ECE 110 Project Proposal

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Graham, The Digital Organoid:

Utilizing Neuromorphic Computing to Model Human Brain Organoid Dynamics

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Background. Human-derived brain organoids are a growing area of neuroscience research enabling new approaches to understanding neurological development, function, and disease. Brain organoids exhibit spiking activity with similar underlying mechanisms to their full-size counterparts, providing an in-vitro solution for modeling complex neural network dynamics [1]. Modeling these spiking neural networks is necessary for understanding normal and diseased brain functions, and developing treatments for neurological diseases. In another rising area of research, neuromorphic computing utilizes the architecture of the brain and neural connectivity to develop novel hardware and software [2]. At a broad level, brain-inspired computational techniques including Spiking Neural Networks (SNNs) leverage the low power consumption of biological neural networks to develop energy-efficient and accelerated processing.

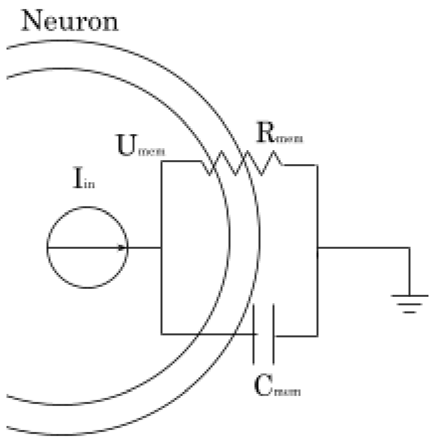
Between these two fields is a largely untapped area of research utilizing the computational power of neuromorphic computing and the likeness to its physical ancestors to decode and model biological neural network dynamics. Previous neuromorphic computing and neuroscience research has led to the notable development of Brian2, an open-source Spiking Neural Network (SNN) simulator designed for computational neuroscience [3]. While Brian2 has enabled the analysis of complex neural networks, the intricacy of biological systems makes it difficult to develop a complete computational model of the brain. Certain biological features and likenesses have been dropped in favor of computational simplicity.

Proposal. As a novel solution, we propose bridging Human Brain Organoid Research and Neuromorphic Computing by taking advantage of the biological likeness of SNNs to develop Graham, the Digital Organoid[1]. Based on a relatively simple model when compared to a human brain, Graham opens up the possibility of a more complex and biologically realistic model, able to mimic firing patterns and respond accordingly to external stimuli. With such lofty ambitions, we decided to decompose Project Graham into three developmental phases.

First is the development of Naive Graham, where the organoid model will utilize a simple SNN to train on electrophysiological (E-Phys) data in an attempt to replicate baseline behavior and random spiking. Graham will be built using the Python snnTorch package, a neuromorphic machine-learning extension of PyTorch [4] [5]. snnTorch includes a variety of neuron models to use in pre-defined networks, each of which provides a tradeoff between biological realism and computational

[1] In honor of the late Graham Chapman who portrays Brian, in *Monty Python's Life Of Brian (1979)*, for which the program Brian2 is named after, which is, in itself, a reference to Python being named after *Monty Python.*

efficiency. To best emulate the network dynamics while maintaining simplicity, we propose starting with the Leaky Integrate and Fire (LIF), default parameters left alone[2]. The LIF neuron model uses an RC circuit to represent ion exchange across an ambiguous membrane, resulting in a crude but functional spiking function analogous to a biological neuron.



$$U_{mem}(t) = I_{in}(t)R + [U_0 - I_{in}(t)]e^{-t/RC}$$

$$\downarrow$$

$$U[t+1] = \beta U(t) + WX[t+1] - S[t]\,U_{th}$$

$$\downarrow$$

Potential = Decay + Input - Reset

Fig. 1.: Leaky Integerate and Fire (LIF) neuron model.
Membrane represented as First Order RC Low Pass circuit then discretized for deep learning application. Figure created by author.

Along with using an SNN, we will replicate the training across other commonly available neural networks including Fully Connected, Convolutional, and Recurrent Neural networks to benchmark the ability of SNNs to generate E-Phys data. The success of each model will be determined by their relative ability to replicate metrics including Inter Spike Intervals (ISIs), Firing Rates (FR), and visual comparisons of raster plots. This phase will serve mainly as a proof of concept and exploration of the tools available within snnTorch.

From here we will advance to Phase two, the Stimulated Naive Gahram, where we introduce external stimuli. We hypothesize that the model will be terrible as it will be trained on data without stimuli, and lacks biologically relevant rules such as Spike Timing Dependent Plasticity (STDP) needed for learning response to input.

Phase three is the Stimulated Learned Gahram which will utilize STDP, and will be trained on E-Phys data with organoid stimulation. Phases two and three will

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[2] While the LIF model is a rational compromise between biological realism and complexity for our proof of concept, we may choose to expand this to utilize more parameters, find a different model or multiple models to better encapsulate other aspects not included by LIF.

primarily serve as future goals, and will only be implemented if we can complete each prior phase.

Materials and Methods. The data sets used to train Gahram will be sorted E-Phys data collected from the UCSC Braingineers consortium, recorded on a Maxwell Biosystems MaxOne High-Density Micro Electrode Array, and run through the spike sorting program KiloSort. Electrophysiology recordings of organoids from the Maxwell Biosystems MaxOne HD MEA encode time points and electrical pulses on a planar sensor, which are sorted by KiloSort to provide firing rates of neurons [6].

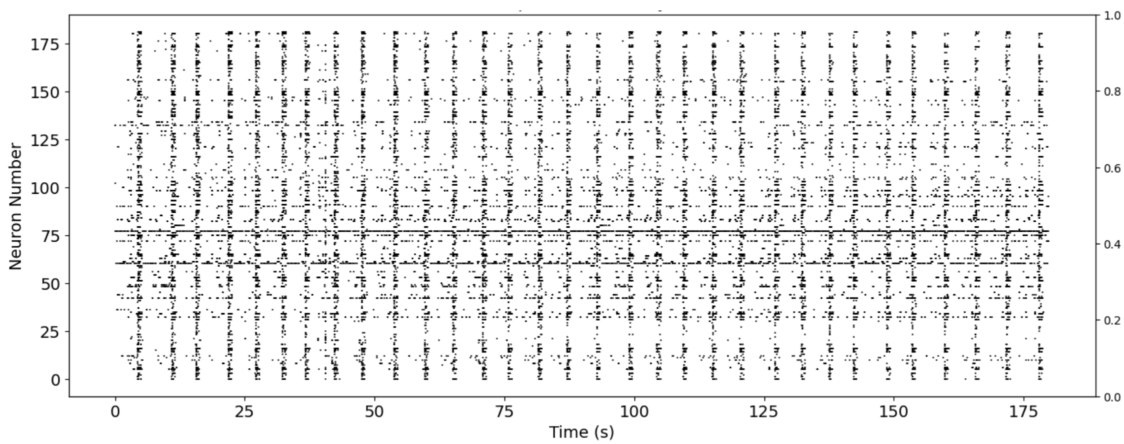

Fig. 2.: Visualization of sorted E-Phys data. Dataset gathered from *Functional Neuronal Circuitry (Sharf, 2022*). Figure created by author [7].

References.

[1] G. Calà, B. Sina, P. De Coppi, G. G. Giobbe, and M. F. M. Gerli, "Primary human organoids models: Current progress and key milestones," *Front. Bioeng. Biotechnol.*, vol. 11, p. 1058970, Mar. 2023, doi: 10.3389/fbioe.2023.1058970.

[2] C. D. Schuman, S. R. Kulkarni, M. Parsa, J. P. Mitchell, P. Date, and B. Kay, "Opportunities for neuromorphic computing algorithms and applications," *Nat Comput Sci*, vol. 2, no. 1, pp. 10–19, Jan. 2022, doi: 10.1038/s43588-021-00184-y.

[3] M. Stimberg, R. Brette, and D. F. Goodman, "Brian 2, an intuitive and efficient neural simulator," *eLife*, vol. 8, p. e47314, Aug. 2019, doi: 10.7554/eLife.47314.

[4] E. Jason, "snnTorch." Accessed: Oct. 24, 2024. [Online]. Available: https://snntorch.readthedocs.io/en/latest/

[5] "PyTorch." [Online]. Available: https://pytorch.org/docs/stable/index.html

[6] M. Pachitariu, S. Sridhar, J. Pennington, and C. Stringer, "Spike sorting with Kilosort4," *Nat Methods*, vol. 21, no. 5, pp. 914–921, May 2024, doi: 10.1038/s41592-024-02232-7.

[7] T. Sharf *et al.*, "Functional neuronal circuitry and oscillatory dynamics in human brain organoids," *Nat Commun*, vol. 13, no. 1, p. 4403, Jul. 2022, doi: 10.1038/s41467-022-32115-4.