Zhiyu (Joe) Zhao

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Professional Profile

Innovative Biophysics Ph.D. with expertise in computational biology and scientific software development. Skilled in molecular dynamics, ligand docking, enhanced sampling, and AI-powered modeling, with a strong foundation in physics and computer science. Independently developed key ligand docking software and simulation analysis tools, contributing significantly to the field. Seeking to apply my experience in biomolecular modeling and algorithm design to support drug discovery on modern cloud platforms.

Education

Ph.D. in Biophysics, **University of Illinois Urbana-Champaign** 08/2015 - 05/2022

Dissertation: Insights into Dynamics of Membrane Transporters from Computational Techniques

Relevant Coursework: Cell & Membrane Physiology, Statistical Physics, Artificial Intelligence

B.S. in Physics, completed CS major coursework, **Shanghai Jiao Tong University** 09/2011 - 07/2015

Research Experience

Postdoc Scholar in Computer Science Department, **Stanford University** 08/2022 - 04/2024

- Led multi-μs-scale MD simulations to investigate biased signaling mechanisms in GPCRs, revealing how ligand-specific conformations influence G protein vs. arrestin pathway selectivity.
- Modeled GPCR-ligand and GPCR-kinase interactions using AlphaFold and DiffDock, gaining hands-on experience with AI-powered tools for structure-based modeling of protein–ligand and protein–protein complexes, directly supporting drug discovery efforts.

Graduate Research Assistant, NIH Center for Macromolecular Modeling and Bioinformatics, **University of Illinois Urbana-Champaign** 01/2016 – 07/2022

- Independently designed and developed a cryo-EM-guided ligand docking toolkit (GOLEM).
  - Implemented an evolutionary search algorithm with gradient descent to efficiently explore ligand binding poses. Designed a physics-based scoring function integrated with cryo-EM density restraints for accurate ligand docking with explicit water modeling.
  - Developed a desktop GUI for non-technical users to launch, monitor, and visualize the docking process in real time, reducing setup time from ∼1 hour to ∼5 minutes via GUI automation.
  - The tool has been adopted by multiple collaborating labs and integrated into ongoing pipelines, contributing to publications in ***Nature***, ***Cell***, and ***JCIM***.
- Executed MD simulations with enhanced sampling techniques (e.g., umbrella sampling, FEP, metadynamics) to quantify how ligand binding modulates protein conformational dynamics. Representative examples:
  - Used steered MD and umbrella sampling to dissect serotonin occlusion in SERT; revealed how ligand-induced interaction networks regulate serotonin import, published in ***Biochemistry*** (2025).
  - Applied FEP to compute binding free energy changes between active/inactive states of a lipid-sensitive ion channel, validating the lipid-modulated activation mechanism (***PNAS***, 2020).
- Collaborated closely with experimental biologists to design simulations aligned with wet-lab hypotheses, interpret modeling results for biological insights, and co-author multi-disciplinary publications.

Technical Skills

Programming	Python	PyTorch	C++	Tcl/Tk	Linux
Software Tools	VMD	NAMD	AMBER	PyMOL	Schrödinger	OpenMM
Expertise	Molecular Dynamics Simulation	Free Energy Calculation	Ligand Docking	Machine Learning	Biological Systems including Membrane Transporters, Ion Channels, and GPCRs

Selected Software Products

GOLEM: an automated and robust ligand docking program to prepare, perform, and visualize cryo-EM-guided ligand docking with explicit water molecules, employed in publications in ***Nature*** and ***Cell***. [Codes available online] [Paper]

Publications

1. **Z. Zhao**, P.-C. Wen, and E. Tajkhorshid. An orchestrated interaction network at the binding site of human SERT enables the serotonin occlusion and import. ***Biochemistry***, in press, **2025**
2. **Z. Zhao** and E. Tajkhorshid. GOLEM: Automated and robust cryo-EM-guided ligand docking with explicit water molecules. ***Journal of Chemical Information and Modeling***, 64(14), 5680-5690, **2024**
3. J. Ge, J. Elferich, S. Dehghani-Ghahnaviyeh, **Z. Zhao**, M. Meadows, H. v. Gersdorff, E. Tajkhorshid, and E. Gouaux. Molecular mechanism of prestin electromotive signal amplification. ***Cell***, 184, 4669–4679, **2021**
4. J. A. Coleman, D. Yang, **Z. Zhao**, P.-C. Wen, C. Yoshioka, E. Tajkhorshid, and E. Gouaux. Serotonin transporter-ibogaine complexes illuminate mechanisms of inhibition and transport. ***Nature***, 569: 141–145, **2019**
5. D. Yang, **Z. Zhao**, E. Tajkhorshid, and E. Gouaux. Structures and membrane interactions of native serotonin transporter in complexes with psychostimulants. ***Proceedings of the National Academy of Sciences***, 120(29), e2304602120, **2023**
6. S. Dehghani-Ghahnaviyeh, **Z. Zhao**, and E. Tajkhorshid. Lipid-mediated prestin organization in outer hair cell membranes and its implications in sound amplification. ***Nature Communications***, 13, 6877, **2022**
7. P. Kumar, Y. Wang, Z. Zhang, **Z. Zhao**, G. D. Cymes, E. Tajkhorshid, and C. Grosman. Cryo-EM structures of a lipid-sensitive pentameric ligand-gated ion channel embedded in a phosphatidylcholine-only bilayer. ***Proceedings of the National Academy of Sciences***, 117: 1788–1798, **2020**
8. J. Li, **Z. Zhao**, and E. Tajkhorshid. Locking two rigid-body bundles in an outward-facing conformation: The ion-coupling mechanism in a LeuT-fold transporter. ***Scientific Reports***, 9: 1–13, **2019**
9. M. L. Starr, R. P. Sparks, A. S. Arango, L. R. Hurst, **Z. Zhao**, M. Lihan, E. Tajkhorshid, and R. A. Fratti. Phosphatidic acid induces conformational changes in Sec18 protomers that prevent SNARE priming. ***Journal of Biological Chemistry***, 294: 3100–3116, **2019**
10. T. Jiang, P.-C. Wen, N. Trebesch, **Z. Zhao**, S. Pant, K. Kapoor, M. Shekhar, and E. Tajkhorshid. Computational dissection of membrane transport at a microscopic level. ***Trends in Biochemical Sciences***, 45: 202–216, **2019**
11. P.-C. Wen, P. Mahinthichaichan, N. Trebesch, T. Jiang, **Z. Zhao**, E. Shinn, Y. Wang, M. Shekhar, K. Kapoor, C. K. Chan, and E. Tajkhorshid. Microscopic view of lipids and their diverse biological functions. ***Current Opinion in Structural Biology***, 51: 177–186, **2018**
12. J. V. Vermaas, N. Trebesch, C. G. Mayne, S. Thangapandian, M. Shekhar, P. Mahinthichaichan, J. L. Baylon, T. Jiang, Y. Wang, M. P. Muller, E. Shinn, **Z. Zhao**, P.-C. Wen, and E. Tajkhorshid. Microscopic characterization of membrane transport function by *in silico* modeling and simulation. ***Methods in Enzymology***, 578: 373–428, **2016**