1 INTRODUCTION

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The second half of the 20th century witnessed the metamorphosis of silicon, an element common in the Earth's crust, into silicon integrated circuits (ICs), complex superstructures that can contain hundreds of millions of complementary-metal-oxide-semiconductor (CMOS) transistors in a tiny footprint of only a few square centimeters. An arsenal of planar microfabrication technologies made possible the rock-to-IC transformation of silicon at surprisingly low costs. Now consider the phenomenal ability of silicon ICs. Hundreds of millions of CMOS transistors interconnected via a labyrinthine maze of metallic wires all work together to process data at gigahertz frequencies.

With their amazing capabilities, inexpensive production, and tiny physical size, ICs have come to have a major affect on our daily lives. As computer microprocessors, they significantly assist our intellectual endeavors. Silicon ICs profoundly enrich our ability to communicate, enabling communication technologies with high speed and data capacity over long distances. In addition, they provide entertainment: music and movies from handheld multimedia devices are a 21st century triumph of silicon technology. People on treadmills with tiny iPods can choose from thousands of musical tunes, ranging from Mariah Carey's songs to Ludwig van Beethoven's symphonies. This scene would be hard to imagine, were it not for silicon ICs.

While the dominance of silicon ICs in data processing, communication, and multimedia will undoubtedly continue into the foreseeable future, there are growing efforts to utilize the power of silicon technology for new types of applications. An important area is biology and medicine. Bioanalytical instruments are being miniaturized to make labs on a chip to perform a variety of experiments: to probe DNA, to monitor electrochemical activity, to examine neural functioning, and to actuate biological cells, for example. Microfluidic systems are being developed to provide a biocompatible environment on chips. By exploiting the power of silicon technology, one can combine CMOS ICs with microfluidic systems to make hybrid chips that perform standardized, and repeatable biological experiments more quickly, with a smaller sample volume, at lower costs than conventional approaches. Research activities in this new field, which we call **CMOS Biotechnology**, are expected to enjoy substantial growth. This trend is reflected by an increasing number of publications in major conferences and journals for IC design.

This book, consisting of ten technical topics contributed by experts in the field, will share some of the exciting developments in CMOS Biotechnology with readers from different disciplines. A large amount of high quality research is being done in this rapidly developing field, making it difficult to select only ten topics. Our selection presents examples of outstanding work to form view of CMOS Biotechnology.

We structured this book by sub-grouping the ten select topics into four parts, based on shared themes.

Part-I Microfluidics for Electrical Engineers (Chapters 2-4) presents an introduction to microfluidics for electrical engineers. Microfluidic systems serve as a biocompatible way to interface biological samples suspended inside them with CMOS chips below. Chapter 2 offers a tutorial on the theoretical foundations of microfluidics. Chapter 3 describes biological applications of microfluidic systems, with special attention to bioanalytical separation operations. Chapter 4 discusses the basic concept and fabrication of a CMOS/Microfluidic hybrid chip consisting of a CMOS IC with a microfluidic system fabricated on top.

Part-II CMOS Actuators (Chapters 5-7) offers examples that show how the CMOS/Microfluidic hybrid chip can be used to manipulate (control the motions of) biological samples ranging from cells to DNA. In Chapters 5 and 6, magnetic and electric manipulations of biological cells are discussed, along with examples of biomedical applications that such manipulation can enable. Chapter 7 describes electrical manipulations of biological objects of much smaller nanoscale size, including DNA for DNA hybridizations.

Part-III CMOS Electrical Sensors (Chapters 8-9) is a sensor counterpart to **Part-II**. Chapter 8 describes a microelectrode array integrated in a

CMOS chip, which can be used to record neural and cardiac cell activities whose signatures are carried by electrical signals. In Chapter 9, a brain-implantable neural recording system based on a CMOS chip is presented. The approach is similar to Chapter 8, but it is more focused on the circuits tailored for implanted sensor applications.

Part-IV CMOS Optical Sensors (Chapters 10-11) presents optical bio-sensing systems built on solid-state imager chips in combination with microfluidic systems. Chapter 10 demonstrates a high-resolution cell imaging experiment made possible by a charge-coupled device (CCD) connected with a microfluidic system. Chapter 11 discusses an example of how a CMOS imager can be utilized to study biological objects at molecular size scales and how it can potentially be exploited for applications like DNA sequencing.