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Advanced materials for neural surface electrodes

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ABSTRACT

Designing electrodes for neural interfacing applications requires deep consideration of a multitude of materials factors. These factors include, but are not limited to, the stiffness, biocompatibility, biostability, dielectric, and conductivity properties of the materials involved. The combination of materials properties chosen not only determines the ability of the device to perform its intended function, but also the extent to which the body reacts to the presence of the device after implantation. Advances in the field of materials science continue to yield new and improved materials with properties well-suited for neural applications. Although many of these materials have been well-established for non-biological applications, their use in medical devices is still relatively novel. The intention of this review is to outline new material advances for neural electrode arrays, in particular those that interface with the surface of the nervous tissue, as well as to propose future directions for neural surface electrode development.

1. Introduction

Great strides have been made over the past decade in the field of neuroscience, leading to ground-breaking technologies, such as optogenetics, for the study of neural circuits and mechanisms [13]. These novel methods not only have revolutionized neural research, but have also opened up new opportunities for neural interface technology. These opportunities, however, come with new specific requirements and challenges. The ability to use optogenetics to stimulate neurons with light allows for precise, controlled activation of specific cell groups [9]. However, exploitation of this technique to its fullest potential, particularly for biomedical applications, requires devices that can be implanted into 3D tissue and animal models. To ensure that the devices can function well for optogenetic application there are several fundamental elements needed, such as incorporation of both light stimulation and transparent recording electrodes, through which light be transmitted. In addition to electrophysiological research, neural interfaces are also useful for a variety of therapeutic applications, including epilepsy mapping, neural prosthetics, deep brain stimulation, pain management, and brain–computer interfacing [4,52,40,38,15]. As the medical understanding of neurological disorders continues to expand, newer and better therapeutic devices must be fabricated for symptom management. Thankfully, advancements in materials science and thin film technology have kept pace with those in the medical field and allowed for the development of smaller, more transparent and more biocompatible neural electrode arrays [29].

Several different types of electrode arrays can be used for neural interfacing, ranging from invasive devices which penetrate into nervous tissue to completely non-invasive electrode caps worn over the skin [20,36]. Although the most invasive devices, such as traditional silicon intracortical probes, provide the highest signal resolution due to their proximity to nerve cell bodies, there is a large trade-off between recorded signal quality and device biocompatibility [53,14]. The primary drawback to these types of devices is that the significant scar tissue formation around the implants often renders them unusable within a short time period after implantation [41]. On the other hand, the most minimally invasive electrode arrays are those that do not penetrate the body at all, such as electroencephalography (EEG) grids worn over the scalp. These devices do not cause any tissue trauma, but the information contained within the recorded signals is significantly degraded by the amount of bone and skin tissue through which the signals have to travel [33]. To develop an implant that will ultimately be acceptable for long-term human use, it is necessary to strike a balance between the invasiveness of the device and the quality of the recorded signals. For this reason, surface electrode arrays, which are implanted within the body but rest atop the neural tissue rather than penetrating into it, have been developed. Examples of these types of devices include electrocorticography grids for recording from and stimulation of the cerebral cortex,

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as well as nerve cuff electrodes, which wrap around peripheral nerves [33,34,46,57].

In order to conform to the non-uniform, curvilinear exterior of neural tissues, such as the cerebral cortex and peripheral nerves, surface electrode arrays must be composed of flexible materials. This means that the substrates of these devices are generally polymeric in nature, due to the intrinsic dielectric and mechanical compliance properties of these materials [19]. Traditional intracortical electrode arrays require rigid substrates, such as silicon, for insertion into neural tissues, but the mechanical impedance mismatch between the soft brain tissue and the stiff devices can cause a large amount of the tissue trauma contributing to glial scar formation [41,48,14]. Therefore, an added benefit of the flexible substrates required for surface electrode arrays that conform to neural structures is that they also allow these devices to move and bend with the soft surrounding tissues, rather than slicing through them. Thus these flexible devices are often more biocompatible in terms of both invasiveness and rigidity.

As previously mentioned, the proximity of neural interfaces to the structures from which they are recording is a crucial factor contributing to the quality and resolution of the acquired signals [53,14]. However, in order to obtain a more biocompatible interface with nervous tissue, which will lead to more stable signal recordings over the long-term, less invasive implants are required. Since neural cell bodies primarily lie in the deeper layers of the cortex and peripheral nerve axons are contained within several layers of connective tissue sheaths, there is an inevitable sacrifice of signal information when shifting to a surface neural recording or stimulating modality. Although this loss of signal resolution is unavoidable, it does not prohibit the use of surface electrode arrays for tasks which require high-information signals to decode user intent, such as brain–computer interfacing and neural prosthetic control [37,63]. In fact, several studies have been performed which validate the employment of micro-electrocorticography (micro-ECoG) surface arrays for such applications [21,32,49].

The validation of surface electrode arrays for neural interfacing tasks has triggered a sea of investigation into developing more advanced, but minimally invasive devices to match the new requirements of the field. This review aims to outline these cutting edge technologies as well as to look forward and propose future directions for the advancement of neural interfaces as tools for research and medical therapy.

2. Current state of the art

State of the art neural surface electrodes aim to incorporate increased biocompatibility with the tools necessary for performing electrophysiological experiments using modern research techniques. Here, we discuss examples of new technologies for enhancing device biocompatibility and function in terms of the novel design modifications employed.

2.1. Open architecture and dissolvable device substrates

One method for reducing the tissue response to implanted medical devices is to minimize the amount of foreign material present. This has been demonstrated in the neural field with histological studies of the cellular response to open-architecture intracortical devices [54]. Through these studies, it has been discovered that not only does the presence of holes through implanted microelectrode arrays allow for tissue integration, but also for diffusion of neural chemicals from one side of the device to the other, another crucial factor for maintaining normal signal transduction and cell health [41,45,47].

Recently, researchers have begun to adopt more open substrate geometries for neural surface electrodes as well. Schendel et al. have developed a 'mesh' micro-electrocorticography (micro-ECoG) grid with individually insulated electrode sites and traces to allow for maximum tissue integration [50]. A comparison of the tissue response to the mesh micro-ECoG array and a standard micro-ECoG array with a single solid Parylene substrate encapsulating all of the electrode sites revealed that a collagen scar tissue formed around both arrays (Fig. 1), but the distribution of the scar tissue around the devices varied. In the case of the mesh device, the tissue grew thinly beneath the array, between the device and the brain, but thickened on top of the array, between the device and the cranial window (used for *in vivo* imaging of the tissue response). Conversely, in the case of the solid device, the tissue grew thick between the device and the brain, but thinly, or sometimes not at all, on top of the device. The dispersion of tissue growth found around the mesh devices was more favorable for neural interfacing applications, since minimization of the amount of material between the electrode sites and the brain is vital to attain maximum recorded signal quality. The results of this study demonstrated that, as has been reported for intracortical devices, open-architecture substrate geometries, similar to the mesh array, are more favorable than traditional solid designs.

Kim et al. have also recognized the benefits of a mesh-like neural surface electrode array, but have taken the idea a step further by not only minimizing the surface area of the substrate material, but also its thickness [27]. As in the case of penetrating electrode arrays, surface devices require a sufficient degree of structural integrity for handling during processing and implantation. However, this mechanical stiffness is not necessary for the function of the device *in vivo*, and in fact can be disadvantageous, causing an increased amount of pressure on neural tissue, which can have harmful effects. Additionally, the increased structural integrity required for device handling results in a decrease in flexibility, diminishing the ability of these devices to conform to non-uniform tissue surfaces. To create a device with adequate mechanical stability to withstand the required processing and implantation procedures, but maximum flexibility to enhance conformity with neural structures, Kim et al. employed the use of a dissolvable silk matrix. This matrix was adhered to a mesh-type micro-ECoG array with a very thin (~2.5 μm) polyimide (PI) layer insulating the traces. The silk matrix was robust enough to permit precise implantation of the electrode arrays over the feline visual cortex,

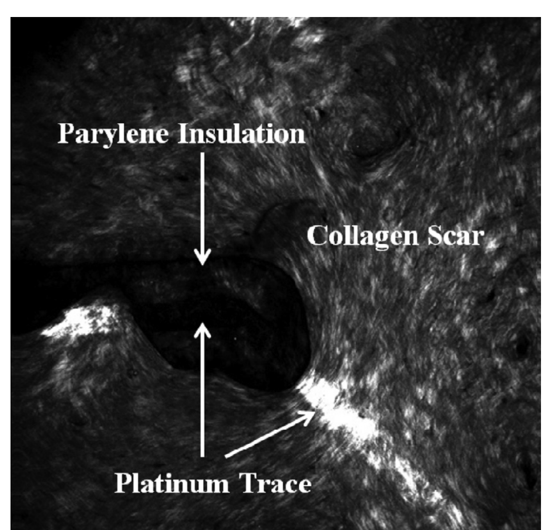

Fig. 1. Second harmonic generation (SHG) image of collagen scar tissue surrounding the trace of a "mesh" micro-ECoG device.