BIOGRAPHICAL SKETCH

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NAME: Sanders, Teresa

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

POSITION TITLE: Assistant 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 MM/YYYY	FIELD OF STUDY
University of Alabama in Huntsville	BS	03/1986	Electrical and Computer Engineering
University of California, Los Angeles	MS	12/1988	Electrical Engineering
Georgia Institute of Technology	PHD	05/2014	Bioengineering
Stanford University, Palo Alto, CA	Other training	2015	Optogenetics Innovation Lab
Emory University / Yerkes National Primate Research Center, Atlanta, GA	Postdoctoral Fellow	06/2016	Neurology / Biology / Yerkes
University of California, Los Angeles, CA	Other training	2016	ICLM/MCCS head-mounted microscope workshop

A. Personal Statement

My role in this project is PI. I will lead the research and coordinate the efforts of personnel. I will also design the experiments and analysis, train postdocs and students on critical aspects of optogenetics and electrophysiology, lead the data analysis and interpretation of results, and guide manuscript preparation. My current research focuses on the role of the hyperdirect pathway in normal and pathological basal ganglia function, particularly in neurodegenerative disorders. I have experience with primate and rodent animal models of Parkinson's disease, as well as with electrophysiology, imaging, optogenetics, and behavioral analysis. During my pre-doctoral research, I performed head-fixed single unit and local field potential recordings in the progressive MPTP monkey model of Parkinson's disease in Thomas Wichmann's lab. Subsequently, as a post-doc I proposed and was awarded a research grant to study optogenetic stimulation of cortico-subthalamic projections in freely moving mice. I performed all aspects of the work including design / construction of the experimental setup and devices for implantable recording / stimulation, planning and performance of surgeries, experimentation with behavioral and electrophysiological recordings, perfusions, histology and microscopy, data analysis, and manuscript preparation. While I accomplished most of the work in the lab of Dieter Jaeger, I completed histological processing and analysis in the lab of Yoland Smith at Yerkes National Primate Center, where I held a formal volunteer research position.

Prior to my PhD, my research (> 14 years) focused on extracting information from complex signals and images, prototyping and testing real-time closed loop systems, simulating complex networks of systems at multiple fidelities, and designing and building imaging missile systems. During my career in industry, I successfully led multiple complex research projects, collaborated with other researchers, and produced prototype technology, advanced models, patents, and/or peer-reviewed publications from each project.

Since returning to academic research, I have used the signal processing and systems analysis expertise I developed in industry to analyze neural systems and extract information from neural signals in novel ways. Using this knowledge, I have decoded speech phonemes, disease severity, and sleep states from electrophysiological signals, and shed new light on gaps in our knowledge about normal and pathological basal ganglia function. My experience in real-time, closed-loop missile systems enabled me to develop and build a system for optogenetic and electrophysiology experiments in freely moving mice. Using this system, I clarified the role of cortico-subthalamic projections in movement, found new clues about the mechanisms of deep brain stimulation, and tested strategies for optogenetic therapies in non-transgenic animals.

The current project builds logically on my prior work in electrophysiology, image and signal processing, basal ganglia circuit analysis, multi-scale modeling, and electronic device implementation. My lab has the equipment and resources to perform the proposed research and I have excellent support at Vanderbilt University. In summary my education, expertise, experience, and resources have prepared me to lead this project for the NIH.

1. Sanders TH, Jaeger D. Optogenetic stimulation of cortico-subthalamic projections is sufficient to ameliorate bradykinesia in 6-ohda lesioned mice. Neurobiol Dis. 2016 Nov;95:225-37. PubMed PMID: 27452483; PubMed Central PMCID: PMC5010926.
2. Sanders TH. Phase-amplitude coupling, an indication of bursting in parkinsonism, is masked by periodic pulses. J Neurophysiol. 2016 Mar;115(3):1587-95. PubMed PMID: 26792883; PubMed Central PMCID: PMC4808129.
3. Sanders TH, Devergnas A, Wichmann T, Clements MA. Canonical Correlation to Estimate the Degree of Parkinsonism from Local Field Potential and Electroencephalographic Signals. Int IEEE EMBS Conf Neural Eng. 2013 Nov;2013:158-161. PubMed PMID: 27099650; PubMed Central PMCID: PMC4834291.
4. Sanders TH, Clements MA, Wichmann T. Parkinsonism-related features of neuronal discharge in primates. J Neurophysiol. 2013 Aug;110(3):720-31. PubMed PMID: 23678015; PubMed Central PMCID: PMC3742985.

B. Positions and Honors

Positions and Employment

1986 - 1991	Member Technical Staff, Hughes Aircraft Company
1991 - 1996	Senior Systems Engineer, Hughes Aircraft Company
1996 - 1997	Consultant, Aerodyne and Stone Engineering
2005 - 2008	Senior Research Engineer, Georgia Tech Research Institute
2008 - 2014	Graduate Research Assistant, Georgia Institute of Technology
2014 - 2016	Postdoctoral Fellow, Emory University / Yerkes National Primate Facility, Atlanta, GA
2016 -	Assistant Professor, Vanderbilt University, Nashville, TN

Other Experience and Professional Memberships

- 1986	President, Student Chapter, Eta Kappa Nu
2008 -	Member, IEEE
2010 -	Member, BMES
2011 -	Member, Society for Neuroscience
2012 -	Member, American Physiological Society

Honors

1990	Cost Improvement Award, Hughes Aircraft
1991	High Performance Team Award, Hughes Aircraft
1996	Outstanding Employee, Hughes Aircraft
2013	Outstanding Research Award, Center for Signal and Information Processing

C. Contribution to Science

1. Discovery that specific optogenetic stimulation of motor cortico-subthalamic projections is sufficient to ameliorate bradykinesia and abnormal neural signaling in parkinsonian mice (reference a). A previous study showed that high frequency stimulation of cortico-subthalamic projections in the Thy1::ChR2 mouse ameliorated rotations in hemi-parkinsonian mice (reference b). However, since the Thy1::ChR2 mouse has opsins in many locations other than the cortico-subthalamic projections and since the ChR2 opsins used were not supportive of the frequencies used for stimulation, there was some concern about the interpretation of the results. In my study, I used a specific dual virus technique to place ultrafast opsins

selectively in the cortico-subthalamic projections. In this way, I discovered that high frequency stimulation specifically targeted to motor cortico-subthalamic projections ameliorated both motor signs and abnormal signaling in parkinsonian mice. This finding is significant from a basic science perspective, but also as a potentially translational discovery because the dual virus transfection technique can be implemented in humans.

a. Sanders TH, Jaeger D. Optogenetic stimulation of cortico-subthalamic projections is sufficient to ameliorate bradykinesia in 6-ohda lesioned mice. Neurobiol Dis. 2016 Nov;95:225-37. PubMed PMID: 27452483; PubMed Central PMCID: PMC5010926.
b. Gradinaru V, Mogri M, Thompson KR, Henderson JM, Deisseroth K. Optical deconstruction of parkinsonian neural circuitry. Science. 2009 Apr 17;324(5925):354-9. PubMed PMID: 19299587.

2. Discovery that phase-amplitude local field potential (LFP) measures from the cortex and subthalamic nucleus correlate with the degree of parkinsonism in the MPTP monkey model (reference a). During my PhD, I analyzed 3 monkeys made increasingly parkinsonian using small injections of MPTP administered over 6 months to 1 year. The monkeys were assigned motor disorder scores and subscores based on a weekly visual assessment. I used signal processing knowledge from my prior missile defense work to interrogate the data and design and evaluate features that best correlated with the degree of parkinsonism from the motor scores. The best correlating feature, phase-amplitude coupling, was later found to also correlate with parkinsonism in humans (references c and d) and is now under test for use in closed-loop deep brain stimulation.

a. Sanders TH, Devergnas A, Wichmann T, Clements MA. Canonical Correlation to Estimate the Degree of Parkinsonism from Local Field Potential and Electroencephalographic Signals. Int IEEE EMBS Conf Neural Eng. 2013 Nov;2013:158-161. PubMed PMID: 27099650; PubMed Central PMCID: PMC4834291.
b. Sanders TH, McCurry M, Clements MA. Sleep stage classification with cross frequency coupling. Conf Proc IEEE Eng Med Biol Soc. 2014;2014:4579-82. PubMed PMID: 25571011.
c. van Wijk BC, Beudel M, Jha A, Oswal A, Foltynie T, Hariz MI, Limousin P, Zrinzo L, Aziz TZ, Green AL, Brown P, Litvak V. Subthalamic nucleus phase-amplitude coupling correlates with motor impairment in Parkinson's disease. Clin Neurophysiol. 2016 Apr;127(4):2010-9. PubMed PMID: 26971483; PubMed Central PMCID: PMC4803022.
d. Shreve LA, Velisar A, Malekmohammadi M, Koop MM, Trager M, Quinn EJ, Hill BC, Blumenfeld Z, Kilbane C, Mantovani A, Henderson JM, Brontë-Stewart H. Subthalamic oscillations and phase amplitude coupling are greater in the more affected hemisphere in Parkinson's disease. Clin Neurophysiol. 2017 Jan;128(1):128-137. PubMed PMID: 27889627.

3. Demonstration of a potential link between synchronized bursting in parkinsonian single cells and phase-amplitude-coupling LFP measures. Understanding the way in which the data from single cells influences LFPs is of great interest, since LFPs are reflective of the population activity that drives behavior. Also LFPs are of interest since they are more readily measured chronically in the human body than single cells. I constructed a stochastically driven biophysical model to show how parkinsonian LFPs may be constructed from synchronized bursting in parkinsonian single cells as described in publication ‘a’ below. The importance of single cell bursting and synchronization in parkinsonism has been observed by others. However, in ‘b’, we showed definitively that single cell features related to bursting and spectral power were more predictive of parkinsonism than firing rate and entropy measures in MPTP monkeys.

a. Sanders TH. Phase-amplitude coupling, an indication of bursting in parkinsonism, is masked by periodic pulses. J Neurophysiol. 2016 Mar;115(3):1587-95. PubMed PMID: 26792883; PubMed Central PMCID: PMC4808129.
b. Sanders TH, Clements MA, Wichmann T. Parkinsonism-related features of neuronal discharge in primates. J Neurophysiol. 2013 Aug;110(3):720-31. PubMed PMID: 23678015; PubMed Central PMCID: PMC3742985.

4. Design, implementation, and test of the first wirelessly networked smartwatch, smartphone, and portable EEG system for analyzing parkinsonism in humans. Parkinson’s disease (PD) patients’ symptoms vary

significantly throughout the day. Physicians try to prescribe therapies that maximize the number of good hours in a patient's day, but this is difficult when prescriptions must be based solely upon observations limited to infrequent office visits. My PhD mentors and I envisioned a home monitoring system for PD patients that would provide additional data to physicians regarding the patients' symptoms over an extended period of time. Using the features discovered in (2) along with accelerometer and gyroscope features found to correlate with parkinsonian movements, I designed and built a networked system for assessing parkinsonism in humans. Each of the 3 devices acquired data from its sensors, then the data were wirelessly transmitted to the smartphone in real-time via a custom app I wrote. The data was then downloaded and parkinsonism assessed using machine learning methods.

   a. Sanders TH, Devergnas A, Wichmann T, Clements Mark A. Remote smartphone monitoring for management of Parkinson's disease. (PETRA) Proceedings of 6th International Conference on PErvasive Technologies Related to Assistive Environments. 2013 May 29;

5. Application of image processing techniques developed for military systems to successfully extract de novo information from biological images.

   a. Sanders TH, Stokes TH, Moffitt RA, Chaudry Q, Parry R, Wang MD. Development of an automatic quantification method for cancer tissue microarray study. Conf Proc IEEE Eng Med Biol Soc. 2009;2009:3665-8. PubMed PMID: 19964806; PubMed Central PMCID: PMC4983438.
   b. Lo TK, Hinkle TA, Ng Lop, Sacks Jack. , inventors. Automatic mask threshold. US 5261010/ 07/766,318. 1993 November 09.

Link to Full Publication List:

https://www.ncbi.nlm.nih.gov/sites/myncbi/teresa.sanders.1/bibliography/49692065/public/?sort=date&direction = descending

D. Additional Information: Research Support and/or Scholastic Performance

Completed Research Support

5T32 NS007480-14 (Levey) 07/01/2014-06/30/2015
Training in Translational Research in Neurology
Role: FEL

001, Georgia Research Alliance (Clements) 01/01/2014-12/31/2015
Mobile device for monitoring and treatment of neurological disorders
Role: GR

001, National Science Foundation (Llewellyn) 06/01/2011-05/30/2012
Science Learning: Integrating Design, Engineering, and Robotics
Role: FEL

001, Georgia Tech Research Institute (Sanders) 01/01/2007-12/30/2007
Military Image Recognition and Search
Role: OP

001, Hughes Aircraft Company (Sanders) 08/01/1989-07/30/1990
Optical Character Recognition with Synthetic Discriminant Function Filters
Role: OP