CMOS INSTRUMENTATION FOR ELECTROCHEMICAL BIOSENSOR ARRAY MICROSYSTEMS

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Understanding the structure and function of proteins has become increasingly important since the completion of the Human Genome Project and the sequencing of several other important genomes. In recent years, lab-on-a-chip systems have introduced some new capabilities for protein analyses. Rapid progress in the field of microsystems, miniaturized devices combining sensor and electronics, facilitates a new generation of miniaturized biosensor arrays utilizing silicon CMOS chips that acquire and process bio-electrochemical signals. Such biosensor array microsystems permit improved sensitivity, measurement throughput and cost per assay. This thesis research addresses the design and development of high performance electrochemical instrumentation circuits that enable simultaneous characterization of multiple protein interfaces in a high throughput chip-scale biosensor arrays microsystem. A CMOS amperometric biosensor readout circuit with current resolution of 1pA has been developed. Furthermore, a new compact, low power, 100fA current resolution impedance analysis circuit that utilizes mixed-mode signal processing to extract real and imaginary impedance components has been developed and tested with an on-chip protein interface. Moreover, to realize a multi-protein array of sensors with different instrumentation needs, a hardware efficient CMOS electrochemical circuit has been designed to achieve both amperometric and impedimetric
measurement while sharing hardware source. Finally, by integrating an understanding of both protein assays challenges and microelectronics design limitations, a novel 1000-element array instrumentation architecture that permits rapid high-throughput characterization of membrane proteins with single protein resolution has been designed. The CMOS instrumentation circuitry developed in this thesis research could significantly advance proteomics research and progress in characterizing newly sequenced genomes.
Publication list

Journal Publications


Journal Papers Submitted or In Preparation


Book Chapter


Conference Publications


CMOS-based sensor array chips provide new and attractive features as compared to today's standard tools for medical, diagnostic, and biotechnical applications. Examples for molecule- and cell-based approaches and related circuit design issues are discussed.

Introduction. Measured electrical, electrochemical, and biological data as well as processing related issues are published elsewhere [12-15].

Recording from nerve cells and neural tissue. CMOS-based biosensor arrays clearly have proven their feasibility, they open the way to novel and user-friendly highly parallel solutions. One of the remaining challenges is to make commercialization a successful story. To integrate an array of amplifiers for parallel electrochemical measurements, a half-shared OPA structure is used, which has been previously studied [11], [12]. The purpose of the half-shared OPA design is to reduce the area required to create a dense sensor array by sharing one non-inverting input with multiple inverting inputs (Fig 5). In the presented device, one non-inverting half of an OPA is shared by groups of 4 TIAs, each of which occupies 30 Å—30 1/4 m2. Å To prepare the monolithic CMOS device for electrochemical applications such as single-cell amperometry, a biocompatible epoxy-based photoresist, SU-8 3010, is used to provide isolation between the electrodes in the electrochemical detector array.

CMOS Microsystems. Main content. The notion of "microsystem" implies that we do not only devise single transducers, i.e., sensors or actuators, but that we develop rather complex systems comprising transducers, associated analog and digital circuitry units, and addressing and interface units on the same microchip. Å We follow the integrated-systems concept in devising and developing complex monolithic CMOS microelectrode and chemo & biosensor chips with large numbers of Å Microelectrode Systems. Large high-density arrays of small electrodes (26,000 Å) Complex integrated systems are developed for electrochemical sensing based on potentiometry or cyclic voltammetry. Applications include the detection of bio- and disease markers or chemo- and bio-agents. Electrochemical biosensors represent a promising diagnostic technology for both humans and animals. Many of these devices can detect biomarkers in body fluids such as blood or urine. However, for continuous and/or local monitoring of specific molecules, implantation of biosensors is needed. Å Using MEMS technology, a detector array having multiple electrodes deposited on a Si wafer was fabricated. Self-assembled monolayer of protein streptavidin was immobilized on the working electrode (Au) surface to capture rRNA from E. coli. It has a sensitivity of detecting 1000 cells and an assay time of 40 min (Gau et al., 2001). Then, electrochemical instrumentation circuits are organized into functional classes, and reported CMOS circuits are reviewed and analyzed to illuminate design options and performance tradeoffs. Finally, recent trends and challenges toward on-CMOS sensor integration that could enable highly miniaturized electrochemical biosensor microsystems are discussed. The information in the paper can guide next generation electrochemical sensor design. Discover the world's research.