BIOGRAPHICAL SKETCH

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NAME: Obara, Christopher John

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

POSITION TITLE: Assistant Professor of Pharmacology, Chemistry & Biochemistry

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 Florida, FL	B.S.	05/2009	Entomology & Nematology
University of Florida, FL	B.A.	05/2009	Physics
National Institutes of Health, Bethesda, MD and Georgetown University, Washington, DC	Ph.D	07/2014	Microbiology & Immunology
HHMI Janelia Research Campus, Ashburn, VA	Post Doc	05/2024	Biophysics & Cell Biology

A. Personal Statement

My laboratory develops custom microscopy and advanced imaging pipelines to try to solve fundamental questions in biophysics, cell biology, and neuroscience. We are especially interested in understanding how the laws of physics acting on single molecules give rise the highly organized functions of cellular life. A central question in our research focus is understanding the spatial and temporal coordination of cellular metabolism, in which incredibly diverse set of small molecules are very specifically targeted and directed through complex metabolic pathways. A lack of imaging tools with the spatial or temporal resolution needed has historically relegated this research question to the realm of classic biochemistry, but through the development of custom-built, super-resolution microscopes and new chemical labels, we are beginning to observe these processes where they occur in living cells.

My research program integrates the power of statistical physics from my educational background with the quantitative experimental tools that I mastered during my PhD and postdoctoral research. During my PhD at the NIH, I began exploring the potential for combining statistical approaches with new tools to drive discoveries in biology. I adapted mathematical approaches from my undergraduate work and combined them with a series of novel flow cytometry-based pipelines for calculating probabilities of virus infection, an approach now commonly used in vaccine efficacy studies. However, this work suffered from an inability to distinguish biological phenomena in spatially distinct regions of cells. This led me to pursue a postdoctoral fellowship under the mentorship of Jennifer Lippincott-Schwartz at HHMI Janelia Research Campus, where I pioneered several microscopy pipelines that have fundamentally changed our understanding of the relationship between organelle structure and function in mammalian cells. My early work on the endoplasmic reticulum (ER) led to the discovery of the ER matrix, a conserved substructure across eukaryotes, providing new insights into the organization and function of this critical organelle (Nixon-Abell, Obara, and Weigel et al., *Science*, 2016). Our follow up work was even able to identify how ER-localized molecules know where they are in a cell: by reading a posttranslational code recorded on microtubules that records local “zip code” and direction (Zheng, Obara et al. *Nature,* 2022).

One of my most significant contributions to the field has been the development of a high-speed microscopy pipeline capable of tracking individual protein-protein interactions in living cells at millisecond timescales. This

innovation allowed me to address long-standing challenges in understanding these crucial signaling hubs, revealing the rapid molecular exchanges that drive cellular communication and coordination (Obara, Nixon-Abell, et al. *Nature*, 2024). These discoveries are paving the way for a deeper understanding of how cells regulate their metabolic processes and make signaling decisions, ultimately bringing us closer to answering the fundamental question of how life converts energy to order and function.

Since establishing my laboratory at UCSD in May 2024, I have been continuing to build on these discoveries, focusing on the role of organelle shaping and trafficking in the regulation of metabolism. My lab is equipped with state-of-the-art imaging facilities, including capabilities for high-speed single molecule imaging, cryogenic fluorescence microscopy, and correlative electron microscopy, which we are leveraging to explore these questions at an unprecedented level of detail. I am committed to advancing the field of cell biology through collaborative research, open access to innovative tools, and the mentorship of the next generation of scientists. My colleagues in the field have recognized and supported me in this commitment—I have been an invited lecturer in advanced microscopy courses numerous times at the NIH, MIT, and the Marine Biology Laboratory at Woods Hole. I have also given invited lectures on designing and using advanced microscopy approaches to communities of imagers across the world, and I am committed to making sure the next generation of imaging technologies are made available to the entire community of researchers. By continuing to push the boundaries of what is possible in cellular imaging, I aim to provide transformative insights into the mechanisms that underpin health and disease, particularly those related to metabolic regulation.

I have not published or created research projects under a different name.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2024-present Assistant Professor, Departments of Pharmacology, Chemistry & Biochemistry, UC San Diego.
2016-2024 HHMI Postdoctoral Fellow, HHMI Janelia Research Campus.
2014-2016 Intramural AIDS Research Fellow, National Institute of Child Health and Human Development, NIH.

Teaching and Academic Activities

2022 Course Instructor, Introduction to single molecule imaging, University of Bergen, Norway.
2021 Guest Lecturer, FAES BioTech Super Resolution Microscopy Course, NIH.
2021 Guest Lecturer, FAES BioTech Quantitative Imaging Microscopy Course, NIH.
2019 Guest Lecturer, FAES BioTech Super Resolution Microscopy Course, NIH.
2018 Course Facilitator, Physiology Course, Marine Biological Laboratory at Woods Hole.
2018 Guest Lecturer, FAES BioTech Super Resolution Microscopy Course, NIH.
2017 Course Facilitator, Physiology Course, Marine Biological Laboratory at Woods Hole.
2017 Guest Lecturer, FAES BioTech Super Resolution Microscopy Course, NIH.
2016 Teaching Assistant, Physiology Course, Marine Biological Laboratory at Woods Hole.
2016 Invited Lecturer, Superresolution Microscopy Course, MIT.
2015 Teaching Assistant, Physiology Course, Marine Biological Laboratory at Woods Hole.

Honors

Awards:

2014-2015 Intramural AIDS postdoctoral research fellowship, NIH Office of AIDS Research.
2009-2010 Intramural AIDS graduate research fellowship, NIH Office of AIDS Research.
2008-2009 Hetrick Scholar for Excellence in Entomology Research.
2005-2009 National Merit Scholar, University of Florida.

Reviewing Experience

2015-present Ad Hoc Reviewer for *Comm. Biology, JCS, JCB, PNAS, Soft Matter, Trends in Cell Biology, Nature Communications, Life Science Alliance*.

Professional memberships: Biophysical Society, American Society for Cell Biology, American Society for Biochemistry and Molecular Biology

C. Contributions to Science

My contributions to science have largely been centered on using and developing quantitative techniques to understand the emergent properties of living systems from the underlying physical principles. Below are my major contributions in this space:

1. One of the most important contributions to science that I have made is the development of custom microscopy approaches and analysis to understand the high-speed behavior of subcellular organelles and components within them. Conventional imaging approaches fail in this system, since dynamic rearrangements of these compartments occur in milliseconds, and structures are often smaller than the diffraction limit of light. To address this, I have developed a series of custom high-speed superresolution imaging approaches using both light and correlative electron microscopy, including high speed structured illumination by grazing incidence, rapid correlative single molecule imaging, and approaches for fluorescence imaging and 3D electron microscopy of high-pressure frozen cells. These technologies have yielded significant insights about the structure, organization, and regulation of organelles in mammalian cells.
   a. **Obara CJ***, Nixon-Abell J*, et al. Motion of VAPB molecules reveals ER-mitochondria contact site subdomains. ***Nature**,* 2024 Feb 1; (626)169–176.
   b. **Obara CJ**, Moore AS, Lippincott-Schwartz J. Structural Diversity within the Endoplasmic Reticulum—From the Microscale to the Nanoscale. ***CSH Perspectives in Biology***, 2022 doi:10.1101/cshperspect.a041259.
   c. Moore AS, Coscia SM, Simpson CL, Ortega FE, Wait EC, Heddleston JM, Nirschl, JJ, **Obara CJ**, Guedes-Dias P, Boecker CA, Chew TL, Theriot JA, Lippincott-Schwartz J, Holzbaur ELF. Actin cables and comet tails organize mitochondrial networks in mitosis. ***Nature*** 2021 Mar 3; 591 (7851), 659-664.
   d. Nixon-Abell J*, **Obara CJ***, Weigel A* et al. Increased spatiotemporal resolution reveals highly dynamic dense tubular matrices in the peripheral ER**.** ***Science*** 2016 Oct 28; 354(6311).

2. I have also made notable contributions to pipelines for quantitative analysis of microscopy data and extraction of relevant biological information by integration of image processing, machine learning, and statistical physics approaches. These analyses are developed to adapt to custom imaging pipelines, and allow quantitative understanding from what would otherwise be qualitative observations.
   a. Sun Y*, Yu Z*, **Obara CJ**, Mittal K, Lippincott-Schwartz J, Koslover EF. Unraveling trajectories of diffusive particles on networks. ***Phys Rev Research*** 2022 Jun 6; 4(023182).
   b. Zheng P, **Obara CJ**, Szczesna E, Nixon-Abell J, Mahalingan KK, Roll-Mecak A, Lippincott-Schwartz J, Blackstone C. ER proteins decipher the tubulin code to regulate organelle distribution. ***Nature*** 2022 Mar 23; 601, 132-138.
   c. Speiser A, Müller LR, Hoess P, Matti U, **Obara CJ**, Legant ER, Kreshuk A, Macke JH, Ries J, Turaga SC. Deep learning enables fast and dense single molecule localization with high accuracy. ***Nature Methods*** 2021 Sep 3; 18, 1082-1090.

3. I have also worked towards the development of novel tools for imaging protein locations and local ion concentrations in quantitative ways. These phenomena are by definition vary rapid, and with the new, high speed imaging approaches described above, the probe response time or conversion frequency can

be limiting. By combining these tools with my custom microscopy approaches, we can push local cellular functions and signaling into the range of superresolution microscopy.

a. Zhang Y, Rózsa M, Liang Y, Bushey D, Wei Z, Zheng J, Reep D, Broussard GJ, Tsang A, Tsegaye G, Narayan S, **Obara CJ**, Lim JX, Patel R, Zhang R, Ahrens MB, Turner GC, Wang SSH, Korff WL, Schreiter ER, Svoboda K, Hasseman JP, Kolb I, Looger LL. Fast and sensitive GCaMP calcium indicators for imaging neural populations. ***Nature*** 2023 Mar 23; 615, 884-891.

b. Mohr MA, Kobitski AY, Sabater LR, Nienhaus K, **Obara CJ**, Lippincott-Schwartz J, Nienhaus GU, Pantazis P. Rational Engineering of Photoconvertible Fluorescent Proteins for Dual-Color Fluorescence Nanoscopy Enabled by a Triplet-State Mechanism of Primed Conversion. ***Angew Chem Int Ed Engl.*** 2017 Sep 11; 56(38):11628-11633.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/christopher.obara.1/bibliography/public/