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Multi-Electrode Arrays Using CMOS Integrated Circuit Technology for Cell-Based Biosensors and Neurobiology

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Introduction

Electrodes that are electrochemically stable, biocompatible, and reasonably priced are needed for the adoption of standard integrated circuit (IC) technology as a transducer in cell-based biosensors for drug discovery pharmacology, brain interface systems, and electrophysiology. The common Complementary Metal Oxide Semiconductor (CMOS) IC technology, however, falls short of the first of these requirements. It has been possible to modify the CMOS in devices only meant for research by using cleanroom facilities during post-processing. However, the economies of scale of CMOS production must be maintained by using only low-cost post-processing techniques in order to enable the acceptance of CMOS as a foundation for commercial biosensors. The approaches used in the design of cell-based biosensors, where CMOS-based integrated circuits (ICs) are a crucial component of the transducer system, are highlighted in this paper. The use of multi-electrode arrays for in vitro neuroscience applications will receive particular attention. When taking into account particular applications, finding appropriate IC packaging techniques brings additional substantial obstacles. A review of the many issues is done, and some potential remedies are offered.

Description

According to the IUPAC, a "biosensor" is "*a device that exploits specialised biochemical reactions mediated by isolated enzymes, immune systems, tissues, orcranelles, or entire cells to detect chemical molecules often by electrical, thermal, or optical signals*." A very interdisciplinary approach is consequently necessary for the advancement and success of biosensor development, and even a single application may call for cutting-edge input from neuroscientists, biologists, semiconductor engineers, electronic hardware designers, pharmacologists, and surgeons [1]. The majority of functional sensors also have two components: a transducer and a biological receptor or bioreceptor that detect the bioreceptor's response to the *analyte* and translate it into an output signal. The bioreceptor is responsible for detecting the presence of the substance being tested (the *analyte*). Typically, the detecting bioreceptor is coated with a substance to prevent natural adhesion processes from occurring or is immobilised on the chemical or physical transducer [2]. The three main categories of transducers are optical, electrochemical, and mass-based detecting techniques. The electrochemical approaches that are more applicable to integrated circuit (IC)-based biosensors and the packaging technologies that are an essential component of such a device are of particular relevance in this review [3]. Examination of pertinent biosensor literature that uses the terms "CMOS" or "integrated circuit" is given. Cell-based kinds are perhaps the most common in actual usage. This fact, together with the authors' particular interest in IC-based biosensors, influenced their decision to make this the article's main topic. The 1965 paper "Biomedical Telemetry" was one of the first to define and discuss biosensors. Integrated circuits (ICs) were still in their infancy at the time, and a patent for a complementary metal oxide semiconductor (CMOS) had just been issued. This technology has since taken root as the undeniable cornerstone of contemporary electronics and today rules the global IC market. Because of economies of scale, CMOS is now quite affordable and widely available, which may be why it is so appealing to the designers of many types of biosensors [4,5]. However, the application of this technology to create a transducer highlights the issue of the analyte/electrode interface as well as potential neurotoxicity concerns because of the specific materials available in a CMOS process (namely, aluminium and its oxide).

Conclusion

In conclusion, this review will first provide a comprehensive overview of the subject before concentrating on CMOS MEAs for in vitro neuroscience applications. The information is organised as follows. The article starts off by giving a general review of transducers as they apply to biosensors before narrowing the discussion to CMOS kinds with a focus on manufacturability. An overview of CMOS technology is given in the article. For researchers interested in using CMOS transducer elements in biosensor applications, we explain the significance of the metal surface and metal-solution interface. This article discusses some of the practical requirements for successful neural recordings and a particularly challenging application, namely neuronal interfaces. The crucial topic of packaging technology is covered in this article, along with barriers to commercialization. A summary of expected future research in this area is provided as the article conclusion.

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