Wei-Tse **Hsu**

Postdoctoral Research Associate
S Parks Rd, Oxford OX1 3QU, UK
wehs766@colorado.edu | weitsehsu.com | wehs7661 | Google Scholar

References: Michael R. Shirts (michael.shirts@colorado.edu), Giovanni Bussi (bussi@sissa.it), and Tarek Sammakia (sammakia@colorado.edu)

Education & Training

University of Oxford
Oxford, UK

Postdoctoral Research Associate in Drug Design — *Starting from Oct. 2024*

- Advisor: Prof. Philip C. Biggin
- Research topics: Deep learning, Cheminformatics, Molecular dynamics, Computational biophysics

University of Colorado, Boulder
Boulder, CO, U.S.A.

Ph.D. in Chemical Engineering — *Sept. 2018 - May 2024*

- Advisor: Prof. Michael R. Shirts
- Research topics: Molecular dynamics, Enhanced sampling methods, Computational biophysics
- Dissertation title: Exploring Conformational Ensembles of Biomolecules Using Molecular Dynamics (defended in Nov. 2023)

National Taiwan University
Taipei, Taiwan

B.Sc. in Chemical Engineering — *Sept. 2013 - June 2017*

- Research advisors: Prof. Steven Sheng-Shih Wang and Prof. Ling Chao

Research Experience

Biggin Lab, Department of Biochemistry, University of Oxford
Oxford, UK

Postdoctoral Research Associate — *Starting from Oct. 2024*

- *Advisor: Prof. Philip Biggin*
- Developing neural networks for binding affinity predictions of protein-ligand complexes.

Shirts Research Group, Department of Chemical and Biological Engineering, University of Colorado, Boulder
Boulder, CO, U.S.A.

Ph.D. Researcher — *Sept. 2018 - Nov. 2023*

- *Advisor: Prof. Michael R. Shirts*
- Developed synchronous replica exchange of expanded ensembles (REXEE) by combining the working principles of replica exchange (REX) and expanded ensemble (EE).
- Developed alchemical metadynamics, which enables alchemical biases in the metadynamics framework and overcomes limitations of traditional alchemical free energy methods.
- Developed methods based on molecular dynamics to predict the proteolytic stability and monomeric propensity of glycosylated insulin.
- Helped design SCALE-MS, an extensible framework aiming to support adapative and asynchronous executions of simulation ensembles.
- Maintained physical_validation, a Python package designed for testing results from molecular dynamics for their physical validity.

Biomolecular Engineering Laboratory, Department of Chemical Engineering, National Taiwan University
Taipei, Taiwan

Undergraduate Researcher/Research Assistant — *July 2016 - April 2018*

- *Advisor: Prof. Steven Sheng-Shih Wang*
- Explored the effects of various small molecules on the amyloid fibrillogenesis of hen egg-white lysozyme (HEWL) with a wide array of spectroscopic experiments.
- Investigated the aggregation process of human γD-crystallin (HGDC) using molecular dynamics and molecular docking.

Biomimetic Membrane Interfacial Phenomena and Engineering Laboratory, Department of Chemical Engineering, National Taiwan University *Taipei, Taiwan*

UNDERGRADUATE RESEARCHER *July 2015 - Feb. 2016*

- *Advisor: Prof. Ling Chao*
- Developed MATLAB codes to accurately estimate fluorophore diffusivity on lipid membranes by fitting fluorescence intensity curves from FRAP (fluorescence recovery after photobleaching) experiments ($R^2 > 0.97$).
- Experimented methods for depositing giant plasma membrane vesicles (GPMVs) on polymer cushions.
- Constructed supported lipid bilayer (SLB) platforms to study membrane protein properties.

Research Output

PUBLICATIONS AND PREPRINTS

8. **Hsu**, W. T., & Shirts, M. R. (2024). Replica Exchange of Expanded Ensembles: A Generalized Ensemble Approach with Enhanced Flexibility and Parallelizability. *Journal of Chemical Theory and Computation*, doi: 10.1021/acs.jctc.4c00484
7. **Hsu**, W. T., Piomponi, V., Merz, T. M., Bussi, G., & Shirts, M. R. (2023). Alchemical metadynamics: Adding alchemical variables to metadynamics to enhance sampling in free energy calculations. *Journal of Chemical Theory and Computation*, doi: 10.1021/acs.jctc.2c01258
6. **Hsu**, W. T., Ramirez, D. A., Sammakia, T., Tan, Z., & Shirts, M. R. (2022). Identifying signatures of proteolytic stability and monomeric propensity in *O*-glycosylated insulin using molecular simulation. *Journal of Computer-Aided Molecular Design*, 1-16. doi: 10.1007/s10822-022-00453-6
5. Merz, P. T., **Hsu**, W. T., Thompson, M. W., Boothroyd, S., Walker, C. C., & Shirts, M. R. (2022). physical_validation: A Python package to assess the physical validity of molecular simulation results. *Journal of Open Source Software*, 7(69), 3981. doi: 10.21105/joss.03981
4. How, S. C., Hsin, A., Chen, G. Y., **Hsu**, W. T., Yang, S. M., Chou, W. L., Chou, S. H., & Wang, S. S. S. (2019). Exploring the influence of brilliant blue G on amyloid fibril formation of lysozyme. *International Journal of Biological Macromolecules*, 138, 37-48. doi: 10.1016/j.ijbiomac.2019.07.055
3. Ulicna, K., Bednarikova, Z., **Hsu**, W. T., Holztragerova, M., Wu, J. W., Hamulakova, S., Wang, S. S. S., & Gazova, Z. (2018). Lysozyme amyloid fibrillization in presence of tacrine/acridone-coumarin heterodimers. *Colloids and Surfaces B: Biointerfaces*, 166, 108-118. doi: 10.1016/j.colsurfb.2018.03.010
2. How, S. C.*, **Hsu**, W. T.*, Tseng, C. P.*, Lo, C. H., Chou, W. L., & Wang, S. S. S. (2018). Brilliant blue R dye is capable of suppressing amyloid fibril formation of lysozyme. *Journal of Biomolecular Structure and Dynamics*, 36(13), 3420-3433. doi: 10.1080/07391102.2017.1388848 (*All these authors contributed equally to this work.)
1. Kuo, C. T., Chen, Y. L., **Hsu**, W. T., How, S. C., Cheng, Y. H., Hsueh, S. S., Liu H. S., Lin T. S., Wu J. W. & Wang, S. S. S. (2017). Investigating the effects of erythrosine B on amyloid fibril formation derived from lysozyme. *International Journal of Biological Macromolecules*, 98, 159-168. doi: 10.1016/j.ijbiomac.2017.01.110

PUBLICATIONS IN PREPARATION

3. **Hsu** W. T., Sammakia, T., Tan, Z., & Shirts, M. R. Deep learning structural determinants for distinguishing conformational ensembles of insulin glycoforms with varying proteolytic stability and dimerization propensity.
2. **Hsu** W. T., Friedman A. J., & Shirts, M. R. Multi-topology alchemical calculations using ensembles of expanded ensemble simulations.
1. Fobe T. L., Walker C. C., **Hsu** W. T., & Shirts, M. R. Prediction and characterization study of terphenyl oligomer foldamer secondary structure using enhanced sampling molecular dynamics.

CONFERENCE ORAL PRESENTATIONS

7. **Hsu**, W. T., Merz, P., Bussi, G., & Shirts, M. R. Accelerated free energy calculations by joint biasing in configurational and alchemical space in metadynamics. AIChE Annual Meeting. Pheonix, AZ, U.S.A. (November, 2022)
6. **Hsu**, W. T., Merz, P., Bussi, G., & Shirts, M. R. Accelerated free energy calculations and enhanced configurational sampling by the introduction of alchemical variables in metadynamics. ACS Fall Meeting, Chicago, IL, U.S.A. (August, 2022)
5. **Hsu**, W. T., Ramirez, D., Tan, Z., Sammakia, T., & Shirts, M. R. Investigating the influence of *O*-linked glycosylation on the proteolytic stability and dimerization propensity of insulin using molecular dynamics. ACS Spring Meeting. San Diego, CA, U.S.A. (March, 2022)
4. **Hsu**, W. T., Merz, P., Bussi, G., & Shirts, M. R. Improved configurational sampling by the the introduction of alchemical variable in metadynamics. AIChE Annual Meeting. Boston, MA (November, 2021)
3. **Hsu**, W. T., Hsin, A., Wu, J. W., & Wang, S. S. S. Brilliant blue G's inhibitory effects on amyloid fibril formation of lysozyme. Green Bioprocessing Engineering Forum. New Taipei, Taiwan (November, 2017)
2. **Hsu**, W. T., Hsin, A., Wu, J. W., & Wang, S. S. S. Investigating the suppressing effects of brilliant blue G on amyloid fibrillogenesis of lysozyme. Annual Meeting of Taiwan Institute of Chemical Engineers (TwIChE). Taipei, Taiwan (December, 2017)
1. **Hsu**, W. T., Hsin, A., Wu, J. W., & Wang, S. S. S. Exploring the inhibitory activity of brilliant blue G toward the formation of amyloid fibrils

derived from lysozyme. BEST Conference & International Symposium on Biotechnology and Bioengineering. Yunlin, Taiwan (June, 2017)

Conference poster presentations

12. **Hsu**, W.T., & Shirts, M. R. Enhancing flexibility and parallelizability of alchemical free energy calculations with replica exchange of expanded ensembles. ACS Fall Meeting, Denver, CO, U.S.A. (August, 2024, Upcoming)
11. **Hsu**, W. T., Ramirez, D., Tan, Z., Lam, A., Sammakia, T., & Shirts, M. R. Guiding chemical synthesis of glycosylated insulin for enhanced oral bioavailability with computational insights. The Joint Symposium of the Taiwan Biophysical Society and International Network of Protein Engineering Centers. Hsinchu, Taiwan. (May, 2024)
10. **Hsu**, W. T., Piomponi, V., Merz, P., Bussi, G., & Shirts, M. R. Innovations in alchemical free energy methods: Introducing alchemical metadynamics and REXEE. 2023 Workshop on Free Energy Methods in Drug Design. Leiden, Netherlands. (May, 2024)
9. **Hsu**, W. T., Piomponi, V., Merz, P., Bussi, G., & Shirts, M. R. Advancing alchemical free energy methods: Enhanced flexibility, parallelizability and configurational sampling. AIChE Annual Meeting, Orlando, FL, U.S.A. (November, 2023)
8. **Hsu**, W. T., Piomponi, V., Merz, P., Bussi, G., & Shirts, M. R. Expanding alchemical free energy calculations: From enhanced configurational sampling to ensemble simulation methods. ACS Fall Meeting, San Francisco, CA, U.S.A. (August, 2023)
7. **Hsu**, W. T., Piomponi, V., Merz, P., Bussi, G., & Shirts, M. R. Enhancing configurational sampling, flexibility, and parallelizability of alchemical free energy methods. The 5th i-CoMSE Workshop: Machine Learning for Molecular Science. Minneapolis, MN, U.S.A. (July, 2023)
6. **Hsu**, W. T., Piomponi, V., Merz, P., Bussi, G., & Shirts, M. R. Alchemical metadynamics: Enhancing configurational sampling in alchemical free energy calculations. 2023 Workshop on Free Energy Methods in Drug Design. Boston, MA, U.S.A. (May, 2023)
5. **Hsu**, W. T., Merz, P., Bussi, G., & Shirts, M. R. Using alchemical variables within the metadynamics framework to improve sampling in free energy calculations. ACS Spring Meeting. San Diego, CA, U.S.A. (March, 2022)
4. **Hsu**, W. T., Ramirez, D., Tan, Z., Sammakia, T., & Shirts, M. R. Gaining mechanistic insights into the influence of *O*-linked glycosylation on insulin properties with molecular dynamics. AIChE Annual Meeting. Boston, MA, U.S.A. (November, 2021)
3. **Hsu**, W. T., Merz, P., Bussi, G., & Shirts, M. R. Introduction of alchemical variables in metadynamics to enhance configurational sampling. Virtual AIChE Annual Meeting. (November, 2020)
2. **Hsu**, W. T., Hsin, A., Wu, J. W., & Wang, S. S. S. Brilliant blue G's inhibitory effects on amyloid fibril formation of lysozyme. Green Bioprocessing Engineering Forum. New Taipei, Taiwan (December, 2017)
1. **Hsu**, W. T., Lin, T. W., & Fu, T. Y. Process optimization and economic assessment of the production of glycerol carbonate from glycerol. Annual Meeting of Taiwan Institute of Chemical Engineers (TwIChE). Taipei, Taiwan (November, 2017)

Invited talks

4. From fundamentals, innovations, to challenges ahead: An overview of enhanced sampling methods in molecular dynamics. Academic Seminar, Institute of Chemistry, Academia Sinica, Taipei, Taiwan (January 2024; link)
3. Developing molecular dynamics-based screening methods for identifying *O*-glycosylated insulin analogs with enhanced proteolytic stability and monomeric propensity. project TYRA Virtual Seminar Series. (May, 2022; link)
2. Investigating the influence of *O*-linked glycosylation on the proteolytic stability and dimerization propensity of insulin using molecular dynamics. Biophysics Supergroup Seminar, University of Colorado, Boulder. (October, 2021; link)
1. Improved methods for sampling the configurational space of flexible biomolecules. project TYRA Virtual Seminar Series. (April, 2021; link)

Open codes

5. **Hsu**, W.T. (2023). sampling_simulator: A Python package for simulating sampling behaviors of enhanced sampling simulations. GitHub.
4. **Hsu**, W. T. (2023). ensemble_md: A Python package for performing GROMACS simulation ensembles. GitHub.
3. **Hsu**, W. T., Piomponi V. (2023). alchemical_metadynamics: A repository for maintaining simulation inputs and analysis codes for alchemical metadynamics. GitHub.
2. **Hsu**, W. T., Ramirez, D. (2022). glycoinsulin_analysis: A python package for assessing the proteolytic stability and dimerization propensity of *O*-glycosylated insulin. GitHub.
1. Merz, P., **Hsu**, W. T., Thompson, M. W., Boothroyd, S., Walker, C. C., & Shirts, M. R. (2022). physical_validation: A Python package to assess the physical validity of molecular simulation results (v1.0.4). Zenodo. doi: 10.5281/zenodo.5815657

Honors & Awards

2023	**Graduate Student Award**, Computational Molecular Science & Engineering Forum (CoMSEF), American Institute of Chemical Engineers (AIChE)	*Orlando, FL, U.S.A.*
2017	**1st Prize**, 3-Minute Thesis Competition - Poster Presentation, 2017 Green Bioprocessing Engineering Forum	*New Taipei, Taiwan*
2017	**2nd Prize**, 3-Minute Thesis Competition - Oral Presentation, 2017 Green Bioprocessing Engineering Forum	*New Taipei, Taiwan*
2017	**1st Prize/Outstanding Research Paper Award**, Oral Presentation Competition, The 64th Annual Meeting of Taiwan Institute of Chemical Engineers	*Taipei, Taiwan*
2017	**3rd Prize**, 2017 Collegiate Process Design Competition, Taiwan Institute of Chemical Engineers	*Taipei, Taiwan*
2017	**1st Prize**, Oral Presentation Competition, 2017 BEST Conference & International Symposium on Biotechnology and Bioengineering	*Yunlin, Taiwan*
2015	**Excellent Work Award**, 2015 National Mechanics Competition, Society of Theoretical and Applied Mechanics of the Republic of China	*Taipei, Taiwan*

Teaching Experience

2023	**Instructor of Enhanced Sampling Virtual School 2023**, Institute for Computational Molecular Science Education (i-CoMSE)	*Online*
2023	**Teaching assistant of The 5th i-CoMSE Workshop: Machine Learning for Molecular Science**, Institute for Computational Molecular Science Education (i-CoMSE)	*Minneapolis, MN, U.S.A.*
2023	**Mentor of 1 graduate researcher (Barbara Morales)**, Shirts Research Group, Department of Chemical and Biological Engineering, University of Colorado, Boulder	*Boulder, CO, U.S.A.*
2022	**Teaching assistant of Molecular Dynamics and Monte Carlo Summer School**, Institute for Computational Molecular Science Education (i-CoMSE)	*Stillwater, OK, U.S.A.*
2020-22	**Mentor of 1 undergraduate researcher (Antonia Lam)**, Shirts Research Group, Department of Chemical and Biological Engineering, University of Colorado, Boulder	*Boulder, CO, U.S.A.*
2021	**Advanced teaching assistant of CHEN 4521: Physical Chemistry for Engineers**, Department of Chemical and Biological Engineering, University of Colorado, Boulder	*Boulder, CO, U.S.A.*
2019	**Teaching assistant of CHEN 3220: Chemical Engineering Separations**, Department of Chemical and Biological Engineering, University of Colorado, Boulder	*Boulder, CO, U.S.A.*

Service & Outreach

Peer Review Service

Jounral Reviewer — *Nov. 2023 - Present*

- Journal of Chemical Theory and Computation

Wei-Tse Hsu Personal Website

Owner/Developer — *Sept. 2022 - Present*

- Website URL: https://weitsehsu.com
- Organized mini-courses in computational chemistry, including
  - Hands-on tutorials: Advanced sampling methods using GROMACS
  - 3rd i-CoMSE Workshop: Methods for Advanced Sampling
- Authored articles about deep learning, computational science, mathematics, and coding tips.

Group of Public Relation, Taiwanese Young Researcher Association (project TYRA)

Core Member & Mentor *Aug. 2020 - Aug. 2022*

- Respectively assisted/led the 2020/2021 mentorship program, which collectively gathered 154 mentors to help 265 Taiwanese mentees with overseas graduate school applications.
- Led the 2021 Summer Workshop in overseas Ph.D. applications and delivered a talk at the workshop.
- Mentored 2 Taiwanese students in overseas Ph.D. applications in 2020 and 2021, respectively.
- Coordinated and promoted weekly academic webinars in various scientific disciplines.

American Institute of Chemical Engineers, National Taiwan University Student Chapter

Founding member & Treasurer *June 2016 - June 2017*

- Initiated the NTU Student Chapter in AIChE and managed financial assets of the organization.

Academic Section in Student Association, Department of Chemical Engineering, National Taiwan University *Taipei, Taiwan*

Minister *June 2015 - June 2016*

- Organized NTU Azalea Festival, a nationwide 2-day exposition introducing departments in NTU.
- Coordinated with department faculty and arranged talks on lab introduction to help undergraduates explore their research interests.

Professional Memberships

American Chemical Society (ACS) *2021 - Present*
American Institute of Chemical Engineers (AIChE) *2020 - Present*

Skills

Molecular simulation	GROMACS, PLUMED, Discovery Studio
Molecular visualization	Visual Molecular Dynamics (VMD), PyMol
Machine learning	Linear/Logistic regression, tree-based models, PCA, SVM, ANNs, CNNs, VAEs, GANs, flow-based models
Programming	Python, Git, LaTeX, MATLAB, Bash
Other applications	Aspen Plus, COMSOL, AutoCAD, Sketchup, GIMP
Wet-lab techniques	Spectroscopy (fluorescence, UV-Vis, CD), FRAP, TEM, ITC, DLS, MTT assay, Cell culture
Languages	Mandarin (native), Taiwanese (native), English (fluent)