

William Yuan-Chi Huang, Ph.D.

Postdoctoral Scholar

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Personal Statement

I have a broad background in biophysics, systems biology, and physical chemistry, with a specific emphasis on applying these perspectives to solve problems in cellular signaling. In particular, I am devoted to understanding signaling reactions at the cell membrane from a physical, dynamical standpoint. My primary approach integrates optical methods, including single-molecule imaging and spectroscopy, and kinetic modeling to analyze biochemically reconstituted reactions. My Ph.D. study focused on resolving the activation mechanisms of membrane-associated proteins, which involves developing extensive imaging-based membrane assays that map complex signaling processes into quantifiable reconstituted systems. I designed a novel type of single-molecule assay that measured the activation time of membrane-associated proteins from membrane recruitment to catalysis (**Science 2019; PNAS 2021**). This was first realized in a reconstituted signaling module of Ras activation by SOS in the MAPK pathway, which revealed unexpected kinetic intermediates and a proofreading mechanism that constitutes the kinetic basis for fidelity control by protein condensates (**PNAS 2016; Biophys. J. 2017; J. Am. Chem. Soc. 2017; Biophys. J. 2020**). My postdoctoral work expands on studying how membrane reactions are dynamically coupled to the cytosol by a total reconstitution approach combining undiluted cell extracts (**Nat. Commun. 2022**) and model membranes. This approach is first demonstrated in a comparative study of reaction kinetics in 2D vs. 3D, which provides empirical support that cell membranes facilitate reactions by reduction-of-dimensionality (**bioRxiv 2022**). Going forward, we will fully develop the hybrid reconstitution approach to resolve signaling modules, with the overarching goal of bridging live-cell studies in formulating a quantitative understanding of cellular signaling, in health and in diseases.

Appointments

Johns Hopkins University 2024/02 –
Assistant Professor, Department of Biophysics

Education

Stanford University 2018 –
Postdoctoral Scholar, Department of Chemical and Systems Biology
Advisor: James E. Ferrell
Topic: Dissecting the dynamics of intracellular signaling by total reconstitution

University of California, Berkeley 2011 – 2016
Ph.D. Chemistry (physical/biophysical division), GPA 4.0/4.0
Advisor: Jay T. Groves
Dissertation: “Statistical analysis of small-scale membrane signaling reactions: the role of membrane recruitment and catalysis in signal transduction”

National Taiwan University 2006 – 2010
B.S. Chemistry, GPA 3.9/4.0
Advisor: Jerry C. C. Chan
Thesis: “Molecular structure study of prion fibrils by molecular dynamics simulations”

Honors & Awards

Mansour Award (Paper Prize), Stanford University 2022
K99/R00 Pathway to Independence Award, National Institutes of Health (impact score: 10) 2022
Finalist, Life Sciences Research Foundation Postdoctoral Fellowship (unfunded) 2020
Government Scholarship to Study Abroad, Ministry of Education, Taiwan 2014 – 2016
Bernice and Yuan-Tseh Lee Undergraduate Award, Chemical Society located in Taipei 2010
Dean’s List, National Taiwan University 2010
Ming-Chen Dai Scholarship, National Taiwan University 2010
Research Grant for Undergraduate Students, National Science Council, Taiwan 2009 – 2010
Presidential Award, National Taiwan University (twice) 2006, 2010

Publications

† = highlights; * = equal contributions

Preprints & Manuscripts in Review

- †**W. Y. C. Huang**[#], S. G. Boxer, and J. E. Ferrell[#]. Membrane localization accelerates association under conditions relevant to cellular signaling. *bioRxiv* **2022** (# = corresponding authors) (in review)

Research Articles

15. **W. Y. C. Huang**, X. Cheng, and J. E. Ferrell. Cytoplasmic organization promotes protein diffusion in *Xenopus* extracts. *Nature Communications* **2022**, 13, 5599.
14. A. A. Lee, **W. Y. C. Huang**, S. D. Hansen, N. H. Kim, S. Alvarez, and J. T. Groves. Stochasticity and positive feedback enable enzyme kinetics at the membrane to sense reaction size. *Proc. Natl. Acad. Sci. U.S.A.* **2021**, 118, e2103626118.
13. **W. Y. C. Huang**, S. Alvarez, Y. Kondo, J. Kuriyan, and J. T. Groves. Relating cellular signaling timescales to single-molecule kinetics: a first-passage time analysis of Ras activation by SOS. *Proc. Natl. Acad. Sci. U.S.A.* **2021**, 118, e2103598118.
12. J. K. Chung*, **W. Y. C. Huang***, C. B. Carbone, A. N. Parikh, R. D. Vale, and J. T. Groves. Coupled membrane lipid miscibility and phosphotyrosine-driven protein condensation phase transitions. *Biophysical Journal* **2021**, 120, 1257-1265.
11. S. D. Hansen, **W. Y. C. Huang**, Y. K. Lee, P. Bieling, S. M. Christensen, and J. T. Groves. Stochastic geometry sensing and polarization in a lipid kinase-phosphatase competitive reaction. *Proc. Natl. Acad. Sci. U.S.A.* **2019**, 116, 15013-15022.
10. †**W. Y. C. Huang**, S. Alvarez*, Y. Kondo*, Y. K. Lee, J. K. Chung, H. Y. M. Lam, K. H. Biswas, J. Kuriyan, and J. T. Groves. A molecular assembly phase transition and kinetic proofreading modulate Ras activation by SOS. *Science* **2019**, 363, 1098-1103.
See also: *Perspectives: Dwelling at membranes promotes decisive signaling. Science*, 2019, 363:1036-1037.
Research Highlight, Nature Reviews Molecular Cell Biology, 2019, 20:263.
LBNL News Center, April 1, 2019.
Recommended by the Faculty of 1000.
9. **W. Y. C. Huang***, J. Ditlev*, H.-K. Chiang, M. K. Rosen, and J. T. Groves. Allosteric modulation of Grb2 recruitment to the intrinsically disordered scaffold protein, LAT, by remote site phosphorylation. *Journal of the American Chemical Society* **2017**, 139, 18009-18015.
8. **W. Y. C. Huang**, H.-K. Chiang, and J. T. Groves. Dynamic scaling analysis of molecular motion within the LAT:Grb2:SOS protein network on membranes. *Biophysical Journal* **2017**, 113, 1807-1813.
7. Y.-H. Hwang Fu, **W. Y. C. Huang**, K. Shen, J. T. Groves, T. Millers, and S. Shan. Two-step membrane binding by the bacterial SRP receptor enable efficient and accurate co-translational protein targeting. *eLife* **2017**, 6, e25885.
6. †**W. Y. C. Huang**, Q. Yan, W.-C. Lin, J. K. Chung, S. D. Hansen, S. M. Christensen, H.-L. Tu, J. Kuriyan, and J. T. Groves. Phosphotyrosine-mediated LAT assembly on membranes drives kinetic bifurcation in recruitment dynamics of the Ras activator SOS. *Proc. Natl. Acad. Sci. U.S.A.* **2016**, 113, 8218-8223.
5. K. H. Biswas*, K. L. Hartman*, C.-H. Yu, O. J. Harrison, H. Song, A. W. Smith, **W. Y. C. Huang**, W.-C. Lin, Z. Guo, A. Padmanabhan, S. M. Troyanovsky, M. L. Dustin, L. Shapiro, B. Honig, R. Zaidel-Bar, and J. T. Groves. E-cadherin junction formation involves an active kinetic nucleation process. *Proc. Natl. Acad. Sci. U.S.A.* **2015**, 112, 10932-10937.
4. A. R. Lowe*, J. H. Tang*, J. Yassif, M. Graf, **W. Y. C. Huang**, J. T. Groves, K. Weis, and J. T. Liphardt. Importin- β modulates the permeability of the nuclear pore complex in a Ran-dependent manner. *eLife* **2015**, 4, e04052.
3. W.-C. Lin*, L. Iversen*, H.-L. Tu, C. Rhodes, S. M. Christensen, J. S. Iwig, S. D. Hansen, **W. Y. C. Huang**, and J. T. Groves. H-Ras forms dimers on membrane surfaces via a protein-protein interface. *Proc. Natl. Acad. Sci. U.S.A.* **2014**, 111, 2996-3001.
2. H.-M. Cheng, **W. Y. C. Huang**, T. W. T. Tsai, Y. Mou, and J. C. C. Chan. Depletion of water molecules near the end stage of steric zipper formation. *Journal of the Chinese Chemical Society* **2013**, 60, 784-800.
1. H.-M. Cheng, T. W. T. Tsai, **W. Y. C. Huang**, H.-K. Lee, H.-Y. Lian, F.-C. Chou, Y. Mou, and J. C. C. Chan. Steric zipper formed by hydrophobic peptide fragment of Syrian hamster prion protein. *Biochemistry* **2011**, 50, 6815-6823.

Conference Proceedings

1. K. A. Rauen, L. Schoyer, L. Schill, B. Stronach, J. Albeck, B. S. Andresen, H. Cavé, M. Ellis, S. M. Fruchtman, B. Gelb, C. Gibson, K. Gripp, E. Hefner, **W. Y. C. Huang**, M. Itkin, B. Kerr, C. Linardic, M. McMahon, B. Oberlander, E. Perlstein, N. Ratner, L. Rogers, A. Schenck, S. Shankar, S. Shvartsman, D. Stevenson, E. Stites, P. Stork, C. Sun, M. Therrien, E. Ullian, B. Widemann, E. Yeh, G. Zampino, M. Zenker, W. Timmer, and F. McCormick. Proceedings of the 5th international RASopathies symposium: when development and cancer intersect. *American Journal of Medical Genetics Part A* **2018**, 176, 2924-2929.

Presentations & Conferences

Annual Retreat, Dept. of Chemical and Systems Biology, Stanford University – talk	2022/10
Science Circle Seminar, Dept. of Chemical and Systems Biology, Stanford University – talk	2022/03
66 th Annual Biophysical Society (BPS) Meeting, San Francisco Moscone Center – talk	2022/02
Science Circle Seminar, Dept. of Chemical and Systems Biology, Stanford University – talk (virtual)	2021/05
Think Tank Seminar, Dept. of Chemical and Systems Biology, Stanford University – talk (virtual)	2020/05
Symposium on Intrinsically Disordered Proteins, LKS Center, Stanford University – attendee	2020/02
GRC Stochastic Physics in Biology, Four Points Sheraton at Ventura – poster	2019/01
62 th Annual Biophysical Society (BPS) Meeting, San Francisco Moscone Center – talk	2018/02
Membrane Supergroup Seminar, Dept. of Molecular and Cell Biology, UC Berkeley – talk	2017/11
5 th International RASopathies Symposium, Renaissance Orlando – invited talk	2017/07
Single-Cell Biophysics, Academia Sinica, Taiwan (hosted by BPS) – poster	2017/06
9 th Biennial Workshop on Single Molecule Biophysics, Aspen Center of Physics (ACP) – poster	2017/01
56 th Annual Am. Soc. for Cell Biol. (ASCB) Meeting, San Francisco Moscone Center – poster	2016/12
60 th Annual Biophysical Society (BPS) Meeting, Los Angeles Convention Center – poster	2016/03
17 th Annual Statistical Mechanics Meeting, UC Berkeley – poster	2016/01
Membrane Supergroup Seminar, Dept. of Molecular and Cell Biology, UC Berkeley – talk	2015/11
58 th Annual Biophysical Society (BPS) Meeting, San Francisco Moscone Center – attendee	2014/02
Graduate Research Conference, Dept. of Chemistry, UC Berkeley – talk	2012/11
Undergraduate Research Conference, Dept. of Chemistry, National Taiwan University – poster	2010/05

Professional Services

Ad-hoc reviewer for *Biophysical Journal*, *Journal of Molecular Biology*

Co-reviewer with advisors for *Science*, *Nature*, *PNAS*, *Biophysical Journal*, *Journal of Biological Chemistry*, *Development*

Teaching Experiences

Graduate Student Instructor (GSI) , Department of Chemistry, UC Berkeley	
Biophysical Chemistry (Chem C130 with Prof. Jay Groves and Prof. Jamie Cate)	2016 Spring
Advanced Biophysical Chemistry I & II (Chem 270AB with Prof. Jay Groves)	2015 Spring
Thermodynamics and Statistical Mechanics (Chem 220A with Prof. Phillip Geissler)	2013 Fall
Physical Chemistry: Quantum Mechanics (Chem 120A with Prof. Martin Head-Gordon)	2013 Spring
Chemical Structure and Reactivity (Chem 3B with Prof. Peter Vollhardt)	2011 Fall
Organic Chemistry Laboratory (Chem 3BL with Prof. Peter Vollhardt)	2011 Fall

References

James E. Ferrell, M.D., Ph.D. – postdoctoral advisor
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Jay T. Groves, Ph.D. – doctoral advisor; thesis committee; instructor of the GSI courses
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