Biological and Hybrid Neural Networks Communication
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BACKGROUND
During initial stages of development, the human brain self assembles from a vast network of billions of neurons into a system capable of sophisticated cognitive behaviors. The human brain maintains these capabilities over a lifetime of homeostasis, and neuroscience helps us explore the brain’s capabilities. The pace of progress in neuroscience depends on experimental toolkits available to researchers. New tools are required to explore new forms of experiments and to achieve better statistical certainty. Significant challenges remain in modern neuroscience in terms of unifying processes at the macroscopic and microscopic scale. Recently, brain organoids, three-dimensional neural tissue structures generated from human stem cells, are being used to model neural development and connectivity. Organoids are more realistic than two-dimensional cultures, recapitulating the brain, which is inherently three-dimensional. While progress has been made studying large-scale brain patterns or behaviors, as well as understanding the brain at a cellular level, it’s still unclear how smaller neural interactions (e.g., on the order of 10,000 cells) create meaningful cognition. Furthermore, systems for interrogation, observation, and data acquisition for such in vitro cultures, in addition to streaming data online to link with these analysis infrastructures, remains a challenge.

TECHNOLOGY DESCRIPTION
To help address this challenge, investigators at UC Santa Cruz (UCSC) have researched and developed a custom autoculture setup for a variety of experimental applications involving organoids. The automated, internet-connected microfluidics prototype delivers precise feeding liquids to individual cerebral organoids in order to optimize their growth without the need for human interference with the tissue culture. UCSC's current demonstration contains a culture plate with 24 individual wells, and each well can be its own experiment in which organoid cultures can be grown independently and fed liquids at varying, programmable concentrations and times. An in-incubator imaging system lets the researchers constantly remotely monitor organoid growth and morphology. The feeding media for each individual culture can be pulled out for analysis at any point during an experiment, which allows researchers to non-invasively measure data such as pH and glucose levels which can be important for monitoring cell growth. This system addresses variation and reproducibility that arises in organoid growth due to “batch effect” issues, where organoids grown at different times or at different labs under similar conditions may vary just because of the complexity of their growth. Moreover, the digital intermediary features of autoculture open the door to new levels of control and observability through flexible and scalable computer-mediated processes.

APPLICATIONS
▶ Neuroscience research
▶ Medical research

ADVANTAGES
▶ Enables simultaneous, multiplexed, 3D study
▶ Minimal/no human intervention with remote controls
▶ Alleviates variation and reproducibility burden
▶ Flexible data formats, fully programmable
▶ Introduces new controls and observability in neural modeling

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