BIOGRAPHICAL SKETCH

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NAME: Dominguez, Roberto

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

POSITION TITLE: Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date	FIELD OF STUDY
Faculty of Physics, Odessa Mechnikov National University, former USSR	B.S., M.S.	09/1982 – 06/1987	Theoretical Physics and Mathematics
Pasteur Institute & University of Paris-Sud, France	Ph.D.	07/1993 – 03/1996	Protein Crystallography and Biochemistry
Rosenstiel Center, Brandeis University, MA	PostDoctoral Fellow	03/1996 – 02/1998	Structural Biology of Molecular Motors

A. Personal Statement

My lab has had a longstanding interest in studying proteins that control cytoskeletal and muscle functions. These proteins regulate numerous physiological processes, including cell locomotion, muscle contraction, and organelle transport. Dysfunction in these proteins can lead to devastating diseases such as musculoskeletal disorders, cancer, and neurodegenerative diseases. Examples of proteins under investigation include Arp2/3 complex, CapZ, tropomodulin, leiomodins, tropomyosin, nebulin, WH2-based actin filament nucleators, formins, gelsolin, MIRO, myosin motors, and spectrin family members (utrophin, dystrophin, α-actinin).

My interest in the cytoskeleton began during my postdoctoral years at Brandeis University, where I determined the first structures of myosin (smooth muscle myosin II) at the beginning of the power stroke under the guidance of Dr. Carolyn Cohen. While myosin motors remain an area of interest, my major focus shifted to actin and actin-binding proteins upon becoming an independent investigator at BBRI (Boston) in 1998. In 2006, my lab relocated to UPenn (Physiology), where I also became a member of the Pennsylvania Muscle Institute (PMI), a world-class organization dedicated to the study of the cytoskeleton.

Our work aims to correlate structure to function by using a broad range of complementary methods and through collaborations within and outside of UPenn. We have ongoing collaborations with Drs. T. Khurana, M. Ostap, E. Holzbaur, H. Stedman, R. Heuckeroth, D. Trauner, E. De la Cruz, P. Lappalainen, A. Gautreau, and G. Romet-Lemonne. Our primary research tools include cryo-EM and X-ray crystallography, which provide atomic-level insights into proteins and their complexes. We also employ a range of other methods, such as cell and molecular biology, bioinformatics, and biophysical and biochemical techniques (ITC, MALS, FRET, TIRF microscopy, proteomics), to connect our structural findings with physiological and cellular activities.

Training: A key aspect of our mission is to mentor and train the next generation of scientists and educators. My lab has trained over 50 postdocs and students. Among former trainees, 9 are now professors (or equivalent) in five different countries, including the USA (Silvia Jansen, David Kast), Belgium (Frédéric Kerff, Mohammed Terrak), France (François Ferron), South Korea (Sung Haeng Lee, Suk Namgoong, InGyun Lee), and the UAE (Saif Alqassim). Several lab alumni are also pursuing successful careers in the biotech industry, including Ludovic Otterbein (Lundbeck, Denmark), Emma Borrego-Diaz (Pfizer, Boston), David Chereau (Biozilla, Sacramento), Adam Zwolak and Bengi Turegun (Janssen, Bala-Cynwyd), Austin Zimmet (McKinsey, Philadelphia), and Peter Carman (GSK). Current lab members include six graduate students (Elana Baltrusaitis, Nicholas Palmer, Kyle Barrie, Shayna Brotzman, Andy Saks, Jonas Cook), a Research Specialist (Erika Ravitch), and two Senior Investigators (Drs. Goska Boczkowska and Greg Rebowski).

Ongoing and recently completed projects:

Ongoing:

R01 GM073791
Dominguez R (PI)
04/01/2023 – 03/31/2027
Structural Basis of Actin Cytoskeleton Dynamics

RM1 GM136511
Ostap EM, Holzbaur E, Lakadamyali M, Dominguez R (MPI)
05/01/2020 – 04/30/2025
Integrative Mechanisms of Organelle Dynamics from the Atomic-to-Cellular Level

R01 DK128282
Heuckeroth RO (PI), Dominguez, R (Co-Investigator)
09/28/2021 – 08/31/2026
Biochemical and cellular mechanisms linking actin mutations to visceral myopathy

Recent Citations:

1. Palmer NJ, Barrie KR, Dominguez R. Mechanisms of actin filament severing and elongation by formins. ***Nature*** (2024) DOI:10.1038/s41586-024-07637-0
2. Barrie KR, Rebowski G, Dominguez R. Mechanism of Actin Filament Severing and Capping by Gelsolin. ***Nat Struct Mol Biol*** (2024) *in press*
3. Ceron RH, Báez-Cruz FA, Palmer NJ, Carman PJ, Boczkowska M, Heuckeroth RO, Ostap EM, Dominguez R. Molecular Mechanisms Linking Missense ACTG2 Mutations to Visceral Myopathy. ***Science Advances*** (2024) **10**(23), DOI: 10.1126/sciadv.adn6615
4. Carman PJ, Barrie KR, Rebowski G, Dominguez R. Structures of the free and capped ends of the actin filament. ***Science*** (2023) **380**:1287-1292, DOI: 10.1126/science.adg6812

B. Positions, Scientific Appointments, and Honors

Scientific Appointments

2010-	Professor of Physiology, U. of Pennsylvania, Perelman School of Medicine, Philadelphia, PA
2006-2010	Associate Professor, U. of Pennsylvania, Perelman School of Medicine, Philadelphia, PA
2001-2006	Principal Scientist (Associate Prof), Boston Biomedical Research Institute, Watertown, MA
1998-2001	Scientist (Assistant Prof), Boston Biomedical Research Institute, Watertown, MA
1996-1998	Postdoctoral Fellow, Rosenstiel Center, Brandeis U, MA (mentor: Dr. C Cohen)
1993-1996	PhD Student, Pasteur Institute & Paris-Sud University, Paris, France (mentor: Dr. PM Alzari)
1992-1993	Pre-doctoral Trainee, EMBL, Heidelberg, Germany (mentor: Dr. D Suck)
1989-1991	Pre-doctoral Trainee, University of Liége, Belgium (mento: Dr. O Dideberg)
1987-1989	Scientist, Center for Genetic Engineering and Biotechnology, Havana, Cuba

Positions and Memberships

2023- present	Member Perelman School of Medicine's Committee on Appointment (COAP)
2021-2022	Member POWER Cluster Hire Committee, Perelman School of Medicine
2021-2022	Chair Physiology Faculty Search Committee
2021-2024	Co-chair Admissions Committee, Biochemistry & Molecular Biophysics Graduate Group
2017-present	Member, Biomedical Research Core Facilities Committee, Perelman School of Medicine
2014-present	Member, Bridge Funding Advisory Committee, Perelman School of Medicine
2015-present	Member, Editorial Board of the Journal of Muscle Research and Cell Motility
2009-2023	Associate Editor, *Cytoskeleton*
2008-2014	Member, Editorial Board of *Biophysical Journal*
2006-2010	Member, NIH Study Section, MSFC
2006-present	Member, American Society for Cell Biology
1998-present	Member, Biophysical Society

Honors

2019	Appointed William Maul Measey Presidential Professor of Physiology
2010	Wenner-Gren Foundation Distinguished Lecturer (FEBS/EMBO meeting, Sweden)

2002-2005 Established Investigator of the American Heart Association
1999-2001 American Heart Association, Grant-in-Aid Junior Investigator
1998-2001 Basil O'Connor Scholar of the March of Dimes
1992-1992 Fellow of the German Academic Exchange Service (DAAD)
1989-1991 Fellow of the Societé Française de Belgique

C. Contributions to Science

1. *Myosin motors structure-function*: As a postdoctoral fellow in Dr. Carolyn Cohen's lab at Brandeis University, I determined the first structures of smooth muscle myosin at the beginning of the power stroke. Our contributions to the study of myosin motors continue to this day and have significantly influenced the field. Many laboratories have utilized our structures to design myosin mutations, position fluorescent probes, analyze cryo-EM maps, and test dynamic models of the actomyosin ATP-dependent mechanochemical cycle.

a. **Dominguez R**, Freyzon Y, Trybus KM, Cohen C. Crystal structure of a vertebrate smooth muscle myosin motor domain and its complex with the essential light chain: visualization of the pre-power stroke state. ***Cell*** (1998) **94**:559-571.

b. Terrak M, Rebowski G, Lu RC, Grabarek Z, **Dominguez R**. Structure of the light chain-binding domain of myosin V. ***PNAS*** (2005) **102**:12718-12723. PMC1200277

c. Shuman H, Greenberg MJ, Zwolak A, Lin T, Sindelar CV, **Dominguez R**, Ostap EM. A vertebrate myosin-I structure reveals unique insights into myosin mechanochemical tuning. ***PNAS*** (2014) **111**:2116-2121. PMC3926069

d. Mentes A, Huehn A, Liu X, Zwolak A, **Dominguez R**, Shuman H, Ostap EM, Sindelar CV. High-resolution cryo-EM structures of actin-bound myosin states reveal the mechanism of myosin force sensing. ***PNAS*** (2018) **115**:1292-1297. PMC5819444

2. *Structural biology and biochemistry of actin and actin-binding proteins: Throughout the years, our lab has been at the forefront of actin structural biology, biochemically characterizing and determining the atomic structures of numerous actin-binding proteins, both in isolation and in complex with actin. We determined the first crystal structure of monomeric, uncomplexed actin, revealing the ADP state for the first time. In collaboration with the Arnesen lab in Norway, we discovered actin's N-terminal acetyltransferase, NAA80, determined its structure in complex with profilin-actin, and revealed the functional implications of this modification. Our research has also addressed many other cytoskeletal regulators, including gelsolin, Ena/VASP, profilin, and CARMIL. Additionally, we have studied the structures and mechanisms of disease-causing mutations in several cytoskeletal proteins, including actin itself, which necessitated the development of novel mammalian cell-based protein expression methods.*

a. Otterbein LR, Graceffa P, **Dominguez R**. The crystal structure of uncomplexed actin in the ADP state. ***Science*** (2001) **293**:616-618. DOI: 10.1126/science.1059700

b. Rebowski G, Boczkowska M, Drazic A, Ree R, Goris M, Arnesen T, **Dominguez R**. Mechanism of actin N-terminal acetylation. ***Science Advances*** (2020) **6**(15). DOI: 10.1126/sciadv.aay8793. PMC7141826

a. Ceron RH, Báez-Cruz FA, Palmer NJ, Carman PJ, Boczkowska M, Heuckeroth RO, Ostap EM, Dominguez R. Molecular Mechanisms Linking Missense ACTG2 Mutations to Visceral Myopathy. ***Science Advances*** (2024) **10**(22). DOI: 10.1126/sciadv.adn6615

b. Palmer NJ, Barrie KR, Dominguez R. Mechanisms of actin filament severing and elongation by formins. ***Nature*** (2024) **632**(8024). DOI:10.1038/s41586-024-07637-0

3. *Muscle cytoskeleton*. Our laboratory has had a long-standing interest in studying the mechanisms that regulate muscle contraction. This includes determining the first structure of a protein phosphatase-1 (PP1)-regulatory subunit complex, that of PP1 with the myosin phosphatase targeting subunit 1 (MYPT1). We also discovered the muscle-specific actin filament nucleator Leiomodin. Another major breakthrough was the determination of the first structures of the pointed and barbed ends of the actin filament, both uncapped and capped by the sarcomeric proteins Tmod and CapZ.

a. Terrak M, Kerff F, Langsetmo K, Tao T, **Dominguez R**. Structural Basis of Protein Phosphatase 1 Regulation. ***Nature*** (2004) **429**:780-784. DOI: 10.1038/nature02582.

b. Chereau D, Boczkowska M, Skwarek-Maruszewska, A, Fujiwara I, Rebowski G, Hayes DB, Lappalainen P, Pollard TD, **Dominguez R**. Leiomodin is an actin filament nucleator in muscle cells. ***Science*** (2008) **320**:239-243. DOI: 10.1126/science.1155313. PMC2845909.

c. Rao JN, Madasu Y, **Dominguez R**. Mechanism of actin filament pointed-end capping by tropomodulin. ***Science*** (2014) **345**:463-467. DOI: 10.1126/science.1256159. PMC4367809

d. Carman PJ, Barrie KR, Rebowski G, Dominguez R. Structures of the free and capped ends of the actin filament. ***Science*** (2023) **380**:1287-1292. DOI: 10.1126/science.adg6812

4. *Actin filament nucleation*. For the last 20 years, our lab has been among the leaders in the field in studying the structural-functional mechanisms of actin filament nucleation, including WH2 domain-based nucleators, Leiomodins, Formins, and the Arp2/3 complex along with its numerous regulators (N-WASP, Arpin, Cortactin, Coronin, etc.).

a. Chereau D, Kerff F, Graceffa P, Grabarek Z, Langsetmo K, **Dominguez R**. Actin-bound structures of Wiskott-Aldrich syndrome protein (WASP)-homology domain 2 and the implications for filament assembly. ***PNAS*** (2005) **102**(46)**:**16644-16649. DOI: 10.1073/pnas.0507021102. PMC1283820

b. Zimmet A, Van Eeuwen T, Boczkowska M, Rebowski G, Murakami K, **Dominguez R**. Cryo-EM Structure of NPF-Bound Human Arp2/3 Complex and Activation Mechanism. ***Science Advances*** (2020) **6**(23), DOI: 10.1126/sciadv.aaz7651. PMC7274804

c. Van Eeuwen T, Boczkowska M, Rebowski G, Carman PJ, Fregoso FE, Dominguez R. Transition State of Arp2/3 Complex Activation by Actin-Bound Dimeric Nucleation-Promoting Factor. ***PNAS*** (2023) **120** (23). DOI: 10.1073/pnas.2306165120. PMC10434305

d. Fregoso FE, Boczkowska M, Rebowski G, Carman PJ, Van Eeuwen T, Dominguez R. Mechanism of synergistic activation of Arp2/3 complex by cortactin and WASP-family proteins. ***Nature Communications*** (2023) **14**(1). DOI: 10.1038/s41467-023-42229-y. PMC10613254

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

BIOGRAPHICAL SKETCH

NAME: Nicholas J. Palmer

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

POSITION TITLE: PhD Candidate

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
Temple University, Philadelphia, PA	BS	06/2020	Biochemistry
Temple University, Philadelphia, PA	Minor	06/2020	Mathematics
University of Pennsylvania, Philadelphia, PA	PhD	06/2025	Biochemistry and Molecular Biophysics

A. Personal Statement

My passion for science began at a young age, when both my parents helped to instill a deep curiosity of the world around me. I have always been interested in the question of how the world works, and since have worked pasionatly to discover as much as I can. Currently, I am a PhD candidate in the Dominguez lab at the University of Pennsylvania, where I focus on employing cryo-electron microscopy (cryo-EM) to explore how the actin cytoskeleton is organized by the hundreds of actin binding proteins which regulate it. My journey in science has been shaped by a diverse set of experiences, starting from my undergraduate studies in Biochemistry at Temple University to my current research endeavors.

From the outset of my academic career, I have been captivated by the complexities of biological systems. I began my undergraduate research experience under Dr. Darius Balciunas in the genetics of zebrafish heart regeneration, where I played a key role in generating loxP inducible zebrafish with CRISPR/Cas9. This work ignited a passion for understanding developmental processes at a molecular level. This initial foray into research taught me the value of interdisciplinary approaches, working as part of a team, and instilled in me a great love of research out of my curiosity. Later, this passion for molecular systems as well as my course work shifted my interest to the biophysics of how molecular interactions work. This brought me to molecular dynamics simulations and structural biology, where I worked with Dr. Paul Axelsen. Here I began to focus heavily on the precise molecular interactions of reverse micelle equilibration and learned a great deal about biophysics and physical chemistry.

As I entered graduate school at the University of Pennsylvania, I was able to rotate in multiple labs using diverse skillsets to understand biology. However, my rotation in the Dominguez lab has led me to a great passion for structural biology. Using knowledge from many fields including computation, biochemistry and physics, endless amount of detail can be uncovered about a molecular system. In the Dominguez lab, I am fortunate to work at the intersection of structural biology and cellular dynamics. Using cryo-EM, I aim to address critical questions regarding how actin binding proteins regulate actin's function in the cell. My commitment to discovery has driven me to publish in high-impact journals such as *Nature*.

I have so far been recognized with several awards for my contributions to research, which affirm my dedication to advancing our understanding of biological processes. However, what truly drives me is the thrill of discovery and the opportunity to contribute to the scientific community. I believe that collaboration and sharing knowledge are fundamental to scientific progress, and I am eager to engage with others who share this vision. As I continue my on my scientific journey, I remain committed to exploring the frontiers of structural biology. I am excited about the potential implications of my research in understanding diseases linked to the actin cytoskeleton and hope to inspire future generations of scientists to embrace curiosity and innovation, like my parents were able to for me.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2015-2018: Undergraduate Researcher at Temple University
2018-2020: Undergraduate Researcher at University of Pennsylvania
2020-Present: PhD Student at University of Pennsylvania

Honors

2020 - 2025	Raiziss Award, University of Pennsylvania
2020	Nina Hillman Award, Temple University
2020	American Institute of Chemists Award, American Institute of Chemists Award

C. Contribution to Science

1. As an undergraduate researcher, I had the opportunity to work with Dr. Darius Balciunas where I aided in generating loxP inducible zebrafish to study heart regeneration using CRISPR/Cas9. There had been a gap in the field understanding the role of developmental genes in heart regeneration in adult Zebrafish, however simple knock outs were embryonic lethal to a Zebrafish embryo. The purpose of this work was to generate an inducible knock out where the gene could be expressed as embryos and knocked out as an adult. We succeeded and became one of the first labs to be able to use CRISPR/Cas9 successfully in Zebrafish. As an undergraduate I also became interested in computational biophysics and shifted toward molecular dynamics simulations. I began working with Dr. Paul Axelsen at the University of Pennsylvania where we used molecular dynamics to simulate reverse micelle equilibration. It was not well understood how reverse micelles exchanged mass to equilibrate to thin size range in solution. Molecular dynamics simulations revealed that reverse micelles exchanged through a series of fission/fusion cycles and stochastically equilibrated mass.

   a. Burg L, **Palmer N**, Kikhi K, Miroshnik ES, Rueckert H, Gaddy E, MacPherson Cunningham C, Mattonet K, Lai SL, Marín-Juez R, Waring RB, Stainier DYR, Balciunas D. Conditional mutagenesis by oligonucleotide-mediated integration of loxP sites in zebrafish. ***PLoS Genet***. 2018 Nov;14(11):e1007754. PubMed Central PMCID: PMC6261631.

   b. **Palmer NJ**, Eskici G, Axelsen PH. Non-Equilibrium Mass Exchange in AOT Reverse Micelles. ***J Phys Chem B***. 2020 Jan 9;124(1):144-148. PubMed PMID: 31793793.

2. As a PhD student I have made numerous publications. However the biggest contributions I have made have been in using cryo-EM to solve high resolution structures of actin and actin binding proteins. I started my PhD work by studying actin mutations that cause visceral myopathy. Using the combination of cryo-EM biophysics and biochemical techniques we found that these mutations disrupted the lateral and longitudinal contacts between actin subunits weakening the overall actin filament. Next, I began working on the mechanism of formin-mediated actin elongation. Formins are a family which regulate the growth of actin filaments. They can both modulate the rate of actin elongation, but also have the unique property of remaining at the end as it grows. Additionally, a specific formin called inverted formin 2 (INF2) has the additional ability to bind the middle of acin filaments and severing them. Both of these mechanisms were unknwon until recently. Using cryo-EM of a mixed system of INF2, profilin, and actin, we discovered a step-by-step mechanism of actin filament elongation by formins. We additionally were able to resolve the structure of INF2 in the middle of the actin filament, which helped build a mechanism for INF2 mediated severing.

   a. Ceron R, Báez-Cruz F, **Palmer N**, Carman P, Boczkowska M, Heuckeroth R, Ostap E, Dominguez R. Molecular mechanisms linking missense ACTG2 mutations to visceral myopathy. ***Science Advances***. 2024 May 31; 10(22):-. Available from: https://www.science.org/doi/10.1126/sciadv.adn6615 DOI: 10.1126/sciadv.adn6615

   b. **Palmer N**, Barrie K, Dominguez R. Mechanisms of actin filament severing and elongation by formins. ***Nature***. 2024 June 06; 632(8024):437-442. Available from: https://www.nature.com/articles/s41586-024-07637-0 DOI: 10.1038/s41586-024-07637-0

YEAR	COURSE TITLE	GRADE
	University of Pennsylvania, PhD in Biochemistry and Molecular Biophysics	
2020	Cell Biology	A
2020	Macromolecular Biophysics: Principles and Methods	A
2020	Macromolecular Crystallography: Methods and Applications	B+
2021	Molecular Basis of Disease I	A
2021	Data Analysis and Scientific Inference	A
2021	Human Physiology	A
2022	Candidacy Exam Course	A

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
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NAME: Ravitch, Erika

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

POSITION TITLE: Research Assistant

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
University of Pennsylvania, Philadelphia, PA	BA	08/2018	05/2022	Biochemistry
University of Pennsylvania, Philadelphia, PA	MS	08/2020	05/2022	Chemistry

A. Personal Statement

My long-standing interest in scientific research has been to understand how a symphony of muscular contractions, heart beats, and nerve impulses potentiate a single movement. The human body is an incredible machine, yet what has always fascinated me is how interactions between proteins and molecules at the nanometer-scale are synthesized into micron-scale and eventually whole-body functions and movements. My interest in muscle and desire to study phenomena beyond the textbook drew me to mechanobiology research. I was hooked the moment I read a paper describing how cellular differentiation could be altered in vitro simply by manipulating the substrate stiffness on which the mesenchymal stem cells were grown. I wanted to understand how muscle cells, especially those in the heart that withstand rhythmic contractions over a lifetime, are equipped to endure their mechanical environment and are remodeled in disease. This drew me to the lab of Professor Ken Margulies. In his lab, I developed a project to investigate how cardiac fibroblasts modulate their Lamin A/C network in response to stiffness and how this contibutes to their differentiation into fibrosis-causing cells. As I was completing my thesis, I felt that there was a disconnect in my ability to consider phenomena at the cellular level, i.e. upregulation of Lamin A/C levels in nuclei, and how I had been trained to think biochemically using sequence, structural, and biophysical analyses. To address this, I pursued an opportunity to train in the lab of Professor Roberto Dominguez, where I have developed my understanding cytoskeleton, which is involved in the transmission of mechanical and stiffness cues into the cell, at the level of individual proteins rather than in cells. Research has challenged me, fueling my curiosity and creativity. At the same time, my clinical experiences have highlighted my passion for patient care and advocacy. An MD/PhD represents the perfect blend of these drives, and I am inspired by the opportunity to push the boundaries of our current understanding of muscular diseases and ultimately translate discoveries made at the bench back to the bedside. My research experiences have uniquely poised me to integrate investigative approaches across scales, from individual proteins to cellular phenomena. I am eager to approach research questions from this perspective, taking insights from patient's specific diseases into the lab to understand how the dysfunction of protein-protein interactions leads to patients' disease phenotypes. An MD/PhD will enable me to integrate this patient-level disease focus into my research questions and allow my future lab to focus on transforming research discoveries into practical treatment options, ultimately bridging my passion for research with my commitment to patient care.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments
2022-present Research Assistant

2020-2022 Master's Thesis Researcher

Honors

2024 Poster Presenter, Biophysical Society Meeting
2023 Poster Presenter, University of Pennsylvania, Department of Physiology Retreat
2022, 2023 Poster Presenter, University of Pennsylvania, Biochemistry and Molecular Biophysics Retreat
2018-2022 Roy and Diana Vagelos Scholar in the Molecular Life Sciences
2016-2018 Intel International Science and Engineering Fair Finalist

C. Contributions to Science

1. **Concurrent Undergraduate and Master's Thesis Research (2020-2022):** Lab of Professor Ken Margulies, MD, Department of Physiology, University of Pennsylvania, March 2020 – April 2022

   During my time in the lab of Dr. Ken Margulies at the University of Pennsylvania, I focused on the mechanisms of load-induced myocardial remodeling that occur during heart disease progression and how cytoskeletal elements contribute to these adaptations. I collaborated with Dr. Jason Choi at Thomas Jefferson University on a project about how mutations in lamin A/C, a cytoskeletal protein that coats the interior of the nuclear envelope, affect cardiomyocytes and cardiac fibroblasts. For my Master's thesis, I investigated how lamin A/C levels in cardiac fibroblasts change in response to substrates that mimic healthy or diseased heart tissue. I discovered that while stiff substrates increased lamin A/C levels, this did not prevent fibroblast differentiation into myofibroblasts, indicating that additional strategies may be necessary to address fibrosis.

2. **Gap Years Research (2022-present):** Lab of Professor Roberto Dominguez, PhD, Department of Physiology, University of Pennsylvania, May 2022 – present

   My ongoing gap years research project focuses on the interactions of two proteins essential for mitochondrial dynamics, especially mitochondrial motility. I have co-led a project to structurally and biophysically characterize the MIRO-TRAK complex, using techniques like isothermal titration calorimetry and cryo-EM to map their interactions. Our findings, published in the Journal of Biological Chemistry, mapped one binding interaction of the MIRO-TRAK interaction and determined its independence of cation and nucleotide regulation. Subsequently, we have determined and mapped a second binding interaction and determined a structure by cryo-EM. .

D. Scholastic Performance

YEAR	COURSE TITLE	GRADE
	University of Pennsylvania, Bachelor of Arts in Biochemistry Summa Cum Laude	
2018	Globalization and Its Historical Significance	A
2018	Structural Biology and Genomics	A
2018	General Chemistry I	A
2018	Calculus II	A-
2018	Physics Principles I (Mechanics)	A
2019	Structural Biology	A
2019	Honors Chemistry II	A-
2019	Physics Principles II (Electricity and Magnetism)	B
2019	Calculus III	B+
2019	American Origins	A
2019	Writing Seminar in the Bibb: The Social Brain	A

YEAR	COURSE TITLE	GRADE
2019	Molecular Biology and Genetics	A
2019	Organic Chemistry I	B+
2019	Literature: From the Classical to the Middle Ages	A
2019	Physics Principles III (Thermodynamics)	A
2019	Physical Modeling of Biological Systems	A-
2020	Microbial Diversity and Pathogenesis	A+
2020	Organic Chemistry II	B+
2020	Principles of Biological Chemistry	A
2020	Gender and Society	A
2020	Computational Physics	A
2020	Physical Chemistry I	A+
2020	Biological Chemistry I	A
2020	Full-Time Biochemical Research	P
2020	Introduction to Experimental Psychology	A
2020	Advanced Spanish II: Grammar/Composition	A
2021	Physical Chemistry II	A
2021	Organic Chemistry Lab I	A
2021	Biological Chemistry II	A
2021	Molecular Spectroscopy	A+
2021	Spanish: Introduction to Literary Analysis	A
2021	Organic Chemistry Lab II	A
2021	Chemical Information	A
2021	Full-Time Biochemical Research	P
2021	Spanish: Contemporary Colombian Fiction	A
2021	Spanish: Afro-Latin America: Knowledge, Culture, Agency?	A+
2022	Human Physiology	A
2022	Biomolecular Spectroscopy and Microscopy	A
2022	Spanish: The Boom in Latin American Literature	A-
	University of Pennsylvania, Master's in Chemistry	
2020	Macromolecular Crystallography: Methods and Application	A
2020	Biological Chemistry I	A
2021	Cryo-EM	A
2021	Biological Chemistry II	A
2021	Integrative Plant and Animal Mechanobiology	A+
2021	Research: Independent Study	A
2022	Mechanobiology of the Cell	A+
2022	Research Independent Study	A

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Saks, Andrew

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

POSITION TITLE: PhD Student

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
The Ohio State University, Columbus, OH	BS	08/2019	05/2023	Chemistry, minor in Mathematics
University of Pennsylvania, Philadelphia, PA	PhD	08/2023	05/2028 (Expected)	Biophysical Chemistry

A. Personal Statement

I have wanted to be a scientist for as long as I can remember. This passion was fostered by my grandfather, who has a PhD in chemistry and worked as a physical chemist. Not only did he inspire me to become a chemist myself, but he also taught me the joy of helping others understand and appreciate our world at a microscopic level. My undergraduate experience was a direct reflection of these values. I attended The Ohio State University where I obtained a bachelor's degree in chemistry and got involved in undergraduate research as a freshman. I joined the lab of Dr. Bern Kohler, a physical chemist who studies the photophysical properties of melanin and DNA-metal complexes. There, I learned to be an independent researcher, as undergraduates in the lab are given their own projects while also helping more senior members with their work. My project culminated in an honors undergraduate thesis that reported the supramolecular assembly of nucleobase-metal polymers using a reporter dye. This dye had not been used in such a way prior to my work. This thesis project is in preparation for a publication on which I will be a co-first author. In helping senior members, I also co-authored a paper on the photophysics of a DNA-silver(I) complex. In addition to pursuing my own scientific goals, I began working as a chemistry tutor during my junior year to teach the subject to >30 younger students. I found this particularly rewarding when I saw their expression change in the instant when they made sense of a difficult concept, causing a transition from frustration to intrigue. Not only did I help them with their course work, I also encouraged students to reach out to me if they needed help with course selection or career advice. During my last semester at Ohio State, I took an introductory biochemistry course, and this was the beginning of a small, but significant, shift in my scientific career. I found the core concepts of the class intriguing, and as such, when I applied to graduate school, I applied for biophysical chemistry programs. I enrolled as a graduate student in biophysical chemistry at the University of Pennsylvania to obtain a PhD and pursue my passion. After rotating in labs which use a variety of biophysical methods, I decided to join the lab of Dr. Roberto Dominguez, who uses structural biology and an array of other biophysical methods to study the actin cytoskeleton. Thus far my work in the group has been centered on interactions between F-actin and actin binding proteins that regulate cell motility and proliferation. The transition from a physical chemist to a biophysical chemist has been challenging, despite the seemingly subtle difference. I have acquired many new skills in my time at Penn, but my experience as an independent undergraduate researcher helped me persevere and find a new, refined version of my passion for molecular science. As I grow as a scientist, I aim to do impactful work by making key discoveries as well as by instilling my passion for biochemistry in younger students, just like my grandfather did for me.

B. Positions and Honors

Positions and Employment

2020-2023: Undergraduate Researcher at The Ohio State University
2021: General Chemistry Lab Teaching Assistant at The Ohio State University
2022-Present: Chemistry Tutor at “Tutoring by a College Professor”
2023-2024: Chemistry and Biochemistry Teaching Assistant at University of Pennsylvania

Professional Memberships:

2022-Present: American Chemical Society
2024-Present: Biophysical Society

C. Contributions to Science

In the lab of Dr. Bern Kohler, I conducted research aimed at uncovering and characterizing novel DNA-metal complexes. During my time in the lab, I worked on two distinct projects. One project examined the photophysical properties of a non-canonical cytosine-cytosine base pair between adjacent single stranded dC_{20} DNA strands. This interaction is made possible by silver ions. My contributions to this work were included in a recent publication in the Journal of the American Chemical Society. This publication is particularly intriguing because it showed a rare triplet excited state in a DNA duplex. In addition to my work on DNA complexes, my undergraduate thesis work was focused on the non-canonical nucleobase, 2-aminopurine, and its ability to form linear polymers and nanofibers in solution. Using a myriad of spectroscopic techniques, I studied the photophysical changes in 2-aminopurine because of metal binding, as well as characterizing thermodynamic and kinetic parameters of supramolecular assembly. Further, I was able to use a rotor dye, thiazole orange, to show that π-stacking is an integral motif in these nano assemblies. This was one of the first known uses of thiazole orange on assemblies lacking a covalent backbone. This project culminated in my honors undergraduate thesis and will result in a co-first author publication.

1. Martínez-Fernández, L.; Kohl, F. R.; Zhang, Y.; Ghosh, S.; Saks, A. J.; Kohler, B. Triplet Excimer Formation in a DNA Duplex with Silver Ion-Mediated Base Pairs. *J. Am. Chem. Soc.* **2024**. https://doi.org/10.1021/jacs.3c08793.

D. Scholastic Performance

YEAR	COURSE TITLE	GRADE
	THE OHIO STATE UNIVERSITY – CUMULATIVE GPA: 3.60	
2019	Arts and Sciences College Survey	S
2019	First-Year Seminar	S
2019	Honors General Chemistry I	A
2019	Calculus 3	B
2019	Spanish 3	A-
2020	Biology: Energy Transfer and Development	B+
2020	Honors General Chemistry II	B+
2020	Honors Principles of Macroeconomics	B+
2020	Spanish 4	A-
2020	English: Language, Identity, and Culture in the U.S. Experience	A
2020	Ordinary and Partial Differential Equations	A
2020	Honors Organic Chemistry I	A-
2020	Organic Chemistry Lab I	A-
2020	Intro to World Cinema	A

YEAR	COURSE TITLE	GRADE
2020	Physics: Electricity, Magnetism, Optics, and Quantum Mechanics	B+
2021	Quantitative Chemical Analysis	A
2021	Organic Chemistry II	A-
2021	Organic Chemistry Lab II	A
2021	Linear Algebra	B+
2021	Inorganic Chemistry	B+
2021	Physical Chemistry I	B+
2021	Honors Undergraduate Research	A
2021	Foundations of Higher Mathematics	B-
2021	Introduction to Social Psychology	A-
2022	Physical Chemistry II	A-
2022	Physical Chemistry Lab	A
2022	Instrumental Chemical Analysis	A
2022	Quantitative Neuroscience	A
2022	Honors Undergraduate Research	A
2022	Instrumental Analysis Lab	A-
2022	Chemical Kinetics	A-
2022	Mathematics: Dynamical Systems	B+
2022	Honors Russian Literature	B+
2022	Honors Undergraduate Thesis	A
2023	Introduction to Biological Chemistry	B+
2023	Honors Undergraduate Thesis	B+
2023	Honors History of East Asian Art	B
2023	History: Science and Society in Early Modern Europe	A-
2023	Golf 1	A
	UNIVERSITY OF PENNSYLVANIA – CUMULATIVE GPA: 3.43	
2023	Statistical Mechanics I	B
2023	Biological Chemistry I	B
2023	Chemical Information for Biological Chemists	B+
2023	Lab Rotation in Chemistry	A
2023	Lab Rotation in Chemistry	A
2024	Biological Chemistry II	B-
2024	Structural and Mechanistic Biochemistry	A
2024	Pre-Dissertation Lab	A+