

Highlights

Research Achievements, Skills & Contributions

- Computational work “*Computer simulations explore how Alzheimer’s disease starts*” is featured in [Rice University News & Media](#), Oct 3, 2016.
- 4 publications from prestigious journals including 1 *PNAS* and 3 *JACS* (out of a total of 14 publications).
- **Molecular dynamics (MD) simulation:** Comprehensive simulation protocols to track a range of short-lived dynamics in molecular detail (usually cannot be obtained via experimental methods alone). Tools include *all-atom models* (timescale: ns ~ μ s) and *coarse-grained models* (timescale: μ s~ms).
- **Statistical analysis for molecular dynamics simulation trajectories:** Incorporation of physical nucleation theory into free energy calculation of protein aggregation due to the finite-size effect in simulation (a novel theoretical approach and necessary correction for connecting simulation result to experimental measurement).
- **Importance (umbrella) sampling for free energy calculation:** Explore the (un)binding free energy landscapes of protein-protein/protein-DNA interactions so as to study their (un)binding/aggregation mechanisms in great detail.
- **Kinetic modeling for biomolecular reactions concerning intermediates:** Dissociation kinetics of transcription factor from DNA; Nucleation-growth kinetics of protein aggregaton.

Academic Background

- Postdoctoral training with Prof. **Peter G. Wolynes** (member of the National Academy of Sciences USA)
- Doctorate under Prof. **Sheng Hsien Lin** (Academician of Academia Sinica, Taiwan ROC)

Teaching & Mentoring

- Mentoring 3 undergrads in the REU program at the Center for Theoretical Biological Physics, Rice

Personal Details

Postdoctoral Research Associate

Wolynes Lab

Department of Chemistry

Rice University

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Professional Experience

Postdoc Research Associate	<u>2015-present</u>
<i>Rice University</i> (with Peter G. Wolynes)	
Postdoc Research Associate	<u>2014-2015</u>
<i>Rice University</i> (co-mentored by Margaret S. Cheung and Peter G. Wolynes)	
R&D fellow, Alternative Military Duty	<u>2011-2014</u>
<i>National Chiao Tung University</i> (with Sheng-Hsien Lin)	

Education

PhD. Physical Chemistry	<u>2006-2011</u>
<i>National Taiwan University</i> (with Sheng-Hsien Lin)	
Thesis title: "Theoretical Studies of Protein Folding: Experimental and Molecular Dynamics Insights the Design of Phenomenological Models"	
Bioinformatics Program	<u>2002-2005</u>
<i>National Taiwan Normal University</i>	
Curriculum of the program includes Cellular & Molecular Biology, Functional Genomics etc.	
BSc. Chemistry	<u>2001-2005</u>
<i>National Taiwan Normal University</i>	
Undergraduate research project with Ying-Chieh Sun	

Teaching and Mentoring Experience

Mentoring Research Intern	<u>2017.8-present</u>
<i>One year internship, extended from Research Experience for Undergraduates (REU) Program</i>	
Mentee: Khoa Pham	
Project name: Effect of DNA mechanical properties on binding of transcription factors to DNA	
Mentor in Frontiers in Science (FIS)	<u>2017.5-7</u>
<i>Research Experience for Undergraduates (REU) Program</i>	
Mentee: Saerom Chang	
Project name: Investigation of the effect of metal ion cofactor on DNA-binding protein	
Mentor in Frontiers in Science (FIS)	<u>2016.5-7</u>
<i>Research Experience for Undergraduates (REU) Program</i>	
Mentee: Nick Anaya	
Project name: Exploring the energy landscape of protein folding & electrostatic effects on protein binding properties	

Teaching Assistant

National Taiwan University

Advanced Physical Chemistry (II), quantum mechanics given by Yit-Tsong Chen	<u>Fall 2008</u>
Advanced Physical Chemistry (III), chemical kinetics given by Sheng-Hsien Lin	<u>Spring 2007</u>
Organic chemistry experiment	<u>2005-2006</u>

Research Interests

- Protein-protein & protein-DNA interactions
- Protein folding, binding, and aggregation
- Protein-carbohydrate interactions
- Small-molecule inhibitors & drug design

Honors and Awards

Grant

- Postdoctoral Research Abroad Program, Ministry of Science Technology (MOST), Taiwan 2013.11

Awards

- National Taiwan University Dean of science award for PhD 2010-2011
- Chinese Chemical Society Dissertation Award of Excellence in Physical Chemistry 2011

Scholarship

- The scholarship of Zhong-Ya Wu Educational Foundation in the year 2006-2007, 2008-2009, 2010-2011
- The scholarship of the Chung Hwa Rotary Educational Foundation in the year 2006-2007
- The scholarship of Xio-Heng Gu Educational Foundation in the year 2005-2006, 2010-2011

Others

- Education Committee Travel Award, Biophysical Society 58th Annual Meeting 2014
- The finalist of poster competition, the 18th Biophysics Conference, Taipei, Taiwan 2013
- The second place of poster competition, the 16th Biophysics Conference, Hualien, Taiwan 2011

Talks

1. “*Why Simulation Matters in Life Sciences*”, **invited talk** for 2017 BioTech Talent Symposium, National Cheng Kung University, Tainan, Dec 23, 2017
2. “*In Silicon Studies of Aggregation of Amyloid Beta Protein Using Energy Landscape Theory*”, **invited talk**, Department of Chemistry, National Taiwan University, Taipei, Dec 15, 2017
3. “*Comparing the Aggregation Free Energy Landscapes of Amyloid Beta (1-42) and Amyloid Beta (1-40)*”, **invited talk**, Institute of Biological Chemistry, Academia Sinica, Taipei, Dec 14, 2017
4. “*In silico Studies of protein-DNA Interaction & Aggregation of Disease-related proteins*”, **invited talk**, Department of Chemistry, National Cheng Kung University, Tainan, Mar 28, 2017
5. “*Facilitated dissociation of DNA-binding proteins: Counterintuitive but forms critical determinant of regulatory functions*”, **invited talk**, Institute of Chemistry, Academia Sinica, Taipei, Oct 12, 2016
6. “*Role of electrostatic interactions between bio-molecules in their functional binding*”, **invited talk**, Chemistry Department, National Taiwan Normal University, Taipei, Oct 5, 2015
7. “*Revisiting protein aggregation kinetics using the mean-field kinetic Ising model*”, selected talk for poster competition award, the 18th Biophysics Conference, Taipei, June 2013
8. “*A Theoretical Study on the Thermodynamics of a β -Hairpin Peptide*”, selected talk for poster competition award, the 16th Biophysics Conference, Hualien, May 2011

Grants

- Postdoctoral Research Abroad Program, Ministry of Science Technology (MOST), Taiwan [Grant no. **103-2917-I-564-015**], 2014.9.1~2015.8.31 (Pinciple investigator). This project aims to use computational methods to explore aggregation energy landscape of poly-glutamines and study its length dependence in aggregation propensity. This project yields two papers: 1. *Protein Sci.* 2016 (first author) and 2. *J. Am. Chem. Soc.* 2016 (second author).

Professional Organizations & Memberships

- Biophysical Society, USA (2012-15, 2017)
- The Protein Society, USA (2017)

Publications

Journal Articles

1. W. Zheng, **M. Y. Tsai**, P. G. Wolynes, “Comparing the Aggregation Free Energy Landscapes of Amyloid Beta(1-42) and Amyloid Beta(1-40),” *J. Am. Chem. Soc.*, **139**, 16666 (2017)
2. **M. Y. Tsai**, B. Zhang, W. Zheng, P. G. Wolynes, “Molecular mechanism of facilitated dissociation of Fis protein from DNA,” *J. Am. Chem. Soc.*, **138**, 13497-13500 (2016)
3. W. Zheng, **M. Y. Tsai**, M. Chen, P. G. Wolynes, “Exploring the Aggregation Free Energy Landscape of the Amyloid- β Protein (1-40),” *Proc. Natl. Acad. Sci. U. S. A.*, **113**, 11835-11840 (2016)
• Featured in [Rice University News & Media](#), Oct 3, 2016
4. M. Chen, **M. Y. Tsai**, W. Zheng, P. G. Wolynes, “The Aggregation Free Energy Landscape of Polyglutamine Repeats,” *J. Am. Chem. Soc.*, **138**, 15197-15203 (2016)
5. G. Parra, N. Schafer, L. Radusky, **M. Y. Tsai**, A. B. Guzovsky, P. G. Wolynes, D. Ferreira, “Protein Frustratometer 2: a tool to localize energetic frustration in protein molecules, now with electrostatics,” *Nucleic Acids Res.*, **44**(W1), W356-360 (2016) doi: 10.1093/nar/gkw304
6. Y. J. Shiu, M. Hayashi, O. Shih, C. Su, **M. Y. Tsai**, Y. Q. Yeh, C. J. Su, Y. S. Huang, S. H. Lin, U. S. Jeng, “Intrinsic Coordination for Revealing Local Structural Changes in Protein Folding-Unfolding,” *Phys. Chem. Chem. Phys.*, **18**, 3179-3187 (2016)
7. **M. Y. Tsai**, W. Zheng, D. Balamurugan, N. P. Schafer, B. L. Kim, M. S. Cheung, P. G. Wolynes, “Electrostatics, Structures Prediction and the Energy Landscapes for Protein Folding and Binding,” *Protein Sci.*, **25**, 255-269 (2016).
8. **M. Y. Tsai**, J. M. Yuan and S. H. Lin, “Thermodynamic Insight into Protein Aggregation Using a Kinetic Ising Model,” *J. Chin. Chem. Soc.*, **62**, 21-25 (2015)
9. **M. Y. Tsai**, J. M. Yuan, M. Yamaki, C.-K. Lin and S. H. Lin, “Molecular Dynamics Insight into the Diverse Thermodynamic Behavior of a Beta-Hairpin Peptide,” *J. Chin. Chem. Soc.* **60**, 915-928 (2013).
10. C.-K. Lin, C.-C. Shih, Y. Niu, **M. Y. Tsai**, Y.-J. Shiu, C. Zhu, M. Hayashi, S. H. Lin, “Theoretical Study on Structure and Sum-Frequency Generation (SFG) Spectroscopy of Styrene-Graphene Adsorption System,” *J. Phys. Chem. C*, **117**, 1754-1760 (2013).
11. **M. Y. Tsai**, J. M. Yuan, Y. Teranishi and S. H. Lin, “Thermodynamics of Protein Folding Using a Modified Wako-Saitô-Muñoz-Eaton model,” *J. Biol. Phys.*, **38**, 543-571 (2012).
12. **M. Y. Tsai**, A. N. Morozov, K. Y. Chu and S.H. Lin, “Molecular Dynamics Insight into the Role of Tertiary (foldon) Interactions on Unfolding in Cytochrome *c*,” *Chem. Phys. Lett.*, **475**, 111-115 (2009).
13. A. N. Morozov, Y. J. Shiu, C. T. Liang, **M. Y. Tsai** and S. H. Lin, “Nonadditive Interactions in Protein Folding: The Zipper Model of Cytochrome *c*,” *J. Biol. Phys.*, **33**, 255-270 (2007).

Book Chapters

14. **M. Y. Tsai**, J. M. Yuan, S. H. Lin, “Thermodynamics and kinetics of protein folding and aggregation.” In *Biophysics and Biochemistry of Aggregation: Experimental and Theoretical Studies on Folding, Misfolding, and Self-Assembly of Amyloidogenic Peptides*, J. M. Yuan, H. X. Zhou, Eds, World Scientific (2017).

Unpublished Work

1. **M. Y. Tsai**, B. Zhang, W. Zheng, M. Chen, P. G. Wolynes, “Binding Configurations of Multiple Fis Proteins Underlie their Dissociation Pathways from DNA,” *manuscript in preparation*