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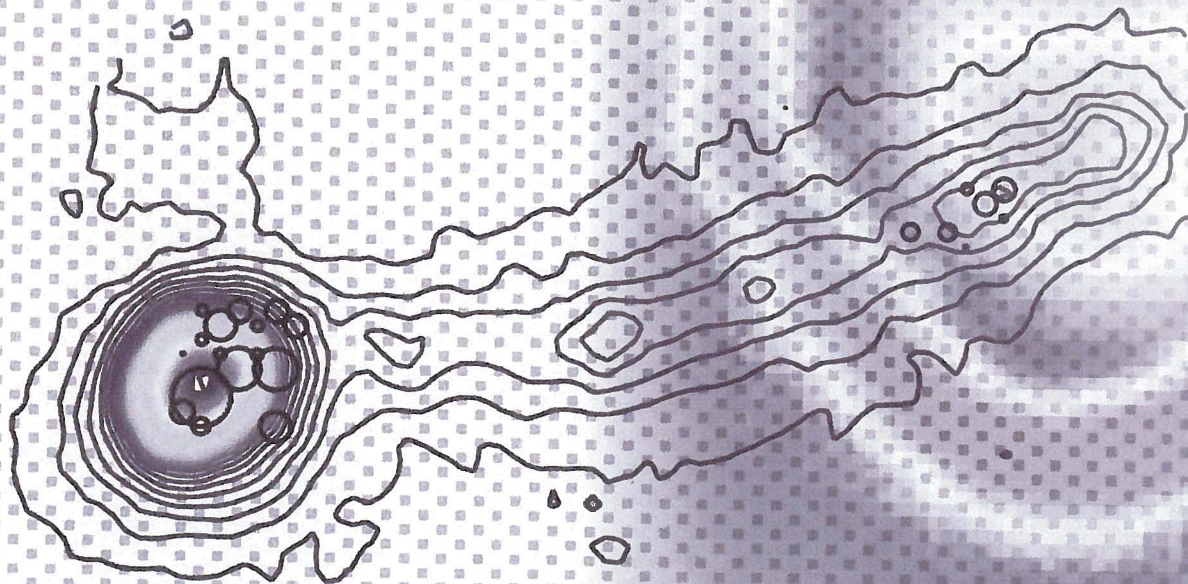

Tübingen Neurotech 2014

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Band 9

Simultaneous Electrical Investigation of Isolated Neurites Using a Neurite-Isolation Device as Neurite Regeneration Model

Johann K. Mika[1], Karin Schwarz[2], Heinz Wanzenböck[1*], Petra Scholze[2], Emmerich Bertagnolli[1]

1 Institute of Solid State Electronics, Vienna University of Technology, Vienna, Austria
2 Center for Brain Research, Medical University of Vienna, Vienna, Austria
* Corresponding author. E-mail address: heinz.wanzenboeck@tuwien.ac.at

Abstract

The understanding of how neurites are guided to each other plays an important role in neurobiology inter alia in regrowth and repair of disconnected nerve cells. In the last decades several neurotrophic factors were identified to promote neurite out-growth and guidance to target links. While the effects of neurotrophins on the molecular properties of neurites are quite well examined, the impact on the electrical functioning was nearly neglected due to the limited possibility for simultaneous recordings with patch clamp technique. Microelectrode Arrays offer a method to overcome this limitation but do not guarantee for a small electrode to neurite distance.

In order to investigate the influence of neurotrophins on the electrical activity of growing neurites we developed a device that separates the neurites from the whole culture and provide microelectrodes near them. Our approach consists of a microfluidic device aligned on top of a multielectrode array. This setup enables the simultaneous recording of neuronal activity of growing neurites through microchannels and optical investigation of the whole growing cell population at the same time. The proof-of-concept was demonstrated with the growth of sympathetic neurons from the superior cervical ganglion of P5 WT mice responding to different levels of nerve growth factor (NGF), one of the most well-studied neurotrophic factors.

Due to the microchannels which act as guidance tubes for neurites the device is capable to act as neurite regeneration model. The approach to combine the guidance tubes with a multielectrode array further helps to verify the effect of neurite growth promoters on metabolical and electrical characteristics. It also enables a universal applicable device for future studies where neurites and somata need to be treated independently of each other.

1 Introduction

The guidance and reconnection of disconnected nerve cells of the central and peripheral nervous system to a target link is currently a strong research topic in neurobiology. In the last decades, several neurotrophins were identified as proteins which induce the survival, development, and function of neurons [1]. In detail, they also promote neurite outgrowth and guidance to target cells [2]. While the effects of neurotrophins on the growth rate and molecular properties were quite well examined in the past, the impact on the electrical functioning of a whole network of neurons was nearly neglected due to the limitation of patch clamp technology. The development of multielectrode arrays by Thomas et al. 1972 [1] and finally the rise of this technology enabled neurobiologists to record nerve signals from a whole culture simultaneously.

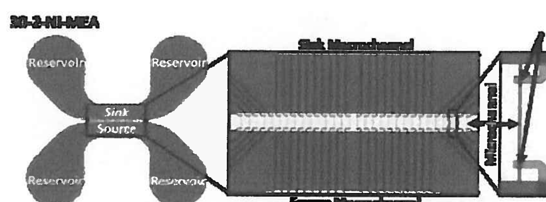

Fig. 1. Schematic drawing of the 30-2-Neurite Isolation-MEA. The NI-part consists of 4 supply reservoirs and a sink and source macrochannel (left, blue). The cells will be seeded either in the source or in both macrochannels. The 30 microchannels (blue) allow only neurites to enter whereas 2 electrodes per channel enable electrical activity recordings of the neurite.

While MEAs broke through the limitation of few electrodes, they did not guarantee a small, defined contact zone between electrode and neurite. To overcome this issue and to investigate electrical signals of multiple neurites our approach consists of a microfluidic neurite-isolation (NI-) device aligned on top of a multielectrode array. Figure 1 shows a schematic view of our device.

This setup enables the simultaneous recording of neuronal activity of growing neurites through microchannels and optical investigation of the whole growing cell population at the same time. We