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Biomedical Sensors and Measurement

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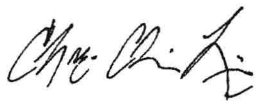
Foreword

This book introduces the basic fundamentals of biomedical sensors and the measurement technology as well as the recent advancements in this field in recent years. There are five chapters in this book which can be subdivided into two major parts. The first part places emphasis on the fundamentals and the development of modern biomedical sensors and the measurement technology including their basic features and special requirement in application. This part also provides essential information on the basic sensitive reaction mechanisms, characteristics and processing approaches of the biomedical sensors. The second part introduces the typical sensors including the physical, chemical and biological sensors as well as the discussion of their measurement techniques. The practical applications of each of these sensors are also described in detail. There are two unique features in this book: (1) The combination of the discussion on the biomedical sensor technologies and their required measurement techniques which include the fundamentals and the practical applications of the biomedical sensors; (2) It The description of the rationale and the needs of the integration of discrete sensing elements into a meaningful and practical sensor array which can become an intelligent sensing system. The authors have given a very persuasive and sound approach in this important scientific and practical endeavor. It also should be acknowledged that the authors have systematically provided a clear roadmap for the development of various sensors by first introducing macro-size sensors for the detection of physical properties and then leading to the advancement of micro-size chemical and biological sensing systems.

The advancement of the micro-size for chemical, biological and biomedical sensors or sensor micro-systems requires multi-disciplinary skills and expertise. This includes the understanding and expertise in microfabrication and micromachining processing, electronic and ionic conductive materials, sensor operational principles, electronic transduction interface technologies and many others. In this book, the authors have logically and systematically discussed and analyzed the interwoven relationship of these techniques and their applications to the development of scientifically and commercially sound practical chemical, biological and biomedical sensors.

The authors, Professor Ping Wang and Associate Professor Qingjun Liu have been engaging, for many years, in the research and teaching of sensor technology, particularly in the field of biomedical sensors. They have been involved in this research effort more than a decade and their appreciation of the multi-disciplinary nature of the sensor research and the unique requirements for the advancement of the biomedical sensors and their measurement techniques can be well recognized throughout this book. As mentioned, this book is derived from the research work on biomedical sensors and measurement, in recent years, at Zhejiang University, Hangzhou, China. Thus, this book will serve as an excellent reference source for researchers in biomedical sensor and measurement. It's intended for scientists, engineers, and manufacturers involved in the development, design, and application of biomedical sensors and measurement. The reference list given in each chapter is very thorough and relevant, this book will also be a very good book for the senior undergraduate and graduate students who wish to pursue a professional career in this field.

Biomedical sensors and the measurement are scientifically and commercially important in numerous applications at this juncture, and this book will be most welcome for researchers and students who wish to understand this field further and to make a meaningful contribution to this important endeavor.



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Preface

In the 20th century, technological innovation has had such a rapid development that science and technology permeates all aspects of our lives, especially in the biomedical field which attracts a large number of professional scientists and engineers. Biomedical engineering is a combination of two developing areas: biomedical and information technology. It promotes the biomedical sensor design and development, as well as applications in clinical diagnosis and treatment technology. Biomedical engineering covers many research areas: bio-mechanics, bio-materials, physiological modeling and sensoring technology, detection technology, signal and image processing. One important research field is biomedical sensoring and detection technology, which obtains original information from primitive organisms (especially human body), one of the most crucial procedures.

In the 1960s, scientists and engineers paid more attention to sensors for they met many of the practical requirements. The development of chemical and biological sensors creates selective sensors, which makes possible the direct detection of a variety of ions and molecules. Micro-sensors and micro-electrodes quickly replaced traditional large-size sensors and were applied to biological and medical fields.

At present, the quick clinical digital thermometer, blood pressure monitors, and wearable home-used blood glucose meter have been widely used. CT (computed tomography scanning) and ultrasound technology are recognized as common advanced diagnostic tools. However, many have omitted that sophisticated sensors play an important role in these instruments. Sensors have brought about revolutionary changes in the field of biomedical diagnostics and application of medical instrumentation, and they will have a positive effect on human life quality in the 21st century. Sensors have the following applications:

- Digital medical image tools like CT, ultrasound, etc.;
- For the traditional image tools such as X-ray machines, it improves and gets more information and reduces the amount of radiation;
- Portable clinical multi-parameter monitoring equipment;
- Portable home-use monitoring and diagnostic equipment;
- Implantable, self-calibration equipment which will be widely used in the future;
- Intelligent systems of sensors can replace our sense system, such as sight, taste, smell, touch, etc.;

■ Rapid diagnosis tools based on immunization and DNA-chip technology.

Although biomedical sensors are being applied more and more, in many cases, the theory is not entirely clear. It's controversial in the expression of stimulus signal theory, signal extraction and measurement. The development of new biomedical sensors indicates a great fundamental research work, which is the key part at present.

Biomedical sensors convert biological signals into easy-to-measure electrical or optical signals. It's the interface between organisms and electronic systems. Meanwhile, effective detection technology, including low-noise and anti-jamming circuits, and data processing techniques are essential during the conversion from bio-medical to electronic signals, as well as for further processing. This book adds the detection technology with sensoring technology according to the actual teaching requirement so that students and other researchers may systematically learn and comprehend the relevant knowledge in this field.

This book can be used as a reference book for researchers and senior undergraduates and graduate students. This book combines detection technology with sensoring technology and strengthens the links between them. In addition, the authors have added an introduction of regular physical sensors and chemical sensors and reorganized and reviewed the latest international development trends of chemical sensors, biological sensors and their intelligent systems, such as electronic nose, electronic tongue, microfluidic chips and micro-nano biosensors and their applications.

Biomedical sensoring and detection techniques require synthesizing the interdiscipline of physics, electronics, materials, chemistry, biology, and medical, etc. The authors are trying to meet this requirement through a detailed description of working principle, sensitive technology, and detection circuit and identification system theory of sensors or devices. We believe that this book will be of great value for those academics, engineers, graduates and senior undergraduates in the biomedical and relevant fields.

The book is composed of five chapters. Chapter 1 introduces the development of biomedical sensoring and detection technology; Chapter 2 describes fundamental knowledge of modern sensoring and detection technologies; Chapter 3 describes the physical sensor and its detection technology; Chapter 4 describes chemical sensors and detection techniques; Chapter 5 describes the biosensors and detection technology. Some content in this book belongs to the international research frontier. Biomedical sensoring and detection technology promotes the reorganization of biomedical information transmission, processing and perception, as well as the development of biomedical engineering and the interdisciplinary field.

The book is the result of several years of study, research and development of the faculties, PhD candidates and many other affiliated to the Biosensor National Special Laboratory of Zhejiang University. We would like to give particular thanks to Jun Wang, Wei Cai, Qi Dong, Gong Cheng, Di Wang, Jun Zhou, Cong Zhao, Lin Wang, Liang Hu, Wei Zhang, Lidan Xiao, Hui Yu, Kai Yu, Wen Zhang, Huixin Zhao, Chunsheng Wu, Liping Du, Ning Hu, Weiwei Ye and Yishan Wang. We sincerely thank them all for their contributions.

And we are deeply grateful to the financial supporting for us overall systematization, teaching, and research work on biomedical topics through the past over ten years: by National Natural Science Foundation and National Distinguished Young Scholars Fund of China (Grant Nos. 30627002, 60725102, 30700167, 30970765, 81027003, 81071226, 31000448), Zhejiang Provincial Natural Science Foundation of China (Grant Nos. 2006CB021, 2010C14006, Y2080673), and National Basic Research Program of China (973 Program, Grant No. 2009CB320303) and National High Technology Research Program of China (863 Program, Grant No. 2007AA09210106), State Key Laboratory of Transducer Technology of China (Grant Nos. SKT0702, SKT0901), etc.

As biomedical sensors and masurement involved in wide interdisciplinary areas, and in consideration of the limit of authors' knowledge and experiences, errors of judgment are, of course, inevitable; comments and suggestions will, therefore, be appreciated.

Ping Wang and Qingjun Liu
Hangzhou, China
January, 2011

Contents

Chapter 1

Introduction

1.1 Definition and Classification of Biomedical Sensors

The sensors are devices that can transform non-electrical signals into electrical signals. The biomedical sensor is a very important kind of sensors. First we will introduce some basic knowledge about biomedical sensors including a definition and classification.

1.1.1 Basic Concept of Sensors

Sensor or transducer is a device which can respond to a measured object and transform it into signals which can be detected. A sensor is usually composed of a sensitive component which directly responds to a measured object, a conversion component and related electronic circuits. Along with the development of modern electronic technology, micro-electronic technology and communication technology, which represent some various useful signals, electrical signals are most convenient for processing, transporting, displaying, and recording.

Sensors often provide information about the physical, chemical or biological state of a system. Measurement is defined as an operation that aims to obtain the measured value of the quantity. Therefore, sensors are defined as devices that can transform non-electrical signals into electrical signals. Sensors often provide information about the physical, chemical or biological state of a system. Measurement is defined as operations that aim to obtain the measured value of the quantity. Therefore, sensor detection technology is one that uses sensors to transform measured quantities into physical quantities which are easy for communication and processing, and then goes on with transformation, communication, displaying, recording and analysising.

Biomedical sensors are special electronic devices which can transfer various non-electrical quantities in biomedical fields into easily detectable electrical quantities. For this reason, they are incorporated into health care analysis. They expand the sensing function of the human sensing organ while the key parts consist of various diagnostic medical analysis instruments and equipment. Biomedical sensing technology is the key to collecting human physiological and pathological information and is also an important disciplinary branch.

1.1.2 Classification of Biomedical Sensors

Biomedical sensors can be classified in the following categories according to their detection quantities. Classified by working principle, sensors include physical sensors, chemical sensors, and biological sensors.

Physical sensors: It refers to the sensor made according to physical nature and effect. This kind of sensors is mostly represented by sensors such as metal resistance strain sensors, semiconductor piezoresistive sensors, piezoelectric sensors, photoelectric sensors, etc.

Chemical sensors: It refers to the sensor made according to chemical nature and effect. This kind of sensors usually uses ion-selective sensitive film to transform non-electricity such as a chemical component, content, density, etc. to related electric quantity, such as various ion sensitive electrodes, ion sensitive tubes, humidity sensors and, etc.

Biological sensors or biosensors: It refers to the sensor using biological active material as a molecule recognition system. This kind of sensors usually uses enzyme to catalyze some biochemical reaction or exams the type and content of large molecule organic substances through some specific combination. It is a newly developed sensor in the second half of the century, and examples include enzyme sensors, microorganism sensors, immunity sensors, tissue sensors, DNA sensors and, etc.

Classified by detection type, there are displacement sensors, flow sensors, temperature sensors, speed sensors, pressure sensors, etc. As for pressure sensors, there are metal strain foil pressure sensors, semiconductor pressure sensors, capacity pressure sensors and other sensors that can detect pressure. As for temperature sensors, it includes thermal resistance sensors, thermocouple sensors, PN junction temperature sensors and other sensors that can detect temperature.

This is also the method that classifies sensors according to the human sense organ that each sensor can replace, such as vision sensors, including various optical sensors and other sensors that can replace the visual function; hearing sensors, including sound pick-up, piezoelectric sensors, capacity sensors and other sensors that can replace the hearing function; olfaction sensors, including various gas sensors and other sensors that can replace the smelling function (Harsányi, 2000). This kind of classification is good for the development of simulation sensors.

In many situations, these classification methods are used together. For example, the strain gauge pressure sensor, conductance cardiac sounds sensor, thermoelectric glucose sensor and so on. The classification has met problems as a result of the diverse development of sensing technology. Therefore the classification methods have their advantages and disadvantages. Any standard classification methods don't exists so far.

1.2 Biomedical Measurement Technology

Biomedical signals are usually weak, random with strong noise and interference, allow dynamic change and exhibit significant individual differences. Therefore, biomedical measurement technologies are more complex and rigid than common industrial detection technology.

Biomedical measurement is a guiding technology in the acquisition and processing of biomedical information, and is directly related to the research of biomedical sensing technology, biomedical measurement methods, electronics and measuring systems. Therefore, the innovative research and development in biomedical measurement has a direct effect on the design and application of sensors and medical instruments.

Biomedical measurement technology involves the detection of physical, chemical and biological signals in different levels of organisms. For example, ECG, EEG, EMG are electrical physiological signals; blood pressure, body temperature, breath, blood flow and pulse are non-electrical physiological signals; blood and urine are chemical or biological signals; enzymes, proteins, antibodies and antigens are biological signals. Similarly, the biomedical measurement systems demands particular reliability and security.

Nowadays the measurement of physical signals has been popularized and many measurements of chemical signals have practical applications. The measurement of biological signals is mostly at the laboratory research stage. With a greater combination of microelectronics, optoelectronics, quantum chemistry and molecular biology with traditional sensing technology, the measurement methods and system for detecting complex organisms will enjoy a bright future. Biomedical measurement technology will also develop into mini-type, multiple parameter and practical applications. The advancements of electronics, IC technology, computer technology and advanced signal processing and intelligent algorithms will promote the application of biomedical measurement.

1.2.1 Bioelectrical Signal Detection

The detection of physiological quantities in the circulatory system and nervous system develops relatively early and rapidly and its importance always leads to a large amount of research reports. Take ECG as an example. Many researchers are still working on automatic extraction and discriminating arrhythmia information from ECG under strong interference. In addition, the detection of the P wave, the ST segment in ECG, research on obtaining an ECG of a fetus from a mother's body surface, on high frequency ECG, on body surface real-time detection and late potential detection have been improved to different extents. ECG detection is mainly applied in diagnosing heart disease and preventing sudden cardiac death. Moreover, it could also aid surgical investigational procedures (Tigaran et al., 2009). Although these research achievements are not mature enough to be put into clinical use, they improve the function of ECG diagnosis and monitoring devices.

1.2.2 Biomagnetic Signal Detection

The biomagnetic field comes from the *in vivo* human body with biological electrical activities, such as MCG, MEG, MMG, etc. In addition, it also includes the magnetic field caused by the magnetic medium in the tissue when affected by an external magnetic field. An invasive strong magnetic mass can also cause an internal biomagnetic field. At present we can detect these magnetic fields in the laboratory. However, commonly a biological magnetic field is very weak. For example, MCG intensity is about 10^{-10} T and MEG is about 10^{-12} T. Therefore SQUID (superconducting quantum interference device) in the liquid nitrogen container is used to detect the biological magnetic field and the measurement system should be placed in a special shielding environment.

In contrast to the detection of bioelectricity, the detection of a biomagnetic field has many features. Take the measurement of MCG as an example. The detection system does not directly come in contact with the organism, which means that the detection uses a detecting coil rather than an electrode to pick up the biological signal. Therefore it receives no effect from the surface of the objects and does not cause an electrode artifact, which is electrically safe. Besides, the detecting signals come from a certain spot or place rather than the difference between two points. Therefore, a location measurement can take place. The magnetoconductivity in tissue is well-distributed which means that biomagnetic signals will not distort when spreading in the body. As a result, research on biomagnetic detecting methods has become one of the pioneering and hot topics and has good application prospects. With the development of room temperature superconductor technology, biomagnetic detection will reach the clinical application stage.

1.2.3 Other Physiological and Biochemical Parameter Detection

It has become a common practice to use sensors non-invasively to detect non-invasive blood pressure, blood flow, breath, pulse, body temperature and cardiac sounds, which lead to wide applications in clinical examinations and other monitoring techniques. The trend is to develop new non-invasive or slightly invasive detecting methods and use one sensor once to detect multiple physiological parameters. For example, use the photoelectric method to detect the pulse as well as other information such as the heart rate, blood pressure, oxygen saturation; use electromagnetic coupling or optical coupling to detect intracranial pressure, and pressure in the mouth. Non-contact and long-distance detection also lead current development trends.

Biochemical parameter detection usually uses blood and body fluid as a sample to conduct the measurement. Therefore, most of the methods are invasive and cannot measure the changes in the parameters over a long-time and in real-time. At present, non-invasive and slightly invasive biochemical parameter detecting methods have received great attention. For example, researchers have detected phenacetin in the saliva and compared it with the results of blood plasma tests; researchers extract lixivium by exerting a small amount of negative pressure on the skin and then use ion field effect transistor sensors to detect blood sugar; dielectric spectroscopy (DS) has been applied to monitor changes in the glucose level by combining electromagnetic and optical sensors (Talary et al., 2007).

1.3 Characteristics of Biomedical Sensors and Measurement

Biomedical measurement has specificity when used for human signal detection and is a non-invasive, safe and reliable measurement. It has become an important research project in recent years. Non-invasive detection, which causes no wound or a slight wound, is easily administered to people. It helps to keep the physiological status of objects, and long-time or real-time monitoring can take place. Therefore it is convenient for clinical examination, monitoring and recovery evaluation. Non-invasive detection has become an important part of biomedical measurement technology.

Biomedical measurement research involve some special measurement methods, e.g., low-noise and anti-interference technology, picking up signals, analyzing and processing technology and measurement system, analog and digital circuits, computer hardware and software and even BCI (brain-computer interface) technology, etc. It also depends on the development of the life sciences (such as cytophysiology, neurophysiology, biochemistry, etc.). The diversity of research objects in biomedical detecting technology makes the research projects dispersive in this field (Wang and Ye, 2003). However, any promotion of detection methods in physiological quantities and biochemical quantities will greatly compel the advancement of the whole of life science as well as the invention of new diagnosis and treatment devices.