BIOGRAPHICAL SKETCH

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NAME: Chou, Steven Ziren

eRA COMMONS USER NAME (credential, e.g., agency login): stevenzchou

POSITION TITLE: Assistant Professor of Molecular Biology and Biophysics

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Jiangsu Normal University, Xuzhou	B.S.	06/2004	Biological Sciences
Chinese Academy of Sciences, Shanghai	Ph.D.	07/2011	Biochemistry (NMR, XRD)
University of Michigan, Ann Arbor	Postdoc Fellow	04/2015	Cryo-EM and Obesity
Yale University, New Haven	Postdoc Assoc	04/2017	Cryo-EM and Cytokinesis
Yale University, New Haven	Assoc Res Sci	06/2022	Cryo-EM and Cell Motility

A. Personal Statement

Scientific training and research. My training in science is mainly in biochemistry, cell biology, genetics, and structural biology, and my research is focused on (1) actin-based cell motility, (2) cytokinesis, and (3) transmembrane signaling.

Driven by my curiosity for how the molecules inside a cell work structurally, I joined an NMR lab (Prof. Hongyu Hu, SIBCB, CAS) as a graduate student. Besides in-depth knowledge and hands-on experience in NMR spectroscopy and protein biochemistry, I also solved protein structures using X-ray crystallography. Frequently challenged by the question of how my proteins work together with their binding partners in large complexes, I performed my first postdoc research in a cryo-EM lab (Prof. Georgios Skiniotis, LSI, UMich) to study the transmembrane signaling through the obesity-related leptin receptor in 2011. The EM structures showed that the ligand leptin induces an architectural change of the recombinant receptor from monomer to dimer. Equipped with state-of-the-art techniques in cryo-EM and fascinated by how cells move and divide, I started my second postdoc research in actin-based cell motility and cytokinesis (Prof. Thomas Pollard, MCDB, Yale) in 2015. During my time at Yale, I got intensive training in molecular complex reconstitution using proteins purified from natural sources (chicken and porcine skeletal muscles, bovine thymuses, human and sheep blood, wild-type yeast, *etc*) and genome editing and phenotype analysis in fission yeast. My structures revealed the long-sought mechanisms of (1) actin assembly and disassembly fueled by ATP hydrolysis, and (2) actin filament branch formation by Arp2/3 complex. Besides sample preparation and structure determination, I also wrote my own computer programs to improve structural analysis in EM (particle picking and sorting, helical indexing, CTF estimation, *etc*).

I started my own lab in the Department of Molecular Biology and Biophysics at UConn Health. My basic research on actin-based cell motility, cytokinesis, and transmembrane signaling will provide structural insights into the pathological mechanism of protein mutations in related diseases, and clues for fighting against these diseases through structure-based and evolution-based protein engineering and targeted protein degradation.

Mentorship and teaching. I have been mentoring the research of three graduate students (Bethlehem Abebe (T32 until November 2025), Wen Liu and Xiaonan Wang) and four undergraduate students (Jieun Park (HRP

fellowship), Jenny Guo (SRP fellowship), Mia Bell and Adam Chen) at UConn Health. One postdoc (Dafeng Liu) is arriving. I mentored an undergraduate student's research at Yale for three years. The student won the prestigious Yale College Dean's Research Fellowship due to her excellence in the mentored research. I was a teaching assistant for the Practical Cryo-EM Workshop (Single Particle and Tomography) organized by the Department of Molecular Biophysics and Biochemistry (course ID: 711) at Yale University. I am committed to helping each member of my lab build a strong skill set to advance their career. To that goal, I design different research projects, provide support in fellowship applications, and encourage lab trainees to attend professional conferences.

Diversity and inclusion. Inclusivity is highly appreciated in all the labs that I attended and is strongly advertised in my own lab. My lab welcomes all people, regardless of gender, age, ethnicity, sexual orientation, or religion. Currently, our lab members have origins in Africa, Asia, and America. Gender equality is promoted not only in the lab but also in all other areas.

Ongoing Research Support.
Startup funds (PI: Chou, S. Z.)
University of Connecticut School of Medicine

Completed Research Support.
None

B. Positions, Scientific Appointments, and Honors

Positions and scientific appointments.

07/2022-	Assistant Professor, Department of Molecular Biology and Biophysics, University of Connecticut Medical Center, Farmington, CT
05/2015-06/2022	Associate Research Scientist, Laboratory of Dr. Thomas D. Pollard, Department of Molecular, Cellular and Developmental Biology, Yale University, New Haven, CT
05/2015-04/2017	Postdoctoral Associate, Laboratory of Dr. Thomas D. Pollard, Department of Molecular, Cellular and Developmental Biology, Yale University, New Haven, CT
10/2011-04/2015	Postdoctoral Research Fellow, Laboratory of Dr. Georgios Skiniotis (now at Stanford U.), Life Sciences Institute, University of Michigan, Ann Arbor, MI
09/2004-06/2011	Graduate student, Laboratory of Dr. Hongyu Hu, Shanghai Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences, Shanghai, China

Fellowships and honors.

2009	Travel Award, Symposium of NMR for Biological Macromolecules, USTC
2008-2009	Merit Student, Chinese Academy of Sciences
2004	Graduation with First-Class Honors, Jiangsu Normal University
2004	ZHU Jingwen Scholarship, Jiangsu Normal University
2001-2002	Merit Student, Jiangsu Normal University
2001-2003	First Place Scholarships, Jiangsu Normal University

Other Experience and Professional Memberships and Service to the Scientific Community.

2023-present	American Biophysical Society member
2016-2017	American Crystallographic Association member
2013-present	*Ad hoc* journal reviewers for Protein Science (2013), Journal of Biomolecular Structure and Dynamics (2014-2023), International Journal of Peptide Research and Therapeutics (2014), Cell Physiology and Biochemistry (2015), Nature Communications (2021-2023), Biochemical Journal (2021), Science Advances (2022-2023), Frontiers Cell and Developmental Biology (2022-2023)

C. Contributions to Science

I. *Actin-Based Cell Motility, Cytokinesis and Related Transmembrane Signaling.* Combining protein biochemistry, cell biology, genetics/genomics, and structural biology, I elucidated the mechanism of actin

filament branch formation, the relationship between actin conformations and nucleotide states, the mechanism of fluorescence change during polymerization of pyrene actin, the structural basis of polarized elongation of actin filaments, and the architectural change of leptin receptor during signaling. Currently, I am striving to explain how straight actin filaments are nucleated by formins, how actin-spectrin junctional complexes are anchored to the plasma membrane and maintain the shape of red blood cells, how the actin-myosin contractile ring is assembled in the middle of the eukaryotic cells during mitosis and meiosis, and the transmembrane signaling required to regulate these processes. (Research with my previous advisor was supported by NIGMS)

- Chavali, S. S. **Chou, S. Z.** Cao, W. X. Pollard, T. D. De La Cruz, E. M. and Sindelar, C. V. (2024). High resolution cryo-EM structures reveal how phosphate release from Arp3 weakens actin filament branches formed by the Arp2/3 complex. ***Nature Communications,*** 000(00):0000–0000
- **Chou, S. Z.** Chatterjee, M. and Pollard, T. D. (2022). Mechanism of actin filament branch formation by Arp2/3 complex revealed by a high resolution cryo-EM structure of the branch junction. ***Proc Natl Acad Sci U S A***, 119(49):0000–0000
- **Chou, S. Z.** and Pollard, T. D. (2020). Cryo-electron microscopy structures of pyrene-labeled ADP-P_i- and ADP-actin filaments. ***Nature Communications***, 11(1):5897 *Article* | Reported in *Faculty Opinions*
- **Chou, S. Z.** and Pollard, T. D. (2019). Mechanism of actin polymerization revealed by cryo-EM structures of actin filaments with three different bound nucleotides. ***Proc Natl Acad Sci U S A***, 116(10):4265–4274 *Article* | Commented in *Proc Natl Acad Sci U S A* | Recommended in *F1000Prime* | Reported in *SciTechDaily* | Reported by Lee, V. in *Yale Scientific Magazine*

II. *Targeted Protein Degradation*. Eukaryotic proteins are targeted for degradation through the ubiquitin-proteasome system (UPS). (1) I entered this field first by doing basic research on protein recognitions: binding of ubiquitin-associated proteins (c-Cbl and Cbl-b) to ubiquitin, removal of the ubiquitin tag by ubiquitin C-terminal hydrolases (UCH-L5, L3, and L1), *etc*. (2) My interest in this field was deepened through my translational research on revealing the mechanism of action of arsenic trioxide for the treatment of Acute Promyelocytic Leukemia (APL), with a 5-year survival rate of 90% now! The zinc cation in the oncoprotein of APL, PML-RARα, can be replaced by arsenic, the replacement destabilizes PML-RARα, and arsenic-bound PML-RARα is later degraded through SUMO modification and UPS. (3) Now, I am applying targeted protein degradation techniques (PROteolysis Targeting Chimeras, PROTACs) to the degradation of proteins with mutations, which cause abnormal transmembrane signaling in disease.

- **Zhou, Z. R.**, Gao, H. C., Zhou, C. J., Chang, Y. G., Hong, J., Song, A. X., Lin, D. H., and Hu, H. Y. (2008). Differential ubiquitin binding of the UBA domains from human c-Cbl and Cbl-b: NMR structural and biochemical insights. ***Protein Sci***, 17(10):1805–14 *(Note: Chou, S. Z. is spelled Zhou, Z. R. using the Pinyin system)*
- **Zhou, Z. R.**, Zhang, Y. H., Liu, S., Song, A. X., and Hu, H. Y. (2012). Length of the active-site crossover loop defines the substrate specificity of ubiquitin C-terminal hydrolases for ubiquitin chains. ***Biochem J***, 441(1):143–9
- Zhang, X. W., Yan, X. J., **Zhou, Z. R.**, Yang, F. F., Wu, Z. Y., Sun, H. B., Liang, W. X., Song, A. X., Lallemand-Breitenbach, V., Jeanne, M., Zhang, Q. Y., Yang, H. Y., Huang, Q. H., Zhou, G. B., Tong, J. H., Zhang, Y., Wu, J. H., Hu, H. Y., de The, H., Chen, S. J., and Chen, Z. (2010). Arsenic trioxide controls the fate of the PML-RARalpha oncoprotein by directly binding PML. ***Science***, 328(5975):240–3

Complete List of Published Work in MyBilbliography (Chou SZ or Zhou ZR):
https://www.ncbi.nlm.nih.gov/myncbi/steven.chou.1/bibliography/public/