

IUCr Final Report: Structural Biology 2.0 Course

Integrating X-ray diffraction and modern computational tools

Institut Pasteur Montevideo, Uruguay | April 21-30, 2025

Executive Summary

The "Structural Biology 2.0: Computational Tools and X-Ray Diffraction - Integrated to Solve and Understand 3D Protein Structures" course successfully achieved all objectives outlined in our IUCr application, delivering comprehensive training in macromolecular crystallography integrated with state-of-the-art computational tools to 24 selected students from 6 countries. The course demonstrated exceptional international appeal with 82 complete applications and successfully prioritized participation from developing countries, particularly Latin America, while maintaining exemplary gender balance as committed in our application.

(I) Financial Support and Utilization

IUCr Support Received: USD \$6,000 total

- General Meeting Support: USD \$3,000 (requested \$8,000)
- Visiting Professorship Program: USD \$3,000 (requested \$4,500)

Funds Utilization:

General Support (\$3,000): These funds were allocated to support travel and subsistence for young scientists from developing countries, enabling participation of students who would otherwise have been unable to attend. The funds supported 16 scholarship recipients from Argentina, Brazil, Chile, and Peru, partially covering their travel expenses and accommodation costs.

Visiting Professorship Support (\$3,000): These funds contributed to the travel expenses of our two IUCr-sponsored visiting professors: Dr. Dorothee Liebschner (Lawrence Berkeley National Laboratory, USA) and Dr. Paul Emsley (MRC Laboratory of Molecular Biology, UK). The IUCr support covered approximately 60% of their combined travel costs, with the remainder supported by other funding sources as outlined in our budget.

(II) Main Results and Impact of the School

This section is outlined according to the objectives that we stated in our original IUCr proposal:

1- Macromolecular Crystallography Training with Computational Integration

FULLY ACHIEVED - The course successfully delivered comprehensive training in macromolecular crystallography seamlessly integrated with AI-based structural prediction algorithms, protein evolution and computational structural analysis tools, exactly as proposed in our application.

Evidence of Achievement:

- Systematic coverage of X-ray diffraction data processing, molecular replacement using both experimental and predicted models, and crystallographic refinement
- Integration of AlphaFold predictions with experimental crystallographic workflows
- Advanced model building and validation techniques combining traditional crystallographic methods with modern computational approaches

- Real-time integration of experimental data processing concepts –extensively using the students’ own real data– with computational structure prediction and analysis throughout the curriculum

2- International Character and Developing Country Focus

EXCEEDED EXPECTATIONS - The course achieved outstanding international representation while successfully prioritizing students from developing countries as specified in our application.

Participation Statistics:

- **Total Applications:** 82 complete applications from multiple countries
- **Selected Students:** 24 (highly competitive 29% acceptance rate)
- **Developing Country Priority:** 23/24 students (96%) from developing countries, primarily Latin America
- **Country Distribution:**
 - Argentina: 10 students (42%)
 - Brazil: 6 students (25%)
 - Uruguay: 5 students (21%)
 - Chile: 1 student (4%)
 - Peru: 1 student (4%)
 - Sweden: 1 student (4% - for international diversity)

This distribution perfectly aligns with IUCr's mission to support crystallography development in regions where it should be enhanced and revitalized.

3- Gender Balance Policy Implementation

EXEMPLARY ACHIEVEMENT - The course achieved perfect gender balance, demonstrating our commitment to IUCr's gender balance policies.

Gender Statistics:

- **Students:** Perfect 50-50 distribution (12 female, 12 male)
- **International Faculty:** 41.6% female representation among invited teachers
- **Local Faculty:** Balanced representation with female leadership in key coordination roles

This represents a significant improvement from our 2017 course (39.1% female) and maintains the excellent balance achieved in our 2021 virtual course (59.1% female), demonstrating sustained commitment to gender equity.

4- High-Quality International Faculty with IUCr Connections

FULLY ACHIEVED - We assembled a world-class teaching team featuring prominent crystallographers with strong IUCr connections, including our two IUCr Visiting Professors.

IUCr Visiting Professors:

Dr. Dorothee Liebschner (Lawrence Berkeley National Laboratory, USA) delivered comprehensive training in:

- Molecular replacement using AlphaFold predictions as search models
- Advanced crystallographic refinement using Phenix
- Integration of experimental phasing with computational predictions
- Map interpretation and model validation techniques

Dr. Liebschner, a key developer of the Phenix software suite, has published extensively in IUCr journals including five recent papers in Acta Crystallographica Section D, making her ideally positioned to teach modern crystallographic methods.

Dr. Paul Emsley (MRC Laboratory of Molecular Biology, UK) provided essential training in:

- Advanced model building using Coot
- Ligand fitting and validation in electron density maps
- ProSMART restraints and advanced refinement techniques
- Integration of crystallographic and cryo-EM model building approaches

Dr. Emsley, creator of the widely-used Coot software, has been a regular contributor to IUCr publications and represents the gold standard in macromolecular model building education.

Additional International Faculty from IUCr Member Countries:

- Germany: EMBL Hamburg (Jan Kosinski, Dimitry Molodenski)
- United Kingdom: MRC Laboratory of Molecular Biology (Lucrezia Catapano)
- USA: Lawrence Berkeley National Lab
- Switzerland: GSK Basel, University of Lausanne
- Brazil: Fiocruz
- Argentina: IBR-CONICET

(III) Program Delivery and Crystallographic Training Outcomes

Theoretical and Practical Integration

The course delivered comprehensive crystallographic training as proposed, with particular emphasis on the modern integration of experimental and computational approaches that defines contemporary structural biology practice.

Core Crystallographic Components Delivered:

- Symmetry and space group theory with practical applications
- Diffraction geometry and data collection strategies
- Data processing from indexing through scaling using autoPROC
- Molecular replacement theory and practice using Phaser
- Crystallographic refinement principles and implementation in Phenix
- Advanced model building and validation using Coot
- Integration of AlphaFold predictions throughout the crystallographic pipeline

Innovative Computational Integration:

- AI-based structure prediction using AlphaFold and related tools
- Protein evolution with a phylogenetics perspective, at the basis of the intimate link between sequence and structure
- Molecular dynamics simulations for understanding protein flexibility
- Modern protein design approaches combining structural and computational methods
- High-throughput structural analysis using computational pipelines

(IV) Hands-on Training with Real Crystallographic Data

EXCEEDED EXPECTATIONS - Students engaged extensively with authentic crystallographic datasets, with 66% bringing their own experimental data for structure solution during the course.

The hands-on training included:

- Processing of students' own diffraction datasets
- Structure solution using molecular replacement with both experimental and predicted search models
- Complete structure determination workflows from data processing through final validation
- Individual access to high-performance computing resources (IPMontevideo cluster with 4 80GB GPUs)
- Real-time problem-solving sessions addressing authentic research challenges

(V) Course Materials and Knowledge Transfer

Comprehensive Resource Development:

- Complete lecture series covering all aspects of modern macromolecular crystallography
- Detailed tutorial guides for major crystallographic software packages
- Hands-on protocols for integrated experimental-computational workflows
- All materials organized in shared repository accessible to participants and available for future IUCr educational initiatives

(VI) Impact on Crystallographic Community Development

Immediate Capacity Building

The course successfully trained 24 researchers from developing countries in state-of-the-art crystallographic methods, directly contributing to IUCr's mission of developing crystallography in underserved regions. Participants now possess integrated skills in experimental data collection, processing, structure solution, and validation combined with modern computational approaches.

Regional Network Strengthening

The course strengthened the South American crystallographic community, building on the established [CEBEM](#) network while creating new international connections. The presence of IUCr Visiting Professors facilitated direct knowledge transfer from leading international laboratories to emerging regional centers.

Educational Model Innovation

The course established a new paradigm for crystallographic education that recognizes the fundamental transformation occurring in structural biology. Rather than treating computational methods as auxiliary tools, the curriculum demonstrated how experimental crystallography and computational prediction now inform each other throughout the structure determination process.

(VII) Challenges and Solutions

High International Demand Management

With 82 applications for 24 positions, we implemented rigorous selection criteria that prioritized developing country participation while maintaining scientific excellence.

Our selection process considered scientific background, potential for applying learned methods, and contribution to regional capacity building.

Technical Infrastructure Requirements

The integration of advanced computational tools required significant technical preparation. We successfully leveraged IPMontevideo's high-performance computing resources while ensuring all participants could access necessary software and datasets.

Curriculum Integration Complexity

Seamlessly integrating experimental and computational approaches required careful curriculum design. We achieved this through daily coordination between theoretical lectures, hands-on tutorials, and practical problem-solving sessions using real data.

Structural Biology 2.0: Integrating X-ray diffraction and modern computational tools Institut Pasteur Montevideo - April 21 -30, 2025

	Day 1 - Monday 21	Day 2 - Tuesday 22	Day 3 - Wednesday 23	Day 4 - Thursday 24	Day 5 - Friday 25	Day 6 - Saturday 26		
08:30-09:00	Registration						08:30-09:00	
09:00-09:30	Overview of the workshop AB	About symmetry and space groups MNL	Phases and the phase problem BG	Introduction to Coot LC/PE	Advanced Model Building with Coot LC/PE	Automatic approaches for model building JP	09:00-09:30	
09:30-10:00	A historic perspective of Structural Biology: integrating crystallography, cryoEM and computational methods AB		AI-based approaches for 3D structure prediction MF				Model quality and validation: concepts & statistics AB	ProSMART and other tools to generate/handle restraints LC/PE
10:00-10:30		Data collection and diffraction geometry BG	Coffee break		Coffee break		10:00-10:30	
10:30-11:00	Coffee break						10:30-11:00	
11:00-11:30	Sequences, alignments, phylogeny: why does it matter to start with this? MG	Coffee break		Introduction to Molecular Replacement FT	Coffee break		11:00-11:30	
11:30-12:00	Lunch	Data Processing: from indexing to scaling MNL	AlphaFold: advanced uses, hands-on tutorial MF & staff	Why do we need to take care about biomolecules' dynamics? MM	Advanced Coot Tutorial I LC/PE & staff	Advanced Coot Tutorial II LC/PE & staff	11:30-12:00	
12:00-12:30		Lunch		Lunch			12:00-12:30	
12:30-13:00		Lunch		Lunch			12:30-13:00	
13:00-13:30	Lunch						13:00-13:30	
13:30-14:00	Basic X-ray crystallography in a nutshell BG	autoPROC Tutorial NL & staff	AlphaFold: advanced uses, hands-on tutorial MF & staff	Xtallographic model refinement: why we need it? Main approaches DL	The very basics of molecular dynamics, proteins on the move AZ	Lunch	13:30-14:00	
14:00-14:30	Computational approaches for structural analysis AZ			Coffee break	Refine in Phenix tutorial DL & staff		Molecular dynamics tutorial I AZ, MM	Molecular dynamics tutorial II AZ, MM
14:30-15:00		Coffee break						
15:00-15:30	Coffee break						15:00-15:30	
15:30-16:00	Coffee break		Molecular replacement and AlphaFold talk to each other DL	While refining: using validation tools in Phenix	Coffee break		15:30-16:00	
16:00-16:30	Working roadmaps in Structural Biology: experimental and computational approaches combined all the way AB	Hands-on problem solving. All participants; working with students' own data	Phaser in Phenix tutorial DL & staff		Coffee break		Coffee break	
16:30-17:00	Discussion and questions session: based on material provided via Moodle - All participants			Coot intro tutorial I LC/PE & staff	Hands-on problem solving. All participants; working with students' own data		Hands-on problem solving. All participants; working with students' own data	
17:00-17:30					Coffee break			
17:30-18:00	Coffee break						17:30-18:00	

	Day 7 - Sunday 27	Day 8 - Monday 28	Day 9 - Tuesday 29	Day 10 - Wednesday 30					
09:00-09:30	Free Time - (tour activity: alternative proposals by the organizers, at the expense of each attendee)	Empowering deep phylogenetics with structural information	MG / DM	Integrative methods in Structural Biology	JK	Structure Analysis: What information can be drawn from an atomic model	AB	09:00-09:30	
09:30-10:00								09:30-10:00	
10:00-10:30		Probing evolutionary relationships with 3D structures	DM	Artificial intelligence for protein design	MM	In-cell structural biology	JK	10:00-10:30	
10:30-11:00				Coffee break				10:30-11:00	
11:00-11:30			Coffee break			Coffee break		11:00-11:30	
11:30-12:00			Structural phylogenetics: a hands-on tutorial	DM & staff	Large protein complexes: structure prediction & analysis, hands-on tutorial	DiM / JK	Engineering new protein functions for Synthetic Biology	FT	11:30-12:00
12:00-12:30									12:00-12:30
12:30-13:00									12:30-13:00
13:00-13:30			Lunch		Lunch		Lunch		13:00-13:30
13:30-14:00									13:30-14:00
14:00-14:30			Modern methods to study conformational ensembles	DA	Protein design hands-on tutorial	MM / FT	"Burning Questions" session - All Participants		14:00-14:30
14:30-15:00									14:30-15:00
15:00-15:30			Introduction to protein design	FT			Final conclusions & Evaluation Form		15:00-15:30
15:30-16:00					Coffee break				15:30-16:00
16:00-16:30			Coffee break						16:00-16:30
16:30-18:00			High-throughput AI-based structure prediction using AlphaFold	DiM / JK	Hands-on problem solving. All participants; working with students' own data				16:30-18:00

Teaching Staff

AB, Alejandro Buschiazio (Inst Pasteur Montevideo, Uruguay)
AZ, Ari Zeida (Univ de la Republica, Uruguay)
BG, Beatriz Guimarães (Fiocruz, Brazil)
DA, Diego del Alamo (GSK Basel, Switzerland)
DiM, Dimitry Molodenski (EMBL Hamburg, Germany)
DL, Dorothee Liebschner (Lawrence Berkeley National Lab, USA)
DM, David Moi (Univ of Lausanne, Switzerland)
FT, Felipe Trajtenberg (Inst Pasteur Montevideo, Uruguay)

JK, Jan Kosinski (EMBL Hamburg, Germany)
LC, Lucrezia Catapano (Lab of Mol Biology / MRC, United Kingdom)
MF, Matheus Ferraz (NEC Bio Therapeutics, Mannheim, Germany)
MG, Martin Graña (Inst Pasteur Montevideo, Uruguay)
MM, Matias Machado (Inst Pasteur Montevideo, Uruguay)
MNL, Maria Natalia Lisa (Inst Biol Mol y Celular de Rosario, Argentina)
NL, Nicole Larrieux (Inst Pasteur Montevideo, Uruguay)
PE, Paul Emsley (Lab of Mol Biology / MRC, United Kingdom)

(VIII) Future Sustainability and Impact

Long-term Regional Development

Participants are now positioned to establish or strengthen crystallographic programs in their home institutions, directly contributing to regional scientific development. The emphasis on integrated methods ensures they can implement modern approaches from the outset.

Educational Resource Dissemination

Course materials developed with IUCr support will be made available to the broader crystallographic community, extending the impact beyond direct participants. These resources represent a model for future integrated crystallographic training programs.

Network Maintenance and Growth

The international connections established during the course, particularly through IUCr Visiting Professor interactions, provide ongoing opportunities for collaboration and knowledge exchange that will benefit the regional crystallographic community for years to come.

Conclusion and Acknowledgments

The "Structural Biology 2.0" course fully achieved its objectives of providing comprehensive training in modern macromolecular crystallography integrated with computational tools. The IUCr's support was instrumental in enabling international participation and securing world-class faculty, particularly through the Visiting Professorship program.

The course successfully demonstrated that experimental crystallography and computational prediction are not competing approaches but complementary methods that together define the future of structural biology. The 24 participants from developing countries now possess the integrated skills necessary to contribute meaningfully to this evolving field.

We gratefully acknowledge the International Union of Crystallography for their financial support and for facilitating the participation of Drs. Liebschner and Emsley through the Visiting Professorship program. Their expertise was invaluable in delivering the high-quality crystallographic training that characterized this course.

The exceptional interest demonstrated by 82 international applications validates the global need for this type of integrated training, while the successful focus on developing country participation directly advances IUCr's mission of promoting crystallographic development worldwide. This course serves as a model for future educational initiatives that can help ensure the global crystallographic community remains at the forefront of structural biology's continuing evolution.