Darren Jason Hsu

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Professional Summary

Solutions Architect at NVIDIA with an extensive background of developing data-driven molecular simulations and machine learning applications in leadership-class high performance computing environments. In addition, I have interests in explaining experimental results with biological simulations, establishing software application workflows, and accelerating codes through algorithmic development and parallelization.

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

NVIDIA Corporation — Remote, USA
Solutions Architect — 2023 – present

– Driving customer adoption of NVIDIA platform products in the healthcare and life science field.

Oak Ridge National Laboratory — Oak Ridge, TN, USA
Postdoctoral Research Associate — 2021 – 2023

– Developed a first-in-class transformer-based AI model to predict bound structures of protein *and* ligand.
– Developed a 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.
– Collaborating with the ExaFEL ECP project to port and debug single particle imaging analysis code `spinifel` on the Crusher supercomputer.

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)
- 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** (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 – 2022
- **Mentor, NERSC Hackathon** July 2021
- **Research Computing Service Data Consultant, Northwestern University** 2020
- **Academics for Careers in Data Science, Northwestern University** 2019 – 2020
- **Research Safety Student Initiative, Northwestern University** 2018 – 2020
- **Teaching Assistant, General Chemistry and Labs, NU and NTU** Feb. 2015 – Dec. 2016

Awards

- **Finalist, 2022 ACM Gordon Bell Special Prize for High Performance Computing-Based COVID-19 Research** 2022
  Submission: TwoFold: highly accurate structure and affinity prediction for protein-ligand complexes from sequences
- **Department of Chemistry Award for Excellence in Graduate Research, Northwestern University** 2020
  Thesis: Characterizing Transient Disordered Protein Structures with Time-Resolved X-Ray Techniques and Molecular Dynamics Simulations
- **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
- **College Student Research Scholarship, Ministry of Science and Technology of Taiwan** 2014
  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, USA** October 2016

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

15. **Darren J. Hsu**, Hao Lu, Aditya Kashi, Michael Matheson, John Gounley, Feiyi Wang, Wayne Joubert and Jens Glaser. TwoFold: Highly Accurate Structure and Affinity Prediction for Protein-ligand Complexes from Sequences. *Accepted, The International Journal of High Performance Computing Applications*

14. **Darren J. Hsu**, Russell B. Davidson, Ada Sedova, Jens Glaser. tinyIFD: A High-throughput Binding Pose Refinement Workflow Through Induced-fit Ligand Docking. *J. Chem. Inf. Model.* **2023**, *63*, 11, 3438-3447.

13. 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. *Angew. Chem. Int. Ed.* **2023**, *e202304615*.

12. Arnold M. Chan, Adam K. Nijhawan, Darren J. Hsu, Denis Leshchev, Dolev Rimmerman, Irina Kosheleva, Kevin L. Kohlstedt, Lin X. Chen. The Role of Transient Intermediate Structures in the Unfolding of the Trp-Cage Fast-Folding Protein: Generating Ensembles from Time-Resolved X-ray Solution Scattering with Genetic Algorithms. *J. Phys. Chem. Lett.* **2023**, *14*, 5, 1133-1139.

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.