## BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
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NAME: **Wacker, Daniel**

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

POSITION TITLE: **Assistant Professor of Pharmacological Sciences, Neuroscience**

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 Munich, Munich, Germany | BSc | 2003-2007 | Chemistry |
| University of Munich, Munich, Germany | MSc | 2007-2009 | Biochemistry |
| Rockefeller University, New York, NY | Technician | 2008-2009 | Cell Biology |
| The Scripps Research Institute, La Jolla, CA | PhD | 2009-2013 | Biophysics |
| University of North Carolina, Chapel Hill, NC | Postdoc | 2014-2018 | Pharmacology |

### A. Personal Statement

The long-term goal of my laboratory at the Icahn School of Medicine is a comprehensive mechanistic understanding of important drug targets involved in a variety of pathologies using structural and pharmacological methods. We are further leveraging these insights in structure-based drug discovery towards the treatment of a variety of disorders. We are particularly interested in the structure and function of membrane receptors and transporters, and aim to design novel, target selective compounds that help delineate the role of these proteins in addiction, learning and cognitive disorders, cancer, as well as other pathologies.

Much of my previous work has focused on crystallographic and pharmacological studies of GPCRs, the largest class of drug targets in the human genome. These studies aimed at elucidating how GPCRs are activated and inhibited by a variety of therapeutic and illicit drugs. Among others, I solved crystal structures of serotonin, dopamine, and opioid receptors. I have since built on these successes in my lab at Mount Sinai, where we have begun investigating the structure and function of understudied membrane drug targets, including several solute carriers (SLCs). In an effort to develop novel therapeutic avenues for treating a variety of pathologies, we are using cutting-edge technologies including membrane protein crystallization and cryo-electron microscopy, quantitative pharmacology, and computational drug design.

Ongoing projects that I would like to highlight include:

**R35 GM133504** (PI: Wacker) 08/01/19 – 04/30/24
NIH/NIGMS
Structural Studies and Drug Discovery Illuminate Serotonin Pharmacology
*Using cryo-EM and x-ray crystallography, we investigate molecular mechanisms of serotonin transporters and receptors, and leverage our insights in computational structure-based ligand discovery.*

**Sloan Research Fellow in Neuroscience** (PI: Wacker) 09/15/19 - 09/14/21
Alfred P. Sloan Foundation
Structural Studies of the Serotonergic System Template Drug Discovery

*We investigate fundamental mechanisms of serotonin signaling, transport, and modulation using a combination of x-ray crystallography, cryo-EM, ligand binding, and in vitro signaling and transport assays.*

**Edward Mallinckrodt, Jr. Foundation Grant** (PI: Wacker) 10/01/19 - 09/30/22
Edward Mallinckrodt, Jr. Foundation
Elucidating the Molecular Mechanisms of Methadone and Fentanyl to Combat the Opioid Epidemic
*Elucidation of how Fentanyl and Methadone signal through the human mu opioid receptor, using a combination of structural and pharmacological techniques*

**McKnight Scholar Award** (PI: Wacker) 07/01/20 – 06/30/23
The McKnight Endowment Fund for Neuroscience
Accelerating Drug Discovery for Cognitive Disorders through Structural Studies of a Serotonin Receptor
*We study the structure and function of the 5-HT7 receptor, a key mediator of the pro-cognitive effects of several antipsychotic, and will discover novel tool compounds to delineate the receptors role in cognition*

## B. Positions, Scientific Appointments, and Honors

### Positions and Scientific Appointments

07/2018 – Present Associate Director, Mount Sinai Center for Therapeutics Discovery
02/2018 – Present Assistant Professor, Department of Pharmacological Sciences, Department of Neuroscience, Icahn School of Medicine at Mount Sinai, New York (NY), USA
01/2014 – 01/2018 Postdoctoral Associate: Structural and functional characterization of G protein-coupled receptor signaling. University of North Carolina, Chapel Hill (NC), USA, Prof. Bryan Roth
07/2009 – 12/2013 Ph.D. and Postdoctoral Research: Structural basis of hallucinogen signaling through serotonin and opioid receptors. The Scripps Research Institute, La Jolla (CA), USA, Prof. Raymond Stevens
03/2008 – 07/2009 Master's Thesis: Structural and functional analysis of yeast Nup133 of the nuclear pore complex. Rockefeller University, New York (NY), USA, Prof. Günter Blobel
08/2006 – 12/2007 Undergraduate Research: Electron-microscopic single particle reconstruction of ribosome complexes. Gene Center Munich, Germany, Prof. Roland Beckmann

### Honors

2016 Keystone Symposia Future of Science Fund scholarship for Keystone Symposia
2016 UNC Department of Pharmacology Retreat Best Oral Presentation Award
2010-2012 Boehringer Ingelheim Fonds PhD Fellowship
2008 MSc Graduation with distinction – among top 10% in class
2008 DAAD Foreign Exchange Research Fellowship

## C. Contributions to Science

1. I have made major contributions towards a structural understanding of G Protein Coupled Receptor (GPCR) function. I contributed to the structural elucidation of numerous therapeutically important GPCRs, including the first crystal structures of the kappa opioid receptor, the glucagon receptor, the D2 and D4 dopamine receptors, and the 5-HT serotonin receptor 5-$HT_{2B}$, 5-$HT_{2C}$, and 5-$HT_{1B}$.

    a. ***#**__**Wacker D**__, #Wang S, #McCorvy JD, Betz RM, Venkatakrishnan AJ, Levit A, Lansu K, Schools Z, Che T, Nichols DE, Shoichet BK, *Dror RO, *Roth BL. Crystal structure of an LSD-bound human serotonin receptor | **Cell** 168, 377-389, (2017) - COVER

    b. __**Wacker D**__, Wang C, Katritch V, Han GW, Huang XP, Vardy E, McCorvy JD, Jiang Y, Chu M, Siu FY, Liu W, Xu HE, Cherezov V, *Roth BL, *Stevens RC. Structural Features for Functional Selectivity at Serotonin Receptors | **Science** 340, 615-619, (2013)

c. *Wang S, Che T, Levit A, Shoichet BK, ***Wacker D**, *Roth BL. Structure of the D2 dopamine receptor bound to the atypical antipsychotic drug risperidone | **Nature** 555, 269-273, (2018)

d. *#Wang S, ***#Wacker D**, #Levit A, Che T, Betz RM, McCorvy JD, Venkatakrishnan AJ, Huang XP, Dror RO, *Shoichet BK, *Roth BL. D4 dopamine receptor high-resolution structures enable the discovery of selective agonists | **Science** 358, 381-386, (2017)

*#co-first authors, *co-corresponding authors*

2. Through combining structural studies with quantitative pharmacological studies, I have contributed to resolving several of the underlying molecular principles that govern how ligands modulate GPCR activity to engage differential signaling pathways. This phenomenon termed functional selectivity or biased signaling can be exploited to design drugs that specifically activate therapeutic over pathological pathways, thereby drastically reducing on-target side effects.

a. **Wacker D**, Wang C, Katritch V, Han GW, Huang XP, Vardy E, McCorvy JD, Jiang Y, Chu M, Siu FY, Liu W, Xu HE, Cherezov V, *Roth BL, *Stevens RC. Structural Features for Functional Selectivity at Serotonin Receptors | **Science** 340, 615-619, (2013)

b. ***#Wacker D**, #Wang S, #McCorvy JD, Betz RM, Venkatakrishnan AJ, Levit A, Lansu K, Schools Z, Che T, Nichols DE, Shoichet BK, *Dror RO, *Roth BL. Crystal structure of an LSD-bound human serotonin receptor | **Cell** 168, 377-389, (2017)

c. Che T, Majumdar S, Zaidi SA, Kormos C, McCorvy JD, Wang S, Mosier PD, Uprety R, Vardy E, Krumm BE, Han GW, Lee MY, Pardon E, Steyaert J, Huang XP, Strachan RT, Tribo AR, Pasternak GW, Carroll IF, Stevens RC, Cherezov V, Katritch V, ***Wacker D**, *Roth BL. Structure of a nanobody-stabilized active state of the kappa opioid receptor | **Cell** 172, 55-67, (2018)

d. **Wacker D**, Stevens RC, *Roth BL. How ligands illuminate GPCR molecular pharmacology | **Cell** 170, 414-427, (2017)

*#co-first authors, *co-corresponding authors*

3. I have also made major contributions to structure-based drug discovery efforts providing GPCR structures for virtual ligand screening campaigns, and identifying and characterizing novel chemical matter for challenging target receptors such as the D4 dopamine receptor. I also determined the first crystal structure of a GPCR ligand developed by structure-based methods, which substantially contributed to the validation and optimization of virtual ligand screening efforts towards novel GPCR compounds.

a. *#McCorvy JD**, #Wacker D**, #Wang S, Agegnehu B, Liu J, Lansu K, Tribo AR, Olsen RHJ, Che T, Jin J, *Roth BL. Structural determinants of 5-HT2B receptor activation and biased agonism | **Nat Struct Mol Biol** 25, 787-796 (2018)

b. *#Wang S, ***#Wacker D**, #Levit A, Che T, Betz RM, McCorvy JD, Venkatakrishnan AJ, Huang XP, Dror RO, *Shoichet BK, *Roth BL. D4 dopamine receptor high-resolution structures enable the discovery of selective agonists | **Science** 358, 381-386, (2017)

c. **Wacker, D.**, Stevens, R.C., *Roth, B.L. How ligands illuminate GPCR molecular pharmacology. **Cell** 170, 414-427, (2017)

d. ***#Wacker D**, #Fenalti G, #Brown MA, Katritch V, Abagyan R, Cherezov V, *Stevens RC. Conserved binding mode of human β2 adrenergic receptor inverse agonists and antagonist revealed by X-ray crystallography | **J Am Chem Soc** 132, 11443-11445, (2010)

*#co-first authors, *co-corresponding authors*

4. In addition to small molecule compounds, antibodies are becoming increasingly useful probes to study GPCR pharmacology. I used both conventional IgG derived antigen-binding fragments (Fabs) and

camelid single-chain antibodies, termed nanobodies, to structurally elucidate GPCR activation mechanisms based on distinct antibody-stabilized GPCR conformations.

a. Che T, Majumdar S, Zaidi SA, Kormos C, McCorvy JD, Wang S, Mosier PD, Uprety R, Vardy E, Krumm BE, Han GW, Lee MY, Pardon E, Steyaert J, Huang XP, Strachan RT, Tribo AR, Pasternak GW, Carroll IF, Stevens RC, Cherezov V, Katritch V, *__Wacker D__, *Roth BL. Structure of a nanobody-stabilized active state of the kappa opioid receptor | **Cell** 172, 55-67, (2018)

b. Ishchenko A, __Wacker D__, Kapoor M, Zhang A, Han GW, Basu S, Patel N, Messerschmidt M, Weierstall U, Liu W, Katritch V, Roth BL, Stevens RC, *Cherezov V. Structural insights into the extracellular recognition of the human serotonin 2B receptor by an antibody | **Proc Natl Acad Sci USA** 114, 8223-8228, (2017)

c. English JG, Olsen RHJ, Lansu K, Patel M, White K, Cockrell AS, Singh D, Strachan RT, __Wacker D__, Roth BL. VEGAS as a Platform for Facile Directed Evolution in Mammalian Cells | **Cell** 178, 748-761, (2019)

**co-corresponding authors*

5. I participated in a larger multi-institutional collaboration with the goal to implement x-ray free-electron laser (XFEL) technology in membrane protein structural biology using crystals generated in lipidic cubic phase. This technology promises to revolutionize structural biology through enabling femtosecond timescale resolved studies, providing high quality data virtually devoid of radiation damage, and requiring minimal crystal optimization.

   a. Liu W, __Wacker D__, Gati C, Han GW, James D, Wang D, Nelson G, Weierstall U, Katritch V, Barty A, Zatsepin NA, Li D, Messerschmidt M, Boutet S, Williams GJ, Koglin JE, Seibert MM, Wang C, Shah STA, Basu S, Fromme R, Kupitz C, Rendek KN, Grotjohann I, Fromme P, Kirian RA, Beyerlein KR, White TA, Chapman HN, Caffrey M, Spence JCH, Stevens RC, *Cherezov V. Serial femtosecond crystallography of G protein-coupled receptors in lipidic cubic phase | **Science** 342, 1521-1524, (2013)

   b. Liu W, __Wacker D__, Wang D, Abola E, *Cherezov V. Femtosecond crystallography of membrane proteins in the lipidic cubic phase | **Phil Trans R So B** 369, (2014)

   c. *Weierstall U, James D, Wang C, White TA, Wang D, Liu W, Spence JC, Bruce Doak R, Nelson G, Fromme P, Fromme R, Grotjohann I, Kupitz C, Zatsepin NA, Liu H, Basu S, __Wacker D__, Han GW, Katritch V, Boutet S, Messerschmidt M, Williams GJ, Koglin JE, Marvin Seibert M, Klinker M, Gati C, Shoeman RL, Barty A, Chapman HN, Kirian RA, Beyerlein KR, Stevens RC, Li D, Shah ST, Howe N, Caffrey M, *Cherezov V. Lipidic cubic phase injector facilitates membrane protein serial femtosecond crystallography | **Nat Commun** 5, 3309, (2014)

   **co-corresponding authors*

**List of published work in MyBibliography:**
https://www.ncbi.nlm.nih.gov/sites/myncbi/wacker.daniel.1/bibliography/54351448/public/?sort=date&direction=ascending

**BIOGRAPHICAL SKETCH**

NAME: **Mathiharan, Yamuna Kalyani**

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

POSITION TITLE: Postdoctoral Fellow

EDUCATION/TRAINING

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | Start Date MM/YYYY | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|---|
| Government College of Technology, Anna University, Coimbatore | B.Tech | 08/2002 | 05/2006 | Industrial Biotechnology |
| A.C.Tech College of Technology, Anna University, Chennai | M.Tech | 08/2006 | 05/2008 | Biotechnology |
| Indian Institute of Science, Bengaluru | PhD | 08/2008 | 07/2015 | Macromolecular Crystallography |
| Life Science Institute, University of Michigan, Ann Arbor | Postdoctoral Fellow | 02/2016 | 06/2017 | Cryo-Electron Microscopy |
| Stanford University, Stanford | Postdoctoral Fellow | 07/2017 | 02/2020 | Cryo-Electron Microscopy |
| Department of Pharmacological Sciences, Mount Sinai, New York | Postdoctoral Fellow | 05/2021 | Present | Cryo-Electron Microscopy |

**A. Personal Statement**

I'm Yamuna Kalyani Mathiharan, a postdoctoral research fellow in Dr Daniel Wacker's lab, Department of Pharmacological Sciences, Mount Sinai, New York, USA. My previous postdoc research experience was in Dr Georgios Skiniotis's lab, Department of Molecular and Cellular Physiology, Stanford University, California, USA, was also part of the Skiniotis lab when it was at University of Michigan. I received my PhD from Molecular Biophysics Unit, Indian Institute of Science, Bengaluru, India under the guidance of Dr. M.R.N Murthy. My area of specialization is structural biology with expertise to solve protein and protein-RNA structures by using cryo-electron microscopy (EM) and macromolecular crystallography. In my PhD studies, have used macromolecular crystallography, mutagenesis and biochemistry to understand the implication of domain swapping in protein oligomerization and function. These studies demonstrate the complexity and interplay of interactions that contribute to the precise oligomeric structure and catalytic function of proteins, the probable role of domain swapping in evolution of unswapped protein oligomers. During my PhD, I've published first authored research articles, have mentored undergraduate and master's students for their thesis project, and helped in managing the lab. As a postdoctoral fellow in Skiniotis lab, was involved in various collaborative projects where I've used cryoEM to solve protein structures; sort conformational heterogeneity and understand their functional relevance. The proteins that I have studied are involved in important regulatory machinery like reverse transcription and membrane proteins involved in neurotransmission. Over the years, I have gained research experience to solve macromolecular structures by using cryo-EM and X-ray crystallography and also equipped to purify high quality recombinant proteins needed for structural studies. I've exhibited ability to carry on research including designing and executing my experiments, also collaborate with others to have an interdisciplinary approach to address my goals which are reflected in my projects. My long-term goal as an independent researcher is to understand membrane proteins involved in neurotransmission and their implication in human diseases.

- ***Mathiharan YK****, Glaaser IW*, Zhao Y*, Robertson MJ, Skiniotis G, Slesinger PA, "Structural basis of GIRK2 channel modulation by cholesterol and $PIP_2$", **(*equally contributed, accepted for publication in Cell Reports)**
- Glassman CR, ***Mathiharan YK****, Jude KM*, Su L, Panova O, Lupardus PJ, Spangler JB, Ely LK, Thomas C, Skiniotis G, Garcia KC, "Structural basis for IL-12 and IL-23 shared receptor usage reveals a gateway for shaping actions on T versus NK cells", **Cell**, 184, 983-999, February 2021 **(*equally contributed).**
- Larsen KP*, ***Mathiharan YK****, Kappel K, Coey AT, Chen DH, Barrero D, Madigan L, Puglisi JD, Skiniotis G and Puglisi EV, "Architecture of an HIV-1 reverse transcription initiation complex", **Nature**, 557 (7703): 118-122, May 2018 **(*equally contributed)**.
- ***Mathiharan YK***, Savithri HS and Murthy MRN, "Insights into stabilizing interactions in the distorted domain swapped dimer of *Salmonella typhimurium* survival protein", **Acta Crystallographica Section D**, 71:1812-1823, September 2015.

**B. Positions, Scientific Appointments, and Honors**

**Positions and Scientific Appointments**

| | |
|---|---|
| **2021 – Present** | **Postdoctoral Researcher, Mount Sinai** |
| **2017 – 2020** | **Postdoctoral Researcher, Stanford** |
| **2016 – 2017** | **Postdoctoral Researcher, University of Michigan** |
| **2015** | **Project officer, IIT Madras** |

**Honors**

| | |
|---|---|
| **2013** | **Department of Biotechnology (DBT), Government of India travel/stay grant** to visit European Synchrotron Radiation Facility (ESRF), Grenoble, France for data collection |
| **2012** | **International Union of Crystallography (IUCr) travel grant,** attend AsCA 12/CRYSTAL 28 |
| **2011** | **International travel grant by Indian Council of Medical Research (ICMR)** to attend PDB40 symposium |
| **2008-2013** | **GATE Life Science PhD Fellowship** |
| **2006-2008** | **GATE Life Science M.Tech Fellowship** |

**C. Contributions to Science**

1. **Early Career:** My early career contributions were focused on applying my knowledge of molecular biology in understanding the importance of epitope regions in filarial ALT protein with an implication of using them as a vaccine candidate. My roles were involved in cloning and expressing the synthetic gene construct containing the epitope of ALT protein (**GenBank: GU596489.1)**.
2. **Graduate Career:** My PhD thesis dwelt on the importance of hinges involved in domain swapping, their implication in protein oligomerization and function - stress protein from *Salmonella typhimurium* and *Sesbania mosaic* virus coat protein was used as examples. By X-ray crystallography, biochemical, biophysical and computational tools, I was able to demonstrate that the hinge sequence indeed has a profound impact on protein structures and the stress protein's function. By these studies, I was able to highlight the importance of intricate network of short- and long-range protein interactions and how it influences the function.

    a) ***Mathiharan YK*** and Murthy MRN, "Molecular dynamics studies on the domain swapped *Salmonella typhimurium* survival protein SurE: insights on the possible reasons for catalytic cooperativity", **Journal of Biomolecular Structure and Dynamics**, 1-9, August 2017.
    b) Hatti K, ***Mathiharan YK***, Srinivasan N and Murthy MRN, "Seeing but not believing: the structure of glycerol dehydrogenase initially assumed to be the structure of a survival protein from

*Salmonella typhimurium*", **Acta Crystallographica Section D**, 73: 609-617, July 2017 (**Cover page article**).

**c)** ***Mathiharan YK***, Savithri HS and Murthy MRN, "Insights into stabilizing interactions in the distorted domain swapped dimer of *Salmonella typhimurium* survival protein", **Acta Crystallographica Section D**, 71:1812-1823, September 2015.

**d)** ***Mathiharan YK***, Pappachan A, Savithri HS and Murthy MRN, "Dramatic structural changes resulting from the loss of a crucial hydrogen bond in the hinge region involved in C-terminal helix swapping in SurE: a survival protein from *Salmonella typhimurium*", **PLoS ONE**, 8(2): e55978, February 2013.

3. **Postdoctoral Career:** As a postdoctoral fellow in Skiniotis lab, one of my study's focus is to use cryo-EM to sort conformational heterogeneity of HIV-1 reverse transcriptase initiation complex, a protein-RNA complex done in collaboration with Dr Elisabetta Viani Puglisi and Dr Joseph D Puglisi, Department of Structural Biology, Stanford. I was involved in cryoEM freezing condition optimization, data-collection, processing, modelling/refinement and structure analysis. This study emphasis the importance of cryo-EM for characterizing RNA plasticity in protein-RNA complexes. I also helped to develop a project where the objective was to capture "open state" conformation of G protein coupled inwardly rectifying potassium channels (GIRK2) upon alcohol/G protein binding, done in collaboration with Dr Paul Slesinger, Nash Family Department of Neuroscience, Icahn School of Medicine, Mount Sinai, New York, USA; I've collected cryoEM data, processed and analyzed GIRK2 structures with different modulators, also optimized GIRK2 nanodisc reconstituted sample for EM studies. This study emphasis the importance of lipids for GIRK2 activation. In another project, I used biochemical approaches including expression in different heterologous hosts like insect and bacterial cells to improve sample quality of module 5, pikromycin polyketide synthase, a multi-domain protein. I was also involved in other collaborative projects where my efforts were to optimize construct and sample quality for structural studies by using negative staining EM or cryo-EM.

**a)** ***Mathiharan YK****, Glaaser IW*, Zhao Y*, Robertson MJ, Skiniotis G, Slesinger PA, "Structural basis of GIRK2 channel modulation by cholesterol and $PIP_2$", **(*equally contributed, accepted for publication in Cell Reports)**

**b)** Glassman CR, ***Mathiharan YK****,* Jude KM*, Su L, Panova O, Lupardus PJ, Spangler JB, Ely LK, Thomas C, Skiniotis G, Garcia KC, "Structural basis for IL-12 and IL-23 shared receptor usage reveals a gateway for shaping actions on T versus NK cells", **Cell**, 184, 983-999, February 2021 **(*equally contributed).**

**c)** Larsen KP*, ***Mathiharan YK****, Kappel K, Coey AT, Chen DH, Barrero D, Madigan L, Puglisi JD, Skiniotis G and Puglisi EV, "Architecture of an HIV-1 reverse transcription initiation complex", **Nature**, 557 (7703): 118-122, May 2018 **(*equally contributed)**.

**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: Gregory Zilberg

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

POSITION TITLE: Graduate Student Research Assistant

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 |
|---|---|---|---|---|
| University of Wisconsin - Madison | BS | 08/2013 | 12/2017 | Biochemistry, Neurobiology |
| Icahn School of Medicine at Mount Sinai | PhD | 08/2018 | XX/2023 | Neuroscience |

## A. Personal Statement

My long term research interests primarily focus on the biochemical determinants of the function of macromolecular complexes that enable pre- and post-synaptic signal transduction and scaffolding. To that end, my undergraduate academic coursework focused on establishing a foundational knowledge of the molecular biology involved in synaptic development and plasticity, and the structure-function relationships of proteins and enzymes. I additionally worked as an undergraduate in Dr. Kate O'Connor-Giles's lab at UW-Madison studying the mechanisms of multiple proteins involved in synaptic development in Drosophila. The four years in this lab resulted in authorship on a publication and a poster presentation at UW-Madison's annual Undergraduate Research Symposia. In my graduate education, in the lab of Dr. Daniel Wacker, I have shifted from phenotypic studies in Drosophila to protein purification and structural determination of GPCR-G protein complexes. For my thesis project, I am focusing on the structural determination and pharmacological characterization of an understudied aminergic receptor type that may yield insights into the atomic level mechanisms of stimulant drug action in neurons and provide a novel target for combating stimulant addiction.

## B. Positions, Scientific Appointments and Honors

**Positions and Employment**

2013 - 2017 Undergraduate Research Assistant, University of Wisconsin - Madison
2018 - Graduate Student Research Assistant, Icahn School of Medicine at Mount Sinai

**Other Experience and Professional Memberships**

2015 – 2016 Content Editor, Journal of Undergraduate Science and Technology
2016 – 2017 Senior Content Editor, Journal of Undergraduate Science and Technology

**Honors**

2013 Undergraduate Research Scholars Program, UW College of Letters and Sciences
2014 Engineering Great People Scholarship, UW Foundation

## C. Contributions to Science

1. **Undergraduate Research:** I was involved in a project in the lab of Dr. Kate O'Connor-Giles at UW – Madison, focusing on the effects of the Drosophila synaptic adaptor protein, Nervous Wreck (Nwk), on pre- and post-synaptic morphological characteristics. This resulted in a poster presentation at UW – Madison's annual Undergraduate Research Symposium. I also assisted in the analysis of electron microscopy tomograms of wild-type and mutant Fife-deficient Drosophila presynaptic densities, leading to an authorship on a publication in the Journal of Cell Biology.
    a. (2015, May). "The Role of Nervous Wreck in Dendritic Patterning and Growth in Drosophila." Poster presented at UW-Madison Undergraduate Research Symposium, Madison, WI.
    b. Bruckner, J.J.; Zhan, H.; Gratz, S.J.; Rao, M.; Ukken, F.; **Zilberg, G.**; O'Connor-Giles, K.M. (2017) "Fife organizes synaptic vesicles and calcium channels for high-probability neurotransmitter release." *J. Cell Biol.* 216(1):231-246.
2. **Graduate Research**: My ongoing predoctoral research focuses on the structural determination and pharmacological characterization of an understudied aminergic receptor type that may yield insights into the atomic level mechanisms of stimulant drug action in neurons and provide a novel target for combating stimulant addiction. I have collected functional data demonstrating novel signaling properties and novel agonists for this receptor that I hope to publish in the coming years alongside a structure of the receptor in complex with one of its signaling transducers, a G protein heterotrimer. I have additionally been asked along with my PI to highlight a publication of a similar nature regarding one of the cannabinoid receptors.
    a. Zilberg, G.; Wacker, D (2020). "A Novel Cryo-EM Structure Enables Development of Selective Cannabinoid Receptor Drugs." *Biochemistry.* 5;59(17):1643-1644.

## D. Scholastic Performance

**Scholastic Performance**

| YEAR | COURSE TITLE | GRADE |
|---|---|---|
| | UNIVERSITY OF WISCONSIN - MADISON | |
| 2013 | General Chemistry 1 | AB |
| 2013 | Calculus and Analytical Geometry 2 | B |
| 2013 | Third Semester Russian | A |
| 2014 | General Chemistry 2 | A |
| 2014 | Statics | B |
| 2014 | Multivariate Calculus | B |
| 2014 | Introductory Biology 1 | AB |
| 2014 | Intro to Organic Chemistry | A |
| 2014 | General Physics 2 | AB |
| 2015 | Introductory Biology 2 | AB |
| 2015 | Intermediate Organic Chemistry | A |
| 2015 | Linear Algebra and Differential Equations | AB |
| 2015 | General Genetics | A |
| 2015 | General Biochemistry 1 | A |
| 2015 | Intro to Organic Chemistry Lab | A |
| 2015 | Resources and People | A |
| 2015 | Neurobiology 1 | A |
| 2016 | Black Music and American Cultural History | A |
| 2016 | General Biochemistry 2 | B |
| 2016 | Neurobiology 2 | B |
| 2016 | Drugs and their Actions | A |
| 2016 | Biochemical Methods | A |
| 2016 | Protein and Enzyme Structure and Function | AB |
| 2016 | Western Intellectual and Religious History Since 1500 | A |

| YEAR | COURSE TITLE | GRADE |
|---|---|---|
| 2016 | Molecular and Cellular Mechanisms of Memory | A |
| 2017 | Fundamentals of Analytical Chemistry | A |
| 2017 | General Physics 1 | A |
| 2017 | Intro to Statistics for the Life Sciences | A |
| 2017 | Development of the Nervous System | A |
| | ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI | |
| 2018 | Cellular and Molecular Neuroscience | A |
| 2018 | Introduction to Biostatistics | A |
| 2018 | Systems Neuroscience | A |
| 2018 | Seminar in Neuroscience | P |
| 2019 | Prominent Biostatistics Concepts | A- |
| 2019 | Behavioral and Cognitive Neuroscience | A |
| 2019 | Neurological and Psychiatric Disorders | A- |
| 2019 | Topics in Clinical Neuroscience | P |
| 2019 | Neuropharmacology | P |
| 2019 | Advanced Topics in Synapses | P |