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14th International Conference on Nanomaterials and Nanotechnology, March 30-31, 2017 | Madrid, Spain-Nano-Architectural Approaches for Improved Intracortical Interface Technologies

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Intracortical microelectrodes (IME) are neural devices that initially were designed to function as neuroscience tools to enable researchers to understand the nervous system. Over the years, technology that aids interfacing with the nervous system has allowed the ability to treat patients with a wide range of neurological injuries and diseases. Despite the substantial success that has been demonstrated using IME in neural interface applications, these implants eventually fail due to loss of quality recording signals. Recent strategies to improve interfacing with the nervous system have been inspired by methods that mimic the native tissue. This review focusses on one strategy in particular, nano-architecture, a term we introduce that encompasses the approach of roughening the surface of the implant. Various nano-architecture approaches have been hypothesized to improve the biocompatibility of IMEs, enhance the recording quality, and increase the longevity of the implant. This review will begin by introducing IME technology and discuss the challenges facing the clinical deployment of IME technology. The biological inspiration of nano-architecture approaches will be explained as well as leading fabrication methods used to create nano-architecture and their limitations. A review of the effects of nano-architecture surfaces on neural cells will be examined, depicting the various cellular responses to these modified surfaces in both in vitro and pre-clinical models. The proposed mechanism elucidating the ability of nano-architectures to influence cellular phenotype will be considered. Finally, the frontiers of next generation nano-architecture IMEs will be identified, with perspective given on the future impact of this interfacing approach. Intracortical microelectrodes (IME) were initially designed for research purposes to enable researchers in the late 1930s an ability to improve the understanding of the nervous system. The first clinical use of neural electrode technology was in 1985, when the FDA approved the use of cochlear prosthetics. Since then, clinical implementation of IME has been employed to treat patients with numerous neurological diseases and injuries, such as amyotrophic lateral sclerosis (ALS) and spinal cord injuries. Unfortunately, an impediment preventing the clinical deployment of IME technology is the complex inflammatory response occurring after electrode implantation, leading to decreased recording quality. The initial insertion of IME produces an injury in the local brain tissue, breaching of the blood brain barrier (BBB), eliciting an influx of chemical and biological markers, resulting in an inflammatory response. The early failure of IME has instigated substantial research in the development of next generation electrodes. There are numerous types of IME, such as silicon microelectrode arrays, metal micro/nano-wires, carbon nano-tubes (CNTs), and conductive polymers, which have been categorized by their backbone material. Nevertheless, biomimetic alterations and advancements have inspired the design of the most recent IME technology. Engineers and scientists reason that biomimetic alterations to create new electrodes that reflect the properties of the brain will allow for better biocompatibility of the implants in vivo, which may lead to improved quality and longevity of recordings have developed stretchable electrode grids that allow for high density and high-quality chronic recordings, which reflect the modulus of the brain better than

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either traditional metal or silicon-based electrode-shave created a flexible electrode grid, neural mesh that, once injected into the brain, unfolds and is able to record freely moving rats with stable recording quality and coherence chronically. This neural mesh is able to follow micro-movements in the brain caused by mechanical movements of the subject or growth, decreasing chances of neural shear damage, and allowing long-term recording. The latter innovation has gained significant interest, most notably, Elon Musk's company Neuralink, has also created a similar neural mesh, called neural lace, which will allow human integration with artificial intelligence.

Amidst the variety of biomimetic electrode types, we introduce the concept of nano-architecture in this review as a class of biomimetic surface alteration for IMEs. We use the term nano-architecture to encompass all topographical surface modifications, such as nano-grooves, nano-pillars, nano-fibers, and materials with inherent structural components. The inspiration of creating nano-architecture on IME surfaces is based on the architecture of the brain, specifically the extracellular matrix (ECM). The ECM is composed of a 3D and high-aspect ratio. The 3D environment allows cells to have topographical cues which will allow them to differentiate and perform their specific functions. Several studies have shown that surfaces that can mimic the architecture of the natural in vivo environment will consequently result in an improved biocompatible response. Nano-architecture substrates indicate increase in initial protein adsorption, thus leading to subsequent attachment and proliferation of cells. Alignment of neuronal cells in the brain has also been shown to depend on the roughness and direction of the substrate surface patterns. Although the exact mechanism is not completely understood, it is thought that nano-architecture is able to indirectly guide the growth and alignment of neurons. Which is beneficial for IME implementation, since enabling neuron growth and proliferation near the implant may allow for improved recording quality. In addition to changes in morphology and protein adhesion, nano-architecture has also been implicated in changes to cell differentiation, phenotype, and gene expression.

The goal of the subsequent sections of this review will be to emphasis the role of the architecture with protein and cell interactions, specifically with the central nervous system cells, in order to convey the rationale behind nano-architecture approaches. The biological inspiration of nano-architecture approaches will be explained as well as leading fabrication methods used to create nano-architecture and their limitations. We will then explore the effects of nano-architecture surfaces on neural cells, depicting the various cellular responses to these modified surfaces in both in vitro and pre-clinical models. The proposed mechanism elucidating the ability of nano-architectures to influence cellular phenotype will be considered. Finally, the frontiers of next generation nano-architecture IMEs will be identified, with perspective given on the future impact of this interfacing approach. In order to convey the rationale behind nano-architecture approaches, an understanding of the brain's ECM is crucial. The brain's ECM is made up of components created by the cells within it: neurons, astrocytes, oligodendrocytes, and microglia. There are three main ECM components, the basement membrane (basal lamina), the perinueonal net, and the neural interstitial matrix. The basement membrane, which lies around the cerebral vasculature, is composed of laminin, collagen IV, nidogen, and heparin sulfate proteoglycans.