Axon-Isolation Device fabricated by Nanoimprintlithography

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The capabilities of micro- and nanostructuring open a way to engineer a well-designed environment for living cells. Especially neurons are interesting from a medical as well as an engineering viewpoint as they are the key to biological signal processing. One key parameters that is still insufficiently understood is the growth of axons and how they connect to other neurons forming a powerful network.
In order to facilitate the investigation of the growth of a single axon a microfluidic structure was fabricated from silicone using a process derived from nanoimprint lithography (NIL). The microfluidic structure features so-called “macrochannels” of a size large enough for seeding the entire cells and “microchannels” with a cross-section too small for the cell soma but sufficiently large for the diameter of an axon (Fig. 1). This way the growth of a single axon can be observed and studied.
A stamp made of Si was fabricated by lithographic patterning and dry etching of a stamp structure. This stamp was used to replicate a silicone elastomere structure acting as axon isolation device (AID). The elastomer was made of PDMS and was attached to a transparent substrate. This setup allowed to optically investigate axon growth of neuronal networks. Fig 2. Shows a microscope image proving that the neurons could be successfully seeded and grown in the macrochannel. The seeding relies on a height difference between the filling chambers so that a hydrodynamic pressure gradient is resulting, that is just sufficient to distribute the cells. In the microchannels the separate growth of single axons small enough to pass these microchannels was observed.
The axon isolation device provides a valuable tool for neurobiologists to study the effect of growth factors and growth inhibitors or even to identify new substances effectively promoting the outgrowth of the axons. Further potential application of this approach for neurobiological investigations and the potential to couple this setup with analysis methods will also be discussed.

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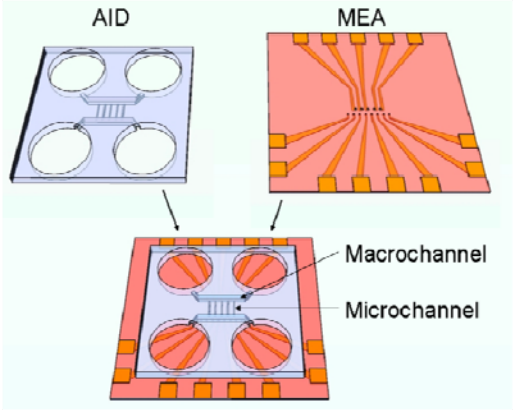

Fig. 1. Concept of PDMS structure of the axon isolation device attached to a transparent substrate with a microelectrode array

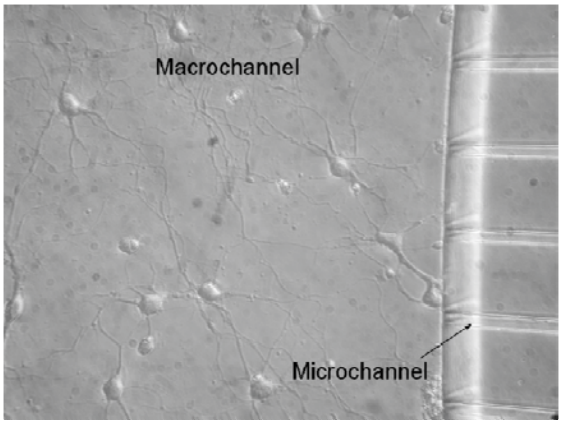

Fig. 2. Microscope image of mouse SCG neurons grown in the microfluidic structure