Brain on a microchip for multiple sclerosis

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What is the problem?

Multiple sclerosis (MS) is the most common long term neuroinflammatory disease that affects the central nervous system. It is estimated that there are over 125,000 people living with MS in the UK, with Scotland having the highest rates. Worldwide, the estimate of people living with MS is about 2.5 million.

MS is not fatal but it dramatically reduces the quality of life of those affected, who have trouble with walking, bad eyesight and tiredness. Currently, therapies only focus on the inflammatory aspect of MS but new therapies need to be developed that target the neurodegenerative aspect of MS.

Healthy neurons (nerve cells) can be likened to electrical cables with the axons of the neurons, which transmit messages by way of electrical signals to and from the brain to the rest of the body, akin to the wire. The axons are covered by a sheath of myelin that acts like a cable's outer plastic insulation (see Figure 1). Myelin is needed for effective transmission of nerve signals and in MS the myelin sheath is damaged, resulting in messages from the brain not being transmitted effectively.

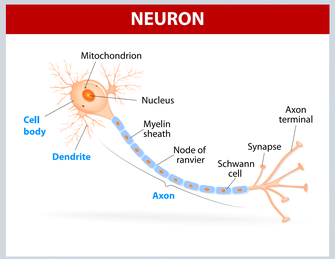

Figure 1 A neuron (nerve cell). Image source: Shutterstock created by Designua (https://www.shutterstock.com/image-vector/anatomy-typical-human-neuron-axon-synapse-163939142?src=8sahUOI9NCbJJ5RIl_SRxA-1-28).

What am I interested in?

I want to develop a device that will allow us to assess how much myelin is on human neurons grown in the device in the lab. Such a device would allow us to test possible new treatments for MS, which are designed to encourage the production of new myelin around damaged neurons.

I want to assess the levels of myelin by detecting electrical signals transmitted by the neurons, so I need:

i) to develop a way to grow human neurons in the device for long enough for them to mature and become electrically active (at least 6 weeks);

ii) to design a way to stimulate the neurons to 'fire' an electrical signal (using a stimulating electrode); and

iii) to design a way to record the transmitted signal (using a recording electrode).

I want the device to have miniature channels which will enable me to position the neurons' cell bodies (which will be stimulated) at one end of the device and for the axons (see Figure 1) to grow along the length of the channels towards the other end of the device, where I can record transmitted signals.

By measuring the speed at which the electrical signals are transmitted from one end of the neurons to the other I will be able to get an indication of the amount of myelin on the axons. I can determine the speed by knowing the distance between the stimulating and recording electrodes and the time it takes for the signal to travel between the two electrodes.

What did I do?

I put together a set-up to allow me to record signals from 16 different sources, simultaneously. My current set-up consists of a digital acquisition system, DC power supply to control the temperature as well as the microscope and a 16 channel amplifier (see Figure 2).

Before making my device, I used commercially available multielectrode arrays (see Figure 3a) and a custom recording device which I had designed (see Figure 3b) to make sure that my set-up was functioning reliably and that I could record signals from the arrays. I used mouse cells at this stage of developing the device because they are easier to grow in the lab than human neurons – they grow much faster and produce spontaneous electrical signals.

I have also been developing a way to grow human neurons in the commercial device and in my new device. I have used a type of cell called a neural stem cell, which can develop in to lots of different types of cell found in the nervous system, and I have persuaded these cells to grow into the type of cell which I am particularly interested in, called cerebral cortical neurons.

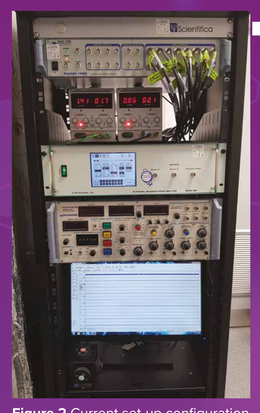

Figure 2 Current set-up configuration.

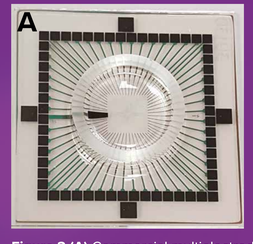

Figure 3 (A) Commercial multielectrode array and **(B)** top view of recording device showing a common single ground (reference) point (black and white cables) and inputs from each side.

What did I find?

When I tested my set up with mouse cells I was able to obtain electrical recordings from them after they'd been grown in the commercially available device for 48 hours (see Figure 4), so I know that my recording set up works.

I have been able to design my device so the miniature channels are large enough to allow the axons to pass through into the second compartment, but small enough so as not to allow the cell bodies to pass through. This means that I can stimulate the cell bodies and record the signals from the axons separately. I was able to do this by making the channels in polydimethylsiloxane (PDMS) (see Figure 5).

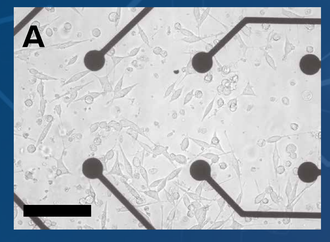

Figure 4A Mouse cells cultured for 48 hours on commercial electrode array. Scale bar = 100µm (1µm = a thousandth of a mm).

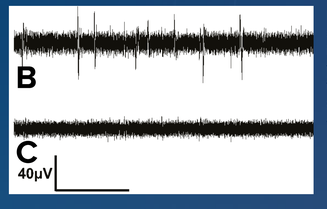

Figure 4B Electrical activity and **(C)** inactivity recorded from the cells after they had been grown for 48 hours.

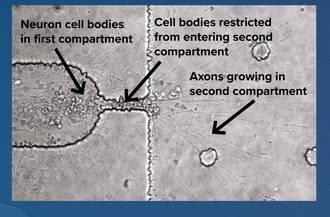

Figure 5 Human neurons grown in my device. The cell bodies, on the left, are restricted by 10µm (10 thousandths of a mm) channels from entering the second compartment on the right.

What does this mean?

In order to design a device that can be used successfully to test possible new MS treatments, I need to perfect the surface properties of the device to enable long term (over 6 weeks) growth of human neurons. I am currently working on a way to do this and hopefully I will soon be able to obtain recordings to determine the amount of myelin on my neurons.

Who am I?

I am currently in the third year of my PhD at Heriot-Watt University in Dr Euan Brown's electrophysiology group. I undertook my BSc (Hons) and MSc by Research in Biological Sciences and Biomedical Sciences at Heriot-Watt University and the University of Edinburgh, respectively.

Kyriakos started his PhD project entitled *'Bioengineering a novel neuronal medical device for Multiple Sclerosis studies'* in 2015 and while principally based at Heriot-Watt University, supervised by Dr Euan Brown, he is also working closely with Epigem Ltd.