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DTU Nanotech Department of Micro- and Nanotechnology



Microfluidic System for Long Term Culturing and Monitoring of Organotypic Brain Tissue and Cells

Tanya Bakmand, Ane R. Sørensen, Fatima A. Alatraktchi, Karsten B. Andersen, Luigi Sasso, Jan B. Gramsbergen Helle S. Waagepetersen, Winnie E. Svendsen



The aim of this project is to combine experience within tissue and cell culturing, electrochemistry and microfabrication to develop a new and innovative culturing and sensor platform that will enable researchers in neurodegenerative diseases to gain new insights into diseases and the effect of drugs, at a timescale and sensitivity that is nor accessible using the methods available today.



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Basic Tissue Requirements

(Continuous) supply of nutrients

Obtained by utilizing a flow of growth medium beneath a culturing membrane. In the preliminary experiments a flow rate of 0.3 µl/min was used.

Continuous waste removal:

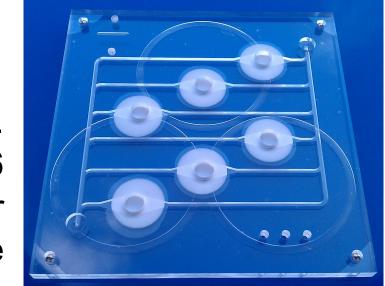
Obtained through the constant flow. It is believed that the flow utilized is low enough to prevent metabolites from building up in the system while still allowing for the presence of e.g. transmitter substances.

Environmental control:

Obtained by keeping the open fluidic device in an incubator at all times, except from occasional visual inspections or similar.

brain tissue.

To the right: Next prototype developed. Capable of parallel culturing of up to 6 individual tissue samples. Used for culturing of embryonic brain tissue for 10 days.



term culturing of embryonic

To the left: Second last prototype capable of coculturing of up to 12 tissue samples. For the newest prototype see poster by Fatima Fatima A. Alatraktchi



Drug Application

When exposing tissue or cell culture to drugs there are mainly two ways of doing it; a constant concentration over a longer timer period or (short) direct application of a limited volume. In this system both are possible:

Steady long term application:

By applying the drug in question to the growth medium before it is enters the culturing cite with the tissue samples a constant concentration of the drug can be obtained for as long as the tissue is being cultured.

Short and instantaneous application:

As this system is produced as an open fluidic system it is possible to directly apply drugs onto the tissue samples being cultured. This have the advantage of instant impact and a high degree of control.

Ideal

Materials

Transparency

All polymers used during the development of prototypes in the presented project have been chosen as based on their transparency and chemical resistance.

Bio-compatibility

The polymers used for prototyping and testing have not all been declared bio-compatible but they are non-cytotoxic.

Sterility

Initially poly(methyl methacrylate) (PMMA) was used for prototyping. It is a polymer that goes well with the fabrication method of choice (micromilling) but as it is not autoclavable it has later been replaced by cyclic olefin copolymer (COC, e.g. TOPAS) and polycarbonate (PC).

Students

Culturing

Device

Interaction with **External Equipment**

Visualization:

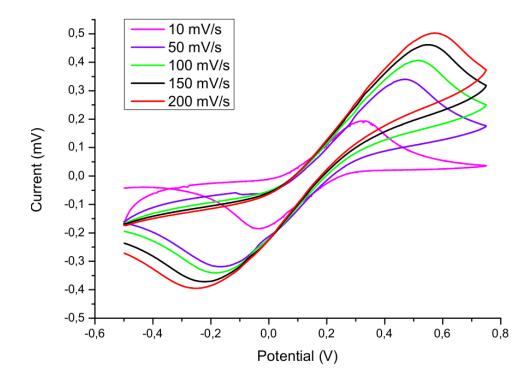
Optical microscopy is possible due to the choice of materials: Polytetrauoroethylene (PTFE) membranes that become transparent in contact with liquid and transparent polymers for the fluidic device.

Other external equipment (e.g. HPLC):

External equipment for analyzing the growth medium before and/or after it has passed the culturing cite can be integrated by inserting valves on the tubing leading to and from the device.

Electrochemical Sensor System

The electrochemical sensor system for integration into the fluidic culturing device is based on a conductive culturing membrane. The initial prototypes have been based on a metal layer on top of a standard culturing membrane, but the vision is to produce an all polymer system in the end.



Above : Cyclic voltammogram of 10 mM ferriferrocyanide obtained using one of the initial sensor prototypes consisting of a gold covered polycarbonate membrane.



Ane Rømer Sørensen



Fatima AlZahra'a Alatraktchi

Build in electrochemical sensor:

Previously work has been put in to the development of a sensor system based on metal electrodes, and detection of the neurotransmitter dopamine has been demonstrated. Currently a material study is conducted in order to find a polymer material suited for the fabrication of the build in sensor system to replace the previously used metal.



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