BIOGRAPHICAL SKETCH

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NAME: Tao, Yizhi Jane

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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)	END DATE MM/YYYY	FIELD OF STUDY
Peking University, Beijing	BS	07/1992	Biophysics
Purdue University, West Lafayette, IN	PHD	05/1999	Biological Sciences
Harvard University/HHMI, Cambridge, MA	Postdoctoral Fellow	2002	Structural Biology

A. Personal Statement

Research in my laboratory focuses on the mechanism of RNA virus assembly, genome replication and packaging. I have had extensive trainings in virology, biochemistry and structural biology during my graduate studies on bacteriophages with Dr. Michael Rossmann at Purdue, and postdoctoral studies on reovirus with Dr. Stephen Harrison at Harvard. At Rice University my lab has performed detailed structural and functional characterization of a number of important RNA viruses and their proteins, including birnavirus, picobirnavirus, influenza A virus, hepatitis E virus, astrovirus, Orsay virus, and the partivirus PsV-F and PsV-S. Meanwhile, my lab also had productive collaboration with others in studying cohesin function, chromosome organization, and histone modification.

I am very excited about the proposed work on CcFV-1. This would be a natural extension of my long-standing interest in dsRNA virus structure and replication since my postdoctoral study on the reovirus polymerase λ3. In the past year, we have obtained a large amount of preliminary data that demonstrate the feasibility of the project. I am confident that our research team has all the biological and technical expertise needed to carry out the proposed work.

1. Collier AM, Lyytinen OL, Guo YR, Toh Y, Poranen MM, Tao YJ. Initiation of RNA Polymerization and Polymerase Encapsidation by a Small dsRNA Virus. PLoS Pathog. 2016 Apr;12(4):e1005523. PubMed Central PMCID: PMC4831847.
2. Pan J, Lin L, Tao YJ. Self-guanylylation of birnavirus VP1 does not require an intact polymerase activity site. Virology. 2009 Dec 5;395(1):87-96. PubMed Central PMCID: PMC2783171.
3. Pan J, Dong L, Lin L, Ochoa WF, Sinkovits RS, Havens WM, Nibert ML, Baker TS, Ghabrial SA, Tao YJ. Atomic structure reveals the unique capsid organization of a dsRNA virus. Proc Natl Acad Sci U S A. 2009 Mar 17;106(11):4225-30. PubMed Central PMCID: PMC2657383.
4. Pan J, Vakharia VN, Tao YJ. The structure of a birnavirus polymerase reveals a distinct active site topology. Proc Natl Acad Sci U S A. 2007 May 1;104(18):7385-90. PubMed Central PMCID: PMC1855279.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2018 -	Professor, BioSciences, Rice University, Houston, TX
2018 - 2021	Adjunct Professor, College of Veterinary Medicine, HuaZhong Agricultural University, Wuhan
2010 - 2018	Associate Professor, Biochemistry & Cell Biology, Rice University, Houston, TX
2002 - 2010	Assistant Professor, Biochemistry & Cell Biology, Rice University, Houston, TX
1999 - 2002	Postdoctoral Fellow, HHMI/Department of Molecular and Cellular Biology, Harvard University, Cambridge, MA
1994 - 1999	Graduate Research Assistant, Purdue University, West Lafayette, IN

Honors

2017	Hamill Innovation Award, Rice University
2009	Image of the Year, Nature
2007	Hamill Innovation Award, Rice University
2005	Research Excellence Award, WM Keck Foundation
2005	Hamill Innovation Award, Rice University
1999	H. Edwin Umbarger Award for outstanding graduate research, Purdue University

C. Contribution to Science

1. Most known dsRNA viruses possess a characteristic, 120-subunit T=1 capsid surrounding their genomes. With viral replicating enzymes packaged inside, such T=1 viral particles of dsRNA viruses function as transcription machines inside infected host cells. Our work on several dsRNA viruses have led to a number of important discoveries: (1) solved the structures of two partitiviruses, Penicillium stoloniferum virus F and S (PsV-F and PSV-S), which reveal a capsid organization and assembly pathway distinct from those of larger dsRNA viruses; (2) elucidated the structure and transcription activity of the picobirnavirus polymerase as a general model for small dsRNA viruses including partitiviruses (to be published); (3) determined the crystal structure and characterized the protein priming activity of two different birnavirus polymerases, both of which have a novel polymerase active site with a permuted topology; (4) solved the crystal structure of the reovirus and rotavirus polymerase, and discovered a cap binding activity of the polymerase that likely functions in the selective copying of the negative-strand viral RNA during transcription.
   a. Collier AM, Lyytinen OL, Guo YR, Toh Y, Poranen MM, Tao YJ. Initiation of RNA Polymerization and Polymerase Encapsidation by a Small dsRNA Virus. PLoS Pathog. 2016 Apr;12(4):e1005523. PubMed Central PMCID: PMC4831847.
   b. Pan J, Dong L, Lin L, Ochoa WF, Sinkovits RS, Havens WM, Nibert ML, Baker TS, Ghabrial SA, Tao YJ. Atomic structure reveals the unique capsid organization of a dsRNA virus. Proc Natl Acad Sci U S A. 2009 Mar 17;106(11):4225-30. PubMed Central PMCID: PMC2657383.
   c. Pan J, Vakharia VN, Tao YJ. The structure of a birnavirus polymerase reveals a distinct active site topology. Proc Natl Acad Sci U S A. 2007 May 1;104(18):7385-90. PubMed Central PMCID: PMC1855279.
   d. Tao Y, Farsetta DL, Nibert ML, Harrison SC. RNA synthesis in a cage--structural studies of reovirus polymerase lambda3. Cell. 2002 Nov 27;111(5):733-45. PubMed PMID: 12464184.

2. Influenza viruses are enveloped viruses with a segmented, (-) RNA genome that is encapsidated in the form of ribonucleoprotein complexes. To provide a better understanding of the influenza virus assembly and replication processes, our laboratory has: (1) determined several crystal structures of the NP proteins from both the influenza A virus and the infectious salmon anemia virus (ISAV); (2) biochemically analyzed NP:RNA interaction with results providing direct support for the existence of protein-free RNAs on the RNP surface; (3) characterized the structure and activity of the recombinant influenza A virus polymerase and its interaction with NP; and (4) solved the full length ISAV M1 protein structure and studied its interaction with membrane and RNP. Our findings have made important contributions to our understanding of orthomyxovirus RNP structure, function, and assembly.
   a. Waters K, Gao C, Ykema M, Han L, Voth L, Tao YJ, Wan XF. Triple reassortment increases compatibility among viral ribonucleoprotein genes of contemporary avian and human influenza A viruses. PLoS Pathog. 2021 Oct;17(10):e1009962. doi: 10.1371/journal.ppat.1009962. eCollection 2021 Oct. PubMed PMID: 34618879; PubMed Central PMCID: PMC8525756.
   b. Waters K, Wan HJ, Han L, Xue J, Ykema M, Tao YJ, Wan XF. Variations outside the conserved motifs of PB1 catalytic active site may affect replication efficiency of the RNP complex of influenza A virus. Virology. 2021 Jul;559:145-155. doi: 10.1016/j.virol.2021.04.001. Epub 2021 Apr 9. PubMed PMID: 33887645.

c. Meyerson NR, Zhou L, Guo YR, Zhao C, Tao YJ, Krug RM, Sawyer SL. Nuclear TRIM25 Specifically Targets Influenza Virus Ribonucleoproteins to Block the Onset of RNA Chain Elongation. Cell Host Microbe. 2017 Nov 8;22(5):627-638.e7. doi: 10.1016/j.chom.2017.10.003. Epub 2017 Nov 5. PubMed PMID: 29107643; PubMed Central PMCID: PMC6309188.

d. Zhang W, Zheng W, Toh Y, Betancourt-Solis MA, Tu J, Fan Y, Vakharia VN, Liu J, McNew JA, Jin M, Tao YJ. Crystal structure of an orthomyxovirus matrix protein reveals mechanisms for self-polymerization and membrane association. Proc Natl Acad Sci U S A. 2017 Aug 8;114(32):8550-8555. PubMed Central PMCID: PMC5559005.

3. For the past seven years my laboratory has been working closely with Dr. Weiwei Zhong in studying the structure and the infection mechanism of the Orsay virus. With our complementary expertise, we are able to perform both structural and functional analyses at the same time, taking advantage of the C. elegans as a convenient model organism for genetic manipulation. Our study of the Orsay δ protein has also yielded exciting new findings indicating that δ plays crucial roles in modulating host cytoskeleton network during infection. Our research on Orsay has the potential to uncover fundamental mechanisms used by viral pathogens to restructure live intestinal cells to facilitate their spread and propagation.
   a. Guo YR, Fan Y, Zhou Y, Jin M, Zhang JL, Jiang H, Holt MV, Wang T, Young NL, Wang D, Zhong W, Tao YJ. Orsay Virus CP-δ Adopts a Novel β-Bracelet Structural Fold and Incorporates into Virions as a Head Fiber. J Virol. 2020 Oct 14;94(21) PubMed Central PMCID: PMC7565637.
   b. Yuan W, Zhou Y, Fan Y, Tao YJ, Zhong W. Orsay δ Protein Is Required for Nonlytic Viral Egress. J Virol. 2018 Jul 15;92(14) PubMed Central PMCID: PMC6026750.
   c. Fan Y, Guo YR, Yuan W, Zhou Y, Holt MV, Wang T, Demeler B, Young NL, Zhong W, Tao YJ. Structure of a pentameric virion-associated fiber with a potential role in Orsay virus entry to host cells. PLoS Pathog. 2017 Feb;13(2):e1006231. PubMed Central PMCID: PMC5344674.
   d. Guo YR, Hryc CF, Jakana J, Jiang H, Wang D, Chiu W, Zhong W, Tao YJ. Crystal structure of a nematode-infecting virus. Proc Natl Acad Sci U S A. 2014 Sep 2;111(35):12781-6. PubMed Central PMCID: PMC4156749.

4. While working as a graduate student with Dr. Michael Rossmann, I obtained the first asymmetric structure of a detailed bacteriophage (i.e. phage phi29) by single particle cryo-EM reconstruction. Using phage mutants and assembly intermediates, I computed a series of phi29 structures that provide important insights into the bacteriophage morphogenesis pathway. Together with Dr. Rossmann, I developed an algorithm for computing EM reconstruction for otherwise highly symmetric particles with local asymmetric structural features. I modified the EM3DR software package to allow reconstruction of asymmetric viral structures. At Purdue I also worked on the crystal structure of the phage T4 fibritin, which forms the whiskers around the neck of the phage that regulate the assembly and host cell attachment of the long tail fiber. In addition to the fibritin E molecule, my laboratory at Rice recently solved the crystal structure of the fibritin B1 mutant, which is a >300Å long coiled coil and likely the longest helical structure ever been solved (to be published).
   a. Tao Y, Strelkov SV, Mesyanzhinov VV, Rossmann MG. Structure of bacteriophage T4 fibritin: a segmented coiled coil and the role of the C-terminal domain. Structure. 1997 Jun 15;5(6):789-98. PubMed PMID: 9261070.
   b. Tao Y, Olson NH, Xu W, Anderson DL, Rossmann MG, Baker TS. Assembly of a tailed bacterial virus and its genome release studied in three dimensions. Cell. 1998 Oct 30;95(3):431-7. PubMed Central PMCID: PMC4167676.
   c. Rossmann MG, Tao Y. Cryo-electron-microscopy reconstruction of partially symmetric objects. J Struct Biol. 1999 Apr-May;125(2-3):196-208. PubMed PMID: 10222275.
   d. Simpson AA, Tao Y, Leiman PG, Badasso MO, He Y, Jardine PJ, Olson NH, Morais MC, Grimes S, Anderson DL, Baker TS, Rossmann MG. Structure of the bacteriophage phi29 DNA packaging motor. Nature. 2000 Dec 7;408(6813):745-50. PubMed Central PMCID: PMC4151180.

5. Chromosome modification, organization and dynamics The structure of human chromosome is highly dynamics in response to cell cycle regulation and cell signaling. Our recent collaboration with Dr. Lu led to the discovery of KAT2A as a novel histone siccinyltransferase that is implicated in many cell signaling

pathways. Moreover, our study on the human cohesin complex over the years have generated several exciting findings, including mapping the interface between SA1/SA2 and Rad21, defining the role of SA1 in telomere maintenance, and implicating SA2 in DNA replication and repair.

a. Pan H, Jin M, Ghadiyaram A, Kaur P, Miller HE, Ta HM, Liu M, Fan Y, Mahn C, Gorthi A, You C, Piehler J, Riehn R, Bishop AJR, Tao YJ, Wang H. Cohesin SA1 and SA2 are RNA binding proteins that localize to RNA containing regions on DNA. Nucleic Acids Res. 2020 Jun 4;48(10):5639-5655. PubMed Central PMCID: PMC7261166.

b. Wang Y, Guo YR, Xing D, Tao YJ, Lu Z. Supramolecular assembly of KAT2A with succinyl-CoA for histone succinylation. Cell Discov. 2018;4:47. PubMed Central PMCID: PMC6079010.

c. Countryman P, Fan Y, Gorthi A, Pan H, Strickland J, Kaur P, Wang X, Lin J, Lei X, White C, You C, Wirth N, Tessmer I, Piehler J, Riehn R, Bishop AJR, Tao YJ, Wang H. Cohesin SA2 is a sequence-independent DNA-binding protein that recognizes DNA replication and repair intermediates. J Biol Chem. 2018 Jan 19;293(3):1054-1069. PubMed Central PMCID: PMC5777247.

d. Wang Y, Guo YR, Liu K, Yin Z, Liu R, Xia Y, Tan L, Yang P, Lee JH, Li XJ, Hawke D, Zheng Y, Qian X, Lyu J, He J, Xing D, Tao YJ, Lu Z. KAT2A coupled with the α-KGDH complex acts as a histone H3 succinyltransferase. Nature. 2017 Dec 14;552(7684):273-277. PubMed Central PMCID: PMC5841452.

BIOGRAPHICAL SKETCH

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NAME: Gao, Yang

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

POSITION TITLE: Assistant 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)	END DATE MM/YYYY	FIELD OF STUDY
University of Science and Technology of China, Hefei, Anhui	BS	05/2007	Life Science
Iowa State University, Ames, IA	PhD	05/2013	Biochemistry

A. Personal Statement

My proposed research aims to illustrate the structure and mechanism of RNA dependent RNA polymerase from CcFV-1. I have acquired adequate expertise to successfully perform the proposed work. I was educated as a structural biologist and biochemist since the beginning of my career. During my PhD studies I employed various techniques to characterize structure and mechanism of proteins in glucose metabolism. My journey on enzymes in nucleic acid metabolism started with my first postdoctoral position in 2013. Subsequently, I have studied double strand break repair nuclease complex Mre11-Rad50, translesion DNA polymerases η and ν, and DNA replisome from bacteriophage T7. These projects prepared me well on reconstituting and characterizing nucleic acid enzymes. I have always been at the technical frontline. I mastered crystallography and molecular dynamics simulations during my Ph. D. During my postdoctoral training at the National Institutes of Health, I adapted the cutting-edge structural techniques time-resolved crystallography and cryo-electron microscope to study mechanisms of DNA replication. My past work has led to 21 publications, including two first-author articles in the prestigious journal Science. In the Science paper published in 2016, I observed the DNA polymerase catalysis in real time at atomic resolution. The molecular movies uncovered the essential roles of multiple metal ions in DNA synthesis. In summary, my extensive experience on DNA polymerases and expertise on various structural techniques prepared me well in studying the structure and function of CcFV-1 polymerase.

1. Gao Y, Cui Y, Fox T, Lin S, Wang H, de Val N, Zhou ZH, Yang W. Structures and operating principles of the replisome. Science. 2019 Feb 22;363(6429) PubMed Central PMCID: PMC6681829.
2. Gao Y, Yang W. Capture of a third Mg^{2+} is essential for catalyzing DNA synthesis. Science. 2016 Jun 10;352(6291):1334-7. PubMed Central PMCID: PMC6320252.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2019 -	Assistant Professor, Rice University, Houston, TX
2014 - 2019	Postdoctoral Fellow , National Institute of Health (NIH), Bethesda, MD
2013 - 2014	Postdoctoral Fellow, Iowa State University, Ames, IA

Honors

2013 - 2013	Teaching Excellence Award, Graduate College, Iowa State Univ.
2011 - 2011	Best Thematic Poster Award, annual Experimental Biology Meeting
2010 - 2010	Graduate Student Teaching Award, Department of Biochemistry, Biophysics and Molecular Biology, Iowa State University
2007 - 2007	Undergraduate Research Excellence Award, University of Science and Technology of China

C. Contribution to Science

1. Structural basis of replisome operation. Since DNA was established as the genetic material and the DNA double-helical structure was proposed, the mechanism of DNA replication has been a central subject in molecular biology research. However, the structural basis of DNA replication was not resolved due to the complexity of DNA replication. To determine replisome structures, I reconstituted the simplest replisome from Bacteriophage T7 and adapted the cutting-edge cryo-electron microscope technique. By solving nearly 20 structures of T7 replisomes on its relevant DNA substrates, I illustrated the mechanism of helicase translocation, helicase-leading strand polymerase coupling and primase-lagging strand polymerase coordination (publication “c”). Based on the first structure of a replisome, I consolidated many years of biochemical data and pointed out the potential mechanisms of replication coupled repair (publication “b”). In addition, I summarized mechanisms of different helicases specialized in different processes of DNA metabolism (publication “a”). In summary, my work provided a scaffold in understanding structural basis of DNA replication.

    a. Gao Y, Yang W. Different mechanisms for translocation by monomeric and hexameric helicases. Curr Opin Struct Biol. 2020 Apr;61:25-32. PubMed Central PMCID: PMC7156327.
    b. Yang W, Seidman MM, Rupp WD, Gao Y. Replisome structure suggests mechanism for continuous fork progression and post-replication repair. DNA Repair (Amst). 2019 Sep;81:102658. PubMed Central PMCID: PMC7467748.
    c. Gao Y, Cui Y, Fox T, Lin S, Wang H, de Val N, Zhou ZH, Yang W. Structures and operating principles of the replisome. Science. 2019 Feb 22;363(6429) PubMed Central PMCID: PMC6681829.

2. Mechanism of metal ion dependent DNA synthesis. DNA polymerases replicate genomic DNA with the assistance of divalent metal ions. It was proposed for decades that two metal ions were required and sufficient for polymerase catalysis. However, the conclusion was mainly based on static crystal structures of polymerases prepared under inhibitory conditions and the dynamic catalytic process was not directly visualized. I investigated the polymerase catalysis with a novel diffusion-based time-resolved crystallography method. By collecting over a hundred crystal structures during polymerase catalysis under different conditions, I for the first time proved that DNA polymerase with well aligned DNA, dNTP and two metal ions are not adequate for the chemical reaction (publication “d”). Only upon the arrival of a third metal ion the reaction proceeds. The third metal ion is present transiently and not directly coordinated by the polymerase, explaining why it escaped from detection for decades. My finding not only illustrated the chemical mechanism of polymerase reaction but also revolutionized how people think about enzyme catalysis. We suspect that the transient bound metal ions play essential roles in all divalent metal ion dependent enzymes in nucleic acid metabolism. To facilitate the research in the field, we summarized our diffusion-based time-resolved crystallography method in great detail in a method paper (publication “c”). DNA is subject to endogenous or environmental consults and specialized translesion DNA polymerases are evolved to bypass various DNA lesions. I have collaborated with an undergraduate student to investigate how a translesion DNA polymerase adds nucleotide against oxidative lesion 8,5′-cyclopurine-2′-deoxynucleosides, which will obstruct replication and transcription if not dealt properly (publication “a”). Our structures and biochemical experiments elucidated how the backbone distorting lesion can be tolerated in polymerase active site in a metal ion dependent manner. Lastly, I have reviewed the common themes in polymerase catalysis and the diverse mechanisms of polymerase bypassing various types of lesions (publication “b”).

    a. Weng PJ, Gao Y, Gregory MT, Wang P, Wang Y, Yang W. Bypassing a 8,5'-cyclo-2'-deoxyadenosine lesion by human DNA polymerase η at atomic resolution. Proc Natl Acad Sci U S A. 2018 Oct 16;115(42):10660-10665. PubMed Central PMCID: PMC6196489.
    b. Yang W, Gao Y. Translesion and Repair DNA Polymerases: Diverse Structure and Mechanism. Annu Rev Biochem. 2018 Jun 20;87:239-261. PubMed Central PMCID: PMC6098713.
    c. Samara NL, Gao Y, Wu J, Yang W. Detection of Reaction Intermediates in Mg^{2+}-Dependent DNA Synthesis and RNA Degradation by Time-Resolved X-Ray Crystallography. Methods Enzymol. 2017;592:283-327. PubMed Central PMCID: PMC6097844.
    d. Gao Y, Yang W. Capture of a third Mg^{2+} is essential for catalyzing DNA synthesis. Science. 2016 Jun 10;352(6291):1334-7. PubMed Central PMCID: PMC6320252.

3. Allosteric communication mechanisms of Mre11-Rad50 (MR) complex. MR complex play pivot roles in DNA double-strand break. The MR complex contains endo- and exo-nuclease activity to initialize DNA recession, ATPase activity to drive DNA translocation, and a several hundred Angstrom long coiled-coil domain that can potentially bridge different DNA strands. How different activities are coordinated within MR complex are not well understood. I have worked with Dr. Nelson for nine months and characterized the allosteric communication of MR complex from bacteriophage T4. I showed that the nuclease activities of Mre11 is autoinhibited by its C-terminal domain and Rad50 binding to the C-terminal domain of Mre11 relieves its autoinhibition (publication “d”). I participated in studying how the long coiled-coil domain mediate MR complex function (publication “c”). In addition, I collaborated with two undergraduate students and investigated the allosteric communication with evolutionary analysis (publication “b”) and characterized the role of Rad50 C-terminus unstructured region in DNA binding (publication “a”). Collectively, my work revealed the working mechanism of the highly conserved MR complex.

    a. Streff HE, Gao Y, Nelson SW. Functional evaluation of the C-terminal region of bacteriophage T4 Rad50. Biochem Biophys Res Commun. 2020 May 28;526(2):485-490. PubMed PMID: 32238267.
    b. Gao Y, Meyer JR, Nelson SW. A network of allosterically coupled residues in the bacteriophage T4 Mre11-Rad50 complex. Protein Sci. 2016 Nov;25(11):2054-2065. PubMed Central PMCID: PMC5079247.
    c. Barfoot T, Herdendorf TJ, Behning BR, Stohr BA, Gao Y, Kreuzer KN, Nelson SW. Functional Analysis of the Bacteriophage T4 Rad50 Homolog (gp46) Coiled-coil Domain. J Biol Chem. 2015 Sep 25;290(39):23905-15. PubMed Central PMCID: PMC4583041.
    d. Gao Y, Nelson SW. Autoinhibition of bacteriophage T4 Mre11 by its C-terminal domain. J Biol Chem. 2014 Sep 19;289(38):26505-26513. PubMed Central PMCID: PMC4176212.