists, chemists, geologists and physicists, all practicing crystallographers in their fields, representing both academia and industry (Appendix A).

Intended Audience and Desired Outcomes These policies are directed towards our scientific colleagues, who may also be practicing crystallographers, as well as all education policy makers of major scientific societies. It is the hope of the ACA and the USNC/Cr that this document, which stands as the white paper on crystallography education and training, provides guidelines to professional societies and academic departments for crafting future crystallography curricula that adequately address the needs of the scientific community. The Continuing Education Committee of the ACA and the USNC/Cr Education Subcommittee will provide guidance and support to interested colleagues and policy makers who wish to put these recommendations into practice.

"The hallmarks of a crystallographer in the 21st century will be his/her skillful analysis of structures in chemical, biological or geological context, knowledge of material preparation and synthetic methods, and a solid repertoire of techniques tailored to the increasingly challenging structural problems in contemporary science."

-K. Kantardjieff and B. Rupp
Zeitschrift für Kristallographie 7 (2002) 328

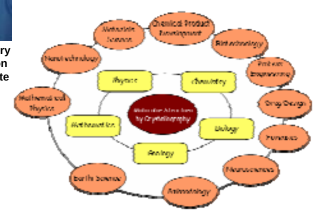
"Friedrich Fröbel, a nineteenth century educator trained as a crystallographer, invented kindergarten. Fröbel's background in crystallography infused every aspect of his conception of kindergarten, especially the self-actuated learning devices or 'gifts' that were the centerpiece of his curriculum."

- B. Kahr
Crystal Growth and Design 4 (2004) 3-9

"Crystallography borders, naturally, on pure physics, chemistry, biology, mineralogy, technology and also on mathematics, but is distinguished by being concerned with the methods and results of investigating the arrangement of atoms in matter, particularly when that arrangement has regular features."

-Paul Ewald
Acta Crystallographica 1 (1948) 2

Students in a senior biochemistry laboratory prepare crystallization screening experiments for lactate dehydrogenase from chicken muscle.



Structure validation workshop held at the ACA national meeting in Orlando, FL 2005.

Left: Crystals of $Cu(SO_4)_2 \bullet 5H_2O$ grown under oil from a saturated solution.

Above: Post-doctoral staff scientist, Brian Schick, aligns a protein crystal sample on a 4-circle goniostat. Right: Post-doctoral staff scientist Matthias Zeller collects low temperature data on a laboratory CCD diffractometer system.

Graduate student Abdul-Basis Alhassan and undergraduate Jennifer Patton discuss sample mounting.

Graduate student James Ongaro cryomounts crystal samples for the synchrotron beamline.

The Laboratório Nacional de Luz Sincrotron (LNLS) in Campinas, Brazil.

Two-year Colleges, Four-year Colleges and Universities

Theme	Life Sciences Undergraduates	Physical Sciences Undergraduates
Intellectual Context	✓ Appreciate the extraordinary wealth of information provided by structural biology and the impact of crystallography on life sciences	✓ Appreciate the technique and vocabulary of X-ray diffraction
Basic Concepts of X-rays and Scattering	✓ Understand the concepts necessary to appreciate the powerful results, as well as the advantages and limitations of the method ✓ Qualitatively understand the interaction of electromagnetic waves with periodic arrays, diffraction and reconstruction to form an electron density image	✓ Appreciate the nature, production and scattering of X-rays
Crystals and Crystallization		✓ Understand the basic properties of crystals, including crystal growth, defects and quality
Solid State and Chemical Bonding		✓ Understand the solid state, including packing and the bonding of molecular, ionic, and extended solids
Symmetry		✓ Be able to identify symmetry elements and nomenclature of molecular point groups, and differentiate chiral and achiral species
Molecular Concepts	✓ Have a solid understanding of the fundamentals of 3D structure in order to communicate and use these concepts in the context of other courses in the curriculum and in their own inquiry and investigation ✓ Understand that the function of a macromolecule is determined by the 3D arrangement of the atoms ✓ Use biomolecular structures derived from crystallographic analysis to develop understanding of protein interactions at the molecular level	✓ Understand the solid state, including packing and the bonding of molecular, ionic, and extended solids
Data Usage and Model Evaluation	✓ Be able to obtain and view X-ray models from databases ✓ Understand the nature, extent, and origins of experimental uncertainties in crystallographically derived results	✓ Understand the nature, extent, and origins of experimental uncertainties in crystallographically derived results ✓ Understand the connection between experimental structural data and theoretical models ✓ Be familiar with crystallographic databases ✓ Be able to interconvert text formulae, line drawings, and 3D representations
Advanced Concepts	✓ Appreciate that biomolecular structure provides the molecular basis of human health and disease ✓ Use results of protein crystallographic analysis to develop understanding of the molecular basis of heredity and biological evolution, as well as matter, energy and organization of living systems	

Post-Baccalaureate Education and Professional Development

Theme	Life Science Practitioners	Physical Science Practitioners	Life Science Users/Consumers	Physical Science Users/Consumers
Intellectual Context	✓ Recognize and appreciate synergy between crystallography and related techniques ✓ Appreciate information content of experimentally derived biomolecular structures and their limitations ✓ Stay current and even anticipate developments	✓ Recognize and appreciate synergy between crystallography and related techniques ✓ Appreciate information content of experimentally derived chemical structures and their limitations	✓ Appreciate extraordinary wealth of information provided by structural biology and impact of crystallography on life sciences	✓ Understand the origin, interpretation, uses and limitations of crystallographic studies
Basic Physics	✓ Understand Thomson scattering, coherence length, beam polarization, anomalous scattering (fluorescence, absorption, Δf', Δf", Kramers-Kronig transform), nature of X-ray optics, production of X-rays (sealed tube, rotating anode and synchrotron)	✓ Understand Thomson scattering, coherence length, beam polarization, anomalous scattering (fluorescence, absorption, Δf', Δf", Kramers-Kronig transform), nature of X-ray optics (cross-fire, bandwidth), production of X-rays (sealed tube, rotating anode and synchrotron)	✓ Understand the concepts as necessary to appreciate the powerful results, as well as the advantages and limitations of the method ✓ Qualitatively understand the interaction of electro-magnetic waves with periodic arrays, diffraction and reconstruction to form an electron density image	✓ Understand the concepts as necessary to appreciate the powerful results, as well as the advantages and limitations of the method ✓ Qualitatively understand the interaction of electro-magnetic waves with periodic arrays, diffraction and reconstruction to form an electron density image
Geometry of Diffraction and Symmetry	✓ Understand Bragg's Law, reciprocal lattice, Ewald construction, unit cells and the asymmetric unit, space groups and implications of symmetry (absences), non-crystallographic symmetry	✓ Understand Bragg's Law, reciprocal lattice, Ewald construction, unit cells and the asymmetric unit, group theory (sub- and super groups/structures), space groups and implications of symmetry (absences), non-crystallographic symmetry	✓ Understand the concepts as necessary to appreciate the powerful results, as well as the advantages and limitations of the method	✓ Understand the concepts as necessary to appreciate the powerful results, as well as the advantages and limitations of the method
X-rays and Diffraction Physics	✓ Anisotropy of sample ordering and absorption, radiation damage, contrast variation/ deuterization, resolution and sin -dependent properties, internal functions of data reduction (indexing, profile fitting, scaling)	✓ Understand the physics of the generation of X-rays and neutrons, scattering phenomena, and how they are related to molecular structure	✓ Understand the concepts as necessary to appreciate the powerful results, as well as the advantages and limitations of the method	✓ Understand the concepts as necessary to appreciate the powerful results, as well as the advantages and limitations of the method
Crystal Physics and the Solid State	✓ Understand the physical properties of crystals and their origins (mosaic spread, flash cooling, phase transition)	✓ Understand the nature of the solid state and its relationship to properties		✓ Understand the nature of the solid state, the types of solid state structures, and their relationship to solution and gas phase structures
Molecular Concepts	✓ Understand basic molecular structure, including bonds, angles, stereochemistry and non-covalent interactions ✓ Understand basic biochemistry, including transcription and translation, enzyme kinetics, thermodynamics, protein-ligand interactions, and the roles of water and metals in structure and function	✓ Understand basic molecular structure, including bonds, angles, stereochemistry and non-covalent interactions ✓ Be able to interpret the results of the experiment and translate these results into an understanding of chemical bonding, packing and other properties	✓ Understand the fundamentals of 3D structure (proteins, ligands, macromolecular structure, structural motifs) to communicate and use concepts in research ✓ Understand how proteins interact dynamically at the molecular level with other proteins, nucleic acids, small molecules, drugs and substrates	✓ Understand basic molecular structure, including bonds, angles, stereochemistry and non-covalent interactions
Crystallization and Sample Preparation	✓ Understand and be able to apply methods of protein expression, purification, production, Se-Met labeling, and the chemistry of heavy-atom derivatization ✓ Understand and be able to apply principles of crystal growth, including supersaturation, kinetics of nucleation and growth, crystal growth methods, crystal stability (osmolality, ionic strength, pH)	✓ Be able to choose and optimize crystallization conditions, select suitable crystalline specimens, and will be familiar with techniques to handle unstable samples	✓ Understand the process of sample preparation, quality and quantity as needed for the objective of the physical characterization	✓ Understand how to prepare and select crystalline samples
Mathematics	✓ Have a solid understanding of Fourier mathematics, least-squares and maximum likelihood, error propagation and statistics, precision vs. accuracy, and Patterson Synthesis	✓ Have a solid understanding of Fourier mathematics, least-squares and maximum likelihood, error propagation and statistics, precision vs. accuracy, and Patterson Synthesis		
Computational Methods, Use of Data, Evaluation of Results	✓ Understand and be able to apply methods of phase determination and heavy atom refinement, including MAD, Molecular Replacement, Direct Methods, Density Modification, NCS averaging ✓ Demonstrate competence in model building, phase bias removal, refinement methods, structure validation, and the use of bioinformatics tools	✓ Be able to confidently apply validation tools and statistics, and understand accuracy and meaningfulness of results	✓ Be able to obtain, view, interpret and evaluate X-ray models competently	✓ Understand the terminology reported in the literature and critically evaluate the results presented ✓ Be able to critically analyze crystallographic results to evaluate their reliability and utility
Practical Knowledge and Skills	✓ Have demonstrated advanced computer skills (OS, programming) ✓ Be able to troubleshoot instrumentation, optimize X-ray beam characteristics to suit an experiment (sources of background, beam collimation, monochromatization, etc) ✓ Be able to handle routine experiments such as cryomounting, selecting data collection strategy, data reduction and sample characterization (effective mosaicity, diffraction limit) ✓ Be able to communicate crystallographic results and methods to both scientists and non-scientists	✓ Have a developed skill set that includes use of advanced instrumentation, presentation of results and 3D visualization ✓ Be able to communicate crystallographic results and methods to both scientists and non-scientists	✓ Understand the capabilities and challenges of the crystallographic process, enabling the user to develop their own realistic structural studies and collaborations	✓ Be aware that although many structures can be solved by individuals with little understanding of crystallography, avoidance of significant but subtle errors requires an awareness of the multiple difficulties that can occur
Advanced Concepts and Applications	✓ Recognize and appreciate the potential of structural genomics, protein engineering, drug discovery, bioinformatics, time-resolved diffraction	✓ Appreciate and understand advances in the modeling of non-routine structural problems, including the concept of chirality and methods of determining absolute structure ✓ Understand and use quantum mechanical and other computational tools as a key part of doing current crystallography	✓ Appreciate the technical aspects involved in crystal structure determination and how these aspects can influence the final results	✓ Have an initial exposure to advanced topics such as charge density diffraction, neutron methods, macromolecular crystallography, etc