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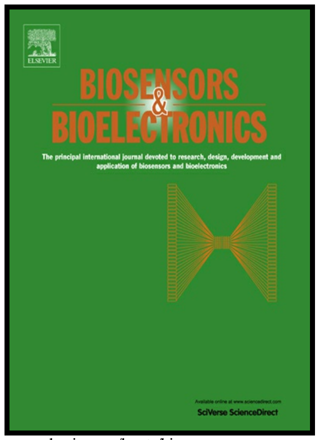

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Modular microstructure design to build neuronal networks of defined functional connectivity

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Abstract

Theoretical and in vivo neuroscience research suggests that functional information transfer within neuronal networks is influenced by circuit architecture. Due to the dynamic complexities of the brain, it remains a challenge to test the correlation between structure and function of a defined network. Engineering controlled neuronal networks in vitro offers a way to test structural motifs; however, no method has achieved small, multi-node networks with stable, unidirectional connections. Here, we screened ten different microchannel architectures within polydimethylsiloxane (PDMS) devices to test their potential for axonal guidance. The most successful design had a probability of 92% of achieving strictly unidirectional connections between nodes. Networks built from this design were cultured on multielectrode arrays and recorded on days in vitro 9, 12, 15 and 18 to investigate spontaneous and evoked bursting activity. Transfer entropy between subsequent nodes showed up to 100 times more directional flow of information compared to the control. Additionally, directed networks produced a greater amount of information flow, reinforcing the importance of directional connections in the brain being critical for reliable communication. By controlling the parameters of network formation, we minimized response variability and achieved functional, directional networks. The technique provides us with a tool to probe the spatio-temporal effects of different network motifs.

Keywords: In vitro neuronal networks, PDMS microstructures, Axon guidance, Functional connectivity, Extracellular recordings, Multi-electrode array, Brains on a chip

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