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Organoid Training System and Methods

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OTHER INFORMATION

KEYWORDS

organoid, cortex organoid, brain organoid, electrophysiology, neural, neuron, neuronal, training neurons, reinforcement learning, neuromorphic

CATEGORIZED AS

- **Computer**
  - Software
- **Medical**
  - Disease: Central Nervous System
  - Research Tools
  - Screening
  - Software
- **Research Tools**
  - Bioinformatics
  - Other
  - Screening Assays
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RELATED CASES

2025-934-0

BACKGROUND

Advances in biological research have been greatly influenced by the development of organoids, a specialized form of 3D cell culture. Created from pluripotent stem cells, organoids are effective in vitro models in replicating the structure and progression of organ development, providing an exceptional tool for studying the complexities of biology. Among these, cerebral cortex organoids (hereafter "organoid") have become particularly instrumental in providing valuable insights into brain formation, function, and pathology. Modern methods of interfacing with organoids involve any combination of encoding information, decoding information, or perturbing the underlying dynamics through various timescales of plasticity. Our knowledge of biological learning rules has not yet translated to reliable methods for consistently training neural tissue in goal-directed ways. In vivo training methods commonly exploit principles of reinforcement learning and Hebbian learning to modify biological networks. However, in vitro training has not seen comparable success, and often cannot utilize the underlying, multi-regional circuits enabling dopaminergic learning. Successfully harnessing in vitro learning methods and systems could uniquely reveal fundamental mesoscale processing and learning principles. This may have profound implications, from developing targeted stimulation protocols for therapeutic interventions to creating energy-efficient bio-electronic systems.

TECHNOLOGY DESCRIPTION

To help fulfil this unmet need, a research team at UC Santa Cruz (UCSC) has developed a framework for real-time neural interfacing. The UCSC closed-loop system operates through discrete timesteps involving three key components: the organoid’s neural activity, the simulated environment, and the training signals chosen by artificial reinforcement learning. The system was evaluated on the inverted pendulum control problem, commonly known as ”cartpole”. Unlike pattern recognition tasks, cartpole requires continuous, active stabilization of an inherently unstable system where small lapses in control lead to failure, making it particularly suitable for assessing both real-time processing and adaptation, akin to organoid environments. Preliminary results demonstrated both the effectiveness of adaptive training. While high-frequency stimulation generally enhanced network performance over baseline, adaptive selection of training signals led to significantly better outcomes than random selection, with proficiency rates doubling in continuous experiments. While almost 23% of cycles reached proficiency under the adaptive training protocol, only about 4% did so with random stimulation, and approximately 2% with no stimulation. Continuous adaptive training, where the adaptive paradigm without cycling between conditions occurred, achieved proficiency in over 45% of trials, substantially higher than the approximate 23% rate observed in adaptive-cycled experiments.

APPLICATIONS

- diagnostics – neuro
- therapeutics – neuro
- research tools – neuro

ADVANTAGES

- To the best of UCSC researchers’ knowledge, this is the first demonstration of goal-oriented learning in brain organoids
- For most organoids, training signals chosen by artificial reinforcement learning outperformed randomly chosen signals or in absence of signals
- Proficiency greater than 45% was achieved in trials using continuous adaptive training

INTELLECTUAL PROPERTY INFORMATION

Patent Pending

RELATED MATERIALS

- Robbins, Ash, et al. "Goal-Directed Learning in Cortical Organoids." bioRxiv (2024): 2024-12. - 12/12/2024

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Telehealth-Mediated Physical Rehabilitation Systems and Methods
- Modern Organoid Research Platform System and Methods
- Ligament-Based Elastic Hybrid Soft-Rigid Joints

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