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Unlocking the Brain — The Transformative Role of High-Density Multielectrode Arrays in Understanding Brain Disorders

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EDITORIAL

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The mature human brain is composed of more than 100 billion neurons, with its vast network is estimated to have more than 60 trillion connections, and orchestrates everything from basic reflexes to sophisticated cognitive processes [1]. Despite remarkable advances in imaging and molecular biology, a comprehensive understanding of neuronal interactions within large-scale networks, both in healthy and pathological conditions, remains elusive. Recently, high-density multielectrode arrays (HD-MEAs) have emerged as a groundbreaking technology, significantly advancing our knowledge of neuronal network functions and their alterations in various neurological and psychiatric disorders.

HD-MEAs are advanced microfabricated devices containing thousands of electrodes densely packed into a small chip that can boast over 4,000 electrodes. This enables simultaneous recording of extracellular activity from hundreds to thousands of individual neurons with exceptional spatiotemporal precision. Specifically, these arrays capture detailed signals such as action potentials, local field potentials, and network oscillations, providing invaluable insights at the single-neuron and subcellular levels [2][3]. The access to the activity of individual neuron at subcellular resolution is particularly valuable in the context of brain disorders including neurodegenerative disease, neurodevelopmental and psychiatric disorders where network dysfunction often underlies clinical symptoms. For instance, in epilepsy, HD-MEAs can detect seizures, network hyperexcitability, and focal points of origin in in vitro and ex vivo models, aiding in both mechanistic understanding and drug screening [4].

The most promising applications of HD-MEAs lies in their integration with neurons derived from human-induced pluripotent stem cell (hiPSC) [5]. These models enable researchers to study patient-specific neural phenotypes, particularly for complex disorders like autism spectrum disorder (ASD) and schizophrenia, where the pathological changes are subtle and network-based. Additionally, HD-MEAs significantly contribute to research on neurodegenerative diseases such as Alzheimer's and Parkinson's, allowing the observation of early changes in neuronal connectivity, synaptic integrity, and firing patterns. These recordings offer potential biomarkers for early diagnosis and serve as valuable platforms for developing targeted therapeutic interventions. HD-MEA recordings from theses disease models allow for real-time monitoring of spontaneous and evoked activity, network bursts, and response to pharmacological agents making them an essential tool for personalized medicine.

In addition, HD-MEAs are being paired with machine learning and computational neuroscience models to manage and interpret the massive datasets they generate. These techniques enable the identification of disease-specific neural signatures, classification of neuronal subtypes based on firing patterns, and prediction of network responses to stimuli or treatments [6]. Furthermore, HD-MEAs support long-term recordings, enabling chronic monitoring of neural cultures or brain tissue slices over days and weeks. This is especially relevant for studying the effects of long-acting drugs or progressive disease models. Their compatibility with optogenetics and microfluidics further broadens their application, allowing for precise stimulation and environmental control.

In conclusion, HD-MEA technology marks a transformative advancement in neuroscience research. By enabling high-resolution and large-scale recordings of neuronal activity, these arrays bridge the critical gap between single-neuron analysis and system-level brain dynamics. As neurodevelopment and psychiatric disorders become an increasing burden on global health, HD-MEAs offer a promising platform to unravel the complexities of neuronal dysfunction and accelerate the development of effective therapies.

Competing interests

The author declares no competing interests.

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