Darren Hsu

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Professional Summary

Computational scientist of biophysics with an extensive research experience in developing data-driven molecular simulations and artificial intelligence applications in leadership-class high performance computing environments. In addition, I have research interests in explaining experimental results with biological simulations, establishing software application workflows, and accelerating codes through algorithm development and parallelization.

Education

Ph.D. in Chemistry, Northwestern University (NU), Evanston, IL (2020)
B.S. in Chemistry, National Taiwan University (NTU), Taipei City, Taiwan (2015)

Work Experiences

Oak Ridge National Laboratory, Oak Ridge, TN (April 2021 – present)
Postdoctoral Research Associate

- Developed a first-in-class transformer-based AI model to predict bound structures of protein and ligand simultaneously. *(2022 ACM Gordon Bell COVID-19 Special Prize Finalist)*
- Developed a high-throughput workflow for induced-fit docking of ligands based on mdgx.cuda molecular dynamics code, achieving 1.18 ms of aggregated simulation in under two hours on Summit supercomputer.
- Developing X-ray scattering-based pose retrieval methods based on crystallographic refinement and molecular dynamics simulations.
- Collaborating with the ExaFEL ECP project by porting and debugging single particle imaging analysis code spinifel on the Crusher supercomputer.

AstraZeneca Pharmaceutical LP, Waltham, MA (October 2020 – April 2021)
Postdoctoral Fellow

- Developed enhanced MD sampling protocols to extract conformational dynamics information from multiple-state CryoEM datasets.
- Simulated activation process and closed-open dimer transition of ataxia telangiectasia-mutated kinase augmented by multiclass CryoEM data.
- Supported MD simulations of G-protein coupled receptors for investigation of extracellular domain motions.

Northwestern University, Evanston, IL (September 2015 – September 2020)
Graduate Research Assistant

- Investigated protein intermediate states through time-resolved X-ray absorption, scattering methods, experimental data-driven MD simulations and metadynamics.
- Commissioned temperature/pH/reductant-jumps with laser pulses for fast and indirect triggering of protein motion at the BioCARS beamline, Advanced Photon Source.
- Developed XSNAMD, a CUDA C code to accelerate X-ray scattering signal calculation in MD simulations by 10,000x. (https://github.com/darrenjhsu/XSNAMD)
- Co-developed pytrx, a python package for X-ray scattering experimental analysis
- (https://github.com/darrenjhsu/pytrx)
- Drafted NIH renewal proposal for the group, with a budget of $1.04 million.
- Collaborated in interdisciplinary projects involving > 25 X-ray scattering, absorption and emission experiments at synchrotrons and international X-ray Free Electron Lasers.

Skills

Computer Programming: Python (SciPy, scikit-learn, Tensorflow, PyTorch, QisKit), C, CUDA, Matlab, Bash, Tcl, High-performance computing, HIP, Slurm and IBM LSF submission scripts
Molecular Simulation: NAMD, GROMACS, AMBER, OpenMM
Computational Chemistry: RDKit, AutoDock, Schrodinger, VMD, PyMOL, Chimera
Productivity Applications: TEX(LaTEX), Vim, Microsoft Office, Git
Scientific Skills: Instrumental analysis (Spectroscopy and X-ray experiments), Signal analysis, Statistical modeling, Machine learning, Numerical simulations, Molecular dynamics simulations, Complex data visualization

Community Services

- Mentor, NERSC Hackathon (July 2021)
- Communications and New Hire Chair, Oak Ridge Postdoctoral Association (July 2021 – September 2022)
- Data Consultant, NU Research Computing Service (March – August 2020)
- Founding Member, NU Academics for Careers in Data Science (November 2018 – September 2019)
- Communications Chair, NU Research Safety Student Initiative (May 2018 – September 2020)
- Teaching Assistant, General Chemistry and Labs, NU (September 2015 – December 2016)
- Teaching Assistant, General Chemistry and Labs, NTU (February 2015 – June 2015)

Awards

- Finalist, 2022 ACM Gordon Bell Special Prize for High Performance Computing-Based COVID-19 Research (October 2022)

Submission: TwoFold: highly accurate structure and affinity prediction for protein-ligand complexes from sequences

- NU Department of Chemistry Award for Excellence in Graduate Research (November 2020)
- Department of Energy Office of Science Graduate Student Research Award (November 2018 – October 2019)
  Proposal: Investigating conformational gating of electron transfer in hybrid hemoglobin through time-resolved X-ray scattering.
- National Institute of Health Molecular Biophysics Training Program (September 2016 – June 2018)
  Proposal: Probing Metal Binding Sites and Conformations of Cytochrome c during its Folding
- College Student Research Scholarship, Ministry of Science and Technology of Taiwan (July 2014 – February 2015)
  Proposal: Potential Energy Surface Interpolation in the Nudged Elastic Band Method

Additional Training

- Qiskit Global Summer School, IBM, Global (July 2022)
- Ultrafast X-ray Summer School, DESY and EuXFEL, Hamburg, Germany (June 2017)
- BioSAXS training course, BioCAT at Argonne National Laboratory, IL, USA (October 2016)

Presentations

Unless otherwise noted presentations are in-person.

1. American Chemical Society Fall 2022 Meeting, Chicago, IL, 2022, "Transformers for Protein-ligand Binding" (talk)
2. Oak Ridge Postdoctoral Association Research Symposium, Oak Ridge, TN, 2022, "High-throughput Pose Refinement Through Induced Fit Ligand Docking" (talk)
3. American Physical Society March Meeting 2022, Chicago, IL, 2022 "High-throughput Pose Refinement Through Induced Fit Ligand Docking" (poster, remote)
4. Northwestern University, Evanston, Illinois, Department of Chemistry, 2021, Experiments Meet Molecular Simulations – Inferring Structural Dynamics Through Experimental Observables" (talk)
5. Science Engagement Section, Oak Ridge National Laboratory, Oak Ridge, TN, 2021, "Experiments Meet Molecular Simulations – Inferring Structural Dynamics Through Experimental Observables" (talk)
6. Oak Ridge Postdoctoral Association Research Symposium, Oak Ridge, TN, 2021, "High-throughput pose refinement for potential SARS-CoV-2 main protease inhibitors" (poster, remote)
7. Oak Ridge National Laboratory, Oak Ridge, Tennessee, Advanced Computing for Chemistry and Materials Group, 2021, "Incorporating X-ray scattering-derived force using GPU for molecular dynamics" (talk)
8. BioCARS Zoom seminar, Argonne, IL, 2020, "Characterizing transient molecular structures using time-resolved X-ray solution scattering" (talk, remote)

9. Nature Conference on Functional Dynamics, Tempe, AZ, 2019, "Tracking protein dynamics with time-resolved X-ray solution scattering coupled to environmental perturbations and molecular dynamics simulations" (poster)
10. NSRRC guest seminar, Hsinchu, Taiwan, 2019, "Tracking structure in real time through X-ray solution scattering" (talk)
11. Small-Angle Scattering Conference 2018, Traverse City, MI, 2018, "Ultrafast time-Resolved X-ray solution scattering at the BioCARS beamline" (talk)
12. Gordon Research Conference on Protein Folding, Galveston, TX, 2018, "Tracking the folding process of carbonmonoxy-cytochrome *c* Initiated by CO photo-dissociation with time-resolved X-ray absorption spectroscopy, X-ray solution scattering, and molecular dynamics simulations" (poster)
13. NTU Department of Chemistry Graduate Poster Presentation, Taipei, Taiwan, 2015, "A nudged elastic band study on rotational mechanisms of a molecular brake" (poster)

Publications

1. Denis Leshchev, Andrew J. S. Valentine, Pyosang Kim, Alexis W. Mills, Subhangi Roy, Arnab Chakraborty, Elisa Biasin, Kristoffer Haldrup, Darren J. Hsu, Matthew S. Kirschner, Dolev Rimmerman, Matthieu Chollet, J. Michael Glownia, Tim B. van Driel, Felix N. Castellano, Xiaosong Li, Lin X. Chen. Beyond the Born-Oppenheimer Approximation: Excited-state Trajectories of a Photoactive Transition Metal Complex in Real Time. Submitted to Nat. Chem.
2. Jens Glaser, Ada Sedova, Stephanie Galanie, Daniel Kneller, Russell Davidson, Elvis Maradzike, Sara Del Galdo, Audrey Labbè, Darren J. Hsu, Rupesh Agarwal, Dmytro Bykov, Arnold Tharrington, Jerry Parks, Dayle Smith, Isabella Daidone, Leighton Coates, Andrey Kovalevsky, Jeremy Smith. Hit expansion of a non-covalent SARS-CoV-2 main protease inhibitor. ACS Pharmacol. Transl. Sci. 2022, 5, 4, 255-265.
3. Michael W. Mara, Brian T. Phelan, Zhulin Xie, Tae Wu Kim, Darren J. Hsu, Xiaolin Liu, Andrew Valentine, Pyosang Kim, Xiaosong Li, Shin-ichi Adachi, Tetsuo Katayama, Karen Mulfort, Lin X. Chen. Unveiling Bridging Ligand Mediated Metal-Metal Interactions in Excited State Bimetallic Complexes. Chem. Sci. 2022, 13, 1715-1724
4. Adam K. Nijhawan, Arnold M. Chan, Darren J. Hsu, Lin X. Chen, Kevin L. Kohlstedt. Resolving dynamics in the ensemble: Finding paths through intermediate states and disordered protein structures. J. Chem. Phys. B 2021, 125, 12401-12412.
5. Darren J. Hsu, Denis Leshchev, Irina Kosheleva, Kevin L. Kohlstedt and Lin X. Chen. Unfolding bovine alpha-lactalbumin with T-jump: characterizing disordered intermediates via time-resolved X-ray solution scattering and molecular dynamics simulations. J. Chem. Phys. 2021, 154, 105121. (Featured, Editor's Choice 2021)
6. Darren J. Hsu, Denis Leshchev, Irina Kosheleva, Kevin L. Kohlstedt and Lin X. Chen. Integrating solvation shell structure in experimentally driven molecular dynamics using X-ray solution scattering data. J. Chem. Phys. 2020, 152, 204115.

7. Allison Devitt, Darren J. Hsu, Jos van den Eijnde, Michael B. Blayney, Rachel D. Dicken. Literature Highlights. ACS Chemical Health & Safety, 2020, 27, 2, 83-85
8. Darren J. Hsu, Denis Lechshev, Dolev Rimmerman, Jiyun Hong, Matthew S. Kelley, Irina Kosheleva, Xiaoyi Zhang and Lin X. Chen. X-ray Snapshots of Protein Folding Reveal Global Conformational Influence on Active Site Ligation. Chem. Sci., 2019, 10, 9788-9800.
9. Dolev Rimmerman, Denis Lechshev, Darren J. Hsu, Jiyun Hong, Baxter Abraham, Irina Kosheleva, Robert Henning and Lin X. Chen. Revealing Fast Structural Dynamics in pH-Responsive Peptides with Time-Resolved X-ray Scattering. J. Phys. Chem. B 2019, 123, 9, 2016-2021.
10. Dolev Rimmerman, Denis Lechshev, Darren J. Hsu, Jiyun Hong, Baxter Abraham, Robert Henning, Irina Kosheleva and Lin X. Chen. Probing Cytochrome c Folding Transitions Upon Photo-Triggered Environmental Perturbations Using Time-Resolved X-Ray Scattering. J. Phys. Chem. B 2018, 122, 20, 5218-5224.
11. Dolev Rimmerman, Denis Lechshev, Darren J. Hsu, Jiyun Hong, Baxter Abraham, Irina Kosheleva, Robert Henning and Lin X. Chen. Insulin hexamer dissociation dynamics revealed by photoinduced T-jumps and time-resolved X-ray solution scattering. Photochem. Photobiol. Sci. 2018, 17, 874-882.
12. Dolev Rimmerman, Denis Lechshev, Darren J. Hsu, Jiyun Hong, Irina Kosheleva and Lin X. Chen. Direct Observation of Insulin Association Dynamics with Time-Resolved X-ray Scattering. J. Phys. Chem. Lett. 2017, 8, 4413-4418.