

An abstract network diagram featuring a complex web of nodes and connecting lines. The nodes are represented by circles of various sizes and colors, including red, blue, orange, purple, and pink. The lines are thin and grey, creating a dense, interconnected pattern. The background is white with faint, larger circles in light blue and purple.

Edited by Isar Mostafanezhad,
Olga Boric-Lubecke, and Jenshan Lin

Medical and Biological Microwave Sensors and Systems

THE CAMBRIDGE RF AND MICROWAVE ENGINEERING SERIES



In this comprehensive work, experts in the field detail recent advances in medical and biological microwave sensors and systems, with chapters on topics such as implantable sensors, wearable microwave tags, and ultra-wideband (UWB) technology.

Each chapter explores the theory behind the technology, as well as its design and implementation. This is supported by practical examples and details of experimental results, along with discussion of system design, design tradeoffs, and possible constraints and manufacturing issues. Applications described include intracranial pressure monitoring, vital signs monitoring, and noninvasive molecular and cellular investigations.

Presenting new research and advances in the field and focusing on the state of the art in medical and biological microwave sensors, this work is an invaluable resource for enthusiastic researchers and practicing engineers in the fields of electrical engineering, biomedical engineering, and medical physics.

Isar Mostafanezhad is the founder and CEO of Nalu Scientific in Honolulu, Hawaii. He has several years of experience in developing and commercializing products in wireless, microwave and medical fields. He is also an Associate Editor for the *IEEE Microwaves and Wireless Components Letters*.

Olga Boric-Lubecke is a Professor of electrical engineering at the University of Hawaii at Manoa. She cofounded and served as Chief Technical Advisor for Kai Medical and has previously worked at Bell Laboratories, researching RF integrated-circuit technology and the biomedical applications of wireless systems.

Jenshan Lin is a Professor at the University of Florida as well as a Fellow of the Institute of Electrical and Electronics Engineers (IEEE). Previously he has worked at Bell Laboratories and has published extensively on the subject of wireless sensors and biomedical applications of microwave technologies. He served as Editor-in-Chief of *IEEE Transactions on Microwave Theory and Techniques* in 2004–2016.

CAMBRIDGE
UNIVERSITY PRESS
www.cambridge.org

ISBN 978-1-107-05660-2



9 781107 056602 >

**Mostafanezhad,
Boric-Lubecke, and Lin**

**Medical and Microwave
Sensors and Systems**

CAMBRIDGE

Medical and Biological Microwave Sensors and Systems

ISAR MOSTAFANEZHAD

University of Hawaii, Nalu Scientific, LLC, Manoa

OLGA BORIC-LUBECKE

University of Hawaii at Manoa

JENSHAN LIN

University of Florida



CAMBRIDGE
UNIVERSITY PRESS

CAMBRIDGE UNIVERSITY PRESS

University Printing House, Cambridge CB2 8BS, United Kingdom

One Liberty Plaza, 20th Floor, New York, NY 10006, USA

477 Williamstown Road, Port Melbourne, VIC 3207, Australia

314–321, 3rd Floor, Plot 3, Splendor Forum, Jasola District Centre, New Delhi – 110025, India

79 Anson Road, #06–04/06, Singapore 079906

It furthers the University's mission by disseminating knowledge in the pursuit of education, learning, and research at the highest international levels of excellence.

www.cambridge.org

Information on this title: www.cambridge.org/9781107056602

10.1017/9781107297302

© Cambridge University Press 2018

This publication is in copyright. Subject to statutory exception and to the provisions of relevant collective licensing agreements, no reproduction of any part may take place without the written permission of Cambridge University Press.

First published 2018

Printed in the United Kingdom by TJ International Ltd. Padstow Cornwall

A catalogue record for this publication is available from the British Library.

Library of Congress Cataloging-in-Publication Data

Names: Mostafanezhad, Isar, editor. | Boric-Lubecke, Olga, 1966– editor. | Lin, Jenshan, 1984– editor.

Title: Medical and biological microwave sensors and systems / [edited by] Isar Mostafanezhad, Olga Boric-Lubecke, Jenshan Lin.

Other titles: Cambridge RF and microwave engineering series.

Description: Cambridge, United Kingdom ; New York : Cambridge University Press, 2017. | Series: The Cambridge RF and microwave engineering series | Includes bibliographical references and index.

Identifiers: LCCN 2016047634 | ISBN 9781107056602 (Hardback : alk. paper)

Subjects: | MESH: Biosensing Techniques | Microwaves—therapeutic use | Wireless Technology | Biomedical Technology

Classification: LCC QP82.2.R33 | NLM QT 36.4 | DDC 612/.014481–dc23

LC record available

at <https://lcn.loc.gov/2016047634>

ISBN 978-1-107-05660-2 Hardback

Cambridge University Press has no responsibility for the persistence or accuracy of URLs for external or third-party Internet websites referred to in this publication and does not guarantee that any content on such websites is, or will remain, accurate or appropriate.

Medical and Biological Microwave Sensors and Systems

In this comprehensive work, experts in the field detail recent advances in medical and biological microwave sensors and systems, with chapters on topics such as implantable sensors, wearable microwave tags, and ultra-wideband (UWB) technology. Each chapter explores the theory behind the technology, as well as its design and implementation. This is supported by practical examples and details of experimental results, along with discussion of system design, design tradeoffs, and possible constraints and manufacturing issues. Applications described include intracranial pressure monitoring, vital signs monitoring, and noninvasive molecular and cellular investigations. Presenting new research and advances in the field and focusing on the state of the art in medical and biological microwave sensors, this work is an invaluable resource for enthusiastic researchers and practicing engineers in the fields of electrical engineering, biomedical engineering, and medical physics.

Isar Mostafanezhad is the founder and CEO of Nalu Scientific in Honolulu, Hawaii. He has several years of experience in developing and commercializing products in wireless, microwave and medical fields. He is also an Associate Editor for the *IEEE Microwaves and Wireless Components Letters*.

Olga Boric-Lubecke is a Professor of electrical engineering at the University of Hawaii at Manoa. She cofounded and served as Chief Technical Advisor for Kai Medical and has previously worked at Bell Laboratories, researching RF integrated-circuit technology and the biomedical applications of wireless systems.

Jenshan Lin is a Professor at the University of Florida as well as a Fellow of the Institute of Electrical and Electronics Engineers (IEEE). Previously he has worked at Bell Laboratories and has published extensively on the subject of wireless sensors and biomedical applications of microwave technologies. He served as Editor-in-Chief of *IEEE Transactions on Microwave Theory and Techniques* in 2004–2016.

The Cambridge RF and Microwave Engineering Series

Series Editor

Steve C. Cripps

Distinguished Research Professor, *Cardiff University*

Editorial Advisory Board

James F. Buckwalter

University of California, Santa Barbara

Jenshan Lin

University of Florida

John Wood

Maxim Integrated Products

Series List

Peter Aaen, Jaime Plá and John Wood, *Modeling and Characterization of RF and Microwave Power FETs*

Dominique Schreurs, Máirtín O'Droma, Anthony A. Goacher and Michael Gadringer (eds.), *RF Amplifier Behavioral Modeling*

Fan Yang and Yahya Rahmat-Samii, *Electromagnetic Band Gap Structures in Antenna Engineering*

Enrico Rubiola, *Phase Noise and Frequency Stability in Oscillators*

Earl McCune, *Practical Digital Wireless Signals*

Stepan Lucyszyn, *Advanced RF MEMS*

Patrick Roblin, *Nonlinear RF Circuits and the Large-Signal Network Analyzer*

Matthias Rudolph, Christian Fager and David E. Root (eds.), *Nonlinear Transistor Model Parameter Extraction Techniques*

John L. B. Walker (ed.), *Handbook of RF and Microwave Solid-State Power Amplifiers*

Anh-Vu H. Pham, Morgan J. Chen and Kunia Aihara, *LCP for Microwave Packages and Modules*

Sorin Voinigescu, *High-Frequency Integrated Circuits*

Richard Collier, *Transmission Lines*

Valeria Teppati, Andrea Ferrero and Mohamed Sayed (eds.), *Modern RF and Microwave Measurement Techniques*

Nuno Borges Carvalho and Dominique Schreurs, *Microwave and Wireless Measurement Techniques*

David E. Root, Jason Horn, Jan Verspecht and Mihai Marcu, *X-Parameters*

Earl McCune, *Dynamic Power Supply Transmitters*

Hossein Hashemi and Sanjay Raman (eds.), *Silicon mm-Wave Power Amplifiers and Transmitters*

T. Mitch Wallis and Pavel Kabos, *Measurement Techniques for Radio Frequency Nanoelectronics*

Giovanni Ghione and Marco Pirola, *Microwave Electronics*

Isar Mostafanezhad, Olga Boric-Lubecke and Jenshan Lin (eds.), *Medical and Biological Microwave Sensors*

Forthcoming

Richard Carter, *Microwave and RF Vacuum Electronic Power Sources*

José Carlos Pedro, David Root, Jianjun Xu and Luis Cotimos Nunes, *Nonlinear Circuit Simulation and Modeling*

Michael Schröter and Martin Claus, *Carbon Nanotube Electronics for Analog Radio-Frequency Applications*

Contributors

Olga Boric-Lubecke

University of Hawaii at Manoa

Kevin Browne

University of Pennsylvania

J. C. Chiao

University of Texas at Arlington

Kacy Cullen

University of Pennsylvania

David Dubuc

LAAS-CNRS, France

Aly Fathy

University of Tennessee

Katia Grenier

LAAS-CNRS, France

Changzhan Gu

Texas Tech University

Usmah Kawoos

Naval Medical Research Center

Francis Kralick

Naval Medical Research Center

Changzhi Li

Texas Tech University

Victor Lubecke

University of Hawaii at Manoa

Danilo Mandic

Imperial College London

Xu Meng

Drexel University

Isar Mostafanezhad

University of Hawaii at Manoa

Smitha Rao

University of Texas at Arlington

Arye Rosen

Drexel University

Aditya Singh

Queens Medical Center, Honolulu, Hawaii

Mohammad-Reza Tofighi

Pennsylvania State University

Yazhou Wang

Boston Design Center

Ehsan Yavari

University of Hawaii

Contents

	<i>List of Contributors</i>	<i>page viii</i>
1	Implantable Wireless Medical Devices for Gastroesophageal Applications	1
	Smitha Rao and J.-C. Chiao	
	1.1 Introduction	1
	1.2 Wireless Communication in Medical Implant Applications	2
	1.3 Implementation Methods	3
	1.4 Endoluminal Capsule Applications	4
	1.5 An Endoluminal Application Example: Reflux Monitoring	6
	1.6 Batteryless Wireless Impedance and pH Sensor Capsule	16
	1.7 Conclusion	30
2	Embedded Wireless Device for Intracranial Pressure Monitoring	40
	Xu Meng, Usmah Kawoos, Francis Kralick, Arye Rosen, and Moahmmad-Reza Tofighi	
	2.1 Introduction	40
	2.2 Existing Technologies for the Measurement and Monitoring of ICP	43
	2.3 Desired Features of the Implant	44
	2.4 Operating Principle	45
	2.5 Antennas	48
	2.6 Packaging Concept of Implant	58
	2.7 Methods for Evaluation of Implant Performance <i>In Vitro</i>	61
	2.8 <i>In Vitro</i> Bench-Test Results	68
	2.9 <i>In Vivo</i> Evaluation of the Implant	73
	2.10 Sources of Error in ICP Measurements	83
	2.11 Discussion	84
	Acknowledgments	85
3	Wireless Intracranial Pressure Systems for the Assessment of Traumatic Brain Injury	89
	Xu Meng, Arye Rosen, Moahmmad-Reza Tofighi, Kevin Browne, and Kacy Cullen	
	3.1 Introduction	89
	3.2 Traumatic Brain Injury	90

3.3	Methods	92
3.4	Dynamic Evaluation of AICP Implants for Assessment of Rotational Head Injury	94
3.5	Design and <i>In Vitro</i> Evaluation of DICP Implants	97
3.6	Dynamic Evaluation of DICP Implants for Assessment of Rotational Head Injury	104
3.7	Conclusion and Future Work	118
4	Microwave Biosensors for Noninvasive Molecular and Cellular Investigations	124
	Katia Grenier and David Dubuc	
4.1	Introduction	124
4.2	Interests in Miniature Microwave-Based Biosensors for Noninvasive Molecular and Cellular Investigations	125
4.3	Microwave Analysis of Biomolecules in Aqueous Solution	131
4.4	Cellular Investigations	137
4.5	Conclusions	148
	Acknowledgments	149
5	Wearable Radar Tag Systems for Physiological Sensing/Monitoring	154
	Aditya Singh, Olga Boric-Lubecke, and Victor Lubecke	
5.1	Introduction	154
5.2	Frequency-Doubling Tags	155
5.3	Experimental Verification	160
5.4	Experimental Verification II	161
5.5	Two-Frequency Radar	163
5.6	Adaptive Noise Cancellation	164
	Summary	168
6	Physiological Radar Sensor Chip Development	172
	Changzhi Li and Changzhan Gu	
6.1	Theory and Recent Advancements	172
6.2	System Integration	176
6.3	Chip Integration	187
6.4	Application Case Studies	197
7	Noise- and Interference-Reduction Methods for Microwave Doppler Radar Vital Signs Monitors	202
	Isar Mostafanezhad, Olga Boric-Lubecke, Danilo Mandic, and Ehsan Yavari	
7.1	Introduction	202
7.2	Cancellation of Unwanted Antenna Motion Using Motion Sensors	203
7.3	Empirical Mode Decomposition	208
7.4	Removing a Subject's Fidgeting Using EMD	212

7.5	Cancellation of Unwanted Antenna Motion Using EMD	219
7.6	Conclusions	225
8	Biomedical Applications of UWB Technology	228
	Aly Fathy and Yazhou Wang	
8.1	Introduction	228
8.2	Overview of UWB Technology for Indoor Positioning Systems	228
8.3	Vital Signs Detection and Human Gait Analysis	239
8.4	Early Breast Cancer Detection	250
	<i>Index</i>	265

1 Implantable Wireless Medical Devices for Gastroesophageal Applications

Smitha Rao and J.-C. Chiao

1.1 Introduction

Advances in low-power-consumption radiofrequency integrated circuits (RFICs), multi-functional integrated circuits, high-sensitivity sensing electrodes, biocompatible materials, and packaging techniques have made implants with wireless communication functionality and/or wireless charging capability more feasible and practical. However, wireless communication or wireless powering has not been widely used in implants. There are several challenges. The implant applications are typically disease oriented and implementation focused. The designs of implants have to address specific needs in the disease diagnosis or treatment modalities, which are strongly related to both electronic and mechanical parameters. The sensing modalities or therapy methods determine the electrical specifications, while the biological environments often present serious design constraints. The implementation has to suit clinical settings for safe, cost-effective, and relatively easy implantation procedures and, most important, the needs and comfort of patients in daily life.

It is obvious that integration of wireless communication functionality in implants can provide critical and increased capabilities in applications. The outbound communication brings sensor signals and device conditions to the reader outside the body. The sensors can monitor physiologic signals, such as blood pressure, intracranial pressure, core temperature, electrical signals of tissue or motility of organs, and biochemical conditions such as pH and certain protein or factor concentrations, of patients *in vivo* and in real time. In addition, the wireless communication can periodically report device conditions such as battery level, electrical resistance of electrodes, and current/voltage delivered to tissues. The inbound communication can be used for device reconfiguration, dosage setting, and condition probing. Bidirectional communication will be ideal for remote access of the implants, adding capabilities for real-time feedback as an integrated system between body and computer. The wireless closed-loop system also can provide real-time patient condition alerts, patient self-diagnosis using smart phones, and autonomous treatment-efficacy studies over a population of patients.

From the perspectives of patients, wireless communication removes the discomfort and inconvenience of tethered wires coming out of the body. Currently, the wires either go through small surgical openings in the body, such as for the extension wire from the head in deep brain stimulation, or an orifice, such as the nostril for stomach stimulation and multichannel intraluminal impedance tests or the urethra for bladder monitoring.

The tethered wires connecting to the external electronic device, either a reader or a pulse generator, obviously bring some inconvenience to patients and sometimes pain, and they often limit patient mobility, hindering quality of life. Often the discomfort and suffering affect patients' daily regular activities and alter their behavior subconsciously or consciously. This could have an effect on the accuracy of monitored physiologic parameters. Given these limitations, it is difficult to use sensors with tethered extension wires in the long term. Many such sensor systems are for short-term or temporary use, lasting from hours to a few days. This limits the possibility of using them to quantitatively monitor patient progress in therapy or as alert monitors continuously checking critical parameters. Treatment systems such as stimulators, because patients depend on them to restore tissue functions, suffer from these unavoidable nuisances and burdens.

1.2 Wireless Communication in Medical Implant Applications

Several electrical implants have been widely used, and more are coming to the market and are being researched in hospitals and laboratories. Cardiac pacemakers for controlling abnormal heart rhythms, implantable cardioverter defibrillators for detecting abnormal ventricular heart rhythms and delivering electrical signals to restore the heart's normal rhythms, and neurostimulators for deep brain stimulation in tremor control for patients with Parkinson's disease and dystonia, as well as in spinal cord stimulation for chronic pain management, have been cleared for wide clinical applications. Research on neurostimulation for obsessive-compulsive disorder, depression, tinnitus, epilepsy, respiratory support, malignant pain, spasticity, amyotrophic lateral sclerosis, Huntington's disease, gastroparesis, irritable bowel syndrome, headaches, traumatic brain injury, angina pain, peripheral vascular disease pain, pelvic pain, incontinence, and sexual dysfunction are on the way to clinical validation.

Most of these devices or systems are still not equipped with wireless communication or wireless powering functionalities. In limited applications, such as neurostimulation, inductive coupling to adjust electrical dosages or wireless rechargeable batteries has been implemented [1,2]. The wireless functions of changing settings or charging are only used for limited time periods instead of continuous communication connection or powering. Nonetheless, it is quite clear that both patients and doctors can greatly benefit from wireless signal transduction and wireless controlling/monitoring of implants; thus manufacturers are working on incorporating these capabilities into the next generation of products.

Two types of implantable systems emerging in recent years require continuous wireless communication between external modules and the implants: cochlear implants and implantable visual prosthetics. Cochlear implants are designed to produce hearing sensations with electrical stimulation of nerves inside the inner ear for patients with severe to profound nerve deafness. The wireless communication carries the signals that are converted from sounds to stimulating electrical pulses from a small module near the ear to the implant. The electrical pulses activate the auditory nerves and create hearing recognition in the brain. Several cochlear implants have been approved by Food and

Drug Administration (FDA) already. Implantable visual prosthetics, such as the Argus II retinal prosthesis system (Second Sight Medical Products, Inc.), have been approved for use as a humanitarian device and are currently being tested clinically for patients with retinal damage (retinitis pigmentosa) [3]. The patient wears a pair of glasses with an attached video camera that captures images. A signal-processing module converts the image signals to electrical stimulation pulse commands for an electrode array, and the commands are wirelessly transmitted into the eye. The electrical pulses then spatially stimulate the retinal cells to induce cellular responses that propagate through optic nerves to the central visual system, resulting in visual percepts. In both cases, the wireless communication carrying the audio signals or visual image data is continuous and conducted within a close distance through tissues around the ear or eye.

1.3 Implementation Methods

Wireless communication and energy transfer enable remote control and signal transduction for devices that are surgically implanted inside the body. Conventional systems require major open surgical procedures or laparotomy with a large incision because the devices are bulky, mostly due to the battery. However, the advances in battery technology and integration of multifunctional chips continue reducing implant sizes. Soon these devices will be sufficiently small to be implanted with minimally invasive surgery that involves a smaller incision to access a body cavity. The advantages of minimally invasive surgery include limited to no trauma on nerves and tissues, less bleeding and scarring, and less pain. In return, these mean a shorter hospital stay, a quicker recovery, less risk, and therefore lower costs. It is clear that miniaturization of wireless implants can enable the advantages of minimally invasive surgical implantation procedures in addition to the advantages of the absence of tethered wires.

Furthermore, endoscopic procedures have also advanced in recent years. Modern endoscopes consist of a long and flexible tube with lighting LEDs and a miniature video camera in the probing end. Real-time images inside the body can be seen on a display screen for visualization and orientation. Operating endoscopes are also equipped with irrigation, suction, and additional working channels that are used for inserting special instruments such as biopsy forceps, scissors, clamps, dissectors, graspers, suturing devices, and other surgical tools. These endoscopic imaging and surgical procedures have been used for the gastrointestinal (GI) tract, including esophagus, stomach and duodenum, bile duct, small intestine, large intestine, colon, rectum, and anus; the respiratory tract inside nose and lower respiratory tract; the ear; the urinary tract; and the female reproductive system, including the cervix, uterus, and fallopian tubes. These procedures are generally outpatient or at least simpler, reducing anesthesia time and/or hospital stays, without significant risk to patients.

Endoscopic procedures have also been researched to access normally closed body cavities through a small internal incision, which is generally called *natural orifice transluminal endoscopic surgery* (NOTES) [4–10]. NOTES is still in the research stage as a new surgical technique. It does not produce external scars when abdominal

operations are performed with an endoscope passed through a natural orifice such as the mouth, nose, urethra, or anus. Recognized advantages include the ones for endoscopic procedures and, additionally, with decreased neurohumoral stress responses, decreased immune suppression, less pain, faster recovery, and decreased wound-related and pulmonary complications, especially a lower incidence of wound infection and incisional hernia [11]. Endoscopic and NOTES procedures open a wide window for wireless implants because they provide an implantation method with more comfort, easier implementation, less pain, fewer risk factors, faster recovery, and thus more affordable cost for patients.

1.4 Endoluminal Capsule Applications

Through endoscopic procedures and NOTES, stomach, liver, pancreas, vagina, bladder, and colon can be accessed with a small internal incision. These organs and nearby cavities thus are good candidates for implanting wireless devices for monitoring or treatment. In particular, endoluminal applications are attractive because the access is easier. For example, currently there are several commercial systems for endoluminal capsule monitoring. A miniaturized wireless radio transmitter is embedded in an ingestible capsule along with certain types of sensors. The patient swallows the capsule with water. The capsule travels through the gastrointestinal tract and broadcasts signals to the outside. The signals contain sensor information such as pH and motility or images. The signals are received by a radio receiver worn on the body. The signals are then processed and stored on a memory card from which data will be transferred to a computer later. Several commercial camera-based imaging capsules [12–15] have been developed targeting esophageal [16,17], colon mucosal [18,19], and small bowel [20–25] visualization. As the capsule travels through the area of interest, it takes photographs with lighting from LEDs mounted at the ends of the capsule. Some examples are shown in Figure 1.1. As disposable devices, the imaging capsules mostly use cost-effective technologies such as complementary metal-oxide semiconductor (CMOS) sensors and coin batteries and operate at a lower frequency band [26]. For example, PillCam capsules, with sizes of 26 or 31 mm in length and 11 mm in diameter, transmit unidirectional signals at 434.1 MHz in a bandwidth of ± 10 MHz with a power consumption of 5.2 mW and a data rate of 2.7 Mb/s [27]. The battery life for imaging the esophagus is designed to be 20 minutes, small bowel is 9 hours, and colon is 10 hours. Another example is the SmartPill, with dimensions of 13 mm in diameter and 26 mm in length, housing three sensors that can measure pressure, pH, and temperature as it travels through the GI tract to assess motility in the evaluation of suspected gastroparesis and colonic transit in the setting of chronic constipation [28,29]. It measures the temperature (25–49°C), pH (0.05–9.0), and pressure (0–350 mmHg) of its immediate surroundings with a battery life of 12 hours. The data are transmitted with amplitude-shift keying (ASK) modulation at 434 MHz to a reader outside.

Telemetry is a critical element in wireless implants or capsules. Endoluminal applications present further technical challenges because the wireless signals have to go