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 focus of my research program is to understand the molecular mechanisms of protein allostery. To do so, my lab uses X-ray scattering, crystallography, cryo-electron microscopy (cryo-EM), and bioinformatics. 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 (*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 that arise from correlated protein motions (*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, *JBC* 2021). As a recognized expert in the structural biology community, I have served in a number of leadership roles. Currently, I am an elected member of the U.S. National Committee for Crystallography (USNC/Cr) and director of the 2022 Erice International School of Crystallography on diffuse scattering.

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. As a leader in the X-ray community, I have actively worked to promote the advancement and education of X-ray science and structural biology. Most recently, as a program chair for the 2020 American Crystallographic Association (ACA) Meeting, I was able to develop a program with a strongly educational theme, geared towards students and postdocs. At Cornell, my graduate course, *CHEM 7880: Structural Methods in Biochemistry*, is first and only course that covers both the theory and practice of X-ray scattering, crystallography, and cryo-EM. At every stage of my career, I have also worked to promote the advancement of women and underrepresented groups in STEM. At Princeton, I served in various capacities to assess departmental climate, improve the experience of women faculty, and create an REU program to increase diversity in STEM. Currently, at Cornell, I am the co-chair of a departmental committee for diversity, equity, and inclusion, and I am also the faculty advisor for the Cornell Chemists for Outreach and Graduate Inclusion (COrGI) Student Organization.

At Cornell and Princeton, I have trained or continue to train 12 undergraduates, 2 rotation students, 9 graduate students, 3 postdoctoral fellows, and 2 research associates.

B. Positions and Honors

Positions and Employment

2001 Visiting Scholar, Center for Materials Science and Engineering, MIT, Cambridge, MA
2001-2008 Graduate Research Assistant, Department of Physics, Cornell University, Ithaca, NY
with Sol M. Gruner (Dept. of Physics and Cornell High Energy Synchrotron Source)
2008-2010 HHMI Postdoctoral Associate, Department of Chemistry, MIT, Cambridge, MA
with Catherine L. Drennan (HHMI, Depts. of Chemistry and Biology)
2010-2014 NIH Postdoctoral Fellow, Department of Chemistry, MIT, Cambridge, MA
with Catherine L. Drennan (HHMI, Depts. of Chemistry and Biology)
2014-2018 Assistant Professor of Chemistry, Princeton University, Princeton, NJ
2018-2021 Assistant Professor of Chemistry & Chemical Biology, Cornell University, Ithaca, NY
2019-present Graduate Faculty, Field of Biophysics, Cornell University, Ithaca, NY
2021-present Associate Professor of Chemistry & Chemical Biology, 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 Member, Structural Biology Oversight Committee, Cornell Cryo-EM Facility
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*
2020-2021 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. Contributions to Science

1) **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. With support from the NIGMS (GM100008, GM124847), my group became the first to provide a full explanation for this signal in terms of protein dynamics at multiple length scales.
    a. 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
    b. 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
    c. Meisburger, S. P. & **Ando, N**. (2017) Correlated motions from crystallography beyond diffraction. *Acc Chem Res* 50: 580–583. PMCID: PMC5663199
    d. **Ando, N**. Protein Folding & Dynamics Webinar (2021): https://youtu.be/jrW5qq5413E?t=438

2) **Evolution of allostery**: Ribonucleotide reductases (RNRs) are essential enzymes for all DNA-based life and have a fascinating evolutionary history that is thought to pre-date the oxygenation of the Earth. Among the RNR family the class Ib RNRs are unusual for two reasons: it lacks a regulatory domain that is prevalent in the rest of the RNR family, and it is found only in bacteria, including a number of well-known human pathogens. Using SAXS, crystallography, and cryo-EM, we discovered that a stunning form of convergent allostery had evolved in this class. This contribution was made possible with NIGMS support (GM124847).
    a. 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
    b. 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
    c. **Ando, N.** American Crystallographic Association (ACA) Etter Award Talk (2020): https://history.amercrystalassn.org/nozomi-ando-video

3) **Complex metalloenzymes**: My group is interested in understanding how life evolves and adapts to unusual environments. With NIGMS support (GM100008, GM124847), we have used various techniques to study the metalloenzymes, proteins that use metal-containing cofactors to perform challenging reactions with biomedical and evolutionary significance.
    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. 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
    c. 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
    d. Corless, E. I., Imran, S. M. S., Watkins, M. B., Bacik, J. P., Mattice, J. R., Patterson, A., Danyal, K., Soffe, M., Kitelinger, R., Seefeldt, L. C., Origanti, S., Bennett, B., Bothner, B., **Ando, N***, Antony, E.*. "The flexible N-terminus of BchL autoinhibits activity through interaction with its [4Fe-4S] cluster and released upon ATP binding." *J Mol. Biol.* (2021) 296, 100107. *co-corresponding. PMID: 33219127

4) **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, a high-pressure small-angle X-ray scattering (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 products from recent

years 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. These contributions have made with long-standing support from NIGMS (GM100008, GM124847).

a. 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
b. 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
c. Meisburger, S.P., Xu, D., **Ando, N.** (2021) *REGALS*: a general method to deconvolve X-ray scattering data from evolving mixtures. *IUCrJ*, in press. https://doi.org/10.1107/S2052252521000555
d. Ando Lab software: https://github.com/ando-lab/

5) **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 class Ia RNR from *E. coli* 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." These contributions were supported by the NIGMS (GM090486, GM100008 to N.A.).

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
c. 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
d. **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. 55, 373–381 (2016). *co-corresponding. PMCID: PMC4722859

D. Additional Information: Research Support

1) Ongoing Research Support

5 R35 GM124847 04 Ando (PI) 8/1/2017-7/31/2022
NIH MIRA R35
Title: Protein Allostery and Catalysis beyond Bragg Diffraction
Goal: The goal of this project is to characterize protein motions that are important for regulation and catalysis by developing X-ray methods, including diffuse scattering, solution small-angle X-ray scattering, and time-resolved crystallography.
Role: As PI, I am responsible for overseeing the project, designing and conducting research, providing guidance to advisees, and disseminating results.

MCB-1942668 Ando (PI) 1/1/2020-12/31/2024
NSF Career
Title: CAREER: Correlated Motions in Protein Allostery
Goal: The goal of this project is to gain molecular level insight into protein allostery in the ribonucleotide reductase family using cryo-electron microscopy and evolutionary bioinformatic methods.
Role: As PI, I am responsible for overseeing the project, designing and conducting research, providing guidance to advisees, and disseminating results.

CBET-1929256 Fasan (PI), Ando (collaborator) 9/15/2019-8/31/2022
NSF

Title: Collaborative Research: Engineering Hyperstable Enzymes via Computationally Guided Protein Stapling
Goal: The goal of this project is to crystallographically characterize myoglobin engineered with staples based on unnatural amino acid incorporation.
Role: As a collaborator on this project, I am responsible for overseeing the structural work done in my lab, exchanging ideas with all participants, and disseminating results.

DMR-1719875 Frank Wise (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 goal of this project is to apply structural methods for macromolecules to understand the functional dynamics of metal-organic frameworks in sensing applications.
Role: As co-PI of this seed grant, I am responsible for overseeing the crystallographic work, providing guidance to advisees, exchanging ideas with all participants, and disseminating results.

2) Completed Research Support

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 was to apply advanced small-angle X-ray scattering methods to characterize transient protein-protein interactions.
Role: As PI, I was responsible for overseeing the project, designing and conducting research, providing guidance to advisees, and disseminating results.