Refinement and Validation of Primary Myelinating Neural Cell Cultures for In Vitro Assessment of Neural Interface Materials

Abstract
Intracortical electrodes for motor control of prosthetics rely on intimate contact with neural tissue for recording signals and stimulating neurons. In vivo approaches for evaluating responses to intracortical devices are complex and prone to adverse events. In vitro models are one alternative to in vivo studies. However, existing models have several limitations which restrict the translation of the cellular reactions to the in vivo scenario. Most notable is no current model includes the four principle cell types critical to the health and function of the central nervous system (CNS). This work investigates the utility and limitations of a primary dissociated mixed myelinating cell (DMMC) culture to model in vivo wound healing responses to biomaterials. The DMMC culture contains biologically relevant ratios of astrocytes, microglia, neurons and oligodendrocytes. The reaction of the DMMC to platinum and a conducting polymer with known in vivo compatibilities were assessed. Whilst, the DMMC was able to yield some insight into relevant cell-material interactions the culture was not robust. However, it was a significant improvement over the clonal cells. To improve the reliability and relevance of the DMMC for recapitulating CNS wound healing a co-culture model using mature mixed glial cells (MGC) was proposed. It was hypothesised that the MGC would improve the attachment and differentiation of the DMMC in control conditions. In adverse conditions the MGC would become reactive and impede the development of the DMMC. The co-culture improved the reliability of the DMMC and revealed clear material specific cellular reactions to the materials. However, the co-culture methodology took up to 63-days before material-specific reactions could be identified. To address this limitation, two alternative co-culture methods were proposed, a layered and a combined method, which reduced the culture time to 35 and 25 days respectively. These models were evaluated for their ability to model the mature CNS and for their ability to model acute implant injury. The combined co-culture showed the most similarity to the CNS and was able mimic several aspects of the acute implant reactions.

About Aaron Gilmour
Aaron Gilmour recently completed his PhD in biomedical engineering at UNSW. He completed his BSc (Psychology and Physiology) and MSc (Physiology) at Massey University (New Zealand). His work focuses on the development and analysis of complex in vitro models of the mammalian CNS for studying how biomaterials might impact neural network development and wound healing in the brain.