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# AUDITORY PHYSIOLOGY RESEARCH IN TORONTO: AN OVERVIEW

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## Introduction

The Canadian Acoustical Association encompasses a wide spectrum of research interests, all linked by the common factor, acoustics, (but perhaps not all soundly linked!) The activities of the CAA parallel in many ways those of its big brother/sister the Acoustical Society of America, but compared to the ASA one area has been largely (but not totally) unrepresented in the CAA, namely auditory physiology. However, recent years have seen the maturation of a number of physiological research groups throughout Canada. One of the main functions of the CAA is to promote interactions between groups or individuals with similar research interests, and the vehicle for such communication is this journal, Canadian Acoustics. To assist the spread of information I have agreed to the request of the editor-in-chief to provide a summary the research in auditory physiology being carried out in laboratories in Toronto, at the Hospital for Sick Children, and at the University.

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Two basic auditory physiology research laboratories are currently operational in Toronto. The first is in the Research Institute of the Hospital for Sick Children (HSC), associated with the Hospital Department of Otolaryngology[1], and the second is part of the university Department of Otolaryngology[2] located in the Institute of Medical Science,the Medical Sciences Building, at the University. Both laboratories are closely linked to the Department of Physiology[3]; the author lectures in auditory physiology at undergraduate and postgraduate levels, in that department, and the laboratories are training grounds for research students in physiology.

The emphases of our basic research are the structure and function of the normal and of the pathological auditory system. The study of structure, (anatomy, histology, light and electron microscopy) is the main activity in the first laboratory (HSC), and auditory function (electrophysiology, and most recently behavioural psychophysics) is the thrust of the second laboratory (U of T). However, it should be noted that rarely do any of our research projects include only one type of investigation (we always attempt to correlate structure and function). In the following, a description of the facilities of each laboratory is presented followed by a brief summary of some of our ongoing projects. The reference list at the end is a small, representative sample of research publications from members of our research group.

## Otological Research Laboratory, Hospital for Sick Children

This laboratory[4] is devoted to anatomical, histological and microscopical studies of the inner ear and the central auditory pathways. The lab is managed by an experienced histologist/electron microscopist[5]. Here, biological material is processed for a variety of morphological studies. Some of the procedures are routine, such as fixation, embedding, and sectioning of specimens, although even those vaguely familiar with the anatomy of the ear will recognise that some specialised techniques are required, to cut or remove the very hard temporal bone surrounding the inner ear without damaging the very delicate sensory structures of the cochlea.

One technique which has proved very useful for observation of cochlear structures has been the micro-dissection of the cochlea followed by special preparation for observation using the scanning electron microscope. Figures 6 and 7 show some views of cochlear structures using this technique. This method has been used to great advantage to study the damage to stereocilia and other hair cell structures which result from various types of cochlear pathology (eg acoustic trauma, ototoxic poisoning, cochlear hypoxia, etc).

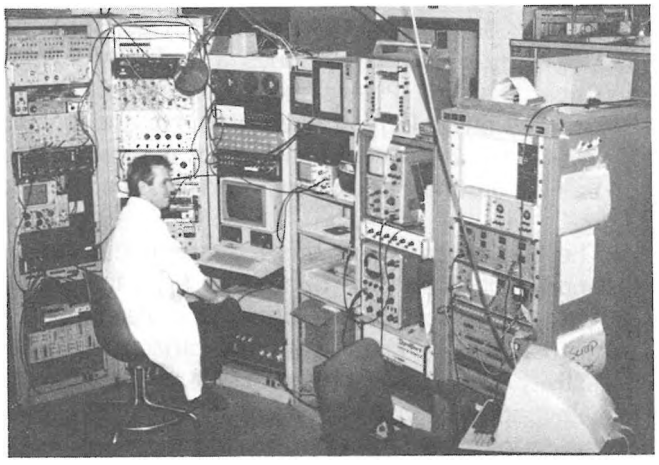

*Figure 1: In the Auditory Physiology Lab, U of T, the author decides which button to press next.*

Serial sectioning of the cochlea is carried out to allow other types of observation, using light microscopy, or transmission electron microscopy. For example, the study of possible ultrastructural changes to hair cells or sensory nerve fibres requires sectioning techniques; cochlear sectioning is currently being used to investigate endolymphatic hydrops, and spiral ganglion cell degeneration in animal models of deafness, (see below).

In addition to studies of the hearing organ, we also have an interest in the vestibular sense organs (e.g. ref 11).

Studies in the laboratory are not confined to the ear, but extend to the central auditory pathways where a different range of techniques is being applied. Anatomical techniques for tracing and assessing the functional integrity of neural pathways of the auditory system include autoradiography (the study of the uptake of radioactive substances into auditory neurones) and labelling of neurones with enzymes such as horse-radish peroxidase.

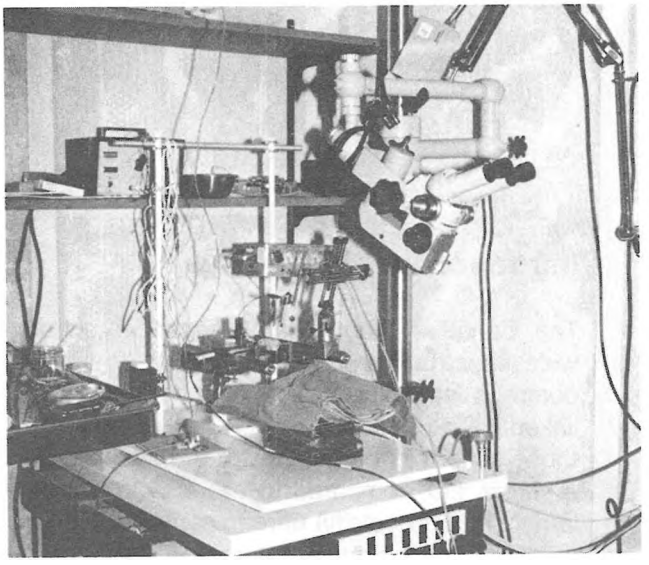

*Figure 2: Stereotaxic equipment to record from single nerve cells in the auditory areas of the brain.*

The laboratory is currently experimenting with new techniques for the quantitative analysis of microscopic images, and for three dimentional reconstruction of cochlear and brain tissue specimens. One example is shown in figure 4.

## Auditory Physiology Laboratory, University of Toronto

This research lab is equipped to carry out a variety of electrophysiological studies into auditory function, (and dysfunction). The techniques currently used include

evoked potential studies, for example the auditory brainstem evoked response (ABR) and cochlear action potential (CAP), in animals with various types of impaired auditory systems. One of our experimental subjects is shown in figure 5.

More detailed information about the function of the cochlea and higher auditory pathways is obtained by inserting recording electrodes directly into the part of the brain under investigation (in fully anaesthetized animals). Micro-electrodes can be used to record from small groups of nerve cells, or from single neurones. Such single unit recording techniques are used to investigate the detailed processing of signals in the auditory pathways, and the deterioration of the same in various types of deafness in our animal models.

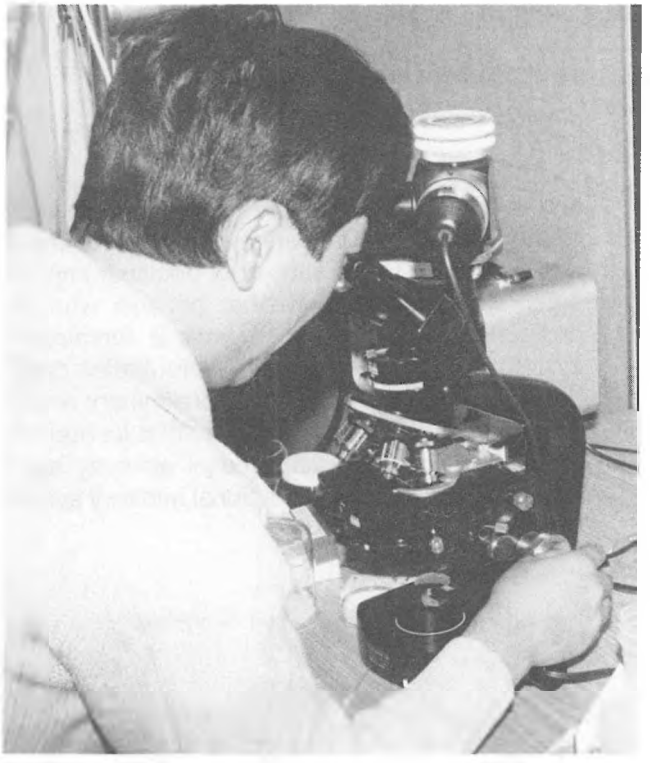

*Figure 3: In the Otological Research Lab, HSC, Dr. N. Fukushima (research fellow from Hiroshima, Japan) studies a cochlear specimen.*

These "animals models of human deafness[6]" include animals exposed to ototoxic drugs, or acoustic trauma, or with surgically induced cochlear dysfunction such as endolymphatic hydrops, or with some genetic disorder such as hereditary nephritis (see below).

In addition to the objective electrophysiological measures of auditory function outlined above, we are also training experimental animals in behavioural psychophysical tasks such that auditory thresholds, masked thresholds, difference limens etc. can be reported by the experimental animals[7]. Such studies are an important link in relating physiological data to hearing disorders in humans where the only real source of scientific information (at least pre mortem) is psychophysical.

## Animal Models of Deafness

For many years we have been using animal models of deafness in an attempt to obtain more insight into the nature and cause of the disease. In the following sections some of our studies with these animal models are briefly described.

### 1) Acoustic trauma

We are interested in how damage to the cochlea, resulting from intense acoustic stimulation, correlates with functional deficits including threshold elevations and other altered aspects of hearing such as frequency selectivity and intensity coding. Most recently, we have started to investigate some of the factors which may be important for optimal recovery of hearing after acoustic trauma. For all these studies it is convenient to use small animals such as the chinchilla or the guinea pig (e.g. refs 1,4).

### 2) Ototoxic drug poisoning

The cochlea is vulnerable to a variety of "ototoxic" drugs. In some studies we take advantage of this fact and use drugs (eg kanamycin) to produce predictable damage to the cochlea, and then assess the specific effects that this damage has on cochlear function using a range of electrophysiological methods (eg. refs 3,4). We also study newly developed drugs which are possibly damaging to the ear, assessing their potential ototoxicity by measuring functional, and anatomical changes caused by the drug (eg. refs 9,10).

### 3) Meniere's disease

In experimental animals, for example guinea pigs, it is possible to induce some of the symptoms of Meniere's disease by a surgical operation which blocks the endolymphatic system of the ear, producing an endolymphatic hydrops. In these "hydrops" animals we are investigating the time-course of changes to the auditory system (eg. fluctuation in low frequency

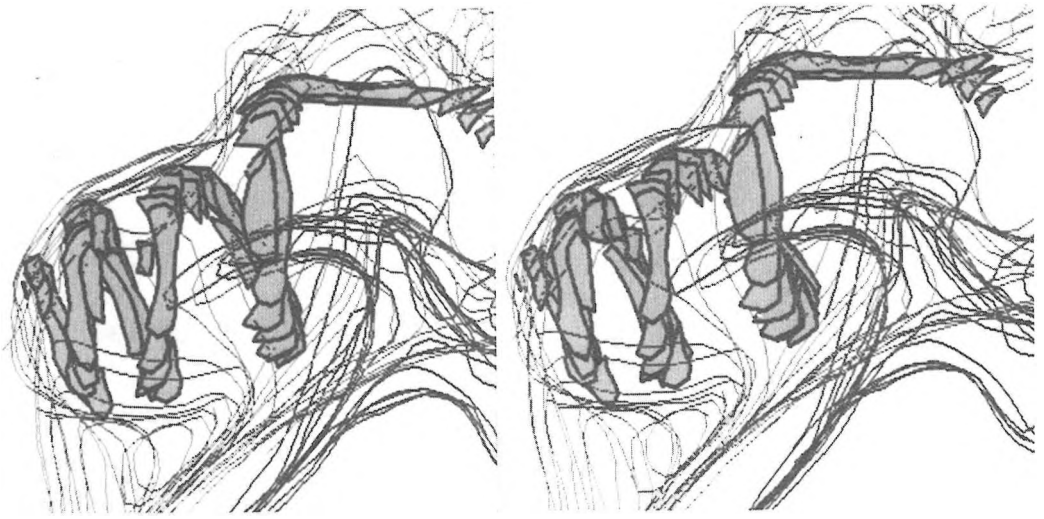

*Figure 4: Computer generated 3-d reconstruction of the cochlear endolymphatic system. (Observe this stereo-pair with a viewer for 3-d image.)*

thresholds of hearing) as well as trying to determine the underlying cause of symptoms in humans. In this respect we are asking whether the spontaneous firing rates of auditory neurones could be a possible underlying cause of tinnitus ("ringing in the ears"). In such animals models of Meniere's disease, functional changes are being compared with any anatomical changes, in particular the volume expansion of the endolymphatic system.

**4. Hereditary deafness**

There are many types of hereditary deafness in man. Unfortunately such types of deafness are difficult to investigate experimentally because they do not often occur in non-human species. We have, however, been monitoring auditory function in dogs with hereditary nephritis, a disease often associated with progressive hearing loss in man (e.g. Alports syndrome). One of the experimental subjects is shown in figure 5. So far, however, we have been unable to characterize a genetically determined hearing loss (ref 13).

**5. Profound deafness**

Animal models of profound deafness can be produced by causing total cochlear degeneration using ototoxic drugs or surgical ablation. Profound hearing loss is not easy to study electrophysiologically (or behaviourally) because, of course, acoustic stimuli cannot be used in experiments to activate the auditory system. However it is possible to determine the integrity of the auditory pathways by a combination of direct electrical stimulation of the cochlea, and evoked potential or single unit recordings, for example from the brain stem or midbrain. Our studies in this area relate to the subject of cochlear implants (ref 7). Thus, we are asking whether patients who have been profoundly deaf from birth have a functional auditory system that can use the limited information provided by a cochlear implant device. Our preliminary results in deaf from birth animal models indicate that an auditory system which has not been activated at an early age may not have developed a fully functional auditory system.

*Figure 5: An experimental subject relaxes for ABR assessment of auditory thresholds.*

## Research Funding

The research lab spaces have been established by the Hospital for Sick Children Research Institute and the University Department of Otolaryngology. Research funding is provided through external agencies, in particular from peer reviewed research grants from the Medical Research Council. Important financial support has also been provided from local agencies, and in particular by the generosity of the Masonic Foundation of Ontario.

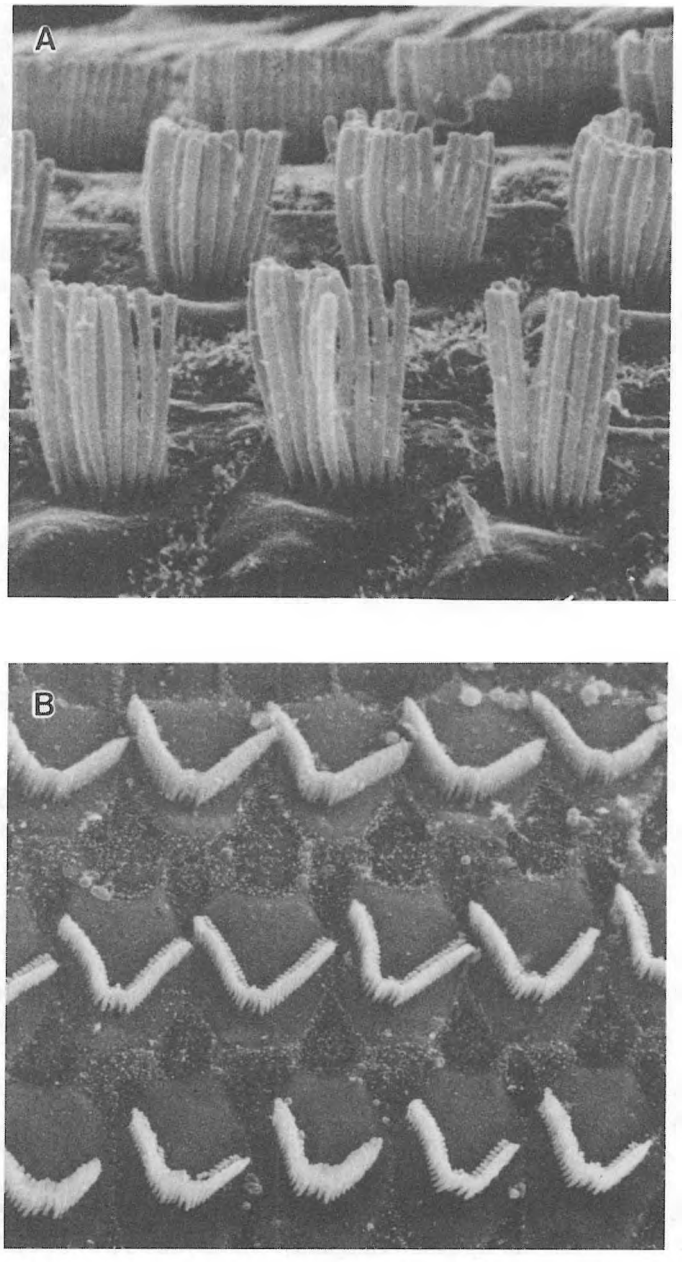


*Figure 6: Scanning electron micrographs of hair-cell stereocilia from the apical (a) and basal (b) regions of the cochlea.*

## Research Training

The research laboratories provide research training to science graduates working toward higher degrees, and to post-docs, for example, MD residents in otolaryngology seeking research experience.

## Applied Research

The major emphasis in our laboratories is basic physiological research. However, being based in a clinical department (otolaryngology) there is sometimes an opportunity to apply some of our techniques and knowledge to clinical problems. Thus for example we have been involved with the provision of cochlear implants to profoundly deaf patients[8] (ref 7) and the development and testing of new implant devices[9] (ref 8).

Evoked potential electrophysiology in humans is now a widely used technique for objective assessment of hearing and other neurological disorders. We have implemented such evoked potentials (ABR, AP) during surgical operations involving the cochlear nerve or auditory brainstem (eg acoustic neuroma removal) to monitor the function of the auditory pathways with the aim of conserving hearing[10] (ref 12).

Thus the basic physiological laboratories described herein enjoy a close relationship with the clinical Department of Otolaryngology, and the related Audiology divisions. The labs serve to promote interaction between clinicians and laboratory scientists, bringing scientific techniques to bear on clinical problems, and allowing new knowledge and techniques generated on the bench to permeate into practical applications.

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[1] Head of Department: Dr. W.S. Crysdale.

[2] Chairman of Department: Dr P.W. Alberti.

[3] Chairman of Department: Dr H. Atwood.

[4] Historical note: the lab was largely established by Dr. Ivan Hunter-Duvar who is now retired, but alive and well, hunting and fishing in Nova Scotia.

[5] Mr. Richard Mount.

[6] The term "deafness" is used here not in its specific sense of total hearing loss but in a general sense to cover all degrees of hearing impairment.

[7] In charge of this research is Dr. David Smith.

[8] In collaboration with Drs. S.M. Abel and J.M. Nedzelski.

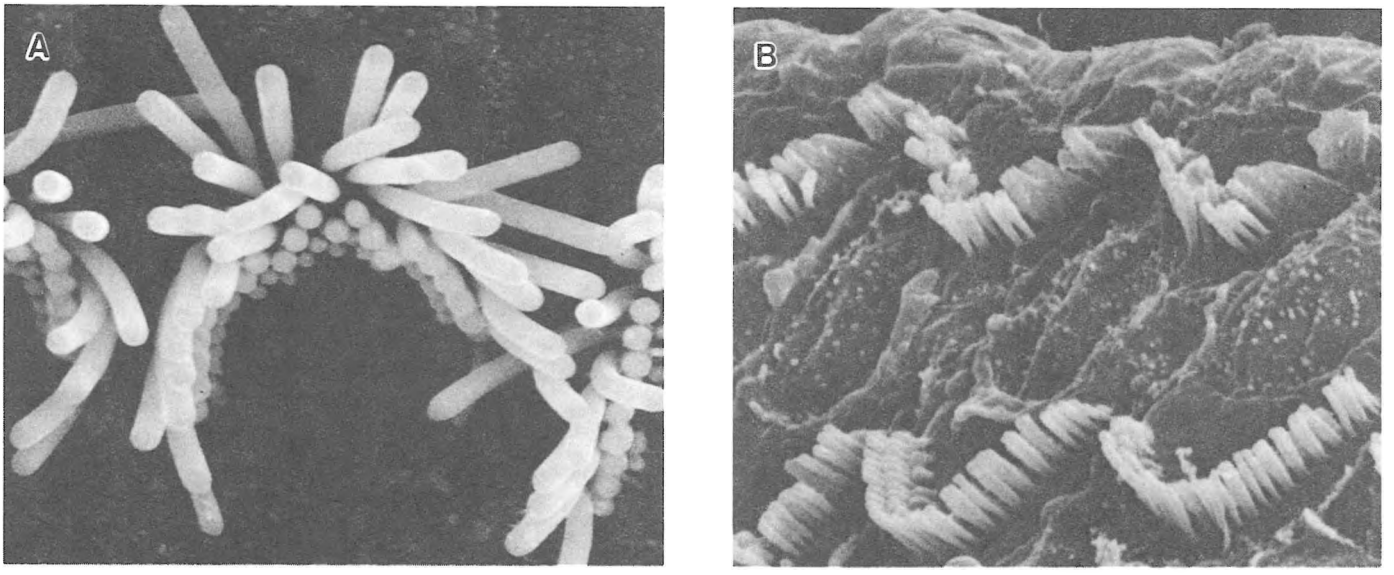


*Figure 7: Some of the effects of acoustic trauma on the stereocilia of hair-cells. Note the splaying (in A) and the fusion of stereocilia (in B).*

[9] In collaboration with Drs. H. Kunov, R. Morris, P. van der Puije and F. Duval.

[10] In collaboration with Dr. J.M. Nedzelski, Dr. D.W. Rowed, Susan Stanton, and Marlene Z. Cashman.

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