Preface

At least 85% of hearing-impaired people – 160 million in Europe alone – suffer hearing problems attributable to their cochlea, for the most of whom a causal therapy is either not available or economically impossible.

The cochlea transforms sound-induced vibrations of the middle ear into electrical signals in the auditory nerve. But to do this, the cochlea must meet specifications not yet achieved by any human-engineered system: i) sensitivity to Ångström displacements, ii) response time in microseconds, iii) operation over an intensity range of 120 dB SPL (a million-fold), iv) frequency range of 100 Hz to 20 kHz, v) detection of intensity changes of 1 dB and frequency changes of 0.1%, and vi) extraction of signals in noisy environments (signal-to-noise ratios of -20 dB). This performance must be achieved by living, self-maintaining structures that are resistant to excessive displacements, are viscous and are inherently slow. The formidable technical specifications of the cochlea are realized by a so-called "cochlear amplifier", an entity whose mode of operation somehow depends on the sound-induced motile response of specialized cells called "outer hair cells". The cochlear amplifier must involve a complex biophysical interplay between molecular, cellular and hydrodynamic processes that, in spite of remarkably rapid progress in hearing research, is still not understood.

This book represents the proceedings of a conference designed to advance our understanding of the biophysical basis of the cochlea. The conference brought together a multidisciplinary group of leading researchers working at the molecular, cellular and cochlear levels and using biological, theoretical and clinical techniques. The form of the conference was based on a series of seven held at intervals of about three years. They are commonly known as the "Mechanics of Hearing" conferences, after the name of the inaugural and exceedingly successful conference organized by E. de Boer in 1983. The conferences are designed to promote the integration of innovative theoretical and experimental aspects of basic and applied auditory research. There is no learned society, no international scientific committee, no institute or funding body that continuously supports or sponsors these conferences. Their success is driven by participants' wish to meet regularly to: i) synthesize results from this rapidly progressing, multidisciplinary research area, ii) target new research goals and generate cutting-edge collaborative projects, and iii) disseminate the information to other researchers.

Where previous conferences in this series included contributions dealing with the mechanics of the input to the cochlea – the middle ear – and with neural encoding at the output of the cochlea – in the auditory nerve -, this conference focused on cochlear processes only. This was necessitated by the recent,

remarkably rapid experimental progress at the genetic, molecular, cellular and whole-organ levels of cochlear processing.

The conference explored mechanisms associated with the non-linear, frequency selectivity of the cochlea produced by electromechanical forces from the outer hair cells. Since the motor molecule responsible for creating electromechanical force in the cell wall has been recently cloned, experiments are now being conducted to understand how these forces arise: how are changes in membrane potential sensed by the motor-complex, and how is the action of this complex harnessed to generate mechanical force by the whole cell.

Entwined with these questions is the so-called "time-constant" problem: the time constant of the basolateral cell membrane is so large that, at high frequencies, the membrane potential – the drive for somatic electromechanics – could be attenuated by as much as two orders of magnitude and its phase delayed by 90°. Consequently, an alternate hypothesis - electromechanical action by the stereocilia themselves - has been postulated as the relevant "amplifying" mechanism at high frequencies. Accordingly, the first set of chapters deals with transduction mechanisms in stereocilia (*I. Stereocilia*) and a second set with transduction mechanisms in the soma of outer hair cells (*II. Hair cells*). Experimental and theoretical aspects of the stereociliary and somatic hypotheses of electromechanics formed the basis of three of the plenary lectures (P. Dallos, P. Martin and G. Zweig).

How electromechanical forces produced by the outer hair cells are coupled into the cochlear partition formed the basis of the third set of chapters (*III. Whole-organ mechanics*), where a central aspect was measurement of the three-dimensional mechanics of the organ of Corti.

The bridge between experiment and theory is the model. Therefore, models form an essential component of each set of chapters; there is also a set of chapters devoted to models of cochlear mechanics (*IV. Cochlear models*).

A by-product of electromechanical transduction is otoacoustic emissions – a pressure change measured in the outer-ear canal which originates from the cochlea. Clinically, the emissions are of paramount importance because they give an objective diagnosis of the condition of the "cochlear amplifier". Such a diagnosis is particularly important for pre-lingual children. Although otoacoustic emissions have become a routine diagnostic tool, poor understanding of the link between emissions and mechanical events in the cochlea has meant that the information gleaned from the emission data remains rudimentary, limiting their full clinical potential. The fifth set of chapters elucidates theoretical and clinical aspects of emissions (*V. Emissions*); the topic is introduced by a plenary lecture (C.A. Shera) that reviews this extensive field.

The final set of chapters is an edited transcript of a recording of the discussion session held on the last evening of the conference (*VI. Discussion session*). Arguably, the most valuable aspect of the book, this section documents current

opinions on outstanding topics of cochlear biophysics and provides directions for future research.

At the end of each manuscript, under "Comments and Discussion", is given (where desired by the participants) a record of the questions that were asked and the answers given after each oral presentation.

Since hearing-impairment can mean severe impairment of the quality of life, it was most appropriate that this conference was made possible by a substantial grant from the European Commission under their programme "Quality of Life and Management of Living Resources" (Proposal No. QLAM-2001-00159; Acronym: BIOCOCHLEA). The international community of hearing scientists is extremely grateful for this far-sighted support. We are also indebted to the financial assistance of the following companies: Adler Werbegeschenke GmbH & Co. KG, Saarbrücken; Attempto Service GmbH, Tübingen; Carl Zeiss, Jena and Oberkochen; Industrial Acoustics Company GmbH, Niederkrüchten; Dr. Koch Computertechnik AG, Tübingen; Polytec GmbH, Waldbronn.

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We dedicate this book to the memories of our recently deceased colleagues and friends: Desmond L. Kirk, Alfons Rüsch, Norma B. Slepecky and Graeme K. Yates, who contributed in different ways to our understanding of the biophysics of the cochlea.

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