Principles of Biomedical Instrumentation

This accessible yet in-depth textbook describes the step-by-step processes involved in biomedical device design. Integrating microfabrication techniques, sensors and digital signal processing with key clinical applications, it covers:

- the measurement, amplification and digitization of physiological signals, and the removal of interfering signals
- the transmission of signals from implanted sensors through the body, and the issues concerning the powering of these sensors
- networks for transferring sensitive patient data to hospitals for continuous home-monitoring systems
- electrical and biological tests for ensuring patient safety
- the cost–benefit and technological trade-offs involved in device design
- current challenges in biomedical device design.

With dedicated chapters on electrocardiography, digital hearing aids and mobile health, and including numerous end-of-chapter homework problems, online solutions and additional references for extended learning, it is the ideal resource for senior undergraduate students taking courses in biomedical instrumentation and clinical technology.

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Preface

The main aim of this textbook is to provide the tools to understand the function and design of different biomedical instruments and devices, and for the reader to be able to use these tools to envision new and improved future technology and designs. Throughout the book the terms medical and biomedical are used interchangeably, and similarly with the terms device and instrument. With several thousand instruments and devices on the market it is clearly impossible to consider more than a handful in detail. Instead, this book concentrates on the following general approach.

(i) What is the clinically relevant measurement that needs to be made?

(ii) What are the pathophysiological mechanisms that give rise to the clinical condition?

(iii) What are the characteristics (e.g. magnitude, frequency, bandwidth) of the signal to be measured? How accurate and reproducible does the measurement have to be? What are the interfering signals that have to be suppressed?

(iv) What are the recommended instrumental specifications for the particular device? How does one design the device to meet these specifications?

(v) How does one test the biocompatibility and electrical safety of such a device, whether it is external or implanted, so that it can operate safely for a number of years?

Traditionally, most of these instruments and devices have been located in a hospital, and patients travel to the clinics for the measurements to be performed by trained personnel. However, this model is changing and nowadays there is an increasing role for what is termed mobile health (m-health), which involves a much greater degree of healthcare being performed by the patients themselves at home. This means that a biomedical device must operate in the patient's home environment without specialized training, as well as transmit the data wirelessly and securely to the physician. This model of **continuous patient monitoring** not only provides a much more complete assessment of the patient's health, but also reduces the number of visits that a patient has to make to the hospital.

The main areas of technological development that have enabled the rapid incorporation of m-health into the healthcare infrastructure are wearable and implantable devices that can transmit data to the physician via mobile phone networks. The integration of micromachined and microfabricated electronics has enabled much smaller high performance devices to be designed. Classic measurement circuits such as the Wheatstone bridge, which used to consist of small lumped element resistors, can now be produced using integrated circuit technology on a submillimetre scale and integrated with amplifiers and filters on a single chip. The role of integrated digital signal processors (DSPs) has become much more important, and has played a key role in fundamental improvements in devices such as hearing aids. The technical challenges of the trade-off between increased signal processing power, miniaturization and battery life are discussed throughout the book.

ORGANIZATION

The skills needed to design and analyze the performance of biomedical instruments come mainly from an engineering background. This book assumes a basic level of understanding of electrical circuits and signal processing, typical of a second-year undergraduate course. No prior knowledge of clinical pathophysiology is assumed, although a basic course in anatomy would be useful.

Chapter 1 outlines the general principles involved in designing a biomedical instrument or device. An outline of the classification schemes used by regulatory bodies and manufacturers is given, along with a general discussion on the steps involved in the design and regulation process. Finally, the various safety standards for biomedical instrumentation are introduced, including testing of hardware, software and user interfaces.

Chapters 2 to 4 cover the basic building blocks of many types of biomedical instrumentation, namely: (i) the transducer/sensor, (ii) the electronic filters and amplifiers, and (iii) the data acquisition system. Analysis of these building blocks involves basic circuit theory and methods. At the end of each of these chapters, examples of the integration of these analysis tools into a real instrument are included. For example, the designs of sequential elements of a pulse oximeter are covered in sections 2.3 (sensor), section 3.6.1 (signal filtering and filtering) and section 4.5.1 (analogue-to-digital conversion).

Chapter 2 begins with a brief introduction to micro-electro-mechanical system (MEMS) devices, which are widely used in modern biomedical devices. Different types of transducers are then described, based on voltage sensors, optical sensors, displacement/pressure sensors, chemical sensors and acoustic sensors. Practical examples are given for each transducer, specifically a biopotential electrode, pulse oximeter, disposable blood pressure monitor, glucose monitor and hearing-aid microphone, respectively.

Chapter 3 concentrates on the design of passive and active filters, as well as the analysis and design of amplification circuits based on operational amplifiers (op-amps). Common higher order filter geometries such as Butterworth, Chebyshev and Sallen–Key are analyzed. Finally, specific amplification and filtering circuits for a pulse oximeter and glucose monitor are shown.

Chapter 4 outlines the different types of analogue-to-digital converter (ADC) architectures that can be used for biomedical instruments, as well as their respective characteristics in terms of resolution and sampling rates. The concepts of oversampling and digital filtering are summarized in the framework of the delta-sigma ADC. The characteristics of different biosignals are described in order to classify them as either deterministic or stochastic: subdivision into different subgroups is also discussed. Finally, different signal processing algorithms including Fourier transformation and time-domain correlation techniques are summarized. Practical examples of correlation analysis in a Swan–Ganz catheter used for cardiac output measurements, as well as short-time Fourier transformation of electroencephalographic signals, are shown.

Chapter 5 deals with the most common measurement using biopotential electrodes, the electrocardiogram (ECG). The design and placement of electrodes, amplification and filtering circuitry, data acquisition system, and integrated signal processing and analysis algorithms are all discussed. Clinical applications that relate the underlying pathophysiology to changes in the ECG signal are outlined, including the most common heart diseases. Finally, the acquisition and analysis of high-frequency ECG signals are described.

Chapter 6 describes the instrumentation associated with a second measurement technique using biopotential electrodes, electroencephalography (EEG). Applications of EEG measurements to diseases such as epilepsy are outlined, as well as its increasing use in monitoring levels of anaesthesia in the operating theatre using the bispectral index. Finally, applications aiding patients with severe physical injuries to communicate and move via brain–computer interfaces are described.

Chapter 7 covers the basics of digital hearing aid design. Different configurations of microphones, and their use in beam-forming techniques to aid speech comprehension in noisy environments, are described. The important role of DSPs in continuous real-time processing within a very small device is discussed in terms of the design trade-offs of performance versus long battery life. Wireless integration of digital hearing aids with external devices, such as mobile phones, is also outlined.

Chapter 8 concentrates on the general topic of m-health and wireless transmission of biomedical data. The role of smartphones and medically related software applications is described, as well as the increasing use of wearable health-monitoring technology. From a medical device point of view the most important developments are the designs of implantable devices, which must be able to connect wirelessly with external transmitters and receivers. Several cardiovascular wireless implanted devices are described, as well as continuous glucose monitors and very new devices such as those for measuring intraocular pressure in patients with glaucoma.

Chapter 9 summarizes the safety issues involved with powered biomedical instruments, both in terms of electrical safety and also biocompatibility. The concepts of electrical macroshock and microshock are introduced, as well as methods of designing equipment to minimize the risks of these events occurring. Equipment for carrying out electrical safety testing is described. The safety of implanted devices is discussed in terms of the biocompatibility of the materials used, as well as their electromagnetic safety. Examples of several biological testing procedures such as cytotoxicity and haemocompatibility are given. Finally, the design of medical devices that can also be used in a magnetic resonance imaging scanner is discussed.

PROBLEMS

The majority of the problems are based specifically around the material in this book, and especially those in Chapters 2 to 4 test knowledge of the circuits, analysis tools and mode of operation of each of the sub-blocks within a biomedical instrument. Some questions may require the writing of relatively simple numerical computer code. Studying instrumentation design is not only a question of understanding the current state of the art but also constitutes a platform to envision alternative approaches, and to speculate on which new technologies and improvements may be incorporated in the future. Therefore, especially in Chapters 5 to 9, there are a number of problems that require the use of external sources in order to investigate devices that are not covered specifically in this book. For example, with the knowledge gained from Chapters 2 to 4 how would one design a new technique for harvesting the body's internal energy for powering an implanted sensor (Problem 8.4). In a similar vein, investigating cases of device failure is a good way to see how apparently watertight safety procedures can, in fact, fail and to consider the implications of these failures for future designs (Problem 1.3).

REFERENCE BOOKS

There is a large number of books covering different aspects of the principles and design of biomedical instrumentation and devices. The unofficial 'bible' of general biomedical instrumentation remains *The Encyclopedia of Medical Devices and Instrumentation* edited by J. G. Webster and published by Wiley-Blackwell in 2004, as well as the distilled classic textbook *Medical Instrumentation: Application and Design*, 4th edition, J. G. Webster, John Wiley & Sons, 2010.

In terms of books that concentrate on one specific aspect of design, the list below represents a partial list that have proved very useful in preparing this current volume.

Chapter 1 Yock, P. G., Zenios, S., Makower, J. *et al.* (eds) *Biodesign: The Process of Innovating Medical Technologies*. Cambridge University Press; 2015.

Chapter 2 Jones D. P. and Watson. J. *Biomedical Sensors* (Sensor Technology Series). Momentum Press; 2010.

Chapter 3 Huijsing, J. *Operational Amplifiers: Theory and Design, 3rd edn*. Springer; 2016.

Chapter 4 Pelgrom, M. J. *Analog-to-Digital Conversion*. Springer; 2013.

Chapter 5 Crawford, J. & Doherty, L. *Practical Aspects of ECG Recording*. M&K Update Ltd; 2012.

Chapter 6 Libenson, M. H. *Practical Approach to Electroencephalography.* Saunders; 2009.

Chapter 7 Popelka, G. R., Moore, B. C. J., Fay, R. R. & Popper, A. N. *Hearing Aids*. Springer; 2016.

Chapter 8 Salvo, P. & Hernandez-Silveira, M. (eds) *Wireless Medical Systems and Algorithms: Design and Applications (Devices, Circuits, and Systems)*. CRC Press; 2016.

Chapter 9 Gad, S. C. & McCord, M G. *Safety Evaluation in the Development of Medical Devices and Combination Products, 3rd edn.* CRC Press; 2008.

Abbreviations

AAMI	Association for the Advancement of Medical Instrumentation
AC	alternating current
ADC	analogue-to-digital converter
ADHF	acute decompensated heart failure
AF	atrial fibrillation
AGC	automatic gain control
ANSI	American National Standards Institute
ASIC	application-specific integrated circuit
ASK	amplitude-shift keying
ATP	adenosine triphosphate
AV	atrioventricular
AVC	automatic volume control
BCI	brain–computer interface
BcSEF	burst-compensated spectral edge frequency
BF	body floating
BILL	bass increase at low level
BIS	bispectral index
BiV	biventricular
BSR	burst-suppression ratio
BTE	behind the ear
BW	bandwidth
CAD	computer-aided design
CE	Conformité Européene
CF	cardiac floating
CFR	Code of Federal Regulations
CGM	continuous glucose monitor
CIC	completely in canal
CIED	cardiovascular implantable electronic device
CMRR	common-mode rejection ratio
CRT	cardiac resynchronization therapy
CSF	cerebrospinal fluid
DAC	digital-to-analogue converter
dB	decibel

DC	direct current
DDD	dual mode, dual chamber, dual sensing
DF	directivity factor
DI	directivity index
DNL	differential non-linearity
DRL	driven right leg
DSP	digital signal processing
EC	European Commission
ECG	electrocardiogram
EDR	electrodermal response
EEG	electroencephalogram
EMG	electromyogram
EMI	electromagnetic interference
EOG	electrooculogram
EPROM	erasable programmable read-only memory
EPSP	excitatory postsynaptic potential
ESI	electric source imaging
FCC	Federal Communications Commission
FDA	Food and Drug Administration
FES	functional electrical stimulation
FET	field-effect transistor
FFT	fast Fourier transform
FIR	finite impulse response
FM	frequency modulation
FSK	frequency shift keying
FT	Fourier transform
GBWP	gain bandwidth product
GDH	glucose-1-dehydrogenase
GFCI	ground-fault current interruptor
GHK	Goldman–Hodgkin–Katz
GOx	glucose oxidase
GPS	global positioning system
GSM	global systems for mobile
GSR	galvanic skin response
HPF	high-pass filter
HR	heart rate
ICA	independent component analysis
ICD	implantable cardioverter–defibrillator
ICNIRP	International Commission on Non-Ionizing Radiation Protection
ICU	intensive care unit

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IDE	investigational device
IEC	International Electrotechnical Commission
IEEE	Institute of Electrical and Electronic Engineers
IHM	implantable haemodynamic monitor
IIR	infinite impulse response
ILR	implantable loop recorder
INL	integrated non-linearity
IOL	intraocular lens
IOP	intraocular pressure
IPAP	implanted pulmonary artery pressure
IPSP	inhibitory postsynaptic potential
ISM	industrial, scientific and medical
ISO	International Organization for Standardization
ITC	in the canal
ITE	in the ear
JFET	junction field-effect transistor
KEMAR	Knowles Electronics Manikin for Acoustic Research
LA	left arm
LBBB	left bundle branch block
LED	light-emitting diode
LIM	line-isolation monitor
LL	left leg
LPF	low-pass filter
LSB	least significant bit
LVDT	linear voltage differential transformer
MD	medical device
MDRS	medical device radiocommunication service
MEMS	micro-electro-mechanical systems
MI	myocardial infarct
MICS	medical implant communication service
MRI	magnetic resonance imaging
MSB	most significant bit
MUX	multiplex
NB	national body
NC	normal conditions
NEC	National Electrical Code
NF	noise figure
NFMI	near-field magnetic induction
NIDCD	National Institute on Deafness and Other Communication Disorders
NSTEMI	non-ST-segment elevated myocardial infarction

OR	operating room
PA	pulmonary artery
PAC	pulmonary artery catheter
PCA	principal component analysis
PDF	probability density function
PDMS	polydimethylsiloxane
PIFA	planar inverted F-antenna
PILL	programmable increase at low level
PIPO	parallel input, parallel output
PISO	parallel input, serial output
PMA	pre-market approval
P-N	positive–negative
PSK	phase shift keying
PSP	postsynaptic potential
PTFE	polytetrafluoroethylene
PVARP	post-ventricular atrial refractory period
PVDF	polyvinyldifluoride
PWM	pulse-width modulation
QSR	quality-system regulation
RA	right arm
RAM	random access memory
RAZ	reduced amplitude zone
RBC	red blood cell
RCD	residual-current device
RF	radiofrequency
RLD	right leg drive
ROC	receiver operator characteristic
ROM	read-only memory
RPM	remote patient monitoring
RV	right ventricle
S/H	sample and hold
SA	sinoatrial
SAR	specific absorption rate
SAR ADC	successive approximation register ADC
SC	single condition
SCP	slow cortical potential
SELV	separated extra-low voltage
SFC	single-fault condition
SFDR	spurious-free dynamic range
SINAD	signal-to-noise and distortion ratio

SIP	signal input
SIPO	serial input, parallel output
SISO	serial input, serial output
SNR	signal-to-noise ratio
SOP	signal output
SPL	sound pressure level
SpO_2	saturation of peripheral oxygen
SSVEP	steady state visual evoked potential
SVI	single ventricular
TARP	total atrial refractory period
THD	total harmonic distortion
TILL	treble increase at low level
UWB	ultrawide band
VEP	visual evoked potential
VLP	ventricular late potential
VOP	venous occlusion plethysmography
WCT	Wilson's central terminal
WDRC	wide dynamic range compression
WMTS	wireless medical telemetry system