BIOGRAPHICAL SKETCH

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NAME: YANG, XIAOJING

eRA COMMONS USERNAME (credential, e.g., agency login): xiaojingyang

POSITION TITLE: Associate 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)*	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
Huazhong Univ. of Sci. & Tech, China	BE	09/1983	07/1987	Biomedical Eng.
Tongji Medical University, China	MS	09/1987	07/1990	Biomedical Eng.
The University of Chicago	MS, PhD	09/1991	12/1995	Structural Biology
Northwestern University	Postdoctoral	04/1996	04/1999	Structural Biology

A. Personal Statement

My long track record in the photoreceptor field includes several landmark crystal structures of bilin-based photoreceptors, dynamic studies of distinct photoreceptors, and method development for diffraction experiments at both cryogenic and room temperatures. The overall goal of my research is to elucidate the general principles of signaling and allosteric regulation in photoreceptors and sensory proteins by provoking and resolving functionally relevant structure dynamics. Central to this endeavor is our integrated approach combining structural biology, biochemistry and spectroscopy, bolstered by technical innovations enabling biophysical interrogation via experimental perturbation and analytical resolution. The current proposal aims to address the fundamental aspects of light signaling, allostery regulation and signal integration in two representative photoreceptor kinases using cryoEM single particle analysis. The feasibility of the proposed studies is supported by our significant preliminary data and our unique leverage in probing structural dynamics. With the support from NIH, my laboratory has established an entire workflow of cryoEM single particle analysis tailored to structural studies of light sensitive proteins. I am a tested investigator with extensive experience in tackling outstanding problems at the frontiers of structural biology. As attested by my productivity in the past 4-5 years and many publications in high-impact journals including Nature, Nature Plants, and PNAS, I am confident that I will successfully lead this research effort and accomplish the goals.

a. Bandara S, Rockwell N, Zeng X, Ren Z, Wang C, Shin H, Martin SS, Moreno MV, Lagarias JC* & Yang X*. Crystal Structure of a far-red-sensing cyanobacteriochrome reveals an atypical bilin conformation and spectral tuning mechanis*m.* **Proc Natl Acad Sci U S A** (2021) doi:10.1073/pnas.2025094118. PubMed PMID: 33727422; PubMed Central PMCID: PMC8000052.

b. Lee SJ, Kim TW, Kim JG, Yang C, Yun SR, Kim C, Ren Z, Kumarapperuma I, Kuk J, Moffat K, Yang X* and Ihee H*. Light-induced protein structural dynamics in bacteriophytochrome revealed by time-resolved x-ray solution scattering. **Science Advances.** (2022) doi: 10.1126/sciadv.abm6278. PubMed PMID: 35622911; PubMed Central PMCID: PMC9140987.

c. Shin H, Ren Z, Zeng X, Bandara S & Yang X*. Structural basis of molecular logic OR in a dual-sensor histidine kinase. **Proc Natl Acad Sci U S A**. (2019) 116:19973 doi:10.1073/pnas.1910855116. PubMed PMID: 31527275; PubMed Central PMCID: PMC6778262.

d. Yang X*, Ren Z, Kuk J, Moffat K. Temperature-scan cryocrystallography reveals reaction intermediates in bacteriophytochrome. **Nature**. (2011) 479(7373):428-32. PubMed PMID: 22002602; PubMed Central PMCID: PMC3337037.

Ongoing and recently completed projects that I would like to highlight include:

National Institutes of Health/NEI
R01 EY024363
06/01/2014 - 05/31/2023
Role: PI
Structures, Dynamics and Signaling Mechanisms of Modular Photoreceptors

National Science Foundation
MCB-2017274
5/1/2020 - 4/30/2024
Role: PI
Collaborative Research: Biochemical, Genetic and Structural Studies of Bilin Lyases

Chicago Biomedical Consortium Catalyst Award
C-086
03/01/2018 - 02/28/2020
Role: PI (with Prof. Minglei Zhao, Univ. of Chicago)
Observing Protein Allostery Dynamics by Single-Particle Imaging

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2020 - now	Associate Professor, Univ. of Illinois at Chicago, Department of Chemistry
2020 - now	Associate Professor, Univ. of Illinois at Chicago, Dept. of Ophthalmology and Visual Sciences
2020 - now	Council Member, American Society for Photobiology
2020 - now	Chair, Award Committee, American Society for Photobiology
2014 - 2020	Assistant professor, Univ. of Illinois at Chicago, Department of Chemistry
2005 - 2014	Senior Research Professional, The University of Chicago
2001 - 2005	Senior Research Associate, Northwestern University, Feinberg School of Medicine
1999 - 2000	Research Specialist, The University of Chicago

C. Contributions to Science

1. **Development and application of dynamic crystallography**: Direct observations of intermediate structures during a biochemical reaction or a biological process hold the key to the mechanistic understanding of protein functions. However, it is technically challenging to obtain dynamic signals at atomic resolution due to their transient and heterogeneous nature. To address these challenges, we have developed a temperature-scan strategy to capture and resolve distinct intermediate structures from a series of difference electron density maps that probe a photoreaction initiated at different cryogenic temperatures. Recently, our laboratory has developed an automated *in situ* serial diffraction platform to facilitate dynamic crystallography experiments at room temperature. This new capability is designed to address two major bottlenecks in current serial crystallography methods, namely sample economy and sample environment. We have successfully applied these dynamic crystallography methods to several photoreceptors including bacteriophytochromes, plant UV-B photoreceptor, and now to modular photoceptors in this proposal.

a. Ren Z*, Wang C, Shin H, Bandara S, Kumarapperuma I, Ren MY, Kang W & **Yang X*** *An automated platform for in situ serial crystallography at room temperature* **IUCrJ. (**2020) 7:1009. doi:10.1107/S2052252520011288. PubMed PMID: 33209315; PubMed Central PMCID: PMC7642789.
b. Ren Z*, Ayhan M, Bandara S, Bowatte K, Kumarapperuma I, Gunawardana S, Shin H, Wang C, Zeng X & **Yang X*.** *Crystal-on-crystal chips for in situ serial diffraction at room temperature.* **Lab on a Chip.** (2018) doi:10.1039/C8LC00489G. PubMed PMID: 29952383**;** PubMed Central PMCID: PMC6057835.
c. Zeng X, Ren Z, Wu Q, Fan J, Peng PP, Tang K, Zhang R, Zhao KH, **Yang X.** Dynamic Crystallography Reveals Early Signalling Events in Ultraviolet Photoreceptor UVR8. **Nat Plants**. (2015) PubMed PMID: 26097745; PubMed Central PMCID: PMC4469132.
d. **Yang X**, Ren Z, Kuk J, Moffat K. Temperature-scan cryocrystallography reveals reaction intermediates in bacteriophytochrome. **Nature**. (2011) Oct 16;479(7373):428-32. PubMed PMID: 22002602; PubMed Central PMCID: PMC3337037.

2. **Structures and signaling mechanisms of bilin-based photoreceptors**: I have determined several landmark crystal structures of bilin-based photoreceptors including the canonical phytochromes and the newly characterized cyanobacteriochromes. These include the first crystal structure for the Pfr state (PNAS, 2008 with 257 citations) and the unusual RpBphP3 (PNAS, 2007 with 151 citations; Structure 2015). We first proposed the "flip-and-rotate" model (PNAS, 2009 with 117 citations) that accounts for light-induced structural changes, which emerges to be a universal photoconversion mechanism for bilin-binding photoreceptors despite their diverse photocycles. In particular, our dynamic crystallographic observations from the photoactive bacteriophytochrome crystals (Nature, 2011) provided direct experimental evidence to support the *15Z/15E* isomerization that helped settle a heated debate on the primary photo-event in bilin-based photoreceptors. Our recent publications in PNAS and Sci. Adv. (Shin et al 2019; Slavov et al 2020; Wang et al 2020; Bandara et al 2021; Lee et al 2022) have further advanced the mechanistic understanding of light signaling in bilin-based photoreceptors.

a. Slavov C, Fischer T, Barnoy A, Shin H, Rao AG, Wiebeler C, Zeng X, Sun Y, Xu Q, Gutt A, Zhao K-H, Gärtner W, Yang X*, Schapiro I* & Wachtveitl J* The interplay between chromophore and protein determines the extended excited state dynamics in a single-domain phytochrome **Proc Natl Acad Sci U S A**. (2020) 117:16356 doi:10.1073/pnas.1921706117. PubMed PMID: 32591422; PubMed Central PMCID: PMC7368379.
b. Yang X, Stojković EA, Ozarowski WB, Kuk J, Davydova E, Moffat K. Light Signaling Mechanism of Two Tandem Bacteriophytochromes. **Structure** (2015) Jul 7;23(7):1179-89. PubMed PMID: 26095026; PubMed Central PMCID: PMC4497868.
c. Yang X, Kuk J, Moffat K. Conformational differences between the Pfr and Pr states in Pseudomonas aeruginosa bacteriophytochrome. **Proc Natl Acad Sci U S A**. (2009) Sep 15;106(37):15639-44. PubMed PMID: 19720999; PubMed Central PMCID: PMC2747172.
d. Yang X, Kuk J, Moffat K. Crystal structure of Pseudomonas aeruginosa bacteriophytochrome: photoconversion and signal transduction. **Proc Natl Acad Sci U S A. (**2008) Sep 23;105(38):14715-20. PubMed PMID: 18799746; PubMed Central PMCID: PMC2567202.

3. **Structures and mechanisms of photoreceptors and bilin lyases**: In collaboration with other research groups, my laboratory has contributed to structural and mechanistic studies on several photoreceptors and enzymes involved in bacterial virulence, photosynthesis and photo-protection. These include but not limited to plant UVR8 (Zeng et al. Nature Plants, 2015), orange carotenoid protein from cyanobacteria (Bandara et al PNAS, 2017), a blue-light photoreceptor (Rinaldi et al. mBio 2021) from pathogenic bacteria, bilin lyases from marine cynaobacteria (Kumarapperuma et al. Structure, 2022). Collectively, these studies have shed light on how the biological systems incorporate the fundamental principles of photochemistry to perceive light as a signal and harvest light as energy.

a. Kumarapperuma I, Joseph K-L, Wang C, Biju LB, Tom IP, Weaver KD, Grebert T, Partensky F, Schluchter MW*, and Yang X* Crystal structure and molecular mechanism of an E/F type bilin lyase-

isomerase. **Structure** (2022) 30: 564-573. PubMed PMID: 35148828; PubMed Central PMCID: PMC8995348.

b. Rinaldi J, Fernández I, Shin H, Sycz G, Gunawardana S, Kumarapperuma I, Paz JM, Otero LH, Cerutti ML, Á Zorreguieta Á, Ren Z, Klinke S*, Yang X*, Goldbaum FA*. Dimer Asymmetry and Light Activation Mechanism in Brucella Blue-Light Sensor Histidine Kinase. **mBio** (2021) doi:10.1128/mBio.00264-21. PubMed PMID: 33879593**;** PubMed Central PMCID: PMC8092228

c. Bandara, S., Ren, Z., Lu, L., Zeng, X., Shin, H., Zhao, K.-H., **Yang, X**.* Photoactivation mechanism of a carotenoid-based photoreceptor. **Proc Natl Acad Sci U S A. (**2017) 114, 6286-6291. doi:10.1073/pnas.1700956114. PubMed PMID: 28559328**;** PubMed Central PMCID: PMC5474822

d. Zhou W, Ding WL, Zeng XL, Dong LL, Zhao B, Zhou M, Scheer H, Zhao KH, Yang X. Structure and mechanism of the phycobiliprotein lyase CpcT. **J Biol Chem**. (2014) Sep 26;289(39):26677-89. PubMed PMID: 25074932; PubMed Central PMCID: PMC4175310.

4. **Structures and mechanism of catalytic RNA and DNA/RNA processing proteins**: In my early career, I studied structures and functions of RNA and protein-RNA interactions by X-ray crystallography. The crystal structures of a ribotoxin and its complex with a 29-mer RNA revealed how a ribonuclease disrupts protein synthesis via hydrolysis of a single phosphodiester bond near the ribosome active site. As a postdoc, I worked on the crystal structure of a ribozyme involved in tRNA maturation, which provided structural insight into a unique RNA-catalyzed reaction mechanism.

   a. Ren Z*, Kang W, Gunawardana S, Bowatte K, Thoulass K, Kaeser G, Lamparter T, Kraub N and Yang X*. Dynamic Interplays between Three Redox Cofactors in DNA Photolyase PhrB. **Cell Reports Physical Sciences.** (2023) doi:10.2139/ssrn.4194951.

   b. Krasilnikov AS, Yang X, Pan T, Mondragón A. Crystal structure of the specificity domain of ribonuclease P. **Nature**. (2003) Feb 13;421(6924):760-4. PubMed PMID: 12610630.

   c. Yang X, Gérczei T, Glover LT, Correll CC. Crystal structures of restrictocin-inhibitor complexes with implications for RNA recognition and base flipping. **Nat Struct Biol**. (2001) Nov;8(11):968-73. PubMed PMID: 11685244.

   d. Yang X, Moffat K. Insights into specificity of cleavage and mechanism of cell entry from the crystal structure of the highly specific Aspergillus ribotoxin, restrictocin. **Structure** (1996) Jul 15;4(7):837-52. PubMed PMID: 8805570.

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https://www.ncbi.nlm.nih.gov/myncbi/xiaojing.yang.1/bibliography/public/