

A perspective on Integrated Biochip System in the Advancement of Health Sector

Abstract

Recent advances in microelectronics and biosensors are enabling developments of innovative biochips for advanced healthcare by providing fully integrated platforms for continuous monitoring of a large set of human disease biomarkers. Continuous monitoring of several human metabolites can be addressed by using fully integrated and minimally invasive devices located in the sub-cutis, typically in the peritoneal region. This extends the techniques of continuous monitoring of glucose currently being pursued with diabetic patients. However, several issues have to be considered in order to succeed in developing fully integrated and minimally invasive implantable devices.

Keywords: biochip • CMOS design • enzymes • biotechnology • nanotechnology • potentiostats • biocompatible membranes • security • privacy

Introduction

According to the Molecular Diagnostics Survey Reports diagnostics testing influences approximately 70% of health care decisions. This means that diagnostics are essential tools for diagnosing and managing numerous health care conditions, ranging from infectious diseases to non-communicable diseases such as diabetes. In fact, non-communicable diseases, or NCDs, are by far the leading cause of death in the world, representing 63% (36 million) of all annual deaths. Fully integrated biochip platforms can build on existing technologies. Continuous monitoring is already in the market with commercially available devices for glucose and lactate while experimental prototypes have been already proposed for other endogenous metabolites, like glutamate and ATP, as well as for exogenous metabolites (typically therapeutic compounds), like cyclophosphamide and naproxen. The technology for continuous monitoring of glucose is robust enough to provide sensors with life-time up to 8 months when implanted in mice and one year in pigs. Sensor performance has been improved to meet sensitivity on physiological concentrations in human blood by using carbon nanotubes in case of both endogenous and exogenous metabolites.

Moreover, the in vivo environment presents unique challenges related to calibration, the foreign body response and signalling. These issues will be critical to the acceptance of these technologies by patients, physicians and regulatory bodies, as well as to their responsible deployment in the field.

Description

Biosensors are based on the principle of converting a biochemical quantity into an electrical signal through the use of electrodes. Currently, a wide variety of different materials are used for the preparation of electrode surfaces for biosensing applications. An increasing number of sensing applications use screen-printed electrodes. Screen-printed electrodes (SPEs) are devices that are produced by printing different conductive inks on various types

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of insulating plastic or ceramic substrates. By using nanostructures, it is possible to control the fundamental properties of electrode materials and enhance the electron transfer between the electrode and the enzyme, thus improving the catalytic reaction. Carbon nanotubes (CNTs) have been recognized as very promising nanomaterials for enhancing electron transfer in biosensing thanks to their electrical and electrochemical properties which make them suitable to be integrated into biological sensors. For these applications, carbon nanotubes present several advantages: small size with larger surface area, high conductivity, high chemical stability and sensitivity, high electrocatalytic effect and a fast electron-transfer rate. Recent studies have demonstrated that CNTs enhance the electrochemical reactivity of proteins or enzymes with retention of their biocatalytic activity.

The nanotubes and enzyme molecules are of similar dimensions, which facilitate the adsorption of the enzyme without significant loss of its biocatalytic shape, form or function. Biofouling is the accumulation of biological material on the device surface. In contrast to biofilms, which consist of bacteria, this biologic material is not causing an infection. This aggregation of cells, macromolecules and small molecules on the biosensor membrane has been extensively reported as detrimental for the sensor function. Biofouling often prevents diffusion of the analyte or adherence of the analyte on the sensor surface. Several strategies have been employed to reduce biofouling, most of them rely on the use of dedicated membranes and coatings. An extensive review about this topic can be found in reference . Below we will briefly describe two techniques for

reducing biofouling: hydrogel overlays and Nafion coatings. Hydrogel overlays, mainly made with poly(hydroxyethylmethacrylate) or poly(ethylene glycol), present a hydrophilic interface which can favor diffusion of water-soluble analytes. Diffusion rate is controlled by changing the crosslinking density of the gel. A drawback of this approach is their poor adhesion to the substrate, and a poor mechanical stability during the implant⁶. Cavallini, A.; De Micheli, G.; Carrara, S. Comparison of Three methods of biocompatible multi-walled carbon nanotubes confinement for the development of implantable amperometric ATP biosensors.

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None

Conflict of Interest

No conflict of interest

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