

BIOGRAPHICAL SKETCH

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NAME: CHIU, Wah

eRA COMMONS USER NAME (credential, e.g., agency login): WAH543

POSITION TITLE: Professor

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
University of California; Berkeley, CA	BA	1969	Physics
University of California; Berkeley, CA	PhD	1975	Biophysics
University of California; Berkeley, CA	Postdoc	1975-1977	Biophysics

A. Personal Statement

- I have developed experimental and computational methodologies for structural determination of biological assemblies by single particle cryo-electron microscopy (cryo-EM) towards atomic resolution for three decades under the support of the P41 Biotechnology Resource Center (P41GM103832). Since 2008, I have established an infrastructure facilitating the determination over 25 single particle structures (a few not yet published), from which the full atom models of the protein components can be obtained without using crystallography. In these investigations, we used different direct detectors (DE12, DE20, K2) and electron microscopes (JEOL and FEI) to record their images and different image processing software to reconstruct their 3D structures. These structures include membrane protein complexes, chaperonins, protein machines and viruses. In addition, we have extensive experience in cryo-electron tomography (cryo-ET) for single particles and cells, which have variable conformations of the molecular components. Recently, my lab moved to the Stanford University to establish a state-of-the-art cryo-EM facility including 3 Krios and 1 Talos-Arctica electron microscopes, which are well suited to collect high resolution single particle images and tomograms of cells.

I was the co-founder and training director of the Keck Center for Computational Biology in Houston involving 7 academic institutions. We administered concurrently multiple NIH training grants for predocs and postdocs from NIGMS and NLM in structural biophysics and biomedical informatics. I mentored many junior scientists who have subsequently become eminent cryo-EM investigators in different academic institutions and industries. To name a few individuals who are now holding independent faculty or managerial positions: Steven Ludtke (Baylor College of Medicine), BVV Prasad (Baylor College of Medicine), Irina Serysheva (U Texas Houston Medical School). Michael Sherman (U Texas Galveston Medical Branch). Irina Orlova (Birkbeck College), Wen Jiang (Purdue U), Hong Zhou (UCLA), Yao Cong (Chinese Academy of Science, Shanghai), Junjie Zhang (Texas A&M U), Wei Dai (Rutgers U), Rui Zhang (Washington U Medical School), Jason Kaelber (Rutgers U), Zhao Wang (Baylor College of Medicine), Christopher booth (Gatan), Benjamin Bammes (Direct Electrons), Jaap Brink (JEOL). My experience in cryo-EM technology development and in training cryo-EM specialists well poises us to participate the proposed research.

- Fan, G, Baker, ML, Wang, Z, Baker, MR, Sinyagovskiy, PA, Chiu, W, Ludtke, SJ, & Serysheva, II (2015) Gating machinery of InsP3R channels revealed by electron cryomicroscopy. *Nature* **527**(7578):336-341. PMID4804758.
- Wang, Z, Fan, G, Hryc, CF, Blaza, JN, Serysheva, II, Schmid, MF, Chiu, W, Luisi, BF, & Du, D (2017) An

- allosteric transport mechanism for the AcrAB-TolC multidrug efflux pump. *Elife* **6**. PMID5404916.
- c. Roh, SH, Hryc, CF, Jeong, HH, Fei, X, Jakana, J, Lorimer, GH, & Chiu, W (2017) Subunit conformational variation within individual GroEL oligomers resolved by Cryo-EM. *Proc Natl Acad Sci U S A* **114**(31):8259-8264. PMID5547627.
- d. Roh, SH, Stam, NJ, Hryc, CF, Couch-Cardel, S, Pintilie, G, Chiu, W, & Wilkens, S (2018) The 3.5-Å CryoEM Structure of Nanodisc-Reconstituted Yeast Vacuolar ATPase Vo Proton Channel. *Mol Cell* 10.1016/j.molcel.2018.02.006.

B. Positions and Honors

Positions

1977-1979	Staff Biophysicist, Lawrence Berkeley National Laboratory, Berkeley
1979-1988	Asst. to Assoc. Professor, Depts of Cell & Dev Bio and Biochem, Univ Arizona, Tucson
1988-2017	Professor, Departments of Biochemistry & Mol Biology, Mol Virology & Microbiology, Mol Physiology & Biophysics, and Mol & Cell Biology, Baylor College of Medicine (BCM)
1988-present	Founding Director, National Center for Macromolecular Imaging (NCMI)
1990-2017	Founding Co-Director, Keck Center for Computational Biology, BCM, Rice Univ, Univ of Houston, MD Anderson Center, UT Health Sci Center, Houston and UTMB, Galveston
1993-2017	Founding Director, Ph.D. Program in Struct. & Comp. Biol. & Mol. Biophys., BCM
2002-2015	Adjunct Professor of Biomedical Informatics, Univ Texas Health Science Center, Houston
2003-2017	Adjunct Professor of Physics, University of Houston, Houston
2004-2017	Adjunct Professor of Computer Science, Rice University, Houston
2009-2014	Visiting Professor, National University of Singapore, Singapore
2011-2012	Visiting Professor, King Saud University, Riyadh, Kingdom of Saudi Arabia
2017-present	Professor, Department of Bioengineering in Engineering School; Department of Microbiology and Immunology in Medical School; and Photon Science in SLAC, Stanford University
2017-present	Adjunct Professor of Biochemistry and Molecular Biology and of Cell Biology, BCM

Honors

Award of Merit from Oakland City Council, 1972; Presidential Scholar of Electron Microscopy Society of America, 1974; Guggenheim Fellow, 1986; Alexander von Humboldt Research Prize, 1996; Alvin Romansky Chair of Biochemistry, 1996; Fellow, Japan Society for the Promotion of Science, 1999; Chinese Biophysicists Network Award, 2003; Presidential Award, American Academy of Nanomedicine, 2006; Elected Academician, Academia Sinica, Taiwan, 2008; Distinguished Service Professor, Baylor College of Medicine, 2010; Elected Member, US National Academy of Sciences, 2012; Elected Member, The Academy of Medicine, Engineering, and Science of Texas, 2013. Distinguished Faculty Award, Baylor College of Medicine Alumni Association, 2013; Honorary Doctorate of Philosophy, University of Helsinki, Finland, 2014; Distinguished Scientist Award, Microscopy Society of America, 2014; Barbara and Corbin J. Robertson Jr. Presidential Award for Excellence in Education, 2015.

Advisory Boards (partial)

Past Advisory Board Membership: NIH Study Sections of Biophysics & Biophysical Chemistry 1984-88, Reserve, 1988-92, Cellular and Molecular Basis of Disease, 1994-98; NIH Center for Scientific Review Working Groups, 1999-01; NIGMS Future Directions in Electron Microscopy, 1998-99 (Chair); Institute of Molecular Bioscience, University of Queensland, Brisbane, AU, 2001-06; The National Academies Advisory Board on DOE Genomics GTL Program, 2005; NIH National Advisory Research Resources Council, 2003-07; Multi-Scale Modeling Research Resource, Scripps Research Institute, La Jolla, 2001-2007; Genomics Medicine Program, Academia Sinica, Taiwan, 2007. HIV Structural Biology Program, NIGMS, NIH (2007-2012); Ministry of Education, Singapore (2007-2015); Structural Genomics Program, NIGMS, NIH (2010-2013); NIGMS Structure Genomics Transition Team (2014-2015); Intramural Program of NIBIB, NIH (2010-2015); Intramural Program of NIAID, NIH (2016); Max Planck Institute of Biochemistry in Martinsried, Germany (2013-2017).

Current Advisory Board Membership: RCSB-Protein Data Bank (2005-present); Swiss National Science Foundation (2007-present); Integrated Structural Biology Infrastructure for Europe: INSTRUMENT (2010-present); Institute of Biological Chemistry, Academia Sinica, Taiwan (2010-present); St. Jude Children's

Research Hospital Structural Biology division (2015-present); Biozentrum, Universität Basel, Basel, Switzerland (2016-present).

Current Editorial Board Membership: Microscopy & Microanalysis (1997-present); Journal of Microscopy (2000-present); Structure (2004-present); Quarterly Reviews of Biophysics (2008-present); Journal of Structural and Functional Genomics (2007-present); Journal of Nanobiotechnology (2011-present); QRB Reports (2015-present).

C. Contributions to Science

2. We were among the first research groups to demonstrate the feasibility of building *de novo* polypeptide backbone topology and identifying side chains of protein components from cryoEM maps of molecular machines without using crystallography. This early work was done with single particle image data collected either on photographic film or CCD cameras in 300 kV JEOL electron microscopes using our own image processing software. Our innovations in this research included skilled imaging; developing software for image reconstruction protocol, and *de novo* modeling in near atomic resolution cryoEM maps.
 - a. Jiang W, Baker ML, Jakana J, Weigele PR, King J, Chiu W (2008) Backbone structure of the infectious epsilon15 virus capsid revealed by electron cryomicroscopy. *Nature*:451(7182):1130-1134. PMID: 18305544
 - b. Ludtke, SJ, Baker, ML, Chen, DH, Song, JL, Chuang, DT, & Chiu, W (2008) De Novo backbone trace of GroEL from single particle electron cryomicroscopy. *Structure* **16**(3):441-448.
 - c. Zhang J, Baker ML, Schroder GF, Douglas NR, Reissmann S, Jakana J, Dougherty M, Fu CJ, Levitt M, Ludtke SJ, Frydman J, Chiu W (2010) Mechanism of folding chamber closure in a group II chaperonin. *Nature*:463(7279):379-383. PMC2834796.
 - d. Liu X, Zhang Q, Murata K, Baker ML, Sullivan MB, Fu C, Dougherty MT, Schmid MF, Osburne MS, Chisholm SW, Chiu W (2010) Structural changes in a marine podovirus associated with release of its genome into Prochlorococcus. *Nature Struct Mol Biol*:17(7):830-836. PMC2924429.
3. I have supported the initiation of a number of image processing software developments for single particle structure determination and modeling. I also promote the importance of cryoEM structure validation with rigorous protocols through a community-wide effort.
 - a. Ludtke, SJ, Baldwin, PR, & Chiu, W (1999) EMAN: semi-automated software for high-resolution single-particle reconstructions. *J Struct Biol* **128**(1):82-97.
 - b. Liu, X, Jiang, W, Jakana, J, & Chiu, W (2007) Averaging tens to hundreds of icosahedral particle images to resolve protein secondary structure elements using a Multi-Path Simulated Annealing optimization algorithm. *J Struct Biol* **160**(1):11-27.
 - c. Baker, ML, Zhang, J, Ludtke, SJ, & Chiu, W (2010) Cryo-EM of macromolecular assemblies at near-atomic resolution. *Nat Protoc* **5**(10):1697-1708. PMCID3107675.
 - d. Henderson, R, Sali, A, Baker, ML, Carragher, B, Devkota, B, Downing, KH, Egelman, EH, Feng, Z, Frank, J, Grigorieff, N, Jiang, W, Ludtke, SJ, Medalia, O, Penczek, PA, Rosenthal, PB, Rossmann, MG, Schmid, MF, Schroder, GF, Steven, AC, Stokes, DL, Westbrook, JD, Wriggers, W, Yang, H, Young, J, Berman, HM, Chiu, W, Kleywegt, GJ, & Lawson, CL (2012) Outcome of the first electron microscopy validation task force meeting. *Structure* **20**(2):205-214. PMCID3328769.
4. I have an active research program in exploring electron cryo-tomography to study mammalian cells, cell-infected with viruses, organelles and protein aggregates followed, in some cases, by annotation and segmentation, and in others, by subvolume extraction, classification and averaging. Our studies have yielded insightful structural mechanisms of different biological processes.
 - a. Koyfman, AY, Schmid, MF, Gheiratmand, L, Fu, CJ, Khant, HA, Huang, D, He, CY, & Chiu, W (2011) Structure of Trypanosoma brucei flagellum accounts for its bihelical motion. *Proc Natl Acad Sci U S A* **108**(27):11105-11108. PMCID3131312.
 - b. Gilliam, JC, Chang, JT, Sandoval, IM, Zhang, Y, Li, T, Pittler, SJ, Chiu, W, & Wensel, TG (2012) Three-dimensional architecture of the rod sensory cilium and its disruption in retinal neurodegeneration. *Cell* **151**(5):1029-1041. PMCID3582337.
 - c. Shahmoradian, SH, Galaz-Montoya, JG, Schmid, MF, Cong, Y, Ma, B, Spiess, C, Frydman, J, Ludtke, SJ, & Chiu, W (2013) TRiC's tricks inhibit huntingtin aggregation. *eLife* **2**:e00710. PMCID3707056.

- d. Dai, W, Fu, C, Raytcheva, D, Flanagan, J, Khant, HA, Liu, X, Rochat, RH, Haase-Pettingell, C, Piret, J, Ludtke, SJ, Nagayama, K, Schmid, MF, King, JA, & Chiu, W (2013) Visualizing virus assembly intermediates inside marine cyanobacteria. *Nature* **502**(7473):707-710. PMID3984937.
5. We have solved many structures of viruses and nucleic acids without symmetry enforcement either by single particle cryo-EM or by cryo-ET using novel data processing protocols or experimental techniques.
- a. Jiang W, Chang J, Jakana J, Weigele P, King J, Chiu W (2006) Structure of epsilon15 bacteriophage reveals genome organization and DNA packaging/injection apparatus. *Nature*:439(7076):612-616. PMID1559657.
- b. Rochat RH, Liu X, Murata K, Nagayama K, Rixon FJ, Chiu W (2011) Seeing the portal in herpes simplex virus type 1 B capsids. *J Virol*:85(4):1871-1874. PMID3028901.
- c. Irobalieva RN, Fogg JM, Catanese DJ, Sutthibutpong T, Chen M, Barker AK, Ludtke SJ, Harris SA, Schmid MF, Chiu W, Zechiedrich L (2015) Structural diversity of supercoiled DNA. *Nature commun* 6:8440. PMID4608029.
- d. Veneziano, R, Ratanalert, S, Zhang, K, Zhang, F, Yan, H, Chiu, W, & Bathe, M (2016) Designer nanoscale DNA assemblies programmed from the top down. *Science* **352**(6293):1534-1542. PMID5111087.

Complete list of published works: <http://www.ncbi.nlm.nih.gov/pubmed/?term=chiu%2C+Wah>
<http://www.ncbi.nlm.nih.gov/sites/myncbi/wah.chiu.1/collections/48036562/public/>

D. Research Support

Ongoing Research Support

P41GM103832	Chiu (PI)	02/15/15-12/31/19
National Institutes of Health		
"3D Electron Microscopy of Macromolecules"		
Goal: To develop experimental and computational methodologies for solving 3-D structures of macromolecular complexes, aggregates and cells towards high resolution using cryoelectron microscopy and tomography. Other activities include collaborative research, service and training.		
R01GM079429	Chiu (PI)	02/01/18 - 01/31/22
National Institutes of Health		
"Unified Data Resource for 3DEM"		
Goal: To establish methodologies and standard for valiating cryoEM maps and models in collaboration with Helen Berman at Rutgers University, leadership team in wwPDB, investigators in European Bioinformatics Institute, UK and the global cryoEM community. Our activities include map and model challenge events for the scientific community with advice from the cryoEM and modeling experts.		
U24GM116787	Chiu (PI)	07/15/16 - 06/30/21
National Institutes of Health		
"CryoEM Data Collection Facility Consortium at NCMI"		
Goal: Establish a cryoEM data acquisition facility for cryoEM specialists in 9 institutions across USA.		
NIH S10OD021600	Chiu (PI)	07/01/16 - 06/30/18
National Institutes of Health		
"Acquisition of a 300 kV Electron Microscope for Structural Biology"		
Goal: Provide a partial fund to purchase a new 300 kV electron cryo-microscope through a high end instrumentation program.		
P01NS092525	L. Thompson, UC Irvine (PI); Chiu (Co-PI)	04/01/16 - 03/31/21
National Institutes of Health		
"From structure to therapy: the TRiC Chaperonin network in Huntington's disease"		
Goal: Use cryoEM and cryoET to study mutant HTT in the context of HD cell model and neuron		
P50GM1003297	A. Telesnitsky U Michigan (PI); Chiu (Co-PI)	09/17/17- 8/31/22
National Institutes of Health		

“The Center for HIV RNA Studies”

Goal: Use cryo-EM to characterize HIV RNA and RNA protein complexes.

P01AI120943 (Gaya Amarasinghe, PI Washington U; Chiu, Co-PI)

07/07/16 - 06/30/21

National Institutes of Health

“Structural and Functional Characterization of the Ebola Virus Replication Complex”

Goal: Use cryoEM to determine structure of molecular complexes relevant to Ebola virus replication.

ONR12151988 (Mark Bathe, PI, M.I.T.; Chiu, Co-PI)

09/01/16 - 08/31/19

N00014-16-1-2953

Office of Naval Research

“DNA Origami Scaffolds for Single-particle Cryo-electron Microscopy of Viral RNA”

Goal: Perform CryoEM to characterize DNA origami with and without RNA.