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: Asrican, Brent	POSITION TITLE Research Assistant Professor
eRA COMMONS USER NAME (credential, e.g., agency login): BASRICAN	

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)*	YEAR(s)	FIELD OF STUDY
Franklin and Marshall College	B.A.	1999	Biological Foundations of Behavior
Brandeis University	Ph.D	2007	Neuroscience
Duke University (Neurobiology)	Postdoctoral	2008-2009	Optogenetics
Duke University (Cell Biology)	Postdoctoral	2009-2013	Adult Neurogenesis

A. Personal Statement

I have over 10 years of experience in electrophysiological and optical research techniques, as well as significant time spent adapting and refining cutting edge techniques and tools to aid in circuit based investigations. During my graduate training, I utilized the rodent hippocampus as a model system to determine molecular mechanisms and circuit modulation of synaptic plasticity. Specifically, I studied the post-synaptic plasticity molecule CaMKII, and its relationship synaptic strength and spine size modification during long-term-potentiation (LTP) in the CA1 region of the rat hippocampus, combining electrophysiological techniques with multi-photon glutamate-uncaging and confocal microscopy. In addition, I have spent significant postdoctoral time dedicated to the development of circuit based optogenetic tools, testing and comparing the role of the conjugated fluorophores on the effectiveness of channelrhodopsins and halorhodopsins. Following this, I was a postdoc, and then senior research associate, in a neurogenesis lab; studying how neuronal circuits regulate postnatal neurogenesis in the mouse subventricular zone (SVZ). There, I combined sophisticated mouse-genetic models with electrophysiology and optogenetic techniques to identify a novel population of cholinergic neurons residing in the SVZ niche that robustly controls stem cell proliferation. Currently, at my current position as Research Assistant Professor in the laboratory of Juan Song at UNC Chapel Hill, I have been investigating the role of circuitry and niche components on the regulation of stem cell proliferation in the mouse dentate gyrus. Using my research expertise in cellular electrophysiology and imaging techniques, I intend to apply my experience in developing my own research career on the unique interactions of neurons and non-neuronal cell types in health and disease. A selection of related publications from my previous work is below:

*__Asrican B, *Wooten J__, Li Y, Quintanilla L, Zhang F, Wander C, Bao H, Yeh, C, Luo Y, Olsen R, Lim S, Hu J, Jin P, Song J. Neuropeptides modulate local astrocytes to regulate adult hippocampal neural stem cells. **Neuron**. **2020** Sep 2;107(5). ***indicates co-first authorship**

***Paez-Gonzalez P**, ***Asrican B**, *Rodriguez E, Kuo C. Identification of distinct ChAT(+) neurons and activity-dependent control of postnatal SVZ neurogenesis. **Nature Neuroscience 2014**. Jul;17(7):934-42 (Cover Story) ***indicates co-first authorship**

Asrican B, Augustine GJ, Berglund K, Chen S, Chow N, Deisseroth K, Feng G, Gloss B, Hira R, Hoffmann C, Kasai H, Katarya M, Kim J, Kudolo J, Lee LM, Lo SQ, Mancuso J, Matsuzaki M, Nakajima R, Qiu L, Tan G, Tang Y, Ting JT, Tsuda S, Wen L, Zhang X, Zhao S. Next-generation transgenic mice for optogenetic analysis of neural circuits. **Frontiers in Neural Circuits 2013** Nov 26; 7: 160 : 1-24

Asrican B, Lisman J, Otmakhov N. Synaptic strength of individual spines correlates with bound CaMKII. **J Neuroscience 2007** Dec 19; 27(51): 14007-14011.

B. Positions, Honors and Professional Experiences

Positions and Employment

2016 -	Assistant Research Professor, Dept. of Pharmacology, University of North Carolina, Chapel Hill
2013 - 2015	Senior Research Associate, Dept. of Cell biology, Duke University
2009 - 2013	Postdoctoral Associate, Dept. of Cell biology, Duke University
2008 - 2009	Postdoctoral Associate, Dept. of Neurobiology, Duke University

Honors

2019	Awarded: Best Poster Presentation: UNC CH Pharmacology Retreat; Chapel Hill NC.
2018	NARSAD Young Investigator (Brain and Behavior Research Foundation)
2017	Junior Faculty Development Award (UNC CH)
2014	Awarded: Best Poster Presentation: Duke Cell Biology Retreat; Beaufort NC.
2001-2007	Igert Associate, Brandeis University
1999	Departmental Honoree, Franklin and Marshall College
1998	Hackman Summer Scholar, Franklin and Marshall College.

Professional Experience

***Ad hoc* reviewer**
Star Protocols

***NIH* reviewer**
CMBG Study Section (ad hoc, October 2021, February 2022)

C. Contribution to Science

1. The early publications during my graduate school training addressed several aspects of hippocampal synaptic function. CA1 pyramidal neurons in the hippocampus integrate information from multiple circuit pathways, primarily cortical inputs via the perforant path and the CA3 inputs along the Schaffer collaterals. We established that the dendritic fields of the CA1 neurons that integrate these inputs were differentially sensitive to neuromodulation by monoamines. We characterized receptor subtypes using a barrage of pharmacological agents. Following that, we developed a means of chemically inducing LTP in the CA1 neurons by blocking inhibition and activating cAMP. This form of NMDA-receptor dependent LTP provides a robust method for inducing plasticity at a large percentage of synapses in the CA1 regions of the hippocampus. Thirdly, we undertook to understand how the post-synaptic plasticity molecule CaMKII is involved in regulating spine size and synaptic strength during LTP induction. Using a GFP-tagged CaMKII, we established how CaMKII translocates into spine-heads and becomes bound in place following LTP induction. We discovered that the amount of bound CaMKII that gets into individual spine heads is correlated with the resulting size and the resulting increases in synaptic strength, consistent with the hypothesis that CaMKII serves as a memory trace.

Asrican B, Lisman J, Otmakhov N. Synaptic strength of individual spines correlates with bound CaMKII. **J Neuroscience 2007** Dec 19; 27(51): 14007-14011.

Otmakhova NA, Lewey J, **Asrican B**, Lisman JE. Inhibition of perforant path input to the CA1 region by serotonin and noradrenaline. **J Neurophysiology 2005** Aug; 94(2):1413-22.

Otmakhov N, Tao-Cheng JH, Carpenter S, **Asrican B**, Dosemeci A, Reese TS, Lisman J. Persistent accumulation of calcium/calmodulin-dependent protein kinase II in dendritic spines after induction of NMDA receptor-dependent chemical long-term potentiation.
J Neuroscience 2004 Oct 20; 24(42):9324-31.

Otmakhov N, Khibnik L, Otmakhova NA, Carpenter S, Riahi S, **Asrican B**, Lisman J. Forskolin-induced LTP in the CA1 hippocampal region is NMDA receptor dependent.
J Neurophysiology 2004 May; 91(5):1955-62.

2. As the field of neurobiology was advancing, it became apparent to many electrophysiologists that more specific tools to probe neural circuits were needed. A means to stimulate or inhibit genetically defined populations of neurons, such as with optogenetics, would greatly facilitate our understanding of circuit dynamics and information flow. However, it was particularly unclear how well particular opsins and associated fluorescent tags worked in practice, since many tools were suddenly being developed and released for public use. To address this question, I did my early postdoctoral work testing variants of halorhodopsins and channelrhodopsins with a variety of promoters and various fluorescent tags. We found that the fluorescent tag on the optogenetic probe had a profound influence on the functionality of the opsin to either stimulate of inhibit neuronal activity. These results established which combinations of elements would be successful for use, and were able to demonstrate how these optogenetic tools can be used, for example, for high-speed mapping of neuronal inputs onto cerebellar Purkinje neurons.

Kim J, Lee S, Tsuda S, Zhang X, **Asrican B**, Gloss B, Feng G, Augustine GJ. Optogenetic Mapping of Cerebellar Inhibitory Circuitry Reveals Spatially Biased Coordination of Interneurons via Electrical Synapses. **Cell Reports 2014**. Jun 12;7(5):1601-13

Asrican B, Augustine GJ, Berglund K, Chen S, Chow N, Deisseroth K, Feng G, Gloss B, Hira R, Hoffmann C, Kasai H, Katarya M, Kim J, Kudolo J, Lee LM, Lo SQ, Mancuso J, Matsuzaki M, Nakajima R, Qiu L, Tan G, Tang Y, Ting JT, Tsuda S, Wen L, Zhang X, Zhao S. Next-generation transgenic mice for optogenetic analysis of neural circuits. **Frontiers in Neural Circuits 2013** Nov 26; 7: 160 : 1-24

3. For my second postdoctoral position, I brought my knowledge of neurobiological tools and circuit based strategies to the field of SVZ neurogenesis and began investigating non-neuronal cells in the CNS. Once such cell type, the ventricular ependymal cell, has the intriguing characteristics of providing ventricular barrier function and active cilia dynamics, while responding to neuronal circuit activity and interacting with the nearby adult neural stem cells (unpublished data). While there were indications that perhaps stem cells also were sensitive to various neurotransmitters, it was not yet clear whether there existed specific neuronal circuits and mechanisms of neuronal activity that could directly regulate the production of newborn neurons. Through collaboration with especially talented colleagues, we discovered a novel cholinergic neuron residing in the stem-cell niche that formed close associations with progenitor-cell populations of the SVZ. Furthermore, we demonstrated, using electrophysiological recordings, and optogenetic control of cholinergic activity, that these cholinergic neurons directly and robustly controlled the production of new neurons from the SVZ stem-cells in the postnatal animal. This represented an exciting new method of synaptic plasticity; circuit based production of new members of a neural circuit.

Asrican B, Paez-Gonzalez P, Erb J, Kuo C. Cholinergic Control of Postnatal Neurogenesis. N**eurogenesis 2016**. Jan;3(1)

***Paez-Gonzalez P**, ***Asrican B**, *Rodriguez E, Kuo C. Identification of distinct ChAT(+) neurons and activity-dependent control of postnatal SVZ neurogenesis. **Nature Neuroscience 2014**. Jul;17(7):934-42 (Cover Story) ***indicates co-first authorship**

4. In my current position as Research Assistant Professor at UNC, I have returned to the hippocampal system to more fully understand the role of circuit based modulation of brain states, with particular emphasis on how subtle modifications in dentate circuitry influence the hippocampus and strongly influence connected brain regions. My long-range goals are to understand how the interface of neuronal and non-neuronal cells influence aspects of brain circuitry relevant to neurodegenerative diseases. I have most recently become particularly interested in understanding the neuroimmune interface and have discovered unique attributes of hippocampal astrocytes in modulating health and disease. I will continue to use innovative techniques in optics, chemogenetics, electrophysiology, and advanced imaging techniques to track and study the factors and implications of circuit dynamics for the benefit of mankind. My most recent work has focused on the role of neuropeptide releasing interneurons in the hippocampus and how they utilize the immune response through astrocyte activation to influence adult neurogenesis and how dysfunction here dramatically results in neuroinflammation and impaired hippocampal function, especially in relation to Alzheimer's Disease.

***Asrican B, *Wooten J**, Li Y, Quintanilla L, Zhang F, Wander C, Bao H, Yeh, C, Luo Y, Olsen R, Lim S, Hu J, Jin P, Song J. Neuropeptides modulate local astrocytes to regulate adult hippocampal neural stem cells. **Neuron**. **2020** Sep 2;107(5). ***indicates co-first authorship**

***Yeh C, *Asrican B,** Moss J, Quintanilla L, He T, Mao X, Cassé F, Gebara E, Bao H, Lu W, Toni N, Song J Mossy cells control adult neural stem cell quiescence and maintenance through a dynamic balance between direct and indirect pathways. **Neuron. 2018** Aug 8;99(3):493-510. ***indicates co-first authorship**

Crowther AJ, Lim SA, **Asrican B**, Albright BH, Wooten J, Yeh CY, Bao H, Cerri DH, Hu J, Ian Shih YY, Asokan A, Song J. An Adeno-Associated Virus-Based Toolkit for Preferential Targeting and Manipulating Quiescent Neural Stem Cells in the Adult Hippocampus. **Stem Cell Reports. 2018** Mar 13;10(3):1146-1159.

***Bao H**, ***Asrican B**, *Li W, Gu B, Wen Z, Lim SA, Haniff I, Ramakrishnan C, Deisseroth K, Philpot B, Song J. Long-Range GABAergic Inputs Regulate Neural Stem Cell Quiescence and Control Adult Hippocampal Neurogenesis. **Cell Stem Cell. 2017** Nov 2;21(5):604-617
(Cover Story). ***indicates co-first authorship**

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/brent.asrican.1/bibliography/40217219/public/?sort=date&direction=descending

D. Research Support

Completed Research Support

1. R01 MH105416 **Kuo (PI)** **11/19/2014 – 10/31/2019**

Control of Postnatal SVZ Neurogenesis via Cholinergic Circuit Activity
The goal of this project is to explore a direct connection between neuronal activity from cholinergic neurons and postnatal SVZ NSC proliferation.
Role: Supported personnel.

2. R01 NS078192 **Kuo (PI)** **03/01/2012 – 02/28/2017**
Ependymal control of new neuron production in the adult brain
The goal of this project is to test the intriguing hypothesis that ependymal cells may hold a key role in controlling new neuron production from stem cells in the adult brain.
Role: Supported personnel.

3. R21 MH106939 **Song (PI)** **06/01/2015 – 05/31/2017**
Mapping Global Brain Connectivity Mediated by DISC1 Gene in Adult-born NeuronsThe goal of this project is to investigate brain circuitry connectivity mediated by newborn neurons with mental disorder risk gene DISC1 deficiency in the adult mouse hippocampus.
Role: Supported personnel.

4. Junior Faculty Career Development Award (UNC) **Asrican (PI)** **1/1/2017-12/31/2017**
Neuropeptide Regulation of Adult Neurogenesis. The goal of this project is to investigate the role of the CCK neuropeptide in the modulation of adult hippocampal neurogenesis in the mouse.
Role: PI

5. 2017 NARSAD Young Investigator Grant (26017) **Asrican (PI)** **1/15/2018-7/14/2020**
Dual Role of Neuropeptide/Neurotransmitter Signaling in Neuropsychiatric Circuit Imbalances. The goal of this project is to investigate how the cholecystokinin peptide and GABA neurotransmitter interact in hippocampal circuits and how dysfunction of this balance might underlie neuropsychiatric diseases such as autism, AD, or schizophrenia.
Role: PI

6. R01 MH111773 **Song (PI)** **09/26/2016 – 07/31/2021**
Neural circuitry mechanisms regulating adult hippocampal neurogenesis. The goal of this project is to determine the role of local inhibitory interneurons and their circuitry connections in the regulation of normal or aberrant neurogenesis the adult mouse hippocampus.
Role: Supported personnel.

Ongoing Research Support

1. R01 NS121300 **Song (PI)** **06/01/2021 – 03/31/2026**
Role of Cholecystokinin in the Dentate Gyrus. The goal of this project is to identify critical neurogenic niche components that promotes sustainable neurogenesis that may enable development of novel strategies to enhance functional repair from endogenous NSCs upon neurodegeneration.
Role: Supported personnel.

2. R21 AG074293 **Asrican (PI)** **09/01/2021 – 08/31/2023**
Altered Diversity of Astrocyte sub-types and Signaling Capabilities in Alzheimer's Disease. The goal of this project is to determine the diversity in astrocyte calcium signaling and molecular expression profiles and the changes that undergo these astrocyte subpopulations in Alzheimer’s disease.
Role: PI.