Specific Aims

Optogenetics is a technique that uses light stimulus to excite or inhibit neurons [10,18,20]. Optogenetics is being used to identify the mechanisms of epileptic seizures and also shows promise as a therapeutic technique to abort seizures [2,3]. Among other limitations, optogenetics instruments currently available for *in vivo* experiments do not allow EEG data to be recorded in freely moving mice. We propose to design a novel optogenetic instrument that overcomes this research barrier and then test it *in vivo.* This instrument will be the world's first to meet all of the following criteria:

1. Capable of recording EEG signals and transmitting them in real time. This allows live data processing and the application of optogenetic stimulus as an immediate response to EEG events.
2. Suitable for use with transgenic mice, giving researchers access to the large range of mouse strains proven as disease models and available for optogenetic research
3. Wireless and fully implantable to allow the animal to move freely and cohabit with other mice
4. Requires no physical interaction from a human after implantation

The instrument will utilize technology proven by our current "Implantable Stimulator with Lamp (ISL)", a wireless optogenetic stimulator and EEG recorder used in rat studies [8,16,30]. **We hypothesize that we can miniaturize this instrument for use with mice and make the instrument reusable.** Like the current ISL, the new instrument will be composed of two subcutaneous components. The Implantable Stimulator and Monitor (ISM) contains the circuit board and battery; it will be implanted in the mouse's abdomen. The satellite component will be the Fiber-Coupled LED (FCL), an ultra-compact head fixture containing the LED lamp and optical fiber which deliver light.

Specific Aim 1: Develop the electronics for a mouse-sized optogenetic stimulator with monitor
- Milestone 1: Reduce the volume of OSI's current ISL electronics from 4.2 mL to 1.5 mL

We will re-design the existing ISL circuit to utilize components in the smallest package sizes available and design a printed circuit board to mount them. We will replace the separate transmission and reception antennas with a single antenna that serves both functions.

- Milestone 2: Add a recharging capability which permits the instrument to be reused

Our current optogenetic instrument is designed to be used for a single experiment and then disposed. We will add circuitry to the instrument which permits recharging and develop a charger. This way, the instrument can be recovered after an experiment and reused indefinitely.

Specific Aim 2: Develop an ultra-efficient, fiber-coupled LED (FCL) appropriate for mice
- Milestone 3: Develop an FCL circuit board using the DA2432 LED die

The proposed device requires a specialized, 300 μm LED for maximum efficiency. This LED is challenging to work with. We will mount a batch of these bare die LEDs on FCL circuit boards.

- Milestone 4: Develop 220 μm diameter fiber tapers and measure optical power

The ISL's current 450 μm optical fiber tapers are too large for use with mice. We will design tapers with a base diameter of 220 μm. We will attach those tapers to the FCL LED and measure power.

Specific Aim 3: Manufacture prototype instruments and conduct an *in vivo* trial.
- Milestone 5: Manufacture 20 instruments We will assemble 20 fully complete instruments
- Milestone 6: Conduct local tests

We will subject 10 of the 20 prototypes to accelerated aging tests and report on performance.

- Milestone 7: Conduct an *in vivo* trial to assess performance

Our collaborators will implant 10 of the 20 prototypes in mice and report on *i)* the device's ability to manipulate observable behavior in response to optogenetic stimulus; *ii)* the device's ability to record EEG signals; and *iii)* device reliability. They will also test the recharging capability post-explant.