Carbon Nanotube-Based Implantable Neural Interfaces

Elissa Grzincic Literature Seminar February 28, 2013

The human nervous system is composed of highly complex networks of nerve cells (neurons), which communicate with each other via electrical signals. Modulation of these electrical signals with man-made electronics can help reinstate neuron communication to improve the condition of patients with diseases such as Alzheimer's disease, Parkinson's disease, schizophrenia, epilepsy and depression and those with loss of hearing or sight.[1] Recording the neuronal signals can assist those with spinal cord injuries to control external devices with volitional thought and can advance research on the basics of neuroscience.[2] Electrodes used to stimulate or record electrical signals in neural tissue are known as neural interfaces or neural electrodes (NE). Some current designs of NE for the central nervous systems are shown in Figure 1. The successful clinical use of NE depends wholly on the ability of the electrode to integrate with the neurons of the brain.

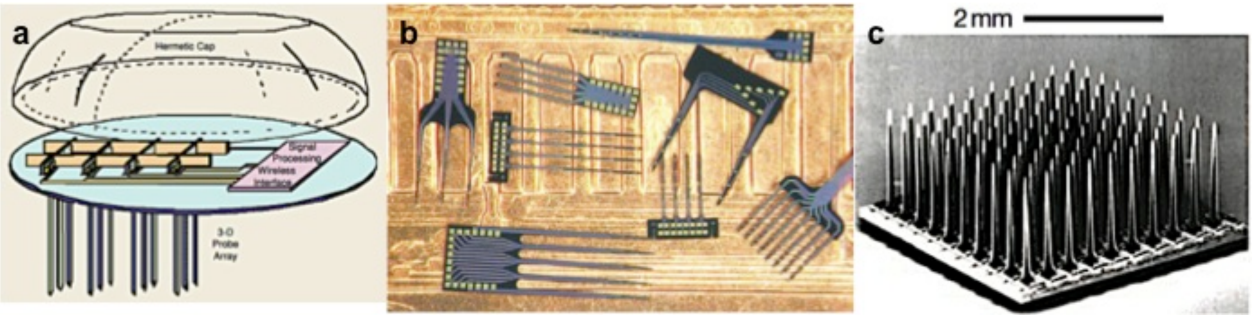

Figure 1: (a) Design for ideal implantable electrode system includes 3D electrode arrays attached to a platform on the cortical surface, where signal processing and wireless communication electronics are located.[3] (b) Examples of silicon probes for electrode systems on the back of a U.S. penny.[3] (c) The Utah Electrode Array design consists of 100 sharp silicon electrodes on a 4 mm x 4 mm substrate.[2]

Great progress has been made in this research area since it's beginning, but some consistent problems have been realized along the way. Although many current devices can work rather well for short periods of time after implantation, chronic or long-term use of neural electrodes has been difficult to achieve. The main reasons for this are 1) degradation of the electrode, 2) using large electrodes to attain sufficient signal-to-noise ratio during recording, and 3) the brain's immune response to implantation over time.[1, 4,5] It is also important that the electrode interact well with the neurons to integrate as seamlessly as possible into the biological environment as possible.

Carbon nanotubes can be utilized to address the most important issues limiting the long-term use of neural electrodes. The unique combination of electrical, mechanical and nanoscale properties of carbon nanotubes (CNT) make them very attractive for use in NE. CNT are nanoscale, strong, tough, flexible, biocompatible and non-faradaic while also having both high electrical conductivity and high surface area.[6,7,8] Correct integration of CNT into NE devices could simultaneously overcome the problems identified easily, cheaply and safely. I chose to focus on ways that CNT can allow for the use of smaller electrodes by reducing impedance, thus improving signal-to-noise ratios[9], and on ways that CNT improve the biological response to neural electrodes. Studies on CNT for neural interfaces are prevalent in scientific literature in the past few years and the studies range from forming different CNT coatings or composites on metal electrodes to growing full electrodes purely from CNT.[10]

Edward W. Keefer and colleagues was the first group to electrically characterize different coatings made with CNT on electrodes and do recording studies.[11] They showed how CNT can help improve the electrode performance during recording. By starting off with planar microelectrode arrays coated in an electrodeposited CNT-gold coating, they were able to show that the CNT lowered the impedance by a factor of 23, increased the charge transfer by a factor of 45 and decreased noise by 65%, when compared to the uncoated indium-tin oxide electrodes. After plating neurons on top of the planar electrode arrays during an *in vitro* experiment and stimulating the neurons with electrical pulses, the threshold for stimulated response recording was decreased by about 530 mV after coating with CNT (Figure 2a). This means that the electrodes could detect smaller signals from the neurons.

The group then moved onto sharpened electrodes for actual *in vivo* experiments.[11] These electrodes were either tungsten or stainless steel and three different CNT coatings were tested. The CNT-gold coating on sharp tungsten and stainless steel compared to the coating on the planar electrodes. CNTs covalently attached to tungsten electrodes increased charge transfer 140-fold and CNT-polypyrrole composite coatings on stainless steel increased charge transfer 1600-fold. The CNT-gold coating on sharp stainless steel electrodes implanted into rat brains greatly increased the recording signal from the bare electrode, as seen in Figure 2b. These results indicate that CNT coatings are promising for improving electrode performance during recording by decreasing impedance, increasing charge transfer and increasing signal-to-noise ratio.

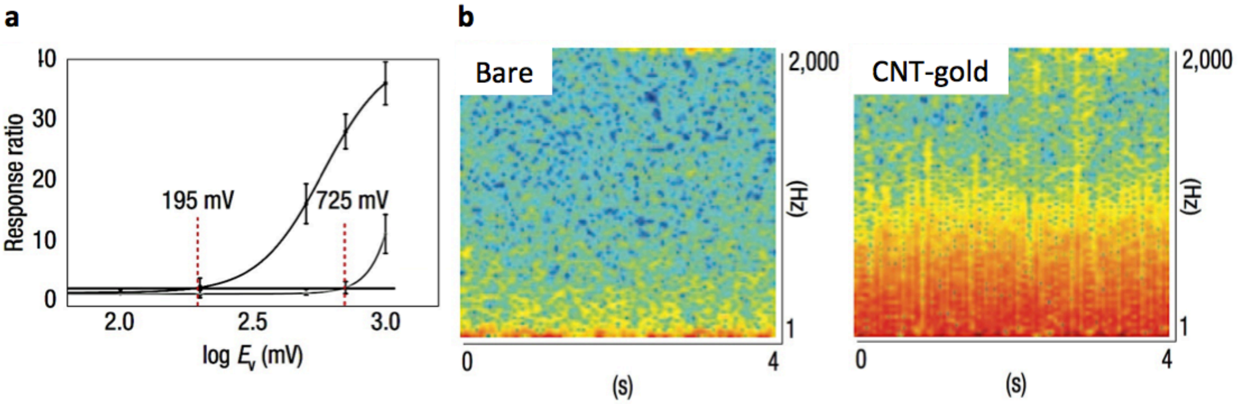

Figure 2: (a) CNT-gold coatings on planar indium-tin oxide microelectrode arrays lowered the threshold for stimulated response from cultured neurons versus bare arrays.[11] (b) CNT-gold coating on sharp stainless steel electrodes increased the recording signal when implanted into rat brains.[11]

Biologically, CNT coatings and electrodes are better choices for integration with brain tissue that materials like metals. CNTs are not only biocompatible in robust coatings, but they are supportive to neuron growth and adhesion. It has been found that the CNTs actually promote neurite growth, neuronal adhesion and viability of cultured neurons under traditional conditions.[12,13,14] The nanoscale dimensions of the CNT allow for molecular interactions with neurons and the nanoscale surface topography is ideal for attracting neurons.[9,15] In fact, they have been shown to improve network formation between neighboring neurons by the presence of increased spontaneous postsynaptic currents, which is a widely accepted way to judge health of network structure.[13] Additionally, functionalization of CNT can be used to alter neuron behavior significantly.[16]

In terms of the brain's immune response, CNT have been shown to decrease the impact of the implanted electrodes. Upon injury to neuronal tissue, microglia (the macrophage-like cells of the nervous system) respond to protect the neurons from the foreign body and heal the injury, and astrocytes change morphology and begin to secrete glial fibrillary acidic protein to form the glial scar.[1,17] This scar encapsulates the electrode and separates it from the neurons it is there to interface with.[18,19] However, carbon nanomaterials have been shown to decrease the number and function of astrocytes in the brain, which in turn decreases the glial scar formation.[18,19]

In these ways and others, CNTs have been shown to be ideal for integration into neural interfaces. The next step is to try to combine the techniques for making these CNT-based electrodes to decrease the relevance of all three issues discussed. Some problems need to be addressed such as experimental inconsistency and the probability of toxicity due to CNT dispersion from coatings. The future directions of this field include elucidation of the mechanism behind NE therapeutics, long-term studies to determine if CNT-induced changes in neuron behavior are harmful and if the changes are reversible, and better separation of metallic and semiconducting CNT for even better electrodes.

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