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Recent advances in neural electrode–tissue interfaces

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Abstract

Neurotechnology is facing an exponential growth in the recent decades. Neural electrode-tissue interface research has been well recognized as an instrumental component of neurotechnology development. While satisfactory performance was demonstrated in some applications, such as cochlear implants and deep brain stimulators, more advanced devices requiring higher resolution for recording or microstimulation still face significant challenges in reliability and longevity. We review the most recent findings that shed light on the sources of poor reliability and longevity in neural electrodes, including the material failure, biological tissue response and the interplay between the two. We introduce newly developed characterization tools from electrophysiology models, molecular and biochemical analysis, material characterization to live imaging. Effective strategies for improving the interface are also highlighted. Finally, we discuss the challenges and opportunities in improving the interface and achieving seamless integration between the implanted electrodes and neural tissue both anatomically and functionally.

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Introduction

Neurotechnology is facing an exponential growth in the recent decades thanks to the advances demonstrated by brain machine interface human trials and clinical successes in neuromodulation therapies. A core component of neurotechnology involves invasive electrode devices interfacing directly with neural tissue for recording and/or stimulation. While satisfactory long-term performance was demonstrated in some applications, such as cochlear implants and deep brain stimulators, more advanced neural interfacing devices requiring higher resolution for single unit recording or microstimulation still face significant challenges in reliability and longevity. The most significant challenge lies in the neural electrode-tissue interface, where a man-made device is brought in contact with biological neural tissue and electrical voltages or currents are being transmitted across the electrode-tissue interface. Like any implantable devices, the highly corrosive and dynamic environment of the host tissue is hostile to implants, among which micro-electronic devices are especially vulnerable. Although an old topic, the material and mechanical reliability of neural electrode arrays continue to be a critical area of research, and in our opinion, deserves more attention especially in the development of newer and more advanced devices. Conversely, the implantation and presence of an artificial device elicits acute injury and chronic inflammatory reactions that lead to tissue remodeling, degeneration and regeneration that alter the microenvironment with which the device is interfacing. Dynamic changes in the neural tissue around the implants affect the quality and stability of the neural electrode recording and/or stimulation performance, and this has been a hot area of research in recent years. Advanced electrodes are being designed to mitigate the issues faced when chronically interfacing with traditional electrodes by changing the geometry, increasing flexibility, and incorporating bioactive coatings and drugs. This article intends to 1) review the most recent findings that contribute to our current understanding of the unsatisfactory quality, stability and longevity of neural recording or stimulation, 2) highlight the development of characterization tools for the study of neural electrode-tissue interface, 3) summarize the strategies that have been applied to improve the interface, and 4) discuss the challenges and opportunities in improving the interface and achieving seamless integration between the implanted electrodes and neural tissue both anatomically and functionally. This article provides an overview of nervous system electrodes, but puts emphasis on central nervous system recording electrodes. For more detailed discussion on peripheral nervous system devices and stimulating electrodes, we would like to kindly direct the reader towards the complementary articles found in this issue of "Current Opinion in Biomedical Engineering" (titled "**Peripheral Nerve Interfaces for Limb Prosthetics**" and "**Central Nervous System Microstimulation**". respectively).

Current understanding of failure mechanisms

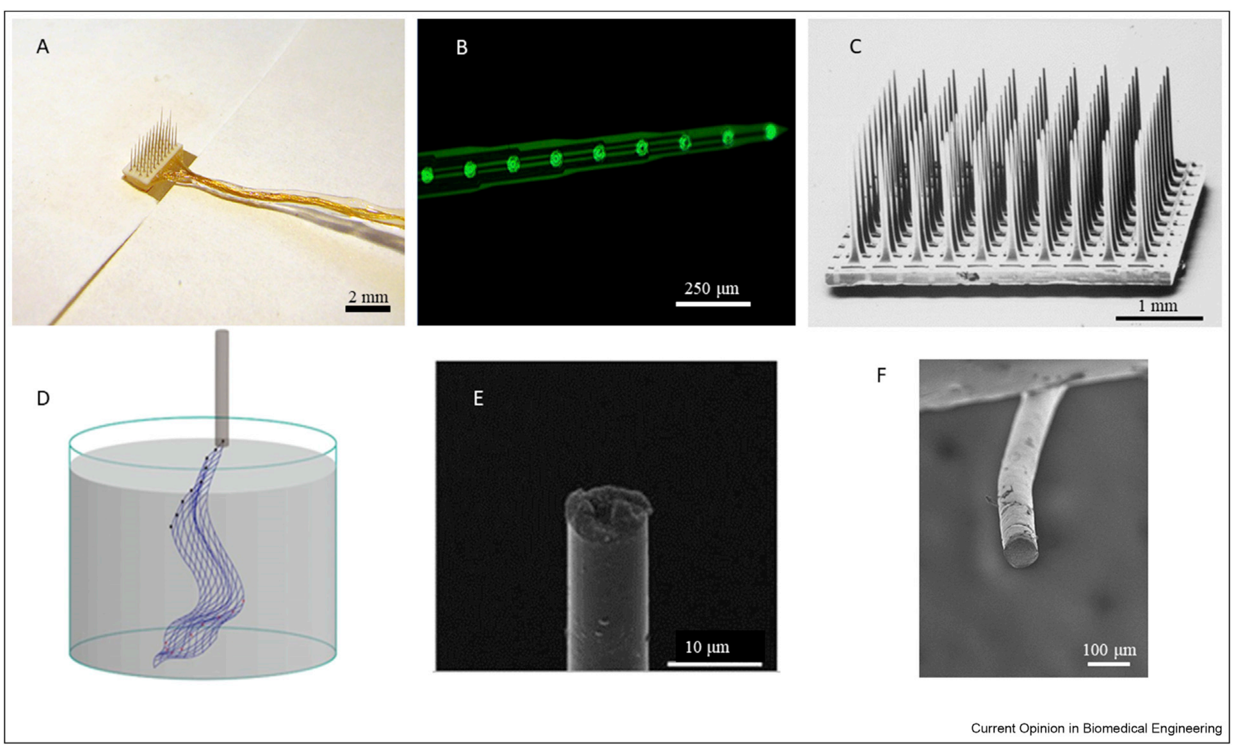
Recording the highest quality single neuron activity in the brain requires penetrating electrodes [1]. While many designs have been utilized for electrode devices implanted in the brain parenchyma, almost all electrodes have certain basic features: electrode sites of a conductive material, conducting leads connecting the electrode sites and external electrical components, and an insulating layer defining the electrode site areas and protecting the connection from electrical shunting. While microwire arrays (bundles of insulated metal wires), Michigan electrodes (planar arrays), and Utah Arrays (bed of needles) are some of the more well-known and studied designs, many new designs and materials have been proposed for neural interfacing (Figure 1). The multitude of device designs and materials is well covered by Patil and Thakor in their review [2]. While neural electrodes have advanced greatly over the past few decades, recording and stimulation performance is highly variable and most devices show failure after chronic implantation ranging from weeks to months and a few years. A summary of device performance from selected studies is shown in Table 1. The causes of variability and long-term failure have been attributed to mechanical/material and biological factors.

Mechanical and material failure

Despite decades of research and development, mechanical and material failures are still a major contributor of performance failure for neural electrode devices. In a non-human primate study examining chronic recording performance of the Utah array (Blackrock Microsystems), mechanical and material failure have been reported to be the greatest cause of failure, accounting for upwards of 48% of all failure in the first year [3]. While many failures occurred at the percutaneous connectors and wire bundles, further difficulties arise with de-insulation, corrosion, and cracking of the electrodes directly interfacing with the neural tissue.

Several recent studies characterized different types of material failures and their recording/stimulation consequences [4,5]. One potential cause of material failure is de-insulation along the electrode or at the electrode tip. De-insulation at the electrode site increases the surface area exposed, decreasing the impedance of the electrode but also decreasing the recording quality [6]. Another notable observation is that failure is variable from animal to animal, with some electrode arrays recording on 80% of channels while others produced no recording [4]. One interesting study focused on the mechanical and material failure mode analysis on chronically implanted planar

Figure 1



Comparison of selected traditional and advanced electrodes. (A) Microwire array, reproduced with permission from Microprobes for Life Sciences Inc. (B) Planar (Michigan) electrode. (C) Bed of needles (Utah) array [112], copyright 1998 Elsevier. (D) Syringe injectable mesh electrode [80], copyright 2017 National Academy of Sciences. (E) Carbon fiber electrode [47], copyright 2012 Nature Publishing. (F) Conducting elastomer microwire electrode [29].