BIOGRAPHICAL SKETCH

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NAME: Robert H Cudmore Jr.

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

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. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
State University of New York at Buffalo, Buffalo, NY	BA	01/1993	Computer Science
University of Pennsylvania, Philadelphia, PA		09/1997	Computer Science
Brandeis University, Waltham, MA	PhD	08/2004	Neuroscience
INSERM UMR-641, Marseille, France	Post-Doc	05/2009	Neuroscience
The Johns Hopkins University, School of Medicine, Baltimore, MD	Post-Doc	09/2015	Neuroscience
The Johns Hopkins University, School of Medicine, Baltimore, MD	Research Associate	1/2019	Neuroscience

A. Personal Statement

I have a long standing interests at the intersection of biology and technology. My initial training in Computer Science and then, for my PhD, in Neurobiology gives me a unique perspective, toolset, and way of thinking that I continuously bring to my basic research. As a graduate student with Gina Turrigiano at Brandeis University, I made significant advances in our understanding of the activity dependent plasticity of both the intrinsic excitability of neurons and in vivo homeostatic scaling of synaptic connectivity. For my initial postdoctoral training with Dominique Debanne in Marseille France, I continued to examine the firing properties of neurons. Here, I described how ion channels can control action potential precision within individual neurons and, interestingly, how this is sufficient to sculpt network synchrony. Having taken a relatively reductionist view by studying neurons in brain slice preparations, I chose to adjust my research focus to a more systems level approach. To do this, I sought training in longitudinal in vivo two-photon microscopy in awake behaving mice with David Linden at The Johns Hopkins University School of Medicine. I have subsequently used in vivo two-photon imaging to address fundamental questions over a wide range of topics including (1) how in vivo sensory experience and (2) biological rhythms can sculpt synaptic structure and connectivity, (3) how neuronal axons can recover from damage, and (4) how cerebral vascular structure is sculpted by behavior.

Most recently, with my newly formed lab at the University of California Davis, we are addressing fundamental questions on the structure and function of the cerebral vasculature in both health and disease. We take a multi-level and multi-disciplinary approach employing in vivo and ex vivo two-photon imaging, whole cell electrophysiology, and image analysis. One axis of the lab is examining the endothelium as a signaling conduit in neurovascular coupling. A second axis is developing the next generation image analysis tools for longitudinal volumetric image analysis.

Four recent manuscripts:

Zhang Y*, **Cudmore RH***, Lin D-T, Linden DJ, Huganir RL (2015) Visualization of NMDA receptor–dependent AMPA receptor synaptic plasticity in vivo. Nat Neurosci 18(3):402-7. * Equal contribution.

Jin Y, Dougherty SE, Wood K, Sun L, **Cudmore RH**, Abdalla A, Kannan G, Pletnikov M, Hashemi P, Linden DJ (2016) Regrowth of Serotonin Axons in the Adult Mouse Brain Following Injury. Neuron 91(4):748-762.

Ye Z, **Cudmore RH**, Linden DJ (2019) Estrogen-Dependent Functional Spine Dynamics in Neocortical Pyramidal Neurons of the Mouse. J Neurosci 39(25):4874-4888.

Cudmore RH, Dougherty SE, Linden DJ (2017) Cerebral vascular structure in the motor cortex of adult mice is stable and is not altered by voluntary exercise. J Cereb Blood Flow Metab 37(12):3725-3743.

B. Positions and Honors

Positions

2019- Assistant Professor, Department of Physiology and Membrane Biology, University of California, Davis.

Honors

2016-2020 American Heart Association, Scientist Development Grant (16SDG27130006).
2011-2013 Young Investigator Grant, NARSAD (17633).
2010-2012 National Institute of Health, Loan Repayment Program (NIH LRP).
2008-2009 Post-doctoral Research Fellowship, Fondation Singer-Polignac.
2006-2008 Post-doctoral Research Fellowship, Assoc. Française contre les Myopathies (AFM).
2005-2006 Post-doctoral Research Fellowship, IBRO/INSERM.

C. Contributions to Science

For a nearly complete publication list, see either
Google Scholar Profile: R.H. Cudmore or NIH Publication List

1. Long-term potentiation of intrinsic excitability (LTP-IE). When I began my PhD, a majority of neuroscience research had focused on how synaptic connections between neurons are modified by particular activity regimes. A compelling body of evidence had demonstrated that the strength, dynamics and distributions of synaptic connections are modulated by activity. Yet, focusing on synaptic plasticity alone could give a flawed and sometimes incorrect understanding of how neural circuits are modified. There is now mounting evidence that intrinsic excitability, the precise way a neuron integrates synaptic input to generate AP output, can be modified by learning and particular activity patterns. Plasticity in intrinsic excitability is evoked by many of the same activity regimes and intracellular signals that mediate synaptic plasticity including a rise in intracellular Ca++ and the activation of protein kinase pathways. Given the overlapping signals which trigger intrinsic and synaptic plasticity, they are likely to be expressed concomitantly. Given the importance of intrinsic excitability in determining the transfer function, it is likely to gate the specific types of activity-dependent synaptic plasticity that occur.

Cudmore RH, Turrigiano GG (2004) Long-term potentiation of intrinsic excitability in LV visual cortical neurons. J Neurophysiol 92(1):341-8.

Cudmore RH, Desai NS (2008) Intrinsic plasticity. Scholarpedia, 3(2):1363.

Cudmore RH, Fronzaroli-Molinieres L, Giraud P, Debanne D (2010) Spike-time precision and network synchrony are controlled by the homeostatic regulation of the D-type potassium current. J Neurosci 30(38): 12885-95.

2. In vivo neuronal and vascular plasticity. Having taken a relatively reductionist approach during my PhD and initial postdoctoral research, I strategically chose to shift my focus using more systems level approaches. This was in part to make my research more validated for translation to the clinic. To achieve this, I took a postdoctoral research position at The Johns Hopkins University working closely with David J Linden and

Richard L Huganir. We set out to employ longitudinal in vivo two-photon imaging in awake behaving mice to tackle a wide range of questions from neuronal spine plasticity to axonal regeneration, to cerebral vascular function. We were one of the first groups to show that sensory experience can induce rapid and persistent changes in individual synaptic spines (Zhang, Cudmore, et al, 2015). We addressed an aging dogma that central nervous system axons cannot regenerate by showing they can (Jin et al, 2016). Finally, in a unique use of two-photon microscopy, we showed incredible stability in the cerebral vasculature (Cudmore, et al, 2017).

Throughout performing this research, I created software, Map Manager - Igor, that drove the research forward and allowed us to ask questions others could not address. Taken what I have learned from extensive user feedback, it is now I am turning my attention to making this software available to the scientific community.

Zhang Y*, **Cudmore RH***, Lin D-T, Linden DJ, Huganir RL (2015) Visualization of NMDA receptor–dependent AMPA receptor synaptic plasticity in vivo. Nat Neurosci 18(3):402-7. * Equal Contribution.

Jin Y, Dougherty SE, Wood K, Sun L, **Cudmore RH**, Abdalla A, Kannan G, Pletnikov M, Hashemi P, Linden DJ (2016) Regrowth of Serotonin Axons in the Adult Mouse Brain Following Injury. Neuron 91(4):748-762.

Cudmore RH, Dougherty SE, Linden DJ (2017) Cerebral vascular structure in the motor cortex of adult mice is stable and is not altered by voluntary exercise. J Cereb Blood Flow Metab 37(12):3725-3743.

Ye Z, **Cudmore RH**, Linden DJ (2019) Estrogen-Dependent Functional Spine Dynamics in Neocortical Pyramidal Neurons of the Mouse. J Neurosci 39(25):4874-4888.

3. Open Source Projects. Please See: **https://github.com/cudmore**
The majority of code I write is made freely available on GitHub. In addition to using a wide range of open source technologies, all of these projects are fully documented for both end users and programmer users. The goal of these projects is first to make useful tools to speed research and discovery and secondly to train and inspire students and researchers to build their own systems.

3.1. **MapManager-Python.** https://github.com/cudmore/PyMapManager

Time-series image volume analysis. A python package backend and both desktop and browser based viewers and editors. The desktop version uses PyQt and the web version uses a client/server model with the frontend web written in Javascript/Angular and the backend in Python/Flask. The API is available as a Python package on PyPi and the backend is distributed in a container (Docker). All components of MapManager-Python will run on Windows, macOS, and Linux.

3.2. **Map-Manager-Matlab.** https://github.com/cudmore/MapManager-Matlab

A fully documented Matlab toolbox to read Map-Manager-Igor datasets and easily extend the analysis.

3.3. **Raspberry Pi Experiments (PiE).** https://github.com/cudmore/pie

A system to perform behavioral experiments using Raspberry Pi computers and Arduino compatible micro-controllers. All configurations use a Python backend, Flask/NGINX web-server, and a Javascript/Angular front end. Features include live streaming video to a browser, 24/7 video recording and environment control of animals in their home-cage, on the scope video recording and experimental control of hardware such as lights, motors, and sensors using an Arduino.

3.4. **SanPy.** https://github.com/cudmore/bAnalysis

Easy to use and full featured spike detection. Has a python backend engine for spike detection, an easy to use API for analysis and plotting, a desktop viewer/editor (PyQt), and a web based editor (Plotly Dash).

4. Map Manager software for genetic linkage analysis. I currently have over 25 years experience in software development which began after completing my BA in computer science, I had the amazing opportunity to be the lead software developer on a major rewrite of a graphical-user-interface desktop application for genetic linkage analysis. My main goals that I achieved was a complete revamping and modernization of an exiting macOS application. This included rewriting the program in C++ and making it cross-platform. I also extended the features to include quantitative trait loci and generalized the statistics to make the software useable not just for mammalian genetics but plant genetics as well. This software is used by ~250 labs and has had a very productive life-cycle. The manuscript describing the software sustained 60+ citations per year for 12 years and peaked at 120+ citations (in 2008). Please note, I am re-using the name Map Manager for my current image analysis project, my goal is to reproduce the success of this genetic mapping software with my new longitudinal image volume analysis software.

Manly KF, **Cudmore RH**, Meer JM (2001) Map Manager QTX, cross-platform software for genetic mapping. Mamm Genome 12(12):930-2.

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

Longitudinal in vivo two-photon imaging of cerebral vascular plasticity — 01/01/2016 - 06/30/2020
American Heart Association - Scientist Development Grant. — 16SDG27130006
Role: PI

The goal of this proposal is to characterize vascular plasticity following ischemic stroke and to determine difference in this plasticity between young and aged mice. There is no overlap with the current application.