CONTENTS

Introduction vii
Contributors ix

1 Middle-Ear Reflectance: Concepts and Clinical Applications 1
Jont B. Allen, Sarah R. Robinson, Judi A. Lapsley Miller,
Patricia S. Jeng, and Harry Levitt

2 Otoacoustic Emissions: Measurement, Modeling, and Applications 41
Glenis Long and Bastian Epp

3 The Audiogram: What It Measures, What It Predicts, and
What It Misses 57
Anthony T. Cacace and Robert F. Burkard

4 Contemporary Issues in Vestibular Assessment 73
Faith W. Akin, Owen D. Murnane, and Kristal Mills Riska

5 Genetics of Deafness: In Mice and Men 99
Mirna Mustapha and Avril Genene Holt

6 Molecular-Based Measures for the Development of Treatment
for Auditory System Disorders: Important Transformative Steps
Toward the Treatment of Tinnitus 107
Avril Genene Holt, Catherine A. Martin, Antonela Muca,
Angela R. Dixon, and Magnus Bergkvist

7 Medical and Surgical Treatment of Inner Ear Disease 131
Lawrence R. Lustig

8 The Future of Cochlear Implants 175
Richard Tyler, Paul R. Kileny, Aniruddha K. Deshpande,
Shruti Balvalli Deshpande, Camille Dunn, Marlan Hansen,
and Bruce Gantz

9 Novel Approaches for Protection and Restoration of Hearing 197
Min Young Lee and Yehoash Raphael

10 The Olivocochlear System: A Current Understanding of Its
Molecular Biology and Functional Roles in Development and
Noise-Induced Hearing Loss 219
Douglas E. Vetter
<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>Current Progress With Auditory Midbrain Implants</td>
<td>255</td>
</tr>
<tr>
<td></td>
<td>Hubert H. Lim, James F. Patrick, and Thomas Lenarz</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Perception and Psychoacoustics of Speech in Cochlear Implant Users</td>
<td>285</td>
</tr>
<tr>
<td></td>
<td>Deniz Başkent, Etienne Gaudrain, Terrin Nichole Tamati, and Anita Wagner</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Theoretical Considerations in Developing an APD Construct:</td>
<td>321</td>
</tr>
<tr>
<td></td>
<td>A Neuroscience Perspective</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dennis J. McFarland and Anthony T. Cacace</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Normal Sound Processing: fMRI</td>
<td>331</td>
</tr>
<tr>
<td></td>
<td>Stefan Uppenkamp and Roy D. Patterson</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>Tinnitus Neurophysiology According to Structural and Functional</td>
<td>351</td>
</tr>
<tr>
<td></td>
<td>Magnetic Resonance Imaging</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dave R. M. Langers and Emile de Kleine</td>
<td></td>
</tr>
</tbody>
</table>

**Index** 371
INTRODUCTION

This is not your typical textbook in audiology; rather, it represents a compendium of state-of-the-art chapters on unique topics dealing with hearing, vestibular, and brain science, the majority of which are not found in standard texts but are highly pertinent to the field. The underlying theme is that audiology is the primary “translational interface” between basic science and clinical concerns. Trained primarily as clinicians and clinical scientists, audiologists are situated in a unique position to implement breakthroughs in engineering, molecular biology, neuroimaging, genetics, medicine, nanobiology, etc., and deliver them to the clinic. However, the underlying advancements require a fundamental understanding of advanced concepts and materials. Therefore, our intent is to provide a foundation for doctoral students in audiology, physics, neurobiology, and engineering and residents in various medical specialties (otolaryngology, neurology, pediatrics, and neurosurgery) with the background and concepts necessary to facilitate understanding in these different areas.

Of the “Current issues” subsumed within this book, we focus on topics that have practical, experimental, and theoretical value. The practical information is clearly apparent and is directly applicable to clinical situations. However, within this material, we also provide insight into basic areas of research where technical information is developing, where our understanding is incomplete, where theory has not been applied in a rigorous manner, and where experimental models can be improved upon to validate our concepts in complex areas. We hope that the end result will inspire new investigators to fill in the gaps and advance the field.

Moreover, it should be obvious that after viewing the table of contents, the topics being covered are expansive. They range from areas of basic science (anatomy, physiology, genetics, gene expression, molecular biology, neurochemistry) and clinical concerns (peripheral and central otopathology) to other relevant domains in assessment and treatment. They cover physical principles of middle ear and inner ear function (auditory, vestibular, balance), molecular and neural substrate underlying normal and pathologic activity in afferent and efferent pathways, implanted devices (cochlear and midbrain implants), mechanisms of speech perception associated with electrical stimulation, to the cortical processing of sound (normal and pathological) using noninvasive methods vis-à-vis magnetic resonance imaging (MRI).

We also consider “Future perspectives” in a similar context to those areas described above. However, these particular areas will no doubt be transformative in nature, where advancements are motivated by the ingenuity of the investigators and where the potential to produce large dividends (successful treatments and potential cures) is on the horizon. One area of interest concerns the combined use of manganese-enhanced MRI (MEMRI), gene expression, and functionalized nanoparticles
to treat noise-induced tinnitus. Another very exciting domain concerns novel approaches for the protection and restoration of hearing. This highly fluid area is expected to have substantial impact on the field, where future developments remain extremely bright.

It is our hope that information derived from these topics expands one’s knowledge base but also provides the incentive to improve the status quo. However, this is not an easy task. To succeed in this ambitious undertaking, we have assembled a stellar array of international world-class scientists, clinicians, and scholars to ensure that state-of-the-art technical information is explicated in an understandable, logical, and cohesive manner. The authors of these chapters have taken this task very seriously and share the common responsibility for giving an expose on potential gaps in knowledge that currently exist in a thoughtful and unselfish manner. We are extremely grateful for their efforts and contributions.

To summarize, we believe that this book will have many beneficiaries. They will be independent of geographical boundaries but will have in common the desire to learn and apply new and advanced concepts to everyday situations. This includes a broad spectrum of individuals from multiple scientific disciplines, including medicine (otolaryngology, pediatrics, neurology, neurosurgery), engineering (biomedical, mechanical, electrical, chemical), basic science (neuro/molecular biology and neurochemistry), rehabilitation, physics, psychology, and of course audiology, where each group will have specific domains-of-interest and applications. We also believe that having a literary source in one book that contains a repository of diverse and highly technical information, presented in a coherent manner, should be extremely valuable to a wide range of individuals, but to our knowledge, such a document does not yet exist. Therefore, this book should fill an important void in the scientific literature as a combined reference text, research guide, and educational tool.

As science in this area evolves, the profession of audiology is in a unique position to integrate advanced technologies developed by clinicians, engineers, and basic scientists and apply them to the clinic. Consequently, audiologists and others in related fields like medicine and engineering represent the “translational interface” between basic science and current clinical concerns. It is a big responsibility to integrate new ideas and concepts into the clinic but it is one that encompasses the technical skills and educational background of those individuals already working in this field.
In this chapter, we will explore the fundamentals of **audiology** and **speech-language pathology**. These fields are dedicated to the assessment, diagnosis, and treatment of hearing and communication disorders. Audiologists and speech-language pathologists work closely with individuals who have difficulties with hearing, speaking, and swallowing. They help patients communicate more effectively and live fuller lives despite challenges.

The contributions of **Faith W. Akin**, **Jont B. Allen**, **Deniz Baskent**, **Robert F. Burkard**, **Anthony T. Cacace**, **Emile de Kleine**, **Aniruddha K. Deshpande**, and **Shruti Balvalli Deshpande** are invaluable in advancing our understanding of these critical areas. Each brings unique expertise and perspectives to the field, expanding the knowledge base for educators, professionals, and students alike.

**Faith W. Akin**, PhD
Vestibular/Balance Laboratory
Mountain Home VA Medical Center
Professor
Department of Audiology and Speech-Language Pathology
East Tennessee State University
Mountain Home, Tennessee
*Chapter 4*

**Jont B. Allen**, PhD
Professor
Department of Computer and Electrical Engineering
University of Illinois
Urbana, Illinois
*Chapter 1*

**Deniz Baskent**, PhD, MSc
Professor
Department of Otorhinolaryngology-Head and Neck Surgery
University of Groningen
University Medical Center Groningen
Groningen, The Netherlands
*Chapter 12*

**Robert F. Burkard**, PhD, CCC-A
Professor and Chair
Department of Rehabilitation Science
University at Buffalo
Buffalo, New York
*Chapter 3*

**Anthony T. Cacace**, PhD
Professor and Director of the Hearing Science Laboratory
Department of Communication Sciences & Disorders
Wayne State University
Detroit, Michigan
*Chapters 3 and 13*

**Emile de Kleine**, PhD
Medical Physicist-Audiologist
University of Groningen
University Medical Center Groningen
Groningen, The Netherlands
*Chapter 15*

**Aniruddha K. Deshpande**, PhD, CCC-A
Assistant Professor
Department of Speech-Language-Hearing Sciences
Hofstra University
Hempstead, New York
*Chapter 8*

**Shruti Balvalli Deshpande**, PhD, CCC-A
Visiting Assistant Professor
Postdoctoral Research Scholar
The University of Iowa
Iowa City, Iowa
*Chapter 8*
Angela R. Dixon, PhD
Postdoctoral Fellow
Department of Anatomy and Cell Biology
Molecular Anatomy of Central Auditory Related Systems
Wayne State University School of Medicine
Detroit, Michigan
Chapter 6

Camille Dunn, PhD
Research Assistant Professor
Department of Otolaryngology
University of Iowa
Iowa City, Iowa
Chapter 8

Bastian Epp, Dr. Rer. Nat.
Assistant Professor
Hearing Systems Group
Department of Electrical Engineering
Technical University of Denmark
Lyngby, Denmark
Chapter 2

Bruce Gantz, MD
Professor and Chair
Department of Otolaryngology
University of Iowa
Iowa City, Iowa
Chapter 8

Etienne Gaudrain, PhD, MSc
Senior Researcher
Lyon Neuroscience Research Center
Auditory Cognition and Psychoacoustics Team
Department of Otorhinolaryngology-Head and Neck Surgery
University of Groningen
University Medical Center Groningen
Research School of Behavioral and Cognitive Neurosciences

Marlan Hansen, MD
Associate Professor
Department of Otolaryngology
University of Iowa
Iowa City, Iowa
Chapter 8

Avril Genene Holt, PhD
Associate Professor
Department of Anatomy and Cell Biology
Molecular Anatomy of Central Auditory Related Systems
Wayne State University School of Medicine
Detroit, Michigan
Chapters 5 and 6

Patricia S. Jeng, PhD
Mimosa Acoustics, Inc.
Mahomet, Illinois
Chapter 1

Paul R. Kileny, PhD
Professor of Otolaryngology
Director, Academic Program–Audiology
Department of Otolaryngology-Head and Neck Surgery
University of Michigan Health System
Ann Arbor, Michigan
Chapter 8

Dave R. M. Langers, PhD
Department of Otorhinolaryngology
University of Groningen
University Medical Center Groningen
Groningen, The Netherlands
Chapter 15
Min Young Lee, MD
Kresge Hearing Research Institute
Department of Otolaryngology-Head and Neck Surgery
University of Michigan Medical School
Ann Arbor, Michigan
Chapter 9

Thomas Lenarz, MD, PhD
Professor and Director
Department of Otolaryngology
Hannover Medical School
Hannover, Germany
Chapter 11

Harry Levitt, BSc, PhD
Professor Emeritus
The City University of New York
Director of Research
Advanced Hearing Concepts
Bodega Bay, California
Chapter 1

Hubert H. Lim, PhD
Assistant Professor
Biomedical Engineering and Otolaryngology
Institute for Translational Neuroscience Scholar
University of Minnesota, Twin Cities
Minneapolis, Minnesota
Chapter 11

Glenis Long, PhD
CUNY Graduate Center
Professor Emerita
Speech-Language-Hearing Science Program
New York, New York
Chapter 2

Lawrence R. Lustig, MD
Howard W. Smith Professor and Chair
Department of Otolaryngology-Head and Neck Surgery
Columbia University Medical Center
New York, New York
Chapter 7

Catherine A. Martin, BA
Kresge Hearing Research Institute
University of Michigan
Ann Arbor, Michigan
Chapter 6

Dennis J. McFarland, PhD
Research Scientist
National Center for Adaptive Neurotechnologies
Wadsworth Center
New York State Department of Health
Albany, New York
Chapter 13

Judi A. Lapsley Miller, PhD
Senior Scientist
Mimosa Acoustics, Inc.
Hearing Research Consultant
Wellington, New Zealand
Chapter 1

Antonela Muca
Wayne State University School of Medicine
Detroit, Michigan
Chapter 6

Owen D. Murnane, PhD
Vestibular/Balance Laboratory
Mountain Home VA Medical Center
Professor
Department of Audiology and Speech-Language Pathology
East Tennessee State University
Mountain Home, Tennessee
Chapter 4
Anita Wagner, PhD, MA
Researcher
Department of Otorhinolaryngology-
Head and Neck Surgery
University of Groningen

University Medical Center Groningen
Research School of Behavioral and
Cognitive Neurosciences
Groningen, The Netherlands
Chapter 12
To my AuD and PhD students for their inspiration and interest in science and research, which in part motivated the need for such a book; To those students, scientists, and clinicians who will continue to advance the field; and To my wife Lydia, for her unwavering support.

—Anthony T. Cacace

To my wife Margreet and our girls Veerle and Céline.

—Emile de Kleine

To my laboratory team for their boundless energy and enthusiasm for science; To my colleagues at Wayne State University and The Kresge Hearing Research Institute, University of Michigan, for thought-provoking and stimulating scientific conversations; To my Saline CoC family for helping me to stay grounded; To my parents for giving me a solid foundation and for their continuous encouragement; and To my husband Ron and our son Parker, who through their support, provide me with the opportunity to continue the work I love.

—Avril Genene Holt

To my wife Jacqueline and children Jop and Jet; and To my scientific colleagues at the University Medical Center Groningen, University of Groningen, University of Oldenburg, Graduate Center of the City University of New York, University of Tübingen, University of Cambridge and University of California, Los Angeles for great collaborations in the past and at present.

—Pim van Dijk
The middle ear is a complex sound transmission system that converts airborne sound into cochlear fluid-born sound, in a relatively efficient way, over the bandwidth of hearing (about 0.1–15 kHz). The middle ear is the gateway to the auditory system, and it is involved in nearly every audiologic test. It is therefore critical to assess middle-ear status in any audiologic evaluation and, in the case of abnormal middle-ear function, pinpoint the source of pathology to enable an appropriate medical intervention. By the use of wideband acoustic measurements, the middle-ear structures can be non-invasively probed across the wide frequency range of hearing, allowing clinicians to make nuanced interpretations of hearing health. The term wideband acoustic immittance (WAI) has recently been coined as an umbrella term to identify a variety of acoustic quantities measured in the ear canal (Feeney et al., 2013). Here we focus primarily on wideband reflectance, from which other WAI quantities may be derived. The reflectance is defined as the ratio of reflected to forward pressure waves.

A middle-ear reflectance measurement involves inserting an acoustic measurement probe into the ear canal, fitted with an ear tip designed to create a sealed ear-canal cavity (Figure 1–1). A hearing aid loudspeaker in the probe transmits wideband sound into the ear canal. Any reflected sound, related to structures of the middle ear, is measured by the probe microphone. This probe is calibrated in such a way that the absorbed and reflected pressures in a cavity may be determined.

Reflectance measurements are clinically practical to make: The measurement takes less than a minute and the ear does not require pressurization. The
same probe can be used for other audiological tests, such as otoacoustic emission (OAE) tests and pure-tone hearing threshold testing. Such testing, when a microphone is used in the ear canal, is known as real-ear testing. Given knowledge of the reflectance, it is possible to correct for troublesome ear canal standing waves, which can produce large artifacts in the real-ear calibrations. Alone, or together with other audiological measurements, middle-ear reflectance measurements can help identify many abnormal conditions which may lead to conductive hearing loss (CHL), including degrees of otitis media, tympanic membrane (TM) perforations, otosclerosis, and ossicular disarticulation. The method is noninvasive, fast, and clinically available.

In this chapter, we cover the theoretical principles of middle-ear reflectance. We then move to clinical applications, showing how normal middle ears behave and how abnormal middle ears differ. We offer advice on how to make quality measurements and provide suggestions for future research.
Background to Middle-Ear Assessment

Noninvasive assessment of middle-ear status is of great importance in hearing health care. An early approach to middle-ear assessment is that of tympanometry (e.g., Feldman, 1976; Shanks, 1988), and it is still the clinical gold standard. The method relies on measurements at low frequencies (e.g., probe tones at 226 Hz and 1,000 Hz are commonly used) and provides no information on the status of the middle ear at higher frequencies relevant to speech perception (e.g., 0.2–8.0 kHz). The methods employed in tympanometry were developed prior to the introduction of digital technology, and these methods reflect the limitations of that era.

Reflectance of sound from the TM and the acoustic impedance of the middle ear are different facets of the same underlying mechanism. Historically, acoustic impedance of the ear was the first to be measured and studied (West, 1928). There is a substantial body of research on the acoustic impedance of the ear. Metz (1946) developed the first clinical instrument for measuring the acoustic impedance of the ear. This instrument was not easy to use and clinical measurement of acoustic impedance proceeded at a slow pace until more practical instruments were developed (Møller, 1960; Terkildsen & Nielsen, 1960; Zwislocki & Feldman, 1970). Tympanometry, the measurement of the middle-ear acoustic impedance as a function of static pressure in the ear canal, provided useful clinical data. Thus, practical instruments were developed for measurements of this type. The 1970s saw a rapid growth in the use of tympanometry, which is widely used today in audiologic evaluations (Jerger, 1970).

The introduction of small, inexpensive computers in the mid-1980s paved the way for a new generation of digital test equipment with capabilities well beyond that of conventional electronic instrumentation. It also facilitated new ways of thinking about audiologic measurement, resulting in the development of innovative wideband techniques. The evolution of wideband reflectance measurement allows for more detailed diagnostic assessment of the middle-ear status than the previous approach based on tympanometry. Early reflectance studies were conducted by Keefe, Ling, and Bulen (1992); Keefe, Bulen, Arehart, and Burns (1993); and Voss and Allen (1994).

The use of reflectance measurements in a computer-based system does not preclude the use of acoustic impedance data, where appropriate. Acoustic reflectance and acoustic impedance are both WAI quantities; different facets of the same underlying mechanism. If one is known, the other can be computed by means of a mathematical transformation. This mathematical transformation can be implemented conveniently in a computer-based instrument.

Acoustics of the Outer and Middle Ear

When a sound wave travels down the ear canal toward the TM, the acoustic power is continuous until it reaches an impedance discontinuity, such as the
Many of the concepts in WAI, including reflectance, are defined in mathematical or physics terms. This creates a problem for clinicians and others without the necessary background. Here we explain some acoustical concepts in lay terms.

The transmission of sound in the ear canal can be approximated quite well by a tube with a fixed diameter equal to that of the average adult ear canal. The tube is terminated at one end by a loudspeaker that delivers an acoustic signal in the frequency range up to at least 10,000 Hz. One may imagine that the air in the tube is partitioned into a very large number of infinitesimally thin discs (Beranek, 1949); each disc can be thought of as consisting of a layer of air particles. These discs of air are compressed or expanded by an applied force, such as a change in air pressure (air molecules will spread out from an area of high pressure to an area of lower pressure), and will return to their original volume once the applied force is removed.

Consider now what happens when the loudspeaker at one end of the tube generates an acoustic signal. When the speaker diaphragm moves inward, it displaces and compresses the adjacent discs of air, which then displace and compress the next layer of air, and so on. By this means, the in and out movements of the transducer diaphragm create a pressure wave that travels down the tube at the speed of sound, about 343 m/s at 20°C. The velocity of each disc of air about its quiescent position (the position of the disc at rest) multiplied by its cross-sectional area is known as the volume velocity, as the product of velocity and cross-sectional area encompasses a moving volume.

The air in the tube opposes being displaced and compressed by the transducer diaphragm. The force exerted by the transducer diaphragm is equal to the pressure times the area of the diaphragm. The work done by the force is equal to force times the displacement, and is stored as energy in the air as it travels along the tube. The acoustic power, $P(f)$ (the force times the volume velocity, often expressed in watts), inserted into the tube is equal to the rate of work done. The power propagated down the tube is transmitted without significant loss through the tube. The acoustic power, $P(f)$, represents the power of the sound wave.

TM. Impedance discontinuities result in frequency-dependent reflections of the sound wave, which we quantify using wideband reflectance.

The acoustic variables discussed in this section may be defined either in the time or frequency domain. It is important to always be aware of which domain is under consideration. In this chapter, we work almost exclusively in the frequency domain, where all variables are functions of frequency, $f$. These variables are also a function of location. For measurements in the ear canal, we define $x = 0$ as the measurement probe location and $x = L$ the TM location.
Pressure and Volume Velocity Waves

We denote the forward traveling pressure wave as \( P_+ (f,x) \) [Pa], using the plus sign subscript to signify the forward direction (toward the TM). This wave is a function of both frequency \( f \) (in Hz) and location and has units of Pascals. Similarly, the reflected, backward traveling retrograde pressure wave is denoted \( P_- (f,x) \). At any location in the ear canal, the total pressure \( P(f,x) \) is defined as

\[
P(f,x) = P_+ (f,x) + P_- (f,x).
\]

(1)

The pressure is a scalar quantity (it has no direction). Any change in the pressure results in a force, which is a vector quantity (it has direction); this force leads to the motion (velocity) of air molecules in the direction of the force.

The corresponding acoustic velocity \( U(f,x) \) may be decomposed into forward \( U_+ (f,x) \) and reverse \( U_- (f,x) \) traveling portions, as

\[
U(f,x) = U_+ (f,x) - U_- (f,x).
\]

(2)

The volume velocity is a vector quantity, which accounts for the change in sign of Equation 2 (here positive \( U_+ \) values indicate propagation of the retrograde wave toward the probe, and positive \( U_- \) values indicate propagation of the forward wave toward the TM).

The complex acoustic reflectance, which we represent using the uppercase Greek letter “Gamma,” is defined as the ratio of retrograde to forward traveling pressure (or velocity) waves

\[
\Gamma(f,x) = \frac{P_- (f,x)}{P_+ (f,x)} = \frac{U_- (f,x)}{U_+ (f,x)}.
\]

(3)

Since \( \Gamma(f,x) \) is complex, it may be expressed either as the sum of real and imaginary parts, or in terms of a magnitude and phase. The utility of the complex reflectance (as compared to other WAI quantities, such as impedance and admittance) is that the acoustic power is proportional to the square of the pressure. Thus, the squared magnitude of the reflectance describes the ratio of reflected to incident power (a value ranging between 0 and 1) as a function of frequency, while the reflectance phase codifies the latency of the reflected power (e.g., the depth at which the reflection occurs). Additionally, power absorbed by ear (potentially including the ear canal, middle ear, and inner ear) may be quantified as one minus the ratio of power reflected. The power reflectance at the probe may be defined as \( |\Gamma(f,0)|^2 \); thus, the power absorbed by the ear is \( 1 - |\Gamma(f,0)|^2 \). These properties of reflectance are more intuitive than impedance for formulating diagnoses of middle-ear pathologies.

For reference, the complex acoustic impedance is defined as the total pressure over the total volume velocity

\[
Z(f,x) = \frac{P(f,x)}{U(f,x)}
\]

(4)

The complex acoustic admittance is given by \( Y(f,x) = \frac{1}{Z(f,x)} \) and various other WAI quantities may be calculated from \( Z(f,x) \) and \( Y(f,x) \), as outlined in Appendix 1–A. This variety of immittance quantities can be confusing, so it is important to remember that they may all be derived from the complex acoustic reflectance. Specifically, the complex impedance is related to the reflectance via

\[
Z(f,x) = \frac{1 + \Gamma(f,x)}{1 - \Gamma(f,x)}.
\]

(5)