Mechanobiology in Epithelial 3D Tissue Constructs

ME3T.

GRK 2415 LECTURES

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Controlled small neural networks on a chip for bottom-up neuroscience

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at 9:00 am

On site:
Seminarraum B1.72
DWI – Leibniz-Institut für Interaktive Materialien
Forckenbeckstraße 50, 52074 Aachen

Zoom:
https://rwth.zoom.us/j/99189331346?pwd=ck5jZ0pFM3V4bVN4dGYzVDVnR1JEdz09
Meeting-ID: 991 8933 1346
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Abstract: The traditional way of addressing questions related to the function of the brain involves studying the nervous system of various organism with the argument: "nature optimized these through millions of years of evolution so we should learn how they function by studying the real system". However, this at the same time means to study something that is highly complex and largely unknown.

Although the tools of neuroscience are becoming more and more advanced, due to the complexity of these systems, it is very difficult to address fundamental questions. Probably this is the reason for the lack of consensus in the field even on seemingly basic questions such as "what is information" and "how is information stored and processed" in the brain. Besides this top-down approach there is also a substantial community (including us) that follows the bottom-up approach[1], *i.e.* trying to learn from small networks of neurons with the advantage that the position and connections of the neurons can be precisely defined and the cells have a good accessibility for recording tools: such as patch clamp[2], microelectrode3[3] or CMOS arrays4, or fluorescence microscopy[5].

This talk will introduce new tools that we developed to create and to interact with well-defined neuronal networks. For example, asymmetric PDMS microchannels can be used to guide the axonal growth in the desired direction on top of microelectrode arrays3[-6] while nanochannels enable the tuning of the connectivity between pre- and postsynaptic neurons[7]. This allows studying fundamental neuroscience paradigms and enables the creation of network architectures with real neurons, including human iPSC-derived cells[6] towards personalized medicine.

I will also present our attempts to automate building the networks using the FluidFM technology[8] and the culturing using custom liquid handling system that also permits reliable changes in the environment including exposure to drugs9.

Overall, the brain-on-a-chip and nerve-on-a-chip technologies presented in this talk are the first necessary step for bottom-up neuroscience, a new approach to study neurons and their networks.

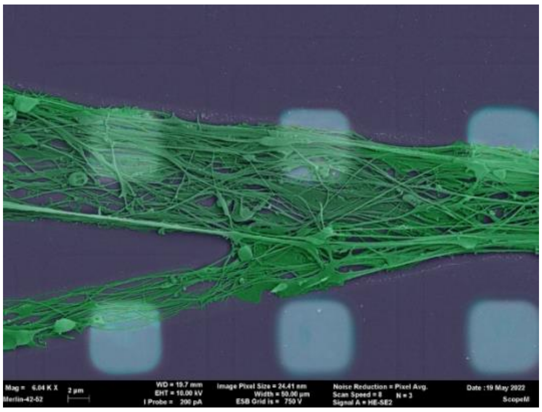

Figure 1: False colored SEM image of axons (green) connecting two nodes of well-defined neural networks on CMOS microelectrode (light blue) arrays.

1. "Brains on a chip": Towards engineered neural networks. Aebersold, M. et al.; *Trends in Analytical Chemistry*; 2016, 78, 60-69.
2. Force-Controlled Patch Clamp of Beating Cardiac Cells. Ossola, D.et al.; *Nano Lett*ers, 2015.
3. An experimental paradigm to investigate stimulation dependent activity in topologically constrained neuronal networks; S.J. Ihle, et al.; *Biosensors and Bioelectronics*, 2021.
4. Engineered biological neural networks on high density CMOS based microelectrode arrays; J. Duru, et al.; *Frontiers in Neuroscience*, 2022.
5. Modular microstructure design to build neural structures with defined functional connectivity; C. Forró, et al.; *Biosensors & Bioelectronics*, 2018.
6. Topologically controlled circuits of human iPSC-derived neurons for electrophysiological recordings; …S. Girardin, et al.; *Lab-on-a-chip*, 2022.
7. Nanoscale patterning of in vitro neuronal circuits; J.C. Mateus and S. Weaver, et al; *ACS-Nano*, 2022.
8. Controlled single-cell deposition and patterning by highly flexible hollow cantilevers; V. Martinez, et al.; *Lab-on-a-chip*, 2016.
9. Engineering circuits of human iPSC-derived neurons and rat primary glia; S. Girardin, et al.; submitted to Frontiers in Neuroscience, 2022. doi: 10.1101/2022.11.07.515431