APPLICANT BIOGRAPHICAL SKETCH

NAME OF APPLICANT: Nathan Yoder

eRA COMMONS USER NAME: yodernat

POSITION TITLE: Graduate Student

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	START DATE MM/YYYY	END DATE *(or expected end date)* MM/YYYY	FIELD OF STUDY
Michigan Technological University	N/A	08/2006	05/2007	Exercise Science
Michigan State University	B.S.	08/2007	05/2011	Physiology
Michigan State University	B.A.	08/2007	05/2011	Chemistry
Oregon Health and Science University	PhD	07/2014	08/2019	Neuroscience

A. Personal Statement

The goal of my proposed research is to combine atomic-level structural studies and functional electrophysiology assays to determine the resting state structure, molecular gating mechanism, and synaptic regulation of an acid-sensing ion channel. An eclectic educational background and extensive multidisciplinary research experience in relevant scientific disciplines make me an ideal candidate to serve as principal investigator for the research I am proposing. As a dual major in physiology and chemistry at Michigan State University, I spent my undergraduate education developing a comprehensive knowledge of the chemical world and how it pertains to the physiological processes of the human body. After graduation, while working at the University of Utah, I led a collaboration between Dr. Jason Shepherd of the Department of Neurobiology and Anatomy and Dr. Adam Frost of the Department of Biochemistry. This collaboration provided opportunities to explore both neurobiology and structural biology research, gain a diverse set of technical skills, and develop cross-disciplinary protocols applicable to research in both laboratories. It was in the Frost laboratory that I was initially exposed to structural biology, utilizing nuclear magnetic resonance spectroscopy, x-ray crystallography, and single particle electron microscopy to explore the structural properties of synaptic proteins. Committed to multidisciplinary research, I chose to pursue a graduate education at Oregon Health and Science University (OHSU), where the strengths in both synaptic physiology and membrane protein structural biology provide a robust environment perfectly tailored to my research interests. I joined the laboratory of Dr. Eric Gouaux due to his outstanding record as a graduate student mentor, his interest in the structural mechanisms of synaptic transmission, as well as his lab's multidisciplinary approach to research. During my first year at OHSU, rotation work with Drs. Gouaux and Laurence Trussell allowed me to gain valuable technical experience pertaining to many of the experiments outlined in this proposal. Specifically, I expressed, purified, and crystallized an acid sensing ion channel during my rotation work with Dr. Gouaux and performed whole-cell patch-clamp electrophysiology experiments in brain slices while working under Dr. Trussell. My proposed research builds upon my past experiences and will allow me to explore important questions in synaptic neurobiology while drawing upon my existing biochemistry, structural biology and patch-clamp electrophysiology skillsets. In summary, independent research experience in relevant disciplines as well as a strong educational background demonstrate my capacity to successfully lead the research I am proposing.

B. Positions and Honors

ACTIVITY/ OCCUPATION	START DATE (mm/yy)	END DATE (mm/yy)	FIELD	INSTITUTION/ COMPANY	SUPERVISOR/ EMPLOYER
Undergraduate Research Assistant	08/09	01/10	Entomology	Michigan State University	Doug Landis, PhD
Undergraduate Research Assistant	12/10	06/11	Psychiatry	Michigan State University	Jesse Bledsoe, PhD
Volunteer Trail Worker	05/11	11/11	Trail work	Montana Conservation Corps (AmeriCorps)	Bobby Grillo
Volunteer Crew Leader	02/12	11/12	Trail work	Montana Conservation Corps (AmeriCorps)	Bobby Grillo
Research Assistant	03/13	06/14	Neurobiology	University of Utah	Jason Shepherd, PhD
Research Assistant	03/13	06/14	Biochemistry	University of Utah	Adam Frost, PhD
Graduate Student	03/15		Neuroscience/ Structural Biology	Oregon Health and Science University	Eric Gouaux, PhD

Academic and Professional Honors

B.S. awarded with honors, Michigan State University, 2011

B.A. awarded with honors, Michigan State University, 2011

Pre-doctoral Training Grant (5T32DK007680-23); Program Director: Dr. Richard Goodman

Pre-doctoral Training Grant (5T32DK007680-24); Program Director: Dr. Richard Goodman

ARCS Foundation Scholarship, 2014-2017

Individual Pre-Doctoral National Research Service Award Fellowship (1F31NS096782-01); 2016-2019

Tartar Trust Fellowship, 2016

Tartar Trust Fellowship, 2017

Tartar Trust Fellowship, 2018

C. Contributions to Science

1. As a graduate student in the Neuroscience Graduate Program working under the supervision of Dr. Eric Gouaux, I have applied structural, biochemical and electrophysiological approaches to elucidate the molecular mechanisms underlying proton-dependent gating in acid-sensing ion channels (ASICs). ASICs are proton-gated channels that activate in milliseconds in response to drops in extracellular pH and completely desensitize within tens to hundreds of milliseconds. As such, the ASIC gating scheme consists of three primary states: high pH resting (closed), low pH open and low pH desensitized. As a graduate student, my primary scientific goal was to solve the elusive high-resolution structure of a resting ASIC at high pH, and, building upon existing x-ray structures of open and desensitized channels, generate a structure-based mechanism for proton-dependent gating. Towards this aim, I successfully applied both x-ray crystallography and single-particle cryo-electron microscopy (cryo-EM) to determine the structures of truncated and full-length ASICs in a resting state at high pH. Subsequently, I generated a comprehensive

molecular mechanism for proton-dependent gating in ASICs and verified this mechanism through engineered disulfide bridges and whole-cell patch-clamp electrophysiology experiments. Finally, I applied anomalous scattering x-ray crystallography experiments to locate binding sites for divalent cations and anions on resting and desensitized ASICs in order to elucidate the molecular mechanisms underlying gating modulation of ASICs by endogenous ions.

a. Yoder N and Gouaux E. Divalent cation and chloride ion sites of chicken acid sensing ion channel 1a elucidated by x-ray crystallography. Plos One. 2018;13(8):e0202134.
b. Yoder N, Yoshioka C, and Gouaux E. Gating mechanisms of acid-sensing ion channels. Nature. 2018;555(7696):397-401.
c. Yoder N, Yoshioka C, and Gouaux E. Structural studies of acid sensing ion channels. Poster session presented at: Cryo-Electron Microscopy and 3D Image Process practical course; 2017 Sept 4-15; London, UK.
d. Yoder N and Gouaux E. Towards the structure of acid sensing ion channel in a resting state at high pH. Poster session presented at: Biophysical Society Annual Meeting; 2017 Feb 14-15; New Orleans, LA.
e. Yoder N and Gouaux E. Crystal structure and ion sites of a resting acid sensing ion channel at high pH. Poster session presented at: Oregon Heath and Science University Neuroscience Graduate Program Retreat; 2016 Sep 12-13; Timberline Lodge, OR.
f. Yoder N and Gouaux E. Pursuing the high pH, resting state structure of acid sensing ion channel 1a. Poster session presented at: Oregon Health and Science University Neuroscience Graduate Program Recruitment; 2016 Feb 29; Portland, OR.
g. Yoder N and Gouaux E. Pursuing the high pH, resting state structure of acid sensing ion channel 1a. Poster session presented at: Oregon Heath and Science University Neuroscience Graduate Program Retreat; 2015 Sep 14-15; Timberline Lodge, OR.
h. Yoder N and Gouaux E. Pursuing the high pH, resting state structure of acid sensing ion channel 1a. Poster session presented at: Oregon Heath and Science University Neuroscience Graduate Program Retreat; 2014 Sep 15-16; Timberline Lodge, OR.

2. While working at the University of Utah in the laboratories of Drs. Jason Shepherd and Adam Frost I spearheaded a collaborative effort to combine structural biology and molecular neurobiology techniques to better understand synaptic plasticity. Though x-ray crystallography has been instrumental in expanding our understanding of protein structures, the dynamic nature of many protein-protein interactions at the synapse limits the conclusions we can make from single protein crystallographic studies. However, recent technological advances in single-particle cryo-EM have rendered this technique suitable for obtaining atomic-level structural data of membrane proteins and protein complexes. As such, cryo-EM is rapidly becoming a useful technique for studying the highly complex and dynamic nature of synaptic protein-protein interactions. In collaboration with neurobiologists and biochemists at the University of Utah, I developed protocols for the expression, purification, and electron microscopy-based imaging of synaptic proteins. Additionally, I was involved in designing and implementing experiments intended to confirm the results of structural experiments in hippocampal culture systems. My contributions have helped expand the techniques available to neurobiologists at Utah wishing to explore the molecular details of protein-protein interactions important for the experience-dependent adjustment of synaptic strength. Additionally, the research I performed helped foster communication and collaboration between independent departments at the university.

   a. Pastuzyn ED, Day CE, Kearns RB, Kyrke-Smith M, Taibi AV, McCormick J, Yoder N, Belnap DM, Erlendsson, S, Morado, DR, Briggs, JAG, Feschotte, C, and Shepherd, JD. *The Neuronal Gene Arc Encodes a Repurposed Retrotransposon Gag Protein that Mediates Intercellular RNA Transfer.* Cell. 2018;172(1-2):275-288 e18.

D. Scholastic Performance

YEAR	SCIENCE COURSE TITLE	GRADE	YEAR	OTHER COURSE TITLE	GRADE

YEAR	SCIENCE COURSE TITLE	GRADE
	MICHIGAN TECHNOLOGICAL UNIVERSITY	
2006	Principles of Biology	AB
2006	University Chemistry 1	A
2006	University Chemistry Laboratory 1	A
2006	Introduction to Exercise Science	A
2006	Calculus with Technology 2	A
	MICHIGAN STATE UNIVERSITY	
2007	Organisms and Populations	3.0
2007	Organic Chemistry 1	2.0
2007	Introduction to Human Nutrition	4.0
2007	Introductory Microbiology	3.5
2008	Engineering Graphics Communications	4.0
2008	Multivariable Calculus	2.0
2008	Calculus Concepts Physics 1	3.5
2008	Personality from a Psychoanalytic Perspective	3.0
2008	Principles of Packaging	4.0
2008	Packaging with Glass and Metal	3.5
2009	Biochemistry 1	3.5
2009	General and Inorganic Chemistry	4.0
2009	Organic Chemistry 2	4.0
2009	Comparative Anatomy and Biology of Vertebrates	4.0
2009	Introduction to Physics Laboratory 1	4.0
2009	Biochemistry 2	3.0
2009	Chemistry Laboratory 2	4.0
2009	Organic Chemistry Laboratory	3.5

YEAR	OTHER COURSE TITLE	GRADE
	MICHIGAN TECHNOLOGICAL UNIVERSITY	
2007	Music History	AB
2007	Cultural Diversity in American Literature	A
2007	Principles of Psychology	A
2007	World Cultures	AB
	MICHIGAN STATE UNIVERSITY	
2008	Independent Study, Study Abroad	4.0
2008	Global Diversity and Interdependence	4.0
2008	Political Sociology	4.0
2008	Introduction to Microeconomics	4.0
2008	Introduction to Marketing	4.0
2008	Management Skills	4.0
2008	Introduction to Supply Chain Management	3.5
2009	Europe and the World	4.0
2011	Sailing and Cruising	4.0

YEAR	SCIENCE COURSE TITLE	GRADE	YEAR	OTHER COURSE TITLE	GRADE
2009	Introduction to Physical Chemistry 1	4.0			
2009	Introduction to Physics Laboratory 2	4.0			
2009	Human Physiology 1	4.0			
2010	Introduction to Physical Chemistry 2	4.0			
2010	Inorganic Chemistry	3.5			
2010	Calculus 1	4.0			
2010	Human Physiology 2	4.0			
2010	Quantitative Analysis	4.0			
2010	Chemical Safety	4.0			
2010	Capstone Laboratory in Physiology	4.0			
2011	Instrumental Methods and Applications	4.0			
2011	Topics in Cell Physiology	4.0			
2011	Topics in Reproductive Physiology	4.0			
	OREGON HEALTH AND SCIENCE UNIVERSITY				
2014	Practice and Ethics of Science	PASS			
2014	Vollum Seminar: Neuroscience	A			
2014	Cellular Neurophysiology	A			
2015	Electron Microscopy Journal Club/Study Group	PASS			
2015	Neuroscience Graduate Program Seminar Course	A			
2015	Cell and Molecular Neurobiology	A			
2015	Electron Microscopy Journal Club/Study Group	PASS			
2015	Vollum Seminar: Neuroscience	A			
2015	Systems Neuroscience	A			

Explanation of grading systems:
A = 4.0, AB = 3.5, B = 3.0, BC = 2.5, C = 2.0, CD = 1.5, D = 1.0. For undergraduate courses, grades 2.0 (C) and above are considered passing. For graduate courses, grades above 3.0 (B) are considered passing.