Biological Question / Opportunity for Knowledge:

The concept of Neural Plasticity, the reorganization of a neural circuit to enhance adaptation to alterations of informational input and transmission, has recently absorbed an increasing amount of attention. It is known that ability for neurons to update their spatial location, to increase or decrease their communication via synaptic connection with other neurons, is essential to the concept of learning and storing knowledge. Details of potential that causes this dismantling and regeneration of neural structure is still unknown. Conceptualizing the stimulus that induces this behavior would result in increasing utility of this process to treat a wide variety of disorders caused by nervous system misalignment. These include Depression, Stroke victims, and even people with sensory malfunctions such as the blind and deaf [4].

Purpose: To construct a model to analyze neural circuit behavior and formation when integrated into a functional information feedback system.

Research Plan/Model:

- To fabricate a neural circuit, Primary rat Cortical Neurons will be with cultured. To do this, rat embryos will be dissected. The cortical tissue will be extracted, dissociated in an enzymatic solution, centrifuged, properly cleansed, and incubated [3]. These cells will then be implemented into a microelectron mechanical systems (MEMS) device (type of microfluid channel) that has three wells . Two wells separated from each other by barrier and the third connected to the two other wells with micro tunnels (custom design) [5]. The Primary cell Cortical Neurons will grow and establish synaptic connections with each other. Neuron populations in well 3 will grow axons through the micro tunnels and make connections to neuron populations in wells 1 and 2. Neurons in well 3 will be stimulated (depolarizing above threshold to create an action potential) by electrodes at a specific frequency. Neurons in cell 2 will have an electrode attached that monitor the signal transmitted from neurons in cell 3. This signal will then go through an electrical circuit that amplifies it and uses it as feedback signal to alter the frequency of stimulation in cell 3. (Example: If recorded signal within neurons in cell 2 do not reach threshold depolarization, circuit will increase input frequency of stimulation to neurons in cell 3) The neurons connecting well 3 to well 2 will be effectively functioning within a feedback circuit. Neurons in cell 1 will be the control group with no feedback applied. The structure and quantity of the neurons in the circuit connecting well 3 to well 1 and from well 3 to well 2 will be observed pre and post stimulation. An increase in quantity of synapses or axons connecting neurons in wells 3 and 2 not seen in wells 3 to 1 could indicate information potential enhancing neural formation.
- Primary Cells Neurons were chosen over immortal cell lines because the function of the neuron, that mimics insitsu behavior, is essential to this study. Organotypic slices were not chosen because the predefined structure could limit any noticeable structural deviations due to the implementation of the feedback circuit. For this experiment, basic elements of neuron communication and connection with each other need to be localized. The Microfluidic tunnels and MEMS device will help guide signal transmission and segregate the control and the subject cells.

References:

[1] DeMarse TB, Pan L, Alagapan S, Brewer GJ, Wheeler BC. Feed-Forward Propagation of Temporal and Rate Information between Cortical Populations during Coherent Activation in Engineered In Vitro Networks. Front Neural Circuits. 2016 Apr 22;10:32. doi: 10.3389/fncir.2016.00032. PMID: 27147977; PMCID: PMC4840215.

[2] Isomura T, Shimba K, Takayama Y, Takeuchi A, Kotani K, Jimbo Y. Signal transfer within a cultured asymmetric cortical neuron circuit. J Neural Eng. 2015 Dec;12(6):066023. doi: 10.1088/1741-2560/12/6/066023. Epub 2015 Nov 3. PMID: 26529359.

[3] "Protocol for Culturing Rat Cortical Neurons." Www.rndsystems.com, www.rndsystems.com/resources/protocols/protocol-culturing-rat-cortical-neurons#:~:text=Warm%20an%20appropriate%20amount%20of%20Complete%20Cortical%20Neuron,Completed%20Cortical%20Neuron%20Culture%20Media%20to%20each%20well.

[4] Rugnetta, Michael. "Neuroplasticity". Encyclopedia Britannica, 3 Sep. 2020, https://www.britannica.com/science/neuroplasticity. Accessed 12 September 2021.

[5] Diagram of custom MEMS device: