

Darren Jason Hsu

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EDUCATION

- **Ph.D. in Chemistry, Northwestern University, Evanston, IL** 2015 – 2020
 - **Dissertation:** Characterizing Protein Folding Intermediates with Time-resolved X-ray Methods and Molecular Dynamics Simulations.
 - **Advisor:** Prof. Lin Chen
- **B.S. in Chemistry, National Taiwan University, Taipei, Taiwan** 2011 – 2015
 - **Project:** Finding the Reaction Trajectory for a Molecular Motor Using Nudged Elastic Band Method.
 - **Advisor:** Prof. Yuan-Chung Cheng

WORK EXPERIENCE

- **Postdoctoral Research Associate, Oak Ridge National Laboratory** 2021 – present
 - Developing AI-based drug binding pose prediction methods based on language models.
 - Developing high-throughput induced-fit docking of ligands based on `mdgx.cuda` molecular dynamics code.
 - Developing X-ray scattering-based pose retrieval methods based on crystallographic refinement and molecular dynamics simulations.
- **Postdoctoral Fellow, AstraZeneca Pharmaceutical LP** 2020 – 2021
 - 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.
- **Graduate Research Assistant, Northwestern University** 2015 – 2020
 - **Advisor:** Prof. Lin Chen
 - Investigated protein intermediate states through time-resolved X-ray absorption/scattering methods and enhanced MD simulations including metadynamics and steering MD.
 - Commissioned temperature/pH/reductant-jumps with laser pulses for fast yet 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>)
 - Collaborated in interdisciplinary projects involving > 25 X-ray scattering, absorption and emission experiments at synchrotrons and international XFELs.
- **Teaching Assistant, General Chemistry and Labs, NU and NTU** 2015 – 2016
 - Prepared lab supplies, lectured and provided help for students in groups of 20 during experiments, graded lab reports, and discussed progress of individual students with lab class organizers.

SKILLS

- **Computational Skills:** **Python** (NumPy, SciPy, Pandas, scikit-learn, Tensorflow, Keras), **C** (CUDA), Matlab, Shell, Linux, Git, High-performance computing, NAMD, GROMACS, Tcl, L^AT_EX
- **Scientific Skills:** Instrumental analysis (Spectroscopy and X-ray experiments), Signal analysis, Statistical modeling, Machine learning, Numerical simulations, Molecular dynamics simulations, Complex data visualization

EXTRACURRICULAR ACTIVITIES

- **Research Computing Service Data Consultant, Northwestern University** 2020
 - Provided consult for Northwestern community on research and coding related questions (machine learning strategies, image processing, Python, R, Matlab, JavaScript, etc.)
- **Academics for Careers in Data Science, Northwestern University** 2019 – 2020
 - Led the “Plover” bird ID project that aims to identify 400 North American bird species from user-uploaded photos through a convolutional neural network.
- **Research Safety Student Initiative, Northwestern University** 2018 – 2020
 - Collaborated with Office of Research Safety, edited bi-monthly newsletters, interviewed professors, and maintained RSSI website to disseminate safety related topics in the University.

AWARDS

- **Department of Chemistry Award for Excellence in Graduate Research, Northwestern University** 2020
- **Department of Energy Office of Science Graduate Student Research Award** 2018 – 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** 2016 – 2018
Proposal: Probing Metal Binding Sites and Conformations of Cytochrome *c* during its Folding
- **Dean’s Award of College of Science, National Taiwan University** 2015
- **Ministry of Science and Technology of Taiwan College Student Research Scholarship** 2014
Proposal: Potential Energy Surface Interpolation in the Nudged Elastic Band Method.

PRESENTATIONS

10. Northwestern University, Evanston, Illinois, Department of Chemistry, 2021, “Experiments Meet Molecular Simulations – Inferring Structural Dynamics Through Experimental Observables” (talk)
9. Oak Ridge National Laboratory, Oak Ridge, Tennessee, Science Engagement Section, 2021, “Experiments Meet Molecular Simulations – Inferring Structural Dynamics Through Experimental Observables” (talk)
8. Oak Ridge Postdoctoral Association Research Symposium, Oak Ridge, TN, 2021, “High-throughput pose refinement for potential SARS-CoV-2 main protease inhibitors” (poster)

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)
6. BioCARS Zoom seminar, Virtual, 2020, "Characterizing transient molecular structures using time-resolved X-ray solution scattering" (talk)
5. 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)
4. NSRRC guest seminar, Hsinchu, Taiwan, 2019, "Tracking structure in real time through X-ray solution scattering" (talk)
3. Small-Angle Scattering Conference 2018, Traverse City, MI, 2018, "Ultrafast time-Resolved X-ray solution scattering at the BioCARS beamline" (talk)
2. 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)
1. NTU Department of Chemistry Graduate Poster Presentation, Taipei, Taiwan, 2015, "A nudged elastic band study on rotational mechanisms of a molecular brake" (poster)

PUBLICATIONS

11. Jens Glaser, Ada Sedova, Stephanie galanie, Daniel Kneller, Russell Davidson, Elvis Maradzike, Sara Del Galdo, Audrey Labbé, **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. *Accepted, ACS Pharmacology & Translational Science*.
10. 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
9. 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.
8. **Darren J. Hsu**, Denis Leshchev, Irina Kosheleva, Kevin L. Kohlstedt and Lin X. Chen. Unfolding bovine α -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**)
7. **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.
6. 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
5. **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.

4. 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.
3. 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.
2. 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.
1. 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.