A polymer chip for the electrochemical detection of neurotransmitters from single cells

Larsen, Simon Tylsgaard; Taboryski, Rafael J.

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Simon Tylsgaard Larsen and Rafael Taboryski

Objective

Secretion of signaling molecules by cellular exocytosis is a key mechanism in many communication processes between living cells. Single exocytotic events can be studied by electrochemical sensing techniques using microelectrodes. The goal of this project is to develop a polymer microchip where neuroactive cells can be easily trapped near microelectrodes and to investigate the potential of the conductive polymer poly(3,4-ethylenedioxythiophene) (PEDOT) to work as microelectrode material for electrochemical detection of the neurotransmitter dopamine.

Fabrication and chip design

Microchips were made by combining two injection molded TOPAS parts. The upper part contained microfluidic channels and openings while the lower part was covered with PEDOT

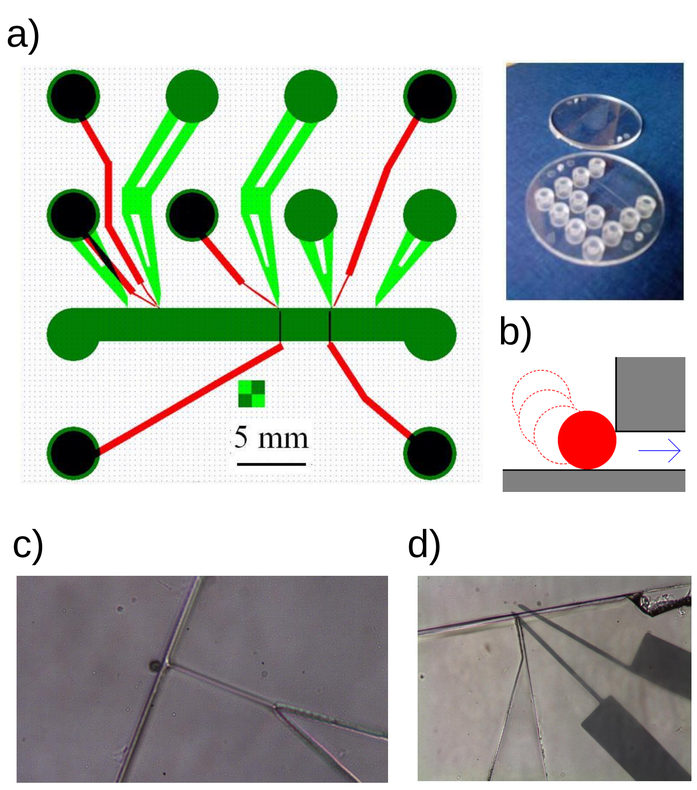

Figure 1: a) Photomask designs for microchip fabrication. Microfluidic channels are shown in green (dark green: 50 µm deep channels, light green: 5 µm deep channels). Electrodes are shown in red. The large circles are chip openings. b) Illustration of cell clamping at a “mouse hole”. The blue arrow indicates suction. c) Living PC12 cells can be trapped at the channel junctions. This microscope image shows a trapped polystyrene microbead of approximately same size as PC12 cells (r = 7,5 µm). d) Microscope image of two PEDOT electrodes aligned with a channel junction.

Electrochemical techniques make it possible to measure the concentration of signaling molecules released from living cells. Integrating these techniques on a polymer microchip would make experiments faster, easier and cheaper. In this study we present a method for trapping single cells close to conductive polymer microelectrodes inside a microfluidic channel system.

microelectrodes. Nickel mold inserts for the injection molding process were made by electroplating of SU-8 templates. The photomask design for the microfluidic channels and electrodes can be seen in fig 1a.

Cell clamping

Living neuroactive PC 12 cells were successfully trapped at a specified site inside a chip using a so-called mouse hole configuration. This configuration consists of a small channel joining a large, cell-containing channel. By applying suction to the small channel, cells can be trapped at the channel end (fig1b,c).

Microelectrodes

The electrodes were aligned with the channel junctions in a way that only the

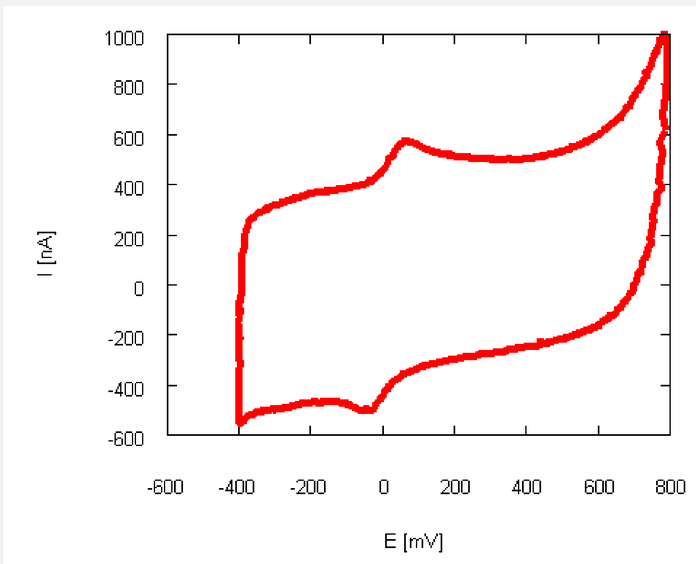

Figure 2: Cyclic voltammogram showing the oxidation and reduction of dopamine on a PEDOT electrode. Dopamine was diluted in phosphate buffer. Concentration: 2,5 x 10^{-4} M, scan rate: 200 mV/s, electrode dimensions: 50 µm X 200 µm.

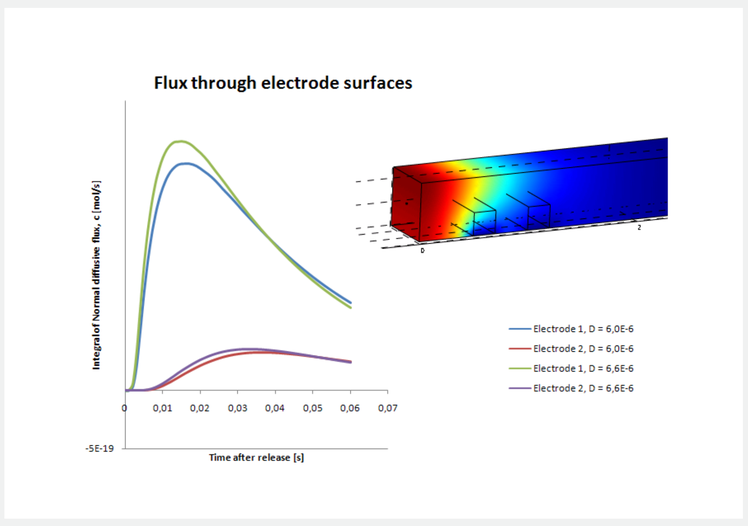

Figure 3: Comsol simulation result for instantaneous release of 100000 molecules at one end of a 5x5 micron cross-section channel. The graph shows the flux at two 2x5 micron electrodes placed 5 and 10 microns from the release site. A 10 percent change in diffusion coefficient resulted in both 10 percent change in spike delay and 10 percent change in spike rise time.

tip was exposed to the microfluidic channels. The tip was placed close to the site where the cell was trapped (fig 1d). The conductive polymer PEDOT was used as electrode material. Cyclic voltammetry experiments showed that the neurotransmitter dopamine can be electrochemically detected on PEDOT electrodes (fig 2).

Chip optimization

COMSOL simulations were used to optimize the chip design. Based on simulation results, the maximum distance between release site and electrode was estimated to be ~2 microns if an average exocytotic event from PC12 cells should be monitored with reasonable signal to noise ratio (fig 3).

Simon Tylsgaard Larsen
PhD Student
sitl@nanotech.dtu.dk

DTU Nanotech
Department of Micro- and Nanotechnology
Technical University of Denmark
www.nanotech.dtu.dk