Programming for Organoid Intelligence

Corina Mills and Dr. Brian Caffo
Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health

Introduction

Research on human stem cell-derived brain organoids aims to establish organoid intelligence (OI) and promote understanding of human neuronal functioning.

OI allows observation of human brain function at a high temporal level which we cannot do otherwise. Such investigation mitigates many of the ethical dilemmas that coincide with human research and bypasses issues that arise from animal testing.

Characterization of human 3D brain microphysiological system

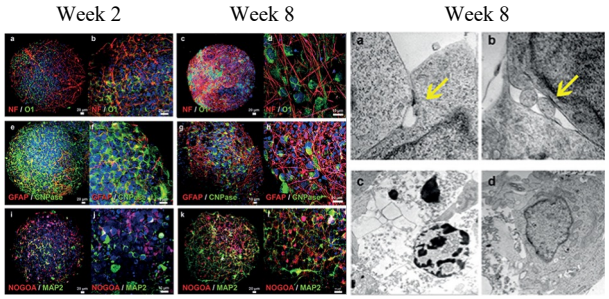


Figure 1a. (left) Comparison of expression of neuronal and glial marker
Figure 1b. (right) Ultrastructure analysis by electron microscopy

Brain organoids are an important model of human brain activity because they provide in vitro reads of functioning human neurons (distinctions between cell lines serve as representations for genetic disorders and/or epigenetic differences).

We hypothesize that spike inter-arrival times of organoid neural activity are dependent on each other and cluster into groups of firing bursts.

Study Aims/Methods

Multi-electrode array (MEA) data collected on brain organoids was loaded in, processed, and analyzed to directly observe function by studying real time neural activity.

We focused on analyzing basic neuronal spike train data (spikes acquired over time) to inform the degree of timing and coordination of neural functioning in the organoid. We worked to develop methods of analysis for inter-arrival time distribution by utilizing various statistical tests and considering the lagged autocorrelation function (ACF).

Results

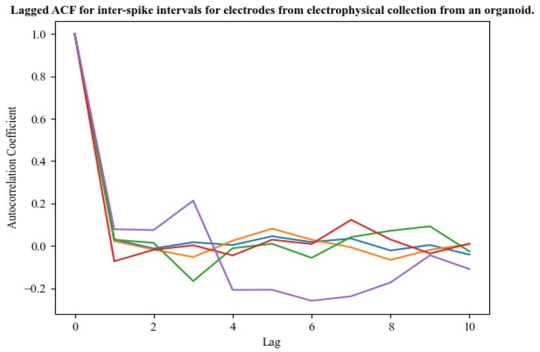


Figure 2. (above) Lagged ACF of 5 sample electrodes of example organoid

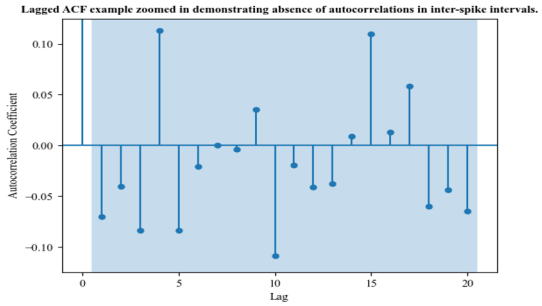


Figure 3. (above) No visible association between interarrival times

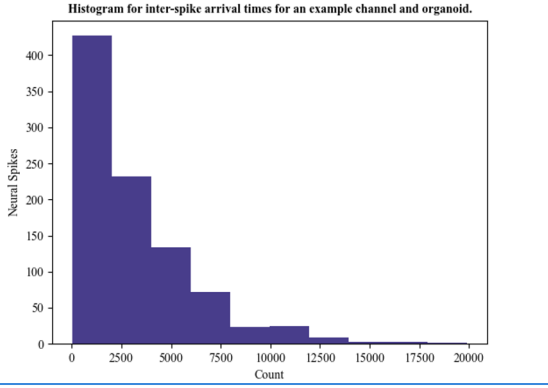
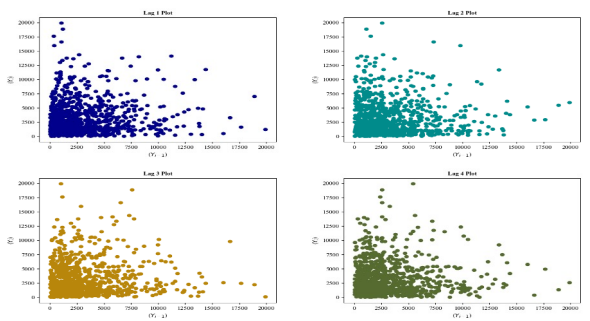


Figure 4. (above) Indicates quantities of spikes inter-arrival times that fall under specified time. 0-2500 ms is highest in prevalence

Results (continued)

Scatterplots of lagged inter-spike arrival times for an example channel and organoid



Summary/Conclusions

The autocorrelation function graphs demonstrate a generally observed absence of lagged correlation in inter-spike arrival times. We disproved our theory that when we stimulate the organoid, electrodes were not evidenced by inter-spike arrival time clustering distribution.

This knowledge can be applied to increase precision of neural network models which will assist in understanding pathophysiology of developmental and degenerative diseases. Further application of this insight in OI-based biocomputing systems will allow the creation of more efficient and effective artificial intelligence.

References

Pamies, D., Barreras, P., Block, K., Makri, G., Kumar, A., Wiersma, D., Smirnova, L., Zang, C., Bressler, J., Christian, K. M., Harris, G., Ming, G. L., Berlinicke, C. J., Kyro, K., Song, H., Pardo, C. A., Hartung, T., & Hogberg, H. T. (2017). A human brain microphysiological system derived from induced pluripotent stem cells to study neurological diseases and toxicity. *ALTEX*, *34*(3), 362–376. https://doi.org/10.14573/altex.1609122

Smirnova, L., Caffo, B. S., Gracias, D. H., Huang, Q., Morales Pantoja, I. E., Tang, B., Zack, D. J., Berlinicke, C. A., Boyd, J. L., Harris, T. D., Johnson, E. C., Kagan, B. J., Kahn, J., Muotri, A. R., Paulhamus, B. L., Schwamborn, J. C., Plotkin, J., Szalay, A. S., Vogelstein, J. T., … Hartung, T. (2023). Organoid Intelligence (OI): The New Frontier in biocomputing and intelligence-in-a-dish. *Frontiers in Science*, *1*. https://doi.org/10.3389/fsci.2023.1017235

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