Microfluidic System for Long Term Culturing of Organotypic Brain Tissue

Bakmand, Tanya; Andersen, Karsten Brandt; Sasso, Luigi; Svendsen, Winnie Edith

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Tanya Bakmand, Karsten B. Andersen, Luigi Sasso and Winnie E. Svendsen

Introduction

RESEARCH in neurodegenerative diseases often utilises explanted organotypic brain tissue for experiments on the effect of various drugs and chemicals. The most widely used method for culturing brain tissue over longer time periods is the membrane interface method [1], which utilises a well plate systems situated inside a standard incubator.

In this work an open microfluidic system for long term culturing of organotypic brain tissue has been developed. The system mimics the in vivo environment of brain tissue by utilising a flow of growth medium underneath a culturing membrane to ensure an adequate supply of nutrients as well as proper waste disposal.

Materials and Methods

Fig. 1 shows an illustration of the developed culturing device. The system was realised by micromilling in poly(methyl methacrylate) (PMMA) and comprises a single fluidic channel that facilitates a flow of growth medium underneath a hydrophilic culturing membrane (JHWP01300, Millipore). A flow rate of 0.3 µL/min, regulated by a syringe pump connected to the fluidic outlet through a piece of microdialysis tubing (AgnTho's), ensures a constant supply of nutrients as well as removal of metabolic waste.

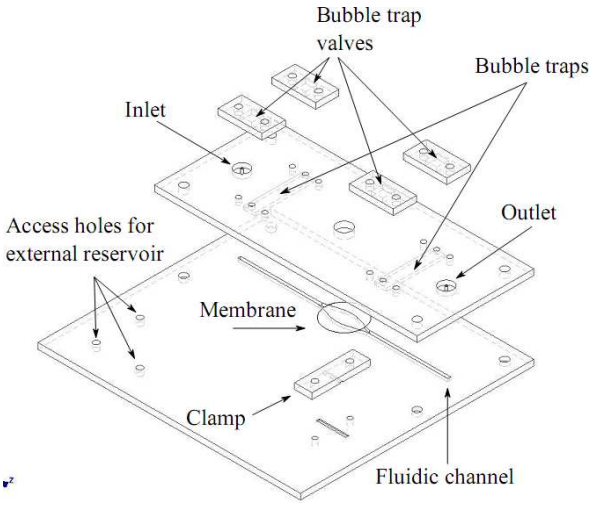

Fig. 1. Illustration of the microfluidic system developed in this work.

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T. Bakmand with the Department of Micro- and Nanotechnology, Technical University of Denmark (phone: +45 26215390; email: tanba@nanotech.dtu.dk).

K. B. Andersen with the Department of Micro- and Nanotechnology, Technical University of Denmark (karsten.andersen@nanotech.dtu.dk).

L. Sasso*Luigi Sasso*[1,2,3]

[1] MacDiarmid Institute for Advanced Materials and Nanotechnology, New Zealand

[2] Biomolecular Interactions Centre and School of Biological Sciences, University of Canterbury, Christchurch, New Zealand

[3] DTU Nanotech, Department of Micro- and Nanotechnology, Technical University of Denmark, Lyngby, Denmark

W. E. Svendsen with the Department of Micro- and Nanotechnology, Technical University of Denmark (Winnie.Svendsen@nanotech.dtu.dk).

The system features two bubble traps, each with a pair of active valves for sterilisation and release of excess air originating from air bubbles. A valve consists of a piece of square PDMS fixated in a matching cavity in a piece of PMMA to be screwed on top of a hole in a bubble trap, see Fig. 1 and 2.

Fig. 2 shows a picture of a finished fluidic prototype utilised for culturing of embryonic brain tissue, including a lowered reservoir preventing flooding of the culturing membrane during culturing. The culturing was performed over three weeks in a standard incubator facilitating a constant temperature, humidity and CO_2 level.

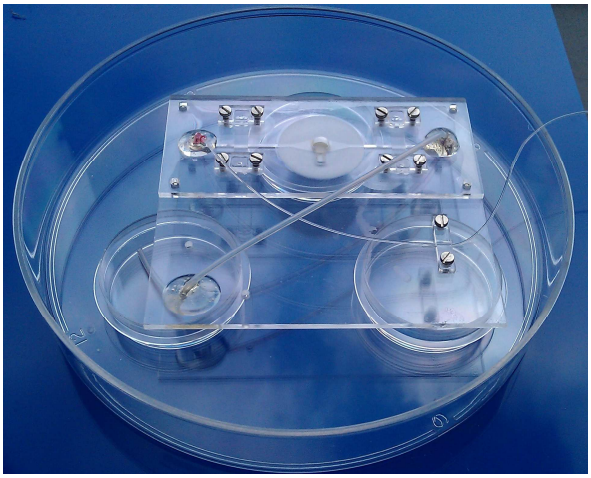

Fig. 1. Picture of the microfluidic system utilised for culturing of embryonic mouse brain tissue over the course of three weeks.

Results

In this work a microfluidic system for long term tissue culturing was developed and the appropriability of the system was demonstrated by culturing a piece of embryonic brain tissue over the course of three weeks.

References

[1] L. Stoppini, P.-A. Buchs and D. Muller. (1991). A simple method for organotypic cultures of nervous tissue. *Journal of Neuroscience Methods.* 37. pp. 173-182.