Towards Mimicking Brain Mechanical Loads: Stretchable Microelectrode Arrays for Brain Spheroid Electrophysiology

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Human neural spheroids, 3D cellular aggregates of neurons and glial cells, are a compelling biological model for studying neuronal communication in physiological and pathological conditions, such as neurodevelopment and traumatic brain injury (TBI), respectively. This study introduces a novel design for a free-standing, fully perforated, and stretchable microelectrode array (MEA) specifically tailored to monitor the electrophysiological activity of brain spheroids under varying static and dynamic mechanical loads.

Our MEAs are fabricated using thin-film technology and composed of a platinum layer sandwiched between two 1 μm thick polyimide films. The stretchability of the MEA is achieved through a Kirigami-based patterning technique, incorporating μm-sized Y-shaped motifs in the MEA that facilitate out-of-plane deflections in plastic/metal/plastic microstructures [1][2]. The thin and freestanding MEAs are clamped between customised holders suitable for electrochemical and mechanical evaluation.

Using finite element modelling, we demonstrated that the electrode geometry, the relative substrate-to-metal width ratio, and metal thickness collectively influenced the overall stretchability of the electrode, affecting the resulting maximum strain on the metallic layer upon elongation. Optimization of these parameters reduced the maximum strain on the metal by half.

Experimental validation involved applying uniaxial elongation at a constant speed (100 µm/s) to the MEA with strain parameters aligned with what is typically seen in TBI (5-30% strain). Scanning electron micrographs of the patterned electrodes upon stretching confirmed the results of the numerical simulations, identifying the electrode as the most fragile component of the MEA. Structural failure was observed at the electrode edge, occurring at 25% strain for the optimized electrodes. To verify the functionality of the electrodes while stretching, we monitored their electrochemical impedance at 1 kHz upon elongation. Optimized electrodes sustained strains up to 10% without a significant increase in their electrochemical impedance amplitude, while unoptimized electrodes sustained strains only up to 7.5% (n_{MEAs} = 3, n_{electr} = 24 per condition).

Additionally, we evaluated the impact of an electrodeposited Poly(3,4-ethylenedioxythiophene) (PEDOT) coating on the electrode stretchability. The PEDOT coating conformed to the patterned electrodes independently of the electrode size and reduced the electrochemical impedance at 1 kHz by 60 folds (n = 24, diameter = 70 µm). The PEDOT coating deformed together with the electrode during elongation. The PEDOT-coated electrodes exhibited more stable impedance under mechanical loading compared to bare platinum electrodes, therefore enhancing both their electrical and mechanical performance.

Finally, we verified the functionality of the stretchable electrodes in recording neural activity from brain spheroids. Each MEA hosted eight Kirigami-patterned recording electrodes (diameter = 70 µm), and a large ground electrode to probe one brain spheroid (spheroid diameter = 500-1000 µm). The MEAs reliably recorded spontaneous neural activity from brain spheroids for up to five days when mounted on a fluidic platform for cell culture media change.

This work paves the way for studying the effect of mechanical loading on neural activity in 3D in vitro brain models.

References:

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