Sensors Applications
Volume 3

Sensors in Medicine and Health Care

Edited by
P. Å. Öberg, T. Togawa, F. A. Spelman

Series Editors:
J. Hesse, J. W. Gardner, W. Göpel

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Preface to the Series

As the use of microelectronics became increasingly indispensable in measurement and control technology, so there was an increasing need for suitable sensors. From the mid-Seventies onwards sensors technology developed by leaps and bounds and within ten years had reached the point where it seemed desirable to publish a survey of what had been achieved so far. At the request of publishers WILEY-VCH, the task of editing was taken on by Wolfgang Göpel of the University of Tübingen (Germany), Joachim Hesse of Carl Zeiss (Germany) and Jay Zemel of the University of Philadelphia (USA), and between 1989 and 1995 a series called *Sensors* was published in 8 volumes covering the field to date. The material was grouped and presented according to the underlying physical principles and reflected the degree of maturity of the respective methods and products. It was written primarily with researchers and design engineers in mind, and new developments have been published each year in one or two supplementary volumes called *Sensors Update*.

Both the publishers and the series editors, however, were agreed from the start that eventually sensor users would want to see publications only dealing with their own specific technical or scientific fields. Sure enough, during the Nineties we saw significant developments in applications for sensor technology, and it is now an indispensable part of many industrial processes and systems. It is timely, therefore, to launch a new series, *Sensors Applications*. WILEY-VCH again commissioned Wolfgang Göpel and Joachim Hesse to plan the series, but sadly Wolfgang Göpel suffered a fatal accident in June 1999 and did not live to see publication. We are fortunate that Julian Gardner of the University of Warwick has been able to take his place, but Wolfgang Göpel remains a co-editor posthumously and will not be forgotten.

The series of *Sensors Applications* will deal with the use of sensors in the key technical and economic sectors and systems: *Sensors in Manufacturing, Intelligent Buildings, Medicine and Health Care, Automotive Technology, Aerospace Technology, Environmental Technology* and *Household Appliances*. Each volume will be edited by specialists in the field. Individual volumes may differ in certain respects as dictated by the topic, but the emphasis in each case will be on the process or system in question: which sensor is used, where, how and why, and exactly what the benefits are to the user. The process or system itself will of course be outlined and the volume will close with a look ahead to likely developments and applications in the future. Actual sensor functions will only be described where it seems necessary for an understanding of how they relate to the process or system. The basic principles can always be found in the earlier series of *Sensors* and *Sensors Update*.

The series editors would like to express their warm appreciation in the colleagues who have contributed their expertise as volume editors or authors. We are deeply indebted to the publisher and would like to thank in particular Dr. Peter Gregory, Dr. Jörn Ritterbusch and Dr. Claudia Barzen for their constructive assistance both with the editorial detail and the publishing venture in general. We trust that our endeavors will meet with the reader's approval.

Oberkochen and Coventry, November 2000

Joachim Hesse
Julian W. Gardner

Preface to Volume 3 of "Sensors Applications"

Diagnosis of disease and its therapy are problems in sensing and control. The patient who seeks information or care wants to learn the state of her organism. The same person, having been diagnosed with a problem seeks to monitor her condition and ensure that the solution offered by the physician is appropriate. In that sense, there are similarities between medical, aerospace, automotive and atmospheric sensing.

The authors of this volume of the Wiley Sensors Applications Series cover biomedical sensing in breadth: ranging from fundamental modalities like optics and imaging, ranging to applications such as hemodynamics, neonatal monitoring and prostheses for the deaf. Each topic is reviewed in depth, so that a practicing biomedical engineer or a bioengineering graduate student could gain insight into a specific topic and learn to apply the principles that are given.

The co-editors P.Å. Öberg, F.A. Spelman and T. Togawa give an introductory review of the history of medical sensing, and use historical examples to point to the future. What will the bioengineers of the future provide to aid diagnosis? Will the dreams of completely non-invasive sensing be reached in the future? Will they be realized in the near future?

Dr. Öberg follows the introduction with an in-depth exposition of optical sensing in medical care. The chapter leads the reader through the fundamental principles of optics and uses those principles to base a discussion of applications of biomedical optics.

Drs. J.D. Newman and A.P.F. Turner review glucose sensing, both invasive and non-invasive approaches. The chapter is tantalizing: if glucose can be sensed, can its level be controlled as well? That is the grail of glucose sensing. Drs. Newman and Turner ask not only if a sensor be built, but whether it can be manufactured.

Dr. S. Ueno presents the principles and application of magnetic resonance imaging (MRI). He describes the techniques employed to acquire detailed images, and delves into the ways that anatomy and physiology can be joined with a sensitive imaging modality.

Dr. K. Yamakoshi describes non-invasive measurement of hemodynamic variables. He provides the principles that have lain behind the sphygmomanometer for more than 100 years, techniques that were limited to measurements of sedentary subjects. He expands his work to review methods by which hemodynamics can be monitored non-invasively in ambulatory subjects. The work is exciting because it invites the possibility of giving information about patients during normal activities as contrasted to measurements that are made while people are sedentary and possibly anxious in a medical setting.

Drs. A. Johansson and B. Hök introduce the respiratory system and methods by which it can be monitored in the clinic and at rest. They present sensors to observe respiratory flows and pressures directly, as well as some devices that measure respiratory rate to indicate the condition of the respiratory system. They provide a clear exposition of the benefits and limits of each of the sensing modalities that they describe.

Dr. P. Rolfe addresses fetal and neonatal monitoring. He covers measurements of both the mother and the infant, and describes the information gained by each measurement. He leads the reader through sensing techniques and describes sampling and processing issues as well.

Dr. T. Tamura brings the reader into the realm of motion and energy analysis. His chapter on body motion analysis develops both direct and indirect methods of sensing, and then shows the applications of those methods. He leads the reader to conclusions about the energy that is consumed by humans in motion.

Drs. B. Hensel, G. Czgan, I. Weiss, and T. Nappholz present information about cardiac pacemaking. They take the reader from an understanding of electrodes that are used both as stimulus sources and as sensors: bidirectional devices. They write about the processing necessary to achieve control of the rhythm of the heart, and offer information about continuous, long-term control of the heart, and the success of the work done in the area.

Dr. F.A. Spelman presents information about cochlear implants. The implant is presented as a substitute for a physiological sensing modality. The principles of design are given, descriptions of the success of the device are offered, and questions whose answers will lead to future designs are presented as well.

Drs. P.J. French, D. Tanase, and J.F.L. Goosen provide an enlightening chapter on the design and application of catheter-based sensors. They give a broad spectrum of applications ranging from blood flow to urology, describing the need for and application of navigational techniques to ensure that the locations of catheter tips are known and controlled. Their practical approach to sensor development and application gives the reader a view of both the process and application by which biomedical engineers approach problems.

Dr. T. Togawa closes this volume with an exposition of home health care and telecare. He describes several sensing applications and the ways by which they can provide information from patients to physicians at a distance. This provocative chapter can lead the reader to think about ways by which health care can be provided efficiently, at low cost and to people who, because of separation from medical centers, would otherwise not be served.

Each author or group of authors has provided an extensive bibliography, so that the readers of this volume can go to the original sources behind the chapters presented here. While the bibliography is not exhaustive, it will lead the inquisitive reader to a rich trove of information.

We thank every author for assembling a comprehensive and interesting chapter. The work done by each is substantial, and, we hope will benefit you as a reader and user of this volume. Special thanks are due to Dr. Martin Ottmar of Wiley-VCH as well as to his staff. Dr. Ottmar was incisive in his comments, helpful at all levels of production and patient to a fault. This volume has benefited greatly from his contributions. Finally, our families deserve thanks for patience and support during the production of this work. The book couldn't be complete without them.

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List of Abbreviations

2D	two dimensional
3D	three dimensional
3D-RA	3D rotational angiography
ABPM	ambulatory BP monitoring
ACOM	ambulatory CO monitoring
ADC	apparent diffusion coefficient
ARTMA	Advanced Real-Time Motion Analysis
AV	anteversion
BBB	blood-brain barrier
BioMEMS	MEMS applied to medicine and biology
BOLD	blood oxygenation level development
BPD	bi-parietal diameter
CBF	cerebral blood flow
CBV	cerebral blood volume
CCD	charge-coupled device
CFNN	compensatory fuzzy neural networks
CMOS	complementary metal oxide semiconductor
CNEP	continuous negative extra-thoracic pressure
CNS	central nervous system
CO	cardiac output
CSF	cerebrospinal fluid
CSI	catheter-system interface
CSI	chemical shift images
CT	computed tomography
DBP	diastolic blood pressure
DLT	direct linear transformation
DPF	differential pathlength factor
DTG	dynamically tuned gyroscope
DURS	direct ultrasound ranging system
DWI	diffusion-weighted imaging
ECG	electrocardiograph
EEG	electroencephalogram
EFM	electronic fetal monitoring

EHG	electrohystography
EM	electromagnetic
EMF	electromotive force
EMG	electromyogram
EOG	electrooculography
EPI	echo-planar imaging
EPS	electrode positioning system
FD	frequency domain
FE	field echo imaging
FES	functional electrical stimulation
FHR	fetal heart rate
FID	free induction decay
FLASH	fast low-angle shot
fMRI	functional MRI
FSR	force-sensitive resistor
FT	Fourier transform
GDH	glucose dehydrogenases
Gox	glucose oxidase
HFP	high-frequency power
HR	heart rate
HSP	hydrostatic pressure difference
IC	integrated circuit
ICP	intracranial pressure
IPPV	intermittent positive pressure ventilation
IR	infrared
IR-SE	inversion-recovery spin echo imaging
ISF	interstitial fluid
ISFET	ion-sensitive field effect transistor
IUGR	intra-uterine growth retardation
IUP	intra-uterine pressure
IVUS	intravascular ultrasound
LDF	laser Doppler flowmetry
LED	light emitting diode
LF	low frequency
LFP	low-frequency power
LITE	low-intensity treadmill exercise
MABP	mean arterial blood pressure
MAP	maximum amplitude of pulsation
MBP	mean blood pressure
MEMS	microelectromechanical systems
MFP	medium-frequency power
MIP	maximum intensity projection
MPG	motion-probing gradient
MRA	magnetic resonance angiography
MRI	magnetic resonance imaging

MRS	magnetic resonance spectroscopy
MSA	muscle sympathetic activity
MSS	Magnetic Surgery System
MTI	magnetic resonance imaging
MV	minute ventilation
NAD	Ch3
NADH	Ch3
NHE	normal hydrogen electrode
NIRS	near infrared spectrophotometry
NMR	nuclear magnetic resonance
Ox	oxidized species
PC	phased-contrast
PGp	photoplethysmography
PPG	photoelectric plethysmography
PPM	pacing pulses per minute
PQQ	pyrroloquinoline quinone
PTA	percutaneous transluminal angioplasty
PTCA	percutaneous coronary angioplasty
PU	polyurethane
PVC	polyvinylchloride
PVD	physical vapor deposition
PVDF	polyvinylidene fluoride
PWM	pulse-width modulated
QD	quadrature demodulation
QT	cardiac repolarization
R	reduced species
RIP	respiratory inductance plethysmograph
RPP	rate pressure product
RRF	rate response factor
RSA	respiratory sinus arrhythmia
SBP	systolic blood pressure
SE	spin echo imaging
SEP	systolic end point
SNR	signal-to-noise ratio
SQUID	superconducting quantum interference device
SV	stroke volume
TD	time domain
THI	tissue hemoglobin index
TOF	time-of-flight
TOI	tissue oxygenation index
TPR	total peripheral resistance
TPSF	temporal point-spread function
TRS	time-resolved spectroscopy
TTI	transthoracic impedance plethysmograph
US	ultrasound

UV	ultraviolet
VER	ventricular evoked response
VIP	ventricular inotropic parameter
WAMAS	Wearable Accelerometric Motion Analysis System

1

Introduction

P. Å. Öberg, F. A. Spelman, and T. Togawa

Measurement is the key to understanding biology and for the diagnosis of pathology. Measurement requires precise sensing to be successful, to allow scientists to advance their knowledge and physicians to control and cure abnormal conditions. In this book, we discuss both measurement and control of physiological variables.

Sensing can focus on the whole human organism as it does in the case of whole-body sensing systems; it can stress the measurement of critical variables such as glucose concentration, temperature, or pressure; it can define the behaviors of particular cells such as single neurons in the brain.

Control can be holistic, as it is in the case of home health care of the elderly or when the condition of a baby is monitored and controlled during the process of birth. Control can be specific when glucose is monitored and held within normal physiological limits, or it can be focused on a particular somatic sense as it is in the cochlear implant that provides hearing to the deaf.

Sensing is critical to all the cases above. It demonstrates a clear need for appropriate transducers that detect one form of energy and convert it to another, either at the input or the output of a specific instrument. Further, sensing implies signal processing. In the chapters that follow, the reader will be exposed to input sensors, output transducers, and the processing that connects them. While sensors are the focus of this volume, output transducers come into play, as does signal processing. As you read the chapters that follow, you will be impressed with the breadth and imagination that are the hallmarks of bioengineering.

1.1

Historical Breakthroughs in Medical Sensing Science

1.1.1

Plethysmography

Plethysmography is one of the earliest methods developed to make non-invasive blood flow measurements in the extremities. It is still one of the most frequently used and accurate methods used to assess peripheral blood flow. A great deal of our knowledge of vascular physiology in health and disease has been derived from data obtained plethysmographically.

Glisson [1] and Swammerdam [2] first employed plethysmography to study isolated muscle contraction. It was not until the latter half of the nineteenth century that this measurement principle was applied to blood flow measurements. Francois-Frank [3] published the first blood flow results in 1876 utilizing the venous occlusion technique. Brodie and Russel [4] studied renal blood flow by enclosing the kidney in a closed chamber in which the volume changes were studied while venous outflow was occluded. Hewlett and Zwaluwenburg [5] investigated blood flow in human limbs with plethysmography, thereby introducing the venous occlusion plethysmograph. Hyman and Winson have reviewed the early development of plethysmography [6].

The word plethysmography is derived from the Greek word for increase (in volume) *plethysmos* and the word to record, to write, *grafein*. Thus, the term plethysmography describes the basic principle of the technique, that is to record changes in the volume of parts of the body. The principle can be applied to the heart, liver, kidney, and to vascular measurements of the limbs and parts thereof. Most transient changes in the volume of organs are related to changes in blood content. Thus, plethysmography can serve to record blood volume as well as changes in blood volume. Since blood flow can be expressed as blood volume change per unit time, we can use plethysmography to measure blood flow. Indeed, plethysmography has been used primarily to assess blood flow to organs.

The most common application is venous occlusion plethysmography, usually used to diagnose obstructions in limb blood vessels. In this method the early influx of arterial blood to a limb is recorded when the venous drainage is stopped temporarily. The volume changes can be assessed in a number of ways, including water-filled cuffs, air-filled cuffs, strain gauges, electrical impedance measurements, and photoelectric probes.

1.1.2
Blood Pressure Measurements

The first blood pressure measurement was made with a very simple sensor. In 1733, the Reverend Stephen Hales [7] introduced glass tubes into the carotid arteries of horses and measured the height of the blood column that arose in the tube. He found it to be 8 feet and 3 inches. The first blood pressure measurement was made. About a century later, Poisieulle [8] studied blood pressure using a mercury manometer, a method for which he received a Gold medal from the Royal Academy of Medicine in Paris. The manometer of Poisieulle was connected to the artery with a leaden cannula.

Ludwig [9], a German professor in Comparative Anatomy at Marburg, improved Poisieulle's device with a recording technique. He recorded the motion of the mercury column on a revolving smoked drum (the kymograph), and dynamic blood pressure measurements were made. Favre [10] used Ludwig's manometer clinically, recording human systolic blood pressure for the first time.

During the 150 years that have elapsed since Ludwig's first invasive human measurement, invasive blood pressure sensors have undergone remarkable development. The most recent devices are based on catheters with microelectronic components, having an outer diameter of 0.35 mm (0.014 inches), which can be introduced into the coronary vessels of the heart. These catheters [11] are used to diagnose coronary obstructive diseases before and after treatment with balloon angioplasty or with intravascular stents. It soon became evident that the early devices were not particularly well-suited for clinical work.

Indirect (non-invasive) blood pressure devices were developed to satisfy the clinical need for systolic blood pressure measurements in humans. The first sphygmomanometer is attributed to Vierordt [12]. Herisson [13] performed the first indirect measurement of blood pressure in humans. The sphygmomanometer used a mercury reservoir covered with a rubber membrane from which a glass column arose. The mercury container was pressed against the radial artery until the oscillations of the mercury column stopped. This point was taken as the systolic pressure level. Inspired by Vierordt and Herisson, many physiologists designed blood-pressure sensing devices in the middle and end of the nineteenth century.

A breakthrough in blood pressure sensors came 1896 when Riva-Rocci [14] presented a new device utilizing an inflatable rubber bladder enclosed in leather, surrounding the upper arm: the modern sphygmomanometer. The pressure in the cuff was increased until the palpated pulse in the radial artery disappeared.

A second milestone in the development of indirect blood pressure measurement was the discovery by a Russian surgeon Korotkov in 1905 [15]. He discovered that if one increased the pressure in the Riva-Rocci cuff to above systolic pressure levels and then slowly decreased the cuff pressure while listening to the sounds from the artery one could associate the sound characteristics with the corresponding pressure levels in the vessel. As long as the cuff pressure exceeds the arterial pressures no sounds are generated. However, when cuff pressure is decreased below systolic pressure and remains above diastolic pressure, the pressure levels correspond to unique changes in the sound from the vessel.

Korotkov's discovery had, and still has, an enormous influence on the quality of non-invasive blood pressure recordings. His method is still frequently used in routine health care, with only small technical improvements. The discoveries of Riva-Rocci and Korotkov are the basis of today's computerized automatic blood-pressure sensors and monitors.

1.1.3
Electrophysiology and Einthoven's Galvanometer

Animals are electrically activated. Animal cells generate electrical activity when they process information or contract. They can be stimulated electrically as well. The history of electrophysiology is long, and guided by distinguished physicians, physiologists, physicists, chemists, and engineers. One interesting story of many is that Volta, having known of Galvani's experiments with the stimulation of nerve, placed an electrode in each ear and detected 'sound…like the bubbling of a viscid fluid…' [16]. The recognition that cellular activity was coupled to electrical signals and that electrical stimulation could excite cells launched the study of electrophysiology.

Electrophysiology has spawned the diagnostic measurement of biopotentials. The most common potential measured is that produced by the heart, the electrocardiogram (ECG), and followed in the clinic by the measurement of the signals that are produced by the brain, the electroencephalogram (EEG), and those produced by somatic muscles, the electromyogram (EMG). The three biopotentials will be discussed in reverse order, since the ECG will be covered in more detail than will the EEG and EMG.

The EMG can be recorded either from the surface or from within muscle tissue. The magnitude of the signal is a nonlinear function of the force exerted by the muscle, but is a linear function of the number of fibers that are recruited to exert that force. Surface recordings produce signals from large volumes of tissue. Indeed, the signals are produced by volumes that are too large for clear interpretation. Intramuscular recordings can be focused on small groups of muscle units and trade patient discomfort for desired detail [17]. The interpretation of the EMG is still an active topic of research [18].

Hans Berger, a German psychiatrist, announced publicly that he could record tiny electric signals from the brain, using external monitoring techniques. His recordings were remarkable considering that they were made in the late 1920s, before the advent of modern electronic instrumentation [19]. While Berger's discovery showed that the general state of the brain could be assessed, it was left to British scientist, W. G. Walter, to demonstrate the diagnostic value of the measurement of the electroencephalogram (EEG). Walter's contribution was one of instrument development, in which he employed a larger number of smaller electrodes than did Berger, and was able to use them to focus on activity in specific regions of the brain [1, 19].

Walter's instrument deserves brief description: he employed 22 cathode ray tubes each connected to a pair of electrodes, to record the activities of different locations within the brain. The display was photographed to develop a snapshot of activity at a particular instant of time [19]. The story shows that innovative instrumentation comes in several eras and from physicians, such as Walter, who have backgrounds in engineering and a keen interest in detailed diagnosis and specific therapy.

The ECG has a long pedigree. In 1842, Carlo Matteucci demonstrated that electric current accompanies each heart beat [20]. The phenomenon remained a laboratory curiosity until the development of the capillary electrometer in 1872. Using a similar technique, Augustus Waller published the first human electrocardiogram in 1887 [20]. In 1889, Willem Einthoven defined the term 'electrocardiogram' for the surface potential field that is produced by the heart. Despite being credited for that definition, Einthoven attributed it to Waller [20]. Work continued with the capillary galvanometer, a device that required tedious mathematical correction to produce a faithful recording of the ECG, until 1902, when Einthoven employed the string galvanometer, a device initially developed by Clement Ader to assess the signals carried by undersea telegraph lines [20].