Title: Exploring Kainic Acid-Induced Alterations in Circular Tripartite Networks with Advanced Analysis Tools

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Abstract
Microelectrode arrays (MEAs) provide a powerful platform for studying neuronal networks, essential for advancing our understanding of brain activity, which depends on the coordinated functioning of interconnected regions. Simplistic traditional in vitro models, often based on single human pluripotent stem cell-derived networks, are currently evolving into complex brain-on-a-chip systems featuring compartmentalized structures and integrated sensors. These innovations enable more accurate modeling of brain functions and generate complex datasets requiring advanced analytical approaches.

Our previously published state-of-the-art brain network model incorporates three MEA compartments, each housing distinct neuronal populations, interconnected through microfluidic tunnels to facilitate axonal communication. This circular tripartite network concept allows the study of both local and global electrophysiological patterns using embedded MEAs. Using this device, we developed an epilepsy-on-a-chip model, inducing seizure-like activity through kainic acid (KA) application in one compartment. To interpret the resulting complex electrophysiological data, we introduced advanced tools for assessing synchronization and functional connectivity across multiple parameters.

Our custom-designed analysis revealed novel multilevel bursting patterns and assessed the interrelations between KA-exposed compartments and non-exposed neighboring compartments. The findings included significant activity shifts in the treated compartments and diverse effects on untreated local networks, confirming the formation of networks with distinct topologies and strengths. However, the global networks' activities were also significantly altered.

Together, our MEA platform and advanced analytical tools offer a robust and promising platform for in vitro disease modeling. In particular, our recent publication demonstrated its advantages for modelling epilepsy.