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Bridging Neuroscience and Engineering with Nano-Neurotechnology

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The past decade has seen an increasing number of technological advances to interface with single neurons and neuronal circuits being applied in vivo. These methods have greatly accelerated our understanding of neural pathways in the brain in health and disease. Additionally, these neurotechnologies hold exciting promise for future neurotherapies.

This issue of *Accounts of Chemical Research* discusses recent advancements of nanomaterials and chemical tools designed for probing and modulating neural activities, aiming to evaluate their impact on diverse aspects of neuroscience and neuroengineering. Key topics include the synthesis of novel nanomaterials with unique properties for neural interfaces, the development of new neural interrogation processes and mechanisms, and the application of these nanoenabled tools in neuroprosthetics, neurosensing, and neuromodulation. Furthermore, the integration of optical, magnetic, photoacoustic, and electrical systems for closed-loop neural monitoring and modulation is explored. Additionally, the challenges for therapeutic applications, such as biocompatibility and long-term stability, are discussed.

Hurdles for long-term applications are that many approaches rely on embedding hard materials, such as electrodes or transducers, into the soft brain or require multiple connected components, such as a power supply, transducers, and sensors. The former is addressed by two papers in this collection documenting the progress in stretchable and flexible neural interfaces. Xiaodong Chen and his team¹ present significant advancements in stretchable microelectrode arrays (MEAs) for neuron–motor system interfacing. Their research focuses on balancing stretchability and electrical conductivity, providing innovative solutions to enhance the biocompatibility and functionality of MEAs in physiological research and clinical applications. Dae-Hyeong Kim, Gi Doo Cha, and their teams² emphasize the integration of nanotechnology with soft bioelectronics. Their work showcases advanced geometric designs and intrinsically stretchable materials that improve the mechanical compatibility and multifunctionality of bioelectronics, paving the way for enhanced neural recording and modulation applications and significantly contributing to the field of neuroengineering. The challenges and possible solutions for compact, completely integrated one-component neuronal interfaces which could open pathways for therapeutic devices are discussed by Philipp Gutruf.³ These innovative neural interfaces overcome traditional challenges by integrating electronics directly onto thin films, reducing displacement volumes, and enhancing energy availability to create

monolithic, wirelessly powered devices. The highlighted device architectures demonstrate the potential of near-field power delivery as a key technique for efficient power transfer, setting a new standard for neural interface technology.

Significant progress has been made in enhancing the biocompatibility of neural interfaces. Xinyan Cui's team⁴ focuses on improving neural probe performance using silica nanoparticles (SiNPs). Their research demonstrates how SiNP coatings can enhance the electrochemical properties and biocompatibility of neural interfaces, offering innovative solutions for chronic neural stimulation and drug delivery. Erin Purcell's team⁵ examines the biological responses to implanted neural electrodes, employing innovative “device-in-slice” techniques to uncover significant structural, functional, and genetic changes in brain tissue surrounding electrodes. These insights are critical for improving the design and integration of neural interfaces, making substantial strides toward more effective and biocompatible neural implants.

Future directions toward translational therapeutic applications likely require innovative neuromodulation techniques and closed-loop systems sensing activity and neuromodulating it.

Tzahi Cohen-Karni's team⁶ presents advancements in using nanostructured electrodes for neural interfaces, discussing hybrid nanomaterials for remote nongenetic optical stimulation, neurotransmitter detection, and electrochemical modulation. The emphasis on closed-loop neural interfacing suggests the potential for these multifunctional nanomaterials to revolutionize the field. Bozhi Tian's team⁷ offers an overview of optoelectronic nanomaterials for neural interfacing, discussing the development of “photoelectrochemicals” that enable high-specificity neuromodulation through minimally invasive optoelectronic systems. The article emphasizes the importance of materials innovation and presents strategic directions for future research, aiming to advance the field of nanoenhanced optoelectronic neuromodulation.

Novel, force-mediated neuromodulation mechanisms are discussed by Guosong Hong and his team.⁸ They categorizing force-mediated techniques into those using focused ultrasound

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and those generating mechanical force from other modalities. This Account showcases the advantages and limitations of each approach, highlighting recent technological advancements and their potential for high-precision neural modulation. Chen Yang and colleagues⁹ highlight the emerging field of photoacoustic neural stimulation, a versatile nongenetic method for high-precision neuromodulation. This technique offers high efficacy and precision without the need for genetic modification, covering the design principles of photoacoustic transducers and highlighting their potential for noninvasive, high-precision brain stimulation. Finally, Jacob Robinson and his team¹⁰ provided a detailed discussion of the progress made in the field of magnetoelectrics for implantable bioelectronics. They reviewed the current advancements, challenges, and potential applications of magnetoelectric materials in bioelectronic devices.

This special issue aims to pave the way for groundbreaking therapies, diagnostics, and technologies that revolutionize neuroscience and improve the lives of those affected by neurological disorders. By integrating advanced nanomaterials and chemical principles, it is set to open new frontiers in neural interfacing, enabling unprecedented precision in monitoring and modulating neural activity at the molecular level. The chemical innovations presented here are poised to lead in creating smarter, more responsive materials and devices that interact seamlessly with the brain's complex biochemical environment. These advancements could lead to personalized neurotherapeutic strategies, transforming treatments for conditions such as Parkinson's disease, epilepsy, and spinal cord injuries. The integrated efforts in this issue enhance our understanding of chemical roles and interactions within neural systems, driving the creation of next-generation neurotechnologies that are minimally invasive, highly efficient, and chemically tailored to individual needs.

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Notes

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