Developing a nerve/electronic interface.

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Project Abstract
Interfacing electronics with the nervous system is a rapidly developing field with many potential applications. The Fawcett group has developed the first practicable method of interfacing with axons in the peripheral nervous system, based on nanotech-derived microchannel recording arrays. Until very recently it has not been practicable to record sensory or motor information from axons in peripheral nerves because the extracellular potential change from action potentials is very small and submerged in noise. This occurs because the ionic current through the membrane is tiny, the extracellular resistance is tiny, so by Ohms law (v=ir) the extracellular voltage change is minute. Enclosing groups of axons in microchannels 100um diameter by 3-5mm in length increases extracellular resistance, amplifies the voltage and allows noise suppression by placing guard electrodes at the channel ends (FitzGerald et al. 2012). Using this microchannel design the lab has achieved long-term stable recording of bladder fullness and emptying as part of an electronic method for bladder control in spinal injury patients (Chew et al. 2013, Granger et al. 2013). Long-term recordings have also been achieved in upper limb nerves, giving sensory information and motor information, both of which could be used to restore limb control or control of a prosthetic limb (FitzGerald et al. 2013).

The project will have two aims: 1) Suppression of the inflammatory foreign body reaction that currently limits microchannel interface effectiveness to 18 months; 2) Develop methods for inserting microchannel interfaces into splanchnic nerves, for control of gut, immune system and hormonal secretion.

1) Foreign body reaction.
As with most materials inserted into the body, a chronic macrophage-driven inflammatory response develops at the surface of the microchannel implant. This leads to a slow build up of scar-like thickening of the nerve sheaths within the microchannels, eventually leading to compromise of the axons and myelin. After 18-14 months many microchannels lose most of their axons.

The project will investigate two methods of overcoming this:
A) The microchannel arrays will by microfabricated to include microfluidic compound delivery channels, so that immunosuppressive substances can be delivered to the microchannels. The first experiments will deliver IL-4 and/or IL-13 to change the macrophage reaction from M1 inflammatory type to M2 healing type. Compounds to manipulate the TGFbeta pathway will also be tested.

B) Our current work has shown that a major cause of the inflammatory reaction of macrophages/microglia is the relative hardness of implanted devices. By matching the compliance of the surface of the device to that of the
surrounding cells, the foreign body reaction is suppressed. Our collaborators at EPFL are creating various types of compliant surface, which will be tested in vivo for effects on the foreign body reaction.

2) Interfacing with different nerve types. Our current work has developed interfaces with limb nerves and bladder nerves. A future opportunity for medicine is control of homeostatic processes via electronics. The project will develop methods for inserting microchannel arrays into the vagus and other splanchnic nerves, with the aim of recording activity and developing closed-loop electronic control strategies for controlling gut, immune and endocrine function.

The project involves collaboration with the Lacour group at EPFL (microchannel nanotechnology), the Donaldson group at UCL (electronic controls and communication), and GSK (control of homeostatic mechanisms).


