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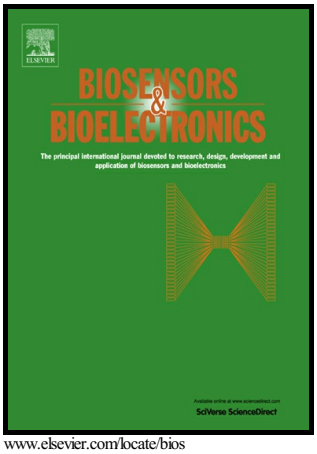

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Electrochemical Biosensor System Using A CMOS Microelectrode Array Provides High Spatially and Temporally Resolved Images

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Abstract

The ability to view biological events in real time has contributed significantly to research in the life sciences. While video capture of real time changes in anatomical relationships is important, it is equally important to visualize real time changes in the chemical communications that drive cell behaviors. This paper describes an electrochemical imaging system capable of capturing changes in chemical gradients in live tissue slices. The system consists of a CMOS microchip with 8,192 configurable Pt surface electrodes, on-chip potentiostat, on-chip control logic, and a microfluidic device designed to interface with the CMOS chip to support *ex vivo* tissue experimentation. All data processing and visualization methods, sensor calibrations, microfluidics fabrication, and tissue preparation and handling procedures are described. Using norepinephrine as a target analyte for proof of concept, the system is capable of differentiating concentrations of norepinephrine as low as 8µM and up to 1,024 µM with a linear response and a spatial resolution of 25.5µm × 30.4µm. Electrochemical imaging was tested using murine adrenal tissue as a biological model and successfully showed caffeine-stimulated release of catecholamines from live slices of adrenal tissue with temporal sensitivity. This system successfully demonstrates the use of a high-density microelectrode array for electrochemical analysis with high spatiotemporal resolution to gather chemical gradient information in parallel with optical microscopy recordings.

Keywords

CMOS Biosensor; Microelectrode Array; Amperometry; Voltammetryl Electrochemistry; Ex Vivo Microfluidics; Data Visualization

1. Introduction

The ability to view biological events in real time contributes significantly to the understanding of critical life processes. Visualizing chemical changes at smaller dimensions and shorter timescales allows scientists to better understand the driving forces that regulate fundamental and obscure biological phenomena, such as chemotaxis and cancer metastasis. Traditional optical microscopy techniques provide a means of observing the movement of small molecules in live biological samples with spatial and temporal resolution, but have limitations. These methods are restricted to a library of inherently colored or fluorescent molecules and those

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