Intelligent implantable microsystems enabling *in situ* anti-epileptic therapies
Prof. Rikky Muller

The focus of my research is to develop implantable microelectronic systems that directly interface with the brain, monitor and treat neurological disorders, enable fundamental neuroscientific discovery. Today, neuroscientists and clinical researchers **lack the tools they need** for the research of neurological disorders. My research develops tools for advanced study of the brain, as well as autonomous devices that will monitor, diagnose, treat and in the long term even cure disease. The devices I develop are comprised of integrated microsystems and circuits that are miniaturized, wireless, remotely powered and **have embedded intelligence to learn the signatures of disease and treat *on demand*.** Such tools will enable a wealth of patient data that cannot be accessed today and will open to door to significant scientific discovery and new treatment paradigms of neurological disorders.

Year 2 Proposal

Hardware development: My group has completed primate testing on WAND: Wireless Artifact-free Neuromodulation Device and submitted a manuscript that is currently in review at Nature Biomedical Engineering (https://arxiv.org/abs/1708.00556). Existing systems are limited by low channel counts, lack of algorithmic flexibility, and distortion of recorded signals from large, persistent stimulation artifacts. We have developed a device that enables new clinical applications requiring high-throughput data streaming, low-latency biosignal processing, and truly simultaneous sensing and stimulation.

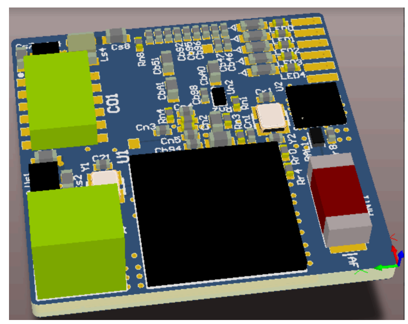

Figure 1: The design of our new WAND Mini boards, 1" x 1"

We are currently working on a re-design the device that will fit into a 1" x 1" form factor. The WAND Mini board shown in Figure 1 will enable *in vivo* studies in rodent models of epilepsy. The new WAND boards can be used to provide therapeutic stimulation or to control the release timing and dosing of anti-epileptic drugs. These devices should be ready by the end of the summer. Our aim for year 2 is complete fabrication and assembly for a rodent-compatible system and to program our seizure detection algorithms into the device to demonstrate a complete closed-loop system for epilepsy. We will be able to use WAND to monitor long-term seizure activity and to validate closed-loop treatment paradigms by programming our seizure detection algorithms into the embedded closed-loop controller.

Algorithm development: Over the past year, my group has been working with a dataset of human intracranial EEG (iEEG) data from epilepsy patients to determine the most efficacious and least computationally complex seizure detection features. We developed a weighted matrix approach that improves sensitivity while minimizing false alarm rates in detecting seizures shown in Figure 2. The algorithm calculates the optimal detection threshold and is trained off line. Last week this project was awarded the **2018 Fung Institute Award for Most Innovative Project**!

In year 2 we will explore adaptive learning techniques in order to train the data set and have it updated on-line. These techniques must have low computational complexity for embedding the algorithm directly onto the low-power microcontroller and FPGA on WAND Mini.

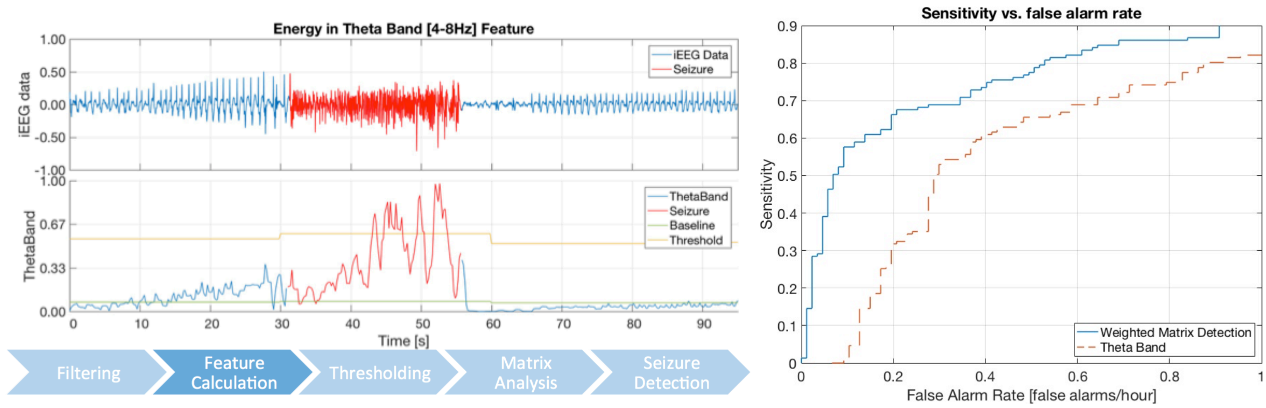

Figure 2: (Left) Seizure detection based on the single best patient-specific feature; (Right) Shows improved sensitivity with lower false alarm rates using our learning-based weighted matrix detection approach.

Our closed-loop patient-specific approach to treatment, enabled by research in machine learning **and accelerated by the Wagner foundation**, will transform patient care. Treatments that learn in a patient-specific manner will be significantly more efficacious while producing minimal side effects. The platform technology developed in this project will also have far reaching applications in neurological disease care and neuroscientific discovery.

Budget

Funds will be used to support one graduate student researcher for one year to conduct and lead this research as well as equipment and supplies for the testing laboratory. Specific items are listed below.
Graduate Student Tuition, Fees and Stipend for 12 months: $72k
Electronic testboards and components for WAND Mini: $10k
Electronic test equipment and lab supplies: $18k

PI Biography

Rikky Muller, Ph.D. is an Assistant Professor of Electrical Engineering and Computer Sciences (EECS) at the University of California, Berkeley. She is Co-director of the Berkeley Wireless Research Center, a Core Member of the Center for Neural Engineering and Prostheses and an Investigator at the Chan-Zuckerberg Biohub. She is also the Co-founder of Cortera Neurotechnologies, Inc. a medical device company founded in 2013 where she held positions as CEO and CTO. Her expertise is in the research and commercialization of implantable medical devices and in developing microelectronic and integrated systems for neurological applications.

Prof. Muller received her BS and MS degrees from MIT and her Ph.D. from UC Berkeley all in EECS. After her graduate studies, she was a McKenzie Fellow and Lecturer of EE at the University of Melbourne in Australia. Prior to her Ph.D. she worked as an IC designer at Analog Devices. Prof. Muller was named one of MIT Technology Review's top 35 global innovators under the age of 35 (TR35) in 2015, and one of MedTech Boston's top 40 healthcare innovators Under 40 in 2016. In 2017, she received the National Academy of Engineering Gilbreth Lectureship, the Chan-Zuckerberg Biohub Investigatorship, and the Keysight Early Career Professorship.