BIOGRAPHICAL SKETCH

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NAME: Ando, Nozomi

eRA COMMONS USER NAME (credential, e.g., agency login): nando1

POSITION TITLE: Assistant Professor of Chemistry and Chemical Biology

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
Massachusetts Institute of Technology	B.S.	06/01	Physics
Cornell University	M.S.	05/04	Physics
Cornell University	Ph.D.	01/09	Physics
Massachusetts Institute of Technology	Postdoctoral	06/14	Chemistry

A. Personal Statement

The fundamental problem that I am interested in solving is that of protein allostery: namely, how distant parts of a protein communicate in order to tune function and perform sequential steps in the correct order. My lab uses X-ray scattering, crystallography, cryo-electron microscopy (cryo-EM), and bioinformatics to understand key relationships between protein structure, dynamics, function, and sequence. We are best known for our innovations in X-ray scattering, which allows us to interpret conformational heterogeneity in terms of protein motions and structural rearrangements (*Chem Rev* 2017). This approach has allowed us to map the conformational landscape of allosteric enzymes and identify evolutionary patterns using small-angle X-ray scattering (SAXS), crystallography, and cryo-EM (*JACS* 2017, *PNAS* 2018, *Nature Comm* 2019). Most recently, we were the first to solve a long-standing problem in X-ray crystallography by explaining the diffuse scattering signal from protein crystals in terms of long-range lattice dynamics and short-ranged protein dynamics, which underlie protein allostery (*Nature Comm* 2020). Many of the systems we study are metalloenzymes as they perform reactions of evolutionary significance, and we are highly experienced in anaerobic methods (*PNAS* 2017, *JACS* 2012).

As a faculty member, I have taken on various roles in service to the scientific community. Of these, my most important work has been focused on two areas: (1) the advancement of women and underrepresented groups in STEM and (2) the advancement and education of structural biology. In the latter category, my lab has produced several highly cited articles: a *Nature Protocols* (2014) article with example data that serves as an introduction to synchrotron-based SAXS. a *Chemical Reviews* (2017) article that serves as a comprehensive guide to X-ray scattering and advanced applications, and a perspective in *Biochemistry* (2018) that serves as a white paper for the future of X-ray science and cryo-EM. In the classroom, I developed a new modern structural biology course at Cornell, *CHEM 7880: Structural Methods in Biochemistry*. This course is unique as it covers both the theory and practice of SAXS, crystallography, and cryo-EM. As a recognized leader in structural biology, I am currently serving as a program chair for the American Crystallographic Association Meeting and elected member of the U.S. National Committee for Crystallography (USNC/Cr). In 2022, I will serve as director of the Erice International School of Crystallography. As relevant to this proposal, I am also a member of the Structural Biology Oversight Committee at Cornell which oversees the Arctica.

Current and former mentees include 12 undergraduates, 2 rotation students, 10 graduate students, 3 postdoctoral fellows, and 1 research scholar.

B. Positions and Honors

Positions and Employment

2001 Visiting Scholar, Center for Materials Science and Engineering, MIT, Cambridge, MA
2014-2018 Assistant Professor of Chemistry, Princeton University, Princeton, NJ
2018-present Assistant Professor of Chemistry & Chemical Biology, Cornell University, Ithaca, NY
2019-present Graduate Faculty, Field of Biophysics, Cornell University, Ithaca, NY

Other Experience and Professional Memberships

2006- Member, Biophysical Society
2007 Mentor, Cornell University Expand Your Horizon Program
2008- Reviewer for *Science, Nature, Nature Comm, JACS, Biochemistry, IUCr, Biophysical Journal, J Phys Chem, Langmuir, Nat Prod Rev, J Mol Biol.*
2008 Training in the teaching of writing at the Cornell University Knight Institute
2009 HHMI MIT Mentoring Program in Chemical Biology
2010-2013 Member, American Physical Society
2010 Member, American Chemical Society
2011 Member, Protein Society
2011-2013 Elected Member, Cornell High Energy Synchrotron Source Executive User Committee
2014-2018 Proposal Reviewer, Cornell High Energy Synchrotron Source
2016 Organizer, *"Biomolecules in Motion"* Workshop, Cornell High Energy Synchrotron Source.
2016 Session chair, 2016 Diffraction Methods Gordon Research Conference
2016 Session chair, 21st Association for Crystallization Technology Larson Workshop
2017 Session chair, 2017 American Crystallographic Association Meeting
2017 Organizer, *"Measurement and Interpretation of Diffuse Scattering in X-Ray Diffraction for Macromolecular Crystallography"* Workshop, NSLS-II and CFN Meeting
2018 Session chair, 2018 Metallocofactors Gordon Conference
2019-present Faculty mentor, Chemical Biology Interface (CBI) Training Program, Cornell University
2019-2021 Elected member, U.S. National Committee for Crystallography (USNC/Cr)

Honors

2007 Best Instrumentation Poster Award, Cornell High Energy Synchrotron Source Users Meeting
2010 National Institutes of Health Ruth L. Kirschstein National Research Service Award (GM090486)
2012 MIT Postdoctoral Association Travel Grant
2012 Plenary speaker for 15th International Small Angle Scattering Conference, Sydney
2012 National Institutes of Health Pathway to Independence Award (GM100008)
2017 Invited Author, *Holy Grails in Chemistry* Special Issue of *Acc Chem Res*
2017 Invited Author, *Chemical Reviews*
2017 *Future of Biophysics* Burroughs Wellcome Fund Symposium Lecture, Biophysical Society.
2017 National Institutes of Health Maximizing Investigators' Research Award
2018 Invited Author, *Future of Biochemistry* Special Issue of *Biochemistry*
2020 Program Chair, American Crystallographic Association Meeting
2020 Margaret C. Etter Early Career Award, American Crystallographic Association
2020 National Science Foundation CAREER Award
2020 *Future of Biophysics* Burroughs Wellcome Symposium Lecture, Biophysical Society
2022 Director, Erice International School of Crystallography

C. Contribution to Science

1) **Service to the structural biology community:** I have a long track record of service to the field of structural biology. In addition to software contributions (described elsewhere), a high-pressure SAXS cell that I designed in my graduate studies has formed the basis for the recently established high-pressure biology (HP-Bio) beamline at the Cornell High Energy Synchrotron Source (CHESS). Notable publications written to serve the structural biology community include a protocol for critically designing and analyzing synchrotron-based SAXS experiments and a piece on the intertwined history and future of X-ray crystallography and cryo-EM, for which we interviewed leading figures, Joachim Frank, Henry Chapman, Sol Gruner, Peter Moore, and Francisco Asturias.

a. **Ando, N.**, Chenevier, P., Novak, M., Tate, M. W., Gruner, S. M. (2008) High hydrostatic pressure small-angle X-ray scattering (SAXS) cell for protein solution studies featuring diamond windows and disposable sample cells. *Journal of Applied Crystallography* **41**, 167-175.
b. Skou, S., Gillilan, R. E., **Ando, N.** (2014) Synchrotron-based small-angle X-ray scattering (SAXS) of biomacromolecules in solution. *Nature Protocols* **9**, 1727–1739. PMCID: PMC4472361
c. Shoemaker, S. C. & **Ando, N**. X-rays in the cryo-electron microscopy era: Structural biology's dynamic future. *Biochemistry* **57,** 277–285 (2018). PMCID: PMC5999524
d. Lecture on SAXS at 3rd Penn State Bioinorganic Workshop (video): https://tinyurl.com/yblxyvaj
e. Software on model-free deconvolution of SAXS data: https://github.com/ando-lab/regals

2) **Diffuse scattering from correlated motions in protein crystals**: Conventional crystallography involves analyzing sharp diffraction patterns, commonly called Bragg data. However, real crystals are not perfectly periodic and produce additional scattering between the Bragg peaks. This smooth background pattern, known as diffuse scattering, contains information about correlated displacements within the crystal but has been exceeding difficult to measure and interpret. My group is the first to provide a full explanation for this signal in terms of protein dynamics at multiple length scales.
   a. Meisburger, S. P., Thomas, W. C., Watkins, M. B. & **Ando, N**. (2017) X-ray scattering studies of protein structural dynamics. *Chem Rev* **117,** 7615–7672. PMCID: PMC5562295
   b. Meisburger, S. P., Case, D. A. & **Ando, N**. (2020) Diffuse X-ray scattering from correlated motions in a protein crystal. *Nature Communications* 11, 1271. PMCID: PMC7062842
   c. Diffuse scattering software: https://github.com/ando-lab/mdx-lib

3) **Allostery in a radical enzyme:** My postdoctoral work on class Ia ribonucleotide reductases (RNRs) set a new precedent for the use of SAXS to study transient and heterogeneous protein complexes. By combining SAXS with other biophysical techniques, we achieved a major milestone in understanding allosteric regulation of the prototypic class Ia RNR and addressed a 50-year old mystery surrounding this complex system. This work has been included in the 6th edition of Lehninger, “Principles of Biochemistry.”
   a. **Ando, N.**, Brignole, E. J., Zimanyi, C. M., Funk, M. A., Yokoyama, K., Asturias, F. J., Stubbe, J., & Drennan, C. L. (2011) Structural interconversions modulate activity of *Escherichia coli* ribonucleotide reductase. *PNAS* 108, 21046–21051. PMCID: PMC3248520
   b. Zimanyi, C. M., **Ando, N.**, Brignole, E. J., Asturias, F. J., Stubbe, J., & Drennan, C. L. (2012) Tangled up in knots: Structures of inactivated forms of *E. coli* class Ia ribonucleotide reductase. *Structure* 20, 1374–1383. PMCID: PMC3459064
   a. Minnihan, E. C., **Ando, N.**, Brignole, E. J., Olshansky, L., Chittuluru, J., Asturias, F. J., Drennan, C. L., Nocera, D., & Stubbe, J. (2013) Generation of a stable, aminotyrosyl radical-induced α2β2 complex of *Escherichia coli* class Ia ribonucleotide reductase. *PNAS* 110, 3835–3840. PMCID: PMC3593893
   b. **Ando, N.*,** Li H., Brignole, E. J., Thompson, S., McLaughlin, M. I., Page, J. E., Asturias, F. J., Stubbe, J., & Drennan, C. L*. Allosteric inhibition of human ribonucleotide reductase by dATP entails the stabilization of a hexamer. *Biochemistry* 55, 373–381 (2016). *co-corresponding. PMCID: PMC4722859

4) **Evolution of allostery**: My group is especially experienced in the treatment of conformational heterogeneity with mathematical decomposition methods. Using this approach, we study the diversity and evolution of allosteric mechanisms in enzyme families. By mapping the conformational landscape of complex allosteric enzymes in solution, we are able to rapidly determine structures by cryo-EM and crystallography that provide detailed insight into allosteric mechanisms.
   a. Meisburger, S. P, Taylor, A. B., Khan, C. A., Zhang, S., Fitzpatrick, P. F., **Ando, N**. (2016) Domain movements upon activation of phenylalanine hydroxylase characterized by crystallography and chromatography-coupled small-angle X-ray scattering. *JACS* **138,** 6506–6516. PMCID: PMC4896396
   b. Parker, M. J., Maggiolo, A. O., Thomas, W. C., Kim, A., Meisburger, S. P., **Ando, N.***, Boal, A. K.*, and Stubbe, J.* (2018) An endogenous dAMP ligand in *Bacillus subtilis* class Ib RNR promotes assembly of a noncanonical dimer for regulation by dATP. *PNAS* **55,** 201800356–10. PMCID: PMC5960316 *co-corresponding

c. Thomas, W. C., Brooks, P. F., Burnim, A. A., Bacik, J.-P., Stubbe, J., Kaelber, J. T., Chen, J. Z., and **Ando, N**. (2019) Convergent Allostery in Ribonucleotide Reductase. *bioRxiv* 504290 doi:10.1101/504290. *Nature Communications* 10, Article number: 2653. PMCID: PMC6572854
d. Software: https://bioxtas-raw.readthedocs.io/en/latest/tutorial/s2_efa.html

5) **Complex metalloenzymes**: My group is interested in understanding how life evolves and adapts to unusual environments. In particular, we use various techniques to study the evolutionary significance of metalloenzymes, proteins that use metal-containing cofactors to perform challenging - and often ancient - chemistry. Our crystallographic work on the dark operative protochlorophyllide oxidoreductase (DPOR) L-protein is currently under review (Corless, *et a*l. "The flexible N-terminus of BchL is autoinhibitory to Protochlorophyllide reduction through interaction with its [4Fe-4S] cluster." bioRXiv. https://doi.org/10.1101/840439).
a. Kung, Y., **Ando, N.**, Doukov, T., Blasiak, L., Bender, G., Ragsdale, S. W., Drennan, C. L. (2012) Visualizing molecular juggling within a B_{12}-dependent methyltransferase complex. *Nature* **484**, 265–269. PMCID: PMC3326194
b. **Ando, N.,** Kung, Y., Can, M., Bender, G., Ragsdale, S. W., & Drennan, C. L. (2012) Transient B_{12}-dependent methyltransferase complexes revealed by small-angle X-ray scattering. *JACS* **134**, 17945–17954. PMCID: PMC3484714
c. Davis, K. M., Schramma, K., Hansen, W., Bacik, J.-P., Khare, S., Seyedsayamdost, M., **Ando, N.** (2017) Structures of the peptide-modifying radical SAM enzyme SuiB elucidate the basis of substrate recognition. *PNAS* **114,** 10420–10425. PMCID: PMC5625900
d. Tinoco, A. et al. Origin of high stereocontrol in olefin cyclopropanation catalyzed by an engineered carbene transferase. ACS Catal 9, 1514–1524 (2019). PMCID: PMC6534153

Complete List of Published Work in Publications:
https://scholar.google.com/citations?user=v-MyIFAAAAAJ&hl=en

D. Research Support

1) Ongoing

5 R35 GM124847 03 Ando (PI) 8/1/2017-7/31/2022
NIH MIRA R35
Title: Protein Allostery and Catalysis beyond Bragg Diffraction
Goal: The goal of this proposal is to characterize protein motions that are important for regulation and catalysis using X-ray scattering methods.

MCB-1942668 Ando (PI) 1/1/2020-12/31/2024
NSF Career
Title: CAREER: Correlated Motions in Protein Allostery
Goal: The major goal of this project is to gain molecular level insight into the correlated motions that give rise to protein allostery using cryo-electron microscopy and bioinformatics methods.

CBET-1929256 Ando (co-PI) 09/15/2019-08/31/2020
NSF
Title: Collaborative Research: Engineering Hyperstable Enzymes via Computationally Guided Protein Stapling
Goal: The major goal of this project is to examine the structure and dynamics of enzymes engineered for industrial applications.

DMR-1719875 Ando (Co-PI), Milner (Co-PI) 9/1/2020-8/31/2021
NSF / Cornell Center for Materials Research Seed Grant
Title: Bio-inspired X-ray Methods to Probe the Structure and Dynamics of Metal-Organic Frameworks
Goal: The major goal of this project is to apply structural methods for macromolecules to understand the functional dynamics of metal-organic frameworks in sensing applications.

2) Completed

5 R00 GM100008 05 Ando (PI) 2/2/2012– 07/31/2017
NIH K99/R00
Title: Structural Characterizations of Transient and Heterogeneous Protein Complexes
Goal: The goal is to apply advanced small-angle X-ray scattering methods to understand catalysis and allostery in dynamic enzymes.
Role: PI