Iris Young

Computational Methods Developer in Structural Biology

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Proficiencies

- **Pump-probe serial XFEL crystallography,** rotation synchrotron crystallography, and knowledge of diffuse scattering, coherent diffractive imaging, and X-ray spectroscopies.
- **Expert Python and bash**, advanced C++, and experience in SQL, MATLAB, HTML, and others.
- **High Performance Computing (HPC)** at (pre)exascale supercomputers (NERSC, ALCF, OLCF).
- **Multiprocessing, multithreading and GPU acceleration** using MPI, OpenMP and Kokkos.
- **Machine learning (ML)** with understanding of CNNs, DL, supervised and unsupervised learning, etc.
- **GUI development** with wxWidgets and wxPython, as well as command line pipeline development.
- **Data visualization** including for time series, non-spatial data, and real-time feedback on streaming data.
- **Large dataset handling** on Lustre filesystems with attention to I/O and in MySQL or SQLite databases.

Research Experience

2022 – 2024 **Computational Project Scientist** Sauter group, Lawrence Berkeley National Laboratory

- Performed scaling and hardening of GPU-accelerated application *diffBragg* for X-ray free electron laser (XFEL) crystallography data processing, including fault tolerance for known problems with experimental XFEL data.
- Demonstrated *diffBragg* application at exascale (5120 nodes, >1 Tb/s data ingest rate) on supercomputer Frontier at Oak Ridge Leadership Computing Facility. Demonstrated performance portability between CUDA and Kokkos implementations on pre-exascale supercomputer Perlmutter at Lawrence Berkeley National Laboratory, and with Kokkos implementation, between Perlmutter (NVIDIA GPUs) and Frontier (AMD GPUs).
- Developed responsive, lightweight desktop application *sim_view* for display of simulated diffraction images and interactive tuning of parameters. Additionally ported *sim_view* to a Google Colab notebook.
- Provided on-site support at XFEL experiments, including as lead or sole member of the live data processing team. Trained newer group members in experiment support.

2018 – 2022 **Postdoctoral Fellow** Fraser lab, University of California, San Francisco

- Developed a python-based tool *qPTxM* for identification of post-transcriptional modifications in rRNA from electron density maps or, if sites of modification are known, as a measure of map quality (feature reliability). Tuned parameters for feature identification using a random forest classifier trained on simulated datasets. This tool aided in the discovery of the mechanism of resistance of bacterial ribosomes to the oxazolidinone class of antibiotics.
- Adapted density modification tool *denmod* for iterative map improvement for use in late stages of single particle cryogenic electron microscopy (cryoEM) map refinement. Incorporated into existing map refinement workflow in a fork of the open-source, GUI-based application *cisTEM*.
- Developed an automated pipeline for rapid, parallel processing of rotation crystallography datasets in a drug fragment screening campaign. Processing is robust to stochastic processing errors and misidentified space groups.

Education

2013 – 2018 **Ph.D., Chemistry** University of California, Berkeley
Mentors: Nicholas Sauter, Jan Kern, Junko Yano, Vittal Yachandra (LBNL)

- Contributed to open source code bases *cctbx.xfel* and *DIALS* for XFEL and synchrotron crystallography data processing, including major components of the *cctbx.xfel* GUI.
- Determined structures of photosystem II (PSII) in multiple metastable and transient illuminated states from XFEL diffraction experiments, leading to elimination of some proposed mechanisms of the water-splitting reaction in oxygenic photosynthesis.
- Extracted and purified PSII from *T. elongatus*, grew and screened crystals, and developed tools for automated refinement and analysis of PSII crystallographic datasets.

2003 – 2006 **B.A., Biological Chemistry** Grinnell College, IA
Coursework heavily concentrated in chemistry and mathematics.

Awards and Fellowships

2018 – 2022 **NIH/NIGMS Kirschstein NRSA (F32) Fellowship**
Disentangling conformational and compositional heterogeneity

2018 **Beverly Green Award for a Graduate Student Speaker**
27th Annual Western Photosynthesis Conference, "XFEL diffraction studies of the oxygen-evolving complex of photosystem II"

2017 **Springer Nature Best Poster Award**
24th Congress and General Assembly of the International Union of Crystallography, Hyderabad, India, "Insights into the oxygen-evolving mechanism of photosynthesis using XFELs"

Service

2023 Co-organizer, Serial Crystallography Methods Workshop, Cornell University
2023 Co-chair, Serial Crystallography session, 73rd ACA Annual Meeting, Baltimore, MD
2023 Workshop co-organizer, 10th BioXFEL International Conference, San Juan, Puerto Rico
2020 – 2021 Co-lead, Crystallography Subgroup, QBI Coronavirus Research Group, UCSF
2018 – 2019 Co-lead, Graduate and Postdoctoral Queer Alliance, UCSF
2017 – 2018 Co-lead, Lambda Alliance, Lawrence Berkeley National Laboratory (LBNL)
2017 – 2018 Co-organizer, Photosynthesis, Carbon Fixation and the Environment Symposium, UC Berkeley
2016 – 2018 Head organizer, Bioenergetics area seminar series at UC Berkeley and LBNL
2013 – 2016 Graduate student instructor for organic chemistry II laboratory, 3 semesters, UC Berkeley
2010 – 2013 Assistant instructor, grader, or tutor for Combinatorics, Linear Algebra, Organic Chemistry I and II, and Introductory Biology, 6 semesters, Grinnell College, IA

Selected Presentations

2023 2023 Structural Biology Summit, Los Angeles, CA
2022 ACA Annual Meeting 2022, Portland, OR
2022 Gordon Research Conference and Gordon Research Seminar: Diffraction Methods in Structural Biology, Lewiston, ME
2022 International School of Crystallography 2022, Erice, Italy
2022 Biophysical Society Meeting 2022, San Francisco, CA
2021 PDB50: A special symposium celebrating the 50th anniversary of the Protein Data Bank, online
2020 Bay Area CryoEM Meeting, Dublin, CA
2019 ImageXD, Berkeley Institute for Data Science, Berkeley, CA
2019 West Coast Structural Biology Workshop, Asilomar, CA
2019 6th Annual BioXFEL International Conference, San Diego, CA
2018 Gordon Research Conference and Gordon Research Seminar: Diffraction Methods in Structural Biology, Lewiston, ME
2018 5th Annual BioXFEL International Conference, New Orleans, LA
2018 27th Annual Western Photosynthesis Conference, Oracle, AZ
2016 Photosynthetic and Respiratory Complexes: From Structure to Function, Verviers, Belgium
2016 25th Western Photosynthesis Meeting, Tabernash, CO

Publications

Interpreting macromolecular diffraction through simulation
Iris D.Young et al. Methods in Enzymology 2023, DOI: 10.1016/bs.mie.2023.06.011

Mapping protein dynamics at high spatial resolution with temperature-jump X-ray crystallography
Alexander M. Wolff et al. Nature Chemistry 2023, DOI: 10.1038/s41557-023-01329-4

Structural characterization of ligand binding and pH-specific activity of mouse Acidic Mammalian Chitinase
Roberto Efraín Díaz et al. eLife 2023, DOI: 10.7554/eLife.89918.1

Structural basis for context-specific inhibition of translation by oxazolidinone antibiotics
Kaitlyn Tsai, Vanja Stojković, D. John Lee et al. Nature Structural and Molecular Biology 2022, DOI: 10.1038/s41594-022-00723-9

Changes in an enzyme ensemble during catalysis observed by high resolution XFEL crystallography
Nathan Smith et al. bioRxiv, forthcoming in Science Advances, DOI: 10.1101/2023.08.15.553460

Directed evolution of the rRNA methylating enzyme Cfr reveals molecular basis of antibiotic resistance
Kaitlyn Tsai et al. eLife 2022, DOI: 10.7554/eLife.70017

De novo determination of mosquitocidal Cry11Aa and Cry11Ba structures from naturally-occurring nanocrystals
Guillaume Tetreau et al. Nature Communications 2022, DOI: 10.1038/s41467-022-31746-x

Structural dynamics in the water and proton channels of photosystem II during the S2 to S3 transition
Rana Hussein et al. Nature Communications 2021, DOI: 10.1038/s41467-021-26781-z

Room temperature XFEL crystallography reveals asymmetry in the vicinity of the two phylloquinones in photosystem I
Stephen M. Keable et al. Scientific Reports 2021, DOI: 10.1038/s41598-021-00236-3

CryoEM and AI reveal a structure of SARS-CoV-2 Nsp2, a multifunctional protein involved in key host processes
Klliment Verba et al. bioRxiv 2021, DOI: 10.1101/2021.05.10.443524

Sentinel cells enable genetic detection of SARS-CoV-2 Spike protein
Zara Y. Weinberg et al. bioRxiv 2021, DOI: 10.1101/2021.04.20.440678

Fragment Binding to the Nsp3 Macrodomain of SARS-CoV-2 Identified Through Crystallographic Screening and Computational Docking
Marion Schuller, Galen Correy, Stefan Gahbauer et al. Science Advances 2021, DOI: 10.1126/sciadv.abf8711

Bi-paratopic and multivalent VH domains block ACE2 binding and neutralize SARS-CoV-2
Colton J. Bracken et al. Nature Chemical Biology 2020, DOI: 10.1038/s41589-020-00679-1

An ultrapotent synthetic nanobody neutralizes SARS-CoV-2 by stabilizing inactive Spike.
Michael Schoof et al. Science 2020, DOI: 10.1126/science.abe3255

Comparative Host-Coronavirus Protein Interaction Networks Reveal Pan-Viral Disease Mechanisms
David E. Gordon et al. Science 2020, DOI: 10.1126/science.abe9403

Untangling the sequence of events during the S2 to S3 transition in photosystem II and implications for the water oxidation mechanism
Mohamed Ibrahim, Thomas Fransson, Ruchira Chatterjee, Mun Hoh Cheah et al. PNAS 2020, DOI: 10.1073/pnas.2000529117

Serial femtosecond crystallography on in vivo-grown crystals drives elucidation of mosquitocidal Cyt1Aa bioactivation cascade
Guillaume Tetreau et al. Nature Communications, DOI: 10.1038/s41467-020-14894-w

Photoreversible Interconversion of a Phytochrome Photosensory Module in the Crystalline State
Sethe Burgie et al. PNAS 2020, DOI: 10.1073/pnas.1912041116

Comparing serial X-ray crystallography and microcrystal electron diffraction (MicroED) as methods for routine structure determination from small macromolecular crystals
Alexander M. Wolff et al. IUCrJ 2020, DOI: 10.1107/S205225252000072X

Assessment of the Nucleotide Modifications in the High-Resolution Cryo-Electron Microscopy Structure of the Escherichia Coli 50S Subunit
Vanja Stojković et al. Nucleic Acids Resaerch 2020, DOI: 10.1093/nar/gkaa037

Processing serial crystallographic data from XFELs or synchrotrons using the cctbx.xfel GUI
Aaron S. Brewster et al. Computational Crystallography Newsletter 2019

Structural Isomers of the S2 state in Photosystem II: Do they exist at room temperature and are they important for function?
Ruchira Chatterjee et al. Physiologia Plantarum 2019, DOI: 10.1111/ppl.12947

Biomaterials in non-integer dimensions (highlight)
Iris D. Young and James S. Fraser Nature Chemistry 2019, DOI: 10.1038/s41557-019-0286-x

Structures of the intermediates of Kok's photosynthetic oxygen clock
Jan Kern et al. Nature 2018, DOI: 10.1038/s41586-018-0681-2

Improving signal strength in serial crystallography with DIALS geometry refinement
Aaron S. Brewster et al. Acta Cryst D 2018, DOI: 10.1107/S2059798318009191

DIALS: implementation and evaluation of a new integration package
Graeme Winter et al. Acta Cryst D 2018, DOI: 10.1107/S2059798317017235

Sample Preparation and Data Collection for High-Speed Fixed-Target Serial Femtosecond Crystallography
Philip Roedig et al. Protocol Exchange 2017, DOI: 10.1038/protex.2017.059

High-speed fixed-target serial virus crystallography
Philip Roedig et al. Nature Methods 2017, DOI: 10.1038/nmeth.4335

Drop-on-demand sample delivery for studying biocatalysts in action at X-ray free-electron lasers
Franklin D. Fuller, Sheraz Gul et al. Nature Methods 2017, DOI: 10.1038/nmeth.4195

Structure of photosystem II and substrate binding at room temperature
Iris D. Young, Mohamed Ibrahim, Ruchira Chatterjee et al. Nature 2016, DOI: 10.1038/nature20161

Processing XFEL data with cctbx.xfel and DIALS
Aaron S. Brewster et al. Computational Crystallography Newsletter 2016f

Structural changes correlated with magnetic spin isomorphism in the S2 state of the Mn4CaO5 cluster in the oxygen-evolving complex of photosystem II
Ruchira Chatterjee et al. Chemical Science 2016, DOI: 10.1039/C6SC00512H

Towards characterization of photo-excited electron transfer and catalysis in natural and artificial systems using XFELs
Roberto Alonso-Mori et al. Faraday Discussions 2016, DOI: 10.1039/C6FD00084C

Concentric-flow electrokinetic injector enables serial crystallography of ribosome and photosystem II
Raymond G. Sierra et al. Nature Methods 2016, DOI: 10.1038/nmeth.3667