传感材料与传感技术丛书

Sensing Material and Sensing Technology Series

BIOMEDICAL SENSORS

EDITED BY **DERIC P. JONES**

影印版

生物医学传感器

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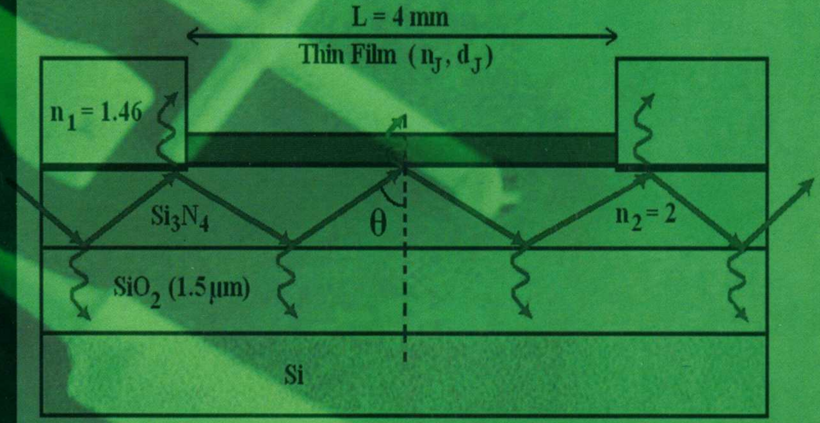

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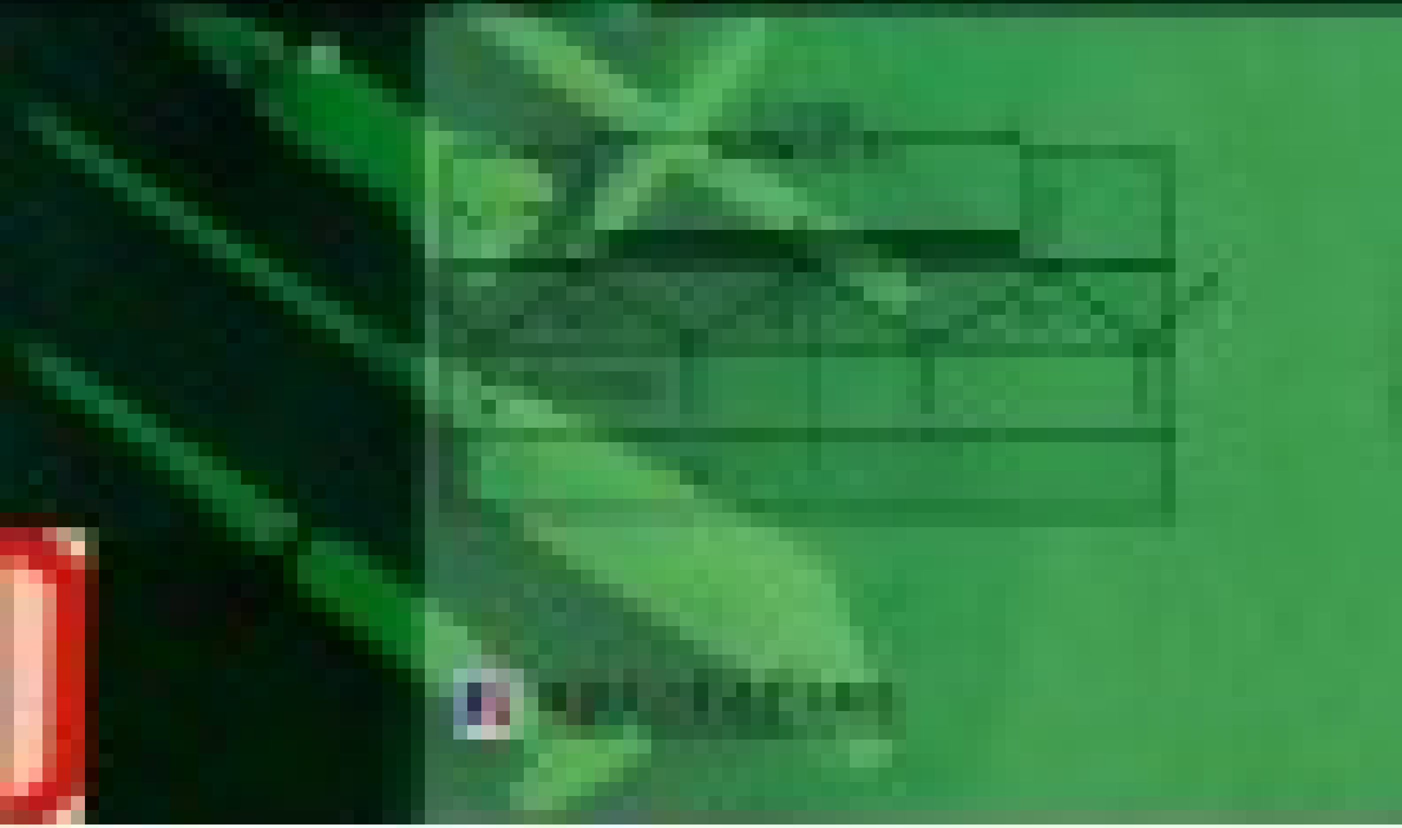

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影 印 版 说 明

1.《传感材料与传感技术丛书》中第一个影印系列 MOMENTUM PRESS 的 *Chemical Sensors:Fundamentals of Sensing Materials & Comprehensive Sensor Technologies*（6 卷，影印为 10 册）2013 年出版后，受到了专家学者的一致好评。为了满足广大读者进一步的教学和科研需要，本次影印其 *Biomedical Sensors*（1 卷，分为上下册影印），本书是下册（5 ~ 9 章内容）。

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SENSORS TECHNOLOGY SERIES EDITOR-IN-CHIEF'S PREFACE

In recent years the interface between the life sciences and the physical sciences has become inhabited by researchers and practitioners with knowledge and expertise in both areas. This is a very welcome trend because traditionally it has been difficult for the physical scientist to appreciate the needs of the life scientist or medical practitioner, and equally difficult for the biomedical community to ascertain what might be possible in physical terms. Happily, this gulf is rapidly being filled. In particular, the development of instruments based on physical, chemical, and biological principles has burgeoned. Inevitably, as with all things, there are downsides, the predominant one in the medical context being related to cost, which for some installations can represent several millions of dollars.

However, rather more modest analytical instruments require sensors of various types as well, and this volume presents a selection of these, complete with detailed background material on the scientific and technical principles relevant to each. Such multifaceted work represents a major ongoing international endeavor and, as such, merits more comprehensive bibliographical material than do some of the more mature topics in other volumes of the series. The descriptive material and relevant bibliographies in the present compilation have been provided by an author list of leading scientists in their various specialties assembled by the volume editor, Deric Jones, who has drawn upon his experience as Head of Medical Electronics & Physics at the Medical School of St. Bartholomew's Hospital in the University of London. These authors have in turn drawn upon their own experiences to present authoritative reviews of sensors ranging from basic devices for measuring temperature and flow, through both ionizing and nonionizing radiation, to transducers for ultrasound, chemical, and biological sensing.

J. Watson
Editor-in-Chief
July 2010

ABOUT THE EDITOR-IN-CHIEF

Joseph Watson is an electrical engineering graduate of the University of Nottingham, England, and the Massachusetts Institute of Technology. He has published books and papers in various areas including electronic circuit design, nucleonics, biomedical electronics, and gas sensors and has been a visiting professor at the University of Calgary, Canada, and the University of California, Davis and Santa Barbara. Dr. Watson has held various consultancies with firms in the United States, Canada, and Japan and since retirement from the University of Wales, Swansea, has continued as chairman of the UK-based Gas Analysis and Sensing Group and as editor-in-chief for the Sensors Technology Series for Momentum Press.

PREFACE

BACKGROUND

In 400 B.C. the Greek physician Hippocrates placed his hand on a patient's forehead and used the sense of touch to estimate body temperature. The five human senses were effectively the only sensors available to the "father of medicine" and his descendents until the seventeenth century when the first objective biomedical sensor in the form of a crude thermometer was devised. However, it was only toward the end of the nineteenth century that developments in science made possible significant advances in biomedical sensor technology. The twentieth century and the modern era of biomedical technology may have been ushered in when, in November 1895, Wilhelm Röntgen astonished the medical profession and the world with an X-ray image of his wife's hand that he obtained using photographic film as a sensor. Twenty-four centuries after Hippocrates, sensors now extend the range of human senses to make possible diagnostic and therapeutic techniques that the ancient Greeks could never have envisioned. Almost all modern biomedical measurement and imaging systems depend upon sensors of one kind or another, although in many cases they are not immediately evident, often being hidden deep within the medical instrument. Today it is quite common for there to be a number of sensors embedded within the same medical device; for example, the ubiquitous hospital blood gas analyzer will routinely incorporate more than half a dozen sensors, one for each gas and substance to be analyzed.

WHAT IS A SENSOR?

The broadest and simplest definition of a *sensor* is "anything that responds to an input of interest." However, a general-purpose dictionary definition is "a device that detects or measures some condition or property and records, indicates, or otherwise responds to the information received." Although this is an excellent everyday definition, for biomedical engineering and medical physics purposes it is too imprecise. A device that merely "detects some condition or property," presumably by registering the presence or absence of a physical quantity with a simple yes-or-no response, would be called a "detector," not a sensor. Although detectors have important uses in medicine, especially as the basis of alarms, they are not generally regarded as sensors. For practical biomedical applications a *sensor* is better defined as "*a device that responds to a physical input of interest with a recordable functionally related output that is usually electrical or optical.*" In a biomedical context, of course, the term *physical input* is taken to include chemical and biochemical quantities and concentrations. A device with an electrical output satisfies the "records or indicates" criterion in the general dictionary definition because electrical signals can be amplified and processed readily to give a display on a monitor, an output on a chart recorder, or an input to a digital data storage system. Sometimes a sensor's optical output signals *are* the required output—in imaging, for example—but any optical output signal can usually be converted fairly easily into an electrical signal by means of a photosensor.

It is the requirement that the output be *functionally related* to the physical quantity of the input that distinguishes a sensor from a yes–no detector. The most desirable functional relationship is a simple linear one, whereby a doubling of the input physical quantity results in a doubling of the electrical or optical output. Such a relationship usually leads to a relatively simple calibration procedure. Unfortunately, many common and widely utilized sensors do not exhibit such linear behavior—a thermistor for temperature measurement, for example—but nevertheless they can still be made into useful practical devices by using suitable, if more elaborate, calibration methods (see Chapter 1).

The terms *sensor* and *transducer* are often used synonymously, although there are times when this may not be appropriate. It seems to be generally accepted in science and technology that a working definition of a *transducer* is "a device that converts one form of energy into another, the latter often being electrical." A sensor usually meets this criterion and can therefore also be described as a transducer. Even sensors of biochemical quantities or concentrations are somehow converting chemical energy into electrical or optical energy. However, a transducer, unlike a sensor, does not necessarily have an electrical or optical output that is intended to be recordable and also functionally related to its input. An example of this is in ultrasonic imaging (see Chapter 6), where the same probe has two quite separate functions: (1) to generate the ultrasonic waves that enter the human body and (2) to respond to, or sense, the ultrasonic echoes from tissue interfaces within the body. In the first case the probe is acting as a *transducer*, converting a short pulse of electrical energy into ultrasonic mechanical energy; in the second case the probe acts as a *sensor*, converting the incident ultrasonic mechanical energy in the echo into an electrical signal that is processed to give the recorded image. On the basis of this distinction, transducers can sometimes be regarded as components of sensors. For example, a diaphragm in a microphone or a pressure sensor converts sound or pressure energy into strain energy in the diaphragm; a second transducer stage is required to convert this strain energy into recordable electrical energy in order to make a complete sound or pressure sensor. The use of the word *sensor* allows a distinction to be made between a device that gives a measurable recordable output that is functionally related to changes in a physical quantity at its input, and a device for converting one form of energy into another—a *transducer*, which may not necessarily have the properties of a sensor.

SCOPE OF THIS VOLUME

This volume includes a wide range of topics in biomedical engineering and medical physics. However, the subject of biomedical sensors has grown very rapidly in the last three decades and now encompasses such a huge field that even a "comprehensive" treatment of this sensor technology must, of necessity, be selective. The choice of topics was influenced principally by their clinical relevance and also to some extent by the contents of a long-established graduate-taught master's course at the Medical School of St. Bartholomew's Hospital, London, UK, that the editor organized. It was decided to include sensors associated with the measurement of temperature, fluid flow, radiation (including ionizing radiation, non-ionizing radiation, and ultrasound), and also chemical and biochemical sensors, including biosensors. Those sensors associated with purely mechanical physical quantities have not been treated as primary subjects in this volume. Hence, sensors for the measurement of position, force, pressure, and acceleration, which are all of particular importance in the field of biomechanics, have been left for the present.

The aim here is to emphasize the technological principles and the practical applications of biomedical sensors rather than the theoretical concepts. The treatments in the chapters usually include details of the technical principles of the sensor together with those of any associated peripheral devices essential for registering the response of the sensor. Examples of the practical applications of the systems associated with the sensors have been included, but detailed discussions of the operations of complete systems have been avoided. Generally the volume concentrates on sensors that are currently used in practice or are likely to be used in the near future. Research laboratory techniques that are speculative or a long way from being practically viable in a clinical context have not been included. Some chapters, where appropriate, contain critical comparisons of manufacturers' sensor data.

READERSHIP

This volume is intended to provide a good initial introduction and reference source for biomedical engineers and medical physicists who need to become acquainted with new fields and topics. It should act as a reliable guide to the bewildering array of more specialized literature and texts on the subject. The contents should be accessible to a broad range of professionals in biomedicine, including practicing experienced biomedical engineers, medical physicists, clinical technologists, and clinicians working in a hospital or other health care environment.

Academics in higher education institutions will find the book an invaluable resource to further their scholarship and advance research projects on sensors and other medical devices. In addition, students should benefit from a well-written, advanced textbook suitable for those final-year undergraduate, postgraduate, and research students aiming to pursue a career in the field of medical physics or biomedical engineering.

Engineers and applied physicists working for health care providers or for the pharmaceutical and medical instrumentation industries will find in this volume a rich source of relevant information. It also contains essential tools to help solve practical problems encountered in both routine applications and the challenges of advanced development work.

THE CONTENTS

The majority of the distinguished authors who have contributed to *Biomedical Sensors* have had decades of practical experience in biomedical engineering and medical physics. Moreover, the authors have well-established international reputations and many are world-renowned experts in their fields.

The chapters are organized according to the measurand being considered, that is, the physical quantity being sensed and measured (e.g., temperature, ionizing radiation, or chemical concentration).

The first chapter deals with the measurement of the temperature of the human body. Temperature has been used by physicians since the earliest times for the diagnosis and monitoring of disease. Given its fundamental importance, it is surprising that there have been so few comprehensive reviews of the subject. It is almost as if it is taken for granted that anyone can measure body temperature accurately if required. This chapter shows that this is not necessarily true, particularly as there are now so many possible techniques, some intended for specific applications, that the choice of an appropriate method to give accurate reliable results is often not easy. Chapter 1 provides a timely overview of modern clinical thermometry and gives a critical assessment of the accuracy and applicability of the various methods available to the physician, surgeon, parents, and others for whom assessing the temperature of the human body is of vital importance.

Chapter 2 is primarily concerned with the most important liquid in the body, which is, of course, blood. The measurement of blood velocity and blood flow in arteries and veins is a major activity for large numbers of biomedical engineers and medical physicists. The quantitative estimation of blood flow in the limbs and in various organs is of great value in many diagnostic investigations, and advances in the subject have made significant contributions to cardiology. The chapter provides a comprehensive review of the traditional flow measurement techniques, such as indicator dilution methods, plethysmography, and ultrasound for arteries and veins. It also covers more modern techniques such as ultrasonic Doppler methods in cardiology and functional magnetic resonance imaging (MRI) in the brain. More advanced topics, such as the use of contrast agents in ultrasonic imaging and MRI in the quantitative analysis of dynamic processes are also discussed. The chapter ends with a brief overview of the measurement of flow in other fluids, including urine, saliva, tears, and gastric acids.

Chapter 3, on respiratory flow sensors, considers another fluid, namely, the gas that flows out of and into the human lung. It requires the use of quite specialized techniques that are different from those outlined in Chapter 2 for liquids. Every large hospital has a pulmonary function laboratory, because respiratory disease is one of the most significant public health burdens in developed countries. Indeed, respiratory diseases account for about one-third of all deaths in the United States. It might be thought that the measurement of airflow is relatively simple, but there are many technical challenges associated with the application of flow sensors in pulmonary medicine. These are dealt with in an exemplary manner in this chapter.

Chapter 4 deals comprehensively with ionizing radiation sensors in medicine, a field that is primarily the preserve of medical physicists, but also engages numerous engineers in the design, development, and maintenance of medical X-ray equipment. The importance of ionizing radiation can be judged from the fact that it is likely that two-thirds or more of all the clinical engineers and scientists working in hospital environments are employed in X-ray or other ionizing radiation–related activities in diagnostic imaging, radiotherapy, nuclear medicine, and radiation protection. The chapter gives an overview of the basic requirements for sensing ionizing radiation, the interactions with materials, and the criteria for assessing the performance of the sensors. It goes on to treat sensors for dosimetry ranging from semiconductors and radiographic film to diamond and outlines their advantages and disadvantages. Next, sensors for imaging are reviewed, including radiographic film and flat-panel detectors, while the characteristics of various scintillator materials for sensors are also outlined. Specific applications and advances in imaging in computed tomography (CT), mammography, single photon emission computed tomography (SPECT), and positron emission tomography (PET) are also covered. The final part deals with sensors for ionizing radiation spectroscopy and concludes with examples of detector selection in a series of case studies.

Chapter 5 deals with nonionizing electromagnetic radiation and radiometric and photometric measurements. Lasers have played an important role in biomedicine for more than three decades, finding significant applications in ophthalmology, surgery, and photodynamic therapy for cancer treatment. In Europe, recent directives on the use of artificial optical radiation in the workplace are being implemented, while in the United States, the Food and Drug Administration (FDA) Center for Devices and Radiological Health produces similar guidance notes. There is also an increasing use of ultraviolet (UV) light therapy for the treatment of eczema and hyperbilirubinemia in newborn babies, up to 60% of whom may suffer from this condition. This authoritative chapter is timely, as there is a growing need to understand the challenges faced in obtaining accurate dosimetry measurements with nonionizing radiation, particularly when it is required to make comparisons with other treatment centers. There is an explanation of radiometric and photometric terms and a review of measurement sensors. Radiometric sensors for the measurement of UV irradiance in phototherapy treatment and their application are discussed. The chapter ends with a section on the objective measurement of solar radiation at the earth's surface and, in particular, the measurement of sun-burning UV radiation, a topic of some importance with the increasing incidence of skin cancer worldwide.

Ultrasonic imaging was originally developed in the 1960s to replace potentially damaging X-rays in fetal imaging. It now finds applications not only in obstetrics, but in a wide range of disciplines from cardiology to ophthalmology and gastroenterology. Chapter 6 reviews in depth the probes that generate and sense the ultrasonic signals that enter the human body in ultrasonic imaging. It complements the sections on ultrasonic flow measurements in Chapter 2. The principles of operation of the probes are outlined and various practical electrical and acoustical models of the sensors are developed. The construction of single-element probes and multielement arrays is considered and the characteristics of various modern piezoelectric materials used to make the probes are compared. Focusing principles and performance criteria are established, followed by some examples of the clinical applications of phased and linear arrays. Finally, advanced topics such as multimode operation and the construction of two-dimensional arrays are considered.

The measurement of the concentrations of the various chemical components of blood is of great importance in the diagnosis and treatment of disease. Blood gas analyzers are among the most significant of medical instruments and operate 24 hours a day, every day, in all major hospitals. Gas sensors also perform a vital role in anesthesia, measuring accurately the concentrations of the anesthetic agents. Chapter 7 is a comprehensive overview of the principles of the sensors used to measure these and other chemical compounds. Electrochemical sensors for the measurement of pH, pO_2 (the partial pressure of oxygen), and pCO_2 (the partial pressure of carbon dioxide) in blood both noninvasively and invasively are described. Advanced miniature microelectromechanical systems (MEMS) for sensing blood pO_2 and pCO_2 and similar ion-selective field effect transistors (ISFETs) for pH are covered. Optical fiber chemical sensors for pH, pCO_2, and invasive and noninvasive blood oximetry are reviewed. The principles of gas phase sensors for the real-time measurement of the concentrations of oxygen, carbon dioxide, and anesthetic gases in respiratory medicine and anesthesia are outlined. There is also a review of a variety of methods for blood glucose sensing from optical and electrochemical sensors to biosensors. Some of the latter part of this section complements the following chapter on biosensors. Finally, a highly sensitive acoustic chemical sensor is described that makes use of a quartz crystal microbalance coated with zeolite to detect acetone in the breath for the diagnosis of diabetes and for other clinical analyses.

Biosensors have evolved from the marriage of two disciplines: optoelectronics technology, exemplified by microcircuits and optical fibers, and molecular biology. They are among the most exciting and challenging developments in analytical devices and have the potential to make continuous measurements of blood chemistry at the bedside or, by means of a chip on a catheter, in a patient's vein. They incorporate a biological recognition element that interacts with a target molecule to provide a highly selective sensor. Drugs, metabolites, proteins, and nucleic acids are all targets for biosensors. Chapter 8 introduces and reviews enzyme-based biosensors—in particular, those based on glucose oxidase, used to estimate blood glucose, and urease for the estimation of blood urea. Enzyme immobilization techniques are described, from physical entrapment and chemical immobilization to surface adsorption. Optical biosensors, including optical fibers, surface plasmon resonance, and attenuated total reflection types are covered. Modified electrochemical biosensors that can be used for home glucose monitoring are also described. Microfabricated enzyme-linked field effect transistors (ENFETs), whole cell biosensors, and nanobiosensors are discussed. Biosensors have enormous potential, but there are also formidable challenges for practical utilization, which are outlined clearly in this chapter. The problems include robustness and lifetime and operational stability, but these are being resolved using a variety of sensors, formatting techniques, and MEMS.

Medical thermography is the ultimate noninvasive investigative technique in which clinically relevant information is obtained without any contact with the patient and without the use of penetrating radiation. It is the subject of the final chapter and uses infrared (IR) radiation that is passively emitted by the human body. Medical thermography is a fine example of "swords into plowshares" technology transfer, because most of the significant advances in the challenging field of IR imaging have been made for military purposes. Thermography is unique in providing quantitative information on inflammatory processes (e.g., in rheumatic diseases), and modern cameras are even capable of detecting infection in passengers at airport gates. In addition, skin diseases, nerve injuries, industrial and sports injuries, and disruptions to the peripheral circulation have all been investigated using IR imaging. This chapter complements Chapter 5, in that it describes a practical application of IR radiometry. It begins with an historical overview of IR detection and imaging and the development of early thermographic cameras. The IR spectrum and its subdivisions and the laws governing the emission of IR radiation are then described. Next, IR camera characteristics and the measurement of IR radiation using IR thermometers and thermal imagers are reviewed, followed by an outline of the development of modern focal-plane imaging arrays. Finally, the characteristics of a variety of sensors, from miniature bolometers to photon detectors, are described and figures of merit for assessing thermal camera performance are discussed.

The design, manufacture, distribution, and maintenance of sensors and the biomedical systems that depend on them are of immense and growing commercial significance. Multimillion-dollar companies, such as the biomedical divisions of General Electric, Philips, and Siemens, together with scores of other smaller enterprises, all base their prosperity on sensors, since virtually all their biomedical products depend critically on the reliable functioning of sensors of one kind or another.

Advanced biomedical sensors represent a commendable application of cutting-edge technology for the benefit of humanity. The practice of modern medicine would be impossible without them. The authors of this volume have communicated not only their consummate expertise, but also their enthusiasm for the subject. Readers will find here a rich source of practical knowledge and, it is hoped, the inspiration to make their own contributions to this rapidly expanding and important field.

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overcome many obstacles to ensure that the series is being published. I am deeply indebted to him for his sound advice, for his unfailing support, and for much more. Finally, I would like to thank my wife, Jennifer, for her forbearance and patience.

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July 14, 2010

ABOUT THE EDITOR

Professor Deric Powell Jones BSc DIC PhD was born in Monmouthshire, South Wales, and received the degrees of BSc in physics and PhD in the superconductivity of alloys from Imperial College, London. He worked as a medical physicist at St. Bartholomew's Hospital and then as a lecturer at the Medical School. During more than twenty-five years spent at St. Bartholomew's he became a reader in the University of London and head of Medical Electronics and Physics in the Medical School. His research interests include the application of opto-electronic techniques in anesthesia and surgery and also the development of new techniques for physiological measurements in respiration and ophthalmology. He is a fellow of the UK Institute of Physics and of the UK Institute of Physics and Engineering in Medicine and a chartered engineer and a senior member of the Institute of Electrical and Electronics Engineers. Professor Jones is currently affiliated to the Biomedical Engineering Department at City University, London.

CONTENTS

CHAPTER 5

NONIONIZING ELECTROMAGNETIC RADIATION

SENSORS FOR RADIOMETRIC AND PHOTOMETRIC MEASUREMENTS

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5.1. INTRODUCTION

Radiometry is defined as the science and technology of the measurement of optical radiation, which is in turn defined as electromagnetic radiation of wavelengths between 1 nm and 1000 μm. Photometry is the science and technology of the measurement of optical radiation as it is perceived by the human eye, and can be considered as a special case of radiometry. The eye is sensitive only to wavelengths in the 360 nm to 830 nm range (CIE, 1983), which is often referred to as "light."

This chapter deals with radiometric, photometric, and spectroradiometric sensors. Radiometric sensors, or "radiometers," are defined as instruments that are designed to measure one or more of the radiometric quantities or parameters used to quantify the characteristics of a source, beam, or field of optical radiation. The term *radiometer* is usually associated with instruments that respond over a relatively wide but well-defined range of wavelengths of optical radiation. This range of wavelengths should be included in the specification of each radiometer.

Photometric sensors or "photometers" are defined as instruments designed to measure one or more of the photometric quantities or parameters used to quantify the characteristics of a source, beam, or field of optical radiation. All photometric measurements are weighted by the spectral response of the human eye. When measurements are made using the eye as the detector, this is referred to as visual photometry. More generally, however, photometric measurements are carried out using photodetectors whose spectral responsivity has been engineered to simulate the spectral response of the average human eye. This is referred to as physical photometry. Physical photometry also includes measurements made using mathematical calculations to correct spectroradiometric measurements for the spectral response of the human eye. In the case of photometers, there is no need to specify a wavelength range of response since the response of a photometer will, by definition, follow the internationally agreed relative spectral responsivity of the average human eye, which is known as the *spectral luminous efficiency function* (CIE, 1983) or the $V(\lambda)$ function.[1]

The optical radiation emission of all sources varies with wavelength, so it is important to know the wavelength distribution of their radiometric parameters. Another class of radiometric sensors has been developed to address this task by dispersing the optical radiation being evaluated into its spectral components. These instruments are known as spectroradiometers. Their design is usually more complex than broadband radiometers and photometers because they employ a component such as a diffraction grating, prism, or Fourier transform (FT) spectrometer that disperses the incident radiation into its component wavelengths.

This chapter will begin by defining the most important radiometric and photometric parameters because it is these parameters that radiometric and photometric sensors are intended to measure. The relation between the various radiometric and photometric parameters will be highlighted because every radiometer and photometer employs a photodetector to convert the total radiant power incident on its active area into an electrical signal. This is convenient if the aim is to measure radiant power, but to measure another radiometric or photometric quantity, the relationship between that quantity and the radiant or luminous power incident on the detector is required for the former to be measured. This is relatively straightforward because the relationship between the various radiometric or photometric parameters is purely geometrical, as will be shown in the next two sections.

5.1.1. DEFINITIONS OF THE MAJOR RADIOMETRIC ENTITIES AND UNITS

Radiant power, sometimes referred to as radiant flux, is defined as the time derivative of radiant energy and represents the rate of flow of that radiant energy. It is denoted by the symbol Φ and has units of watts. Radiant power is used, for example, to quantify the power of a laser beam. Total radiant power or flux is frequently encountered in radiometry, and this is the total radiant power emitted by a source in all directions. Note that radiant energy or "exposure" can be calculated by integrating the radiant power over a period of time. Radiant intensity[2] is the radiant power radiated from a source into a unit solid angle[3] in a defined direction and is expressed in units of watts per steradian (W sr^{-1}). Radiant intensity is denoted by the symbol I and is associated with point, isotropic[4] sources and sources whose dimensions are small compared to the distance between the source being characterized and the observer. Irradiance is the radiant power incident on a surface per unit surface area from a hemisphere. It is denoted by the symbol E and has units of watts per square meter (W m^{-2}). Radiant exitance refers

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[1] $V(\lambda)$ corresponds to photopic vision. For scotopic vision, an alternative $V'(\lambda)$ is defined (CIE, 1983).

[2] The term intensity has different meanings when it is used in different fields. In radiometry it is defined as radiant power per unit solid angle and has units of watts per steradian (W sr^{-1}). The same term is (wrongly) used to mean irradiance or radiant power and it is even used to denote radiance in atmospheric physics (Palmer, 1993).

[3] Solid angle is the three-dimensional (3-D) equivalent of the plane angle. The solid angle of a cone is defined as the ratio of the area cut out on a spherical surface with its center at the apex of that cone divided by the square of the radius of the sphere. It has units of steradians (sr). A hemisphere has a solid angle of 2π sr.

[4] An isotropic source is a spherical source that radiates uniformly in all directions, that is, its radiant intensity is the same in all directions.