EE 301 Final Report

12/3/2019

Professor

Dr. Ada Poon is an associate professor of electrical engineering whose research focuses on developing biomedical electronic devices. These technologies are intended to serve as tools for scientific discovery (such as midfield wireless power transfer systems that enable more flexible electrophysiological mouse experiments), systems for recording or modulating biological activity (such as a wireless, optogenetic neuromodulation implant), and devices for restoring lost biological function (such as the Alzheimer's project discussed in this report). Dr. Poon's current research thrusts target heart disease, diabetes, cancer, and Alzheimer's disease.

Topic

Therapeutic electronic implant intended to delay onset of debilitating Alzheimer's symptoms by enabling retrieval, and thus long-term potentiation, of short-term memories

High-Level Overview

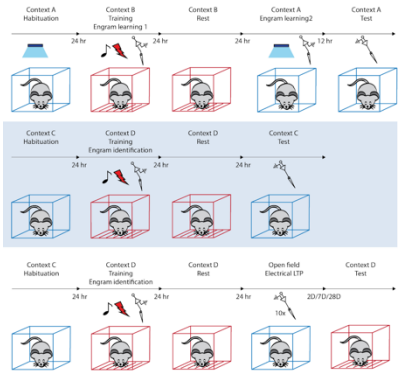
Approximately 4% of people over the age of 60, and 33% of people over the age of 85, suffer from dementia in the form of Alzheimer's disease. Dementia is a debilitating condition that robs people of their memory and cognitive function that disproportionately affects the elderly. Previous research on Alzheimer's suggested that the disease occurred due to an inability of the brain to store new memories. However, recent studies have uncovered evidence that suggests the initial stages of Alzheimer's are actually primarily characterized by the brain's inability to *recall* memories – the memory storage mechanisms remain largely intact.

Dr. Poon's research focuses on developing devices to exploit this discovery – if neurons that store memories can be activated at will to enable Alzheimer's patients to recall targeted memories, the early symptoms of the disease can potentially be delayed and cognitive function augmented. In addition, research suggests that activating otherwise-unreachable neurons promotes healthier cell growth, indicating that this technology may not only improve the quality of life of Alzheimer's patients, but also their overall prognoses.

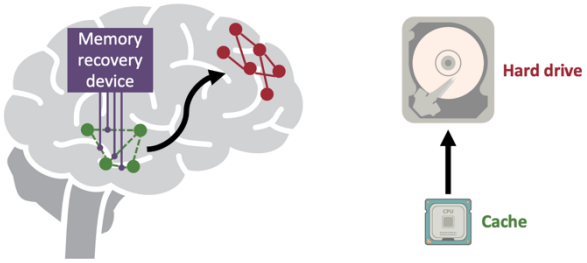
Details

The experimental basis of Dr. Poon's work largely stems from the lab of Dr. Susumu Tonegawa at MIT. Dr. Tonegawa studies engrams, the physical traces of memory in the brain that are manifested as, for example, changes in synaptic connections between neurons or variations in the density of dendritic spines. Dr. Tonegawa's typical experimental procedure is as follows: first, neurons in the dentate gyrus region of the brain are monitored during some learning experience. The dentate gyrus is a portion of the hippocampus thought to be responsible for episodic memory formation. Neurons in this region of the brain that express certain genes (known as IEGs, or immediate early genes) during the learning experience are hypothesized to be part of the memory formation process and are tagged with a protein called channelrhodopsin-2. This protein enables the neurons to later be artificially stimulated with

blue light. This allows researchers to observe whether activity among the population of neurons that was active during a learning experience, even some time period after the actual experience, can reproduce a learned response in an animal.



This experimental procedure has revealed that in populations of mice with early-onset Alzheimer's, difficulties in memory recall can be ameliorated by the direct stimulation of labelled engram cells. In the most cited experiment, mice are exposed to a contextual fear stimulus and the extent of their "freezing" response is measured. What is often observed is that Alzheimer's mice freeze when initially presented with the stimulus, don't freeze at a later time, but do freeze when the neurons that were active during the initial freezing are stimulated, regardless of whether or not the fear stimulus is present also. This suggests that memories are being created but are unable to be retrieved. One other key result is that repeated activation of engram cells can result in long-term potentiation which is hypothesized to be the means behind long-term memory storage. Thus, stimulation of these cells can help not only diminish the effects of Alzheimer's, but reverse them as well.



To take advantage of this discovery, Dr. Poon has designed a wireless implant device for the targeted stimulation of engram cells. The device is powered electromagnetically and draws on Dr. Poon's work with wireless powering of devices within tissue. It is still under development, but it will ideally be deployed to human Alzheimer's patients to help them improve their memory retrieval abilities. While Dr. Poon did not share the specifications of the current device, her previous work, such as "An RF-Powered FDD Radio for Neural Microimplants" demonstrated the operation of a device that sustained a 58 Mb/s data rate at 93 microwatts of power. This device can be powered by an antenna directly on the skin, negating the need for a through-skin implant or head-mount, and would be ideal for this application.

Takeaways

I was fascinated by Dr. Poon's talk, especially by the idea that technology, rather than drugs, could be used to treat something as pervasive and challenging as Alzheimer's. I will be rotating in Dr. Poon's lab next quarter, and I plan to assist in the development of the Alzheimer's device. My role will be to modify the packaging and system integration to ensure that the separate components of the device, the stimulator and the wireless power unit, operate cohesively and with high efficiency.