Darren Jason Hsu

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EDUCATION

Northwestern University   Evanston, IL, USA
Ph.D. in Chemistry, Advisor: Prof. Lin Chen   2015 – 2020

– Dissertation: "Characterizing Protein Folding Intermediates with Time-resolved X-ray Methods and Molecular Dynamics Simulations"

National Taiwan University   Taipei, Taiwan
B.S. in Chemistry, Advisor: Prof. Yuan-Chung Cheng   2011 – 2015

– Project: "Finding the Reaction Trajectory for a Molecular Motor Using Nudged Elastic Band Method"

WORK EXPERIENCES

Oak Ridge National Laboratory   Knoxville, TN, USA
Postdoctoral Research Associate   2021 – present

– Developing AI-based drug binding pose prediction methods based on language models.

– Developing high-throughput workflow for 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.

AstraZeneca Pharmaceutical LP   Waltham, MA, USA
Postdoctoral Fellow   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.

Northwestern University   Evanston, IL, USA
Graduate Research Assistant   2015 – 2020

– 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.

Skills

- **Computer Programming**: **Python** (NumPy, SciPy, Pandas, scikit-learn, Tensorflow, PyTorch), C, CUDA, Matlab, Bash, Tcl, High-performance computing

- **Molecular Simulation**: NAMD, GROMACS, AMBER

- **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

- **Executive Committee, Oak Ridge Postdoctoral Association (ORPA)**   2021 – present
    - Served as New Hire and Communications Committees Chair that offered guidance to new postdocs and communicated to 300 postdocs and 250 staff in Oak Ridge National Lab through newsletters and website. Helped organize the 10th ORPA Research Symposium.

- **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

Unless otherwise noted presentations are in-person.

13. American Chemical Society Fall 2022 Meeting, Chicago, IL, 2022, "Transformers for Protein-ligand Binding" (talk)

12. Oak Ridge Postdoctoral Association Research Symposium, Oak Ridge, TN, 2022, "High-throughput Pose Refinement Through Induced Fit Ligand Docking" (talk)

11. American Physical Society March Meeting 2022, Chicago, IL, 2022 "High-throughput Pose Refinement Through Induced Fit Ligand Docking" (poster, remote)

10. Northwestern University, Evanston, Illinois, Department of Chemistry, 2021, "Experiments Meet Molecular Simulations – Inferring Structural Dynamics Through Experimental Observables" (talk)

9. Science Engagement Section, Oak Ridge National Laboratory, Oak Ridge, TN, 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, 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)

6. BioCARS Zoom seminar, Argonne, IL, 2020, "Characterizing transient molecular structures using time-resolved X-ray solution scattering" (talk, remote)

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. *ACS Pharmacol. Transl. Sci.* **2022**, *5*, 4, 255-265.

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.