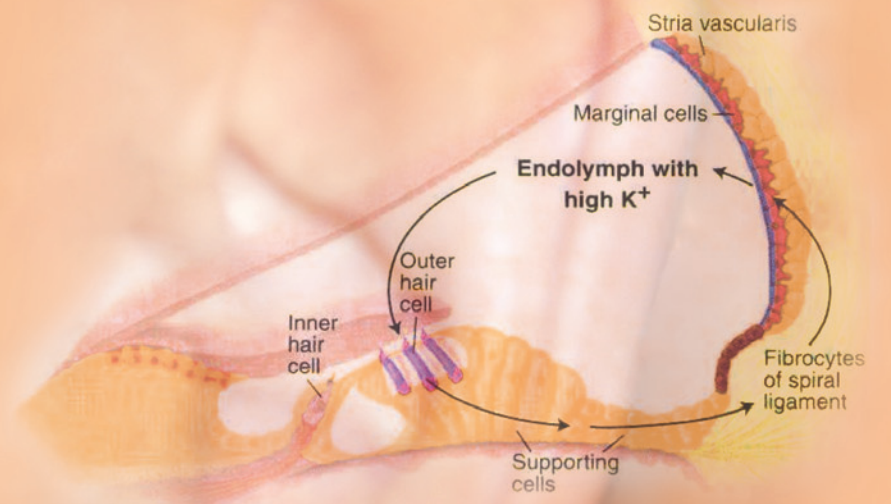
Acoustics Australia



SPECIAL ISSUE: MECHANISMS OF HEARING DAMAGE

- ***Spatial perception and masking***
- ***Plasticity in the adult auditory system***
- ***Efferent control of hearing***
- ***Genetics of hearing loss***
- ***Mitochondria, cell death and deafness***
- ***Cochlear mechanics and masking***
- ***Servo control in the cochlea***

Australian Acoustical Society ***Vol. 34 No. 1 April 2006***

Acoustics Australia

Acoustics Australia
General Business
(subscriptions, extra copies, back issues, advertising, etc.)

Mrs Leigh Wallbank
P O Box 579
CRONULLA NSW 2230
Tel (02) 9528 4362
Fax (02) 9589 0547
wallbank@zipworld.com.au

Acoustics Australia
All Editorial Matters
(articles, reports, news, book reviews, new products, etc)

The editors, Acoustics Australia
School of Physics
University of New South Wales
Sydney 2052 Australia
61-2-93854954 (tel)
61-2-93856060 (fax)
aaeds@phys.unsw.edu.au
www.acoustics.asn.au
AcousticsAustralia@acoustics.asn.au
www.acoustics.asn.au

Australian Acoustical Society
Enquiries see page 60

Acoustics Australia is published by the Australian Acoustical Society (A.B.N. 28 000 712 658)

Printed by
Cliff Lewis Cronulla Printing Co
91-93 Parraweena Rd,
CARINGBAH NSW 2229
Tel (02) 9525 6588
Fax (02) 9524 8712
email: scott@clp.com.au
ISSN 0814-6039

Vol 34 No 1 April 2006

CONTENTS

PAPERS

FORUM

Cover illustration by Heidi Hereth.
Potassium cycling: see the paper by Dahl et al, p25.

From the President

It is with great sadness and shock that I write this President's Message due to the tragic death of Andrew Wearne at the end of last month. We have lost Australia's best – and probably one of the world's top five – railway noise and vibration acoustic engineers. I attended his memorial service along with approximately 800 others and there was overwhelming praise and recognition for Andrew's achievements from friends, colleagues and clients.

I was quite surprised how much this loss affected me personally, given that I only knew Andrew as a fellow professional and didn't know him socially. Although we had worked together on a number of projects over the last 13 or so years and others in our office had been working more closely with him recently, his name was always mentioned with the utmost respect.

I believe the real reason behind my feelings was the fact that Andrew was always so polite, easy to deal with and a true professional that you subconsciously knew what he would have been like as a husband, father, team mate and friend, hence you actually felt that you knew him well. I know that many other acousticians were similarly shocked and it was wonderful to see so many of his peers attend the memorial service which was a celebration of his life and achievements.

It is tragic circumstances like this that make you pause for a moment and take stock of your life. Do I enjoy my job? Do I have the right work / life balance? Am I contributing to society making the world a better place? The memorial service certainly indicated the great contribution Andrew has made through his skills as an engineer and also his dedication to friends in his local Berowra community. I trust that we can all reflect on the way we behave both professionally and socially to achieve the right outcomes. Hopefully this involves compromise and resolution rather than argument and conflict.

In our Articles of Association, the Acoustical Society is termed a "learned" society. Today we are a little less "learned". Andrew will be truly missed. The family has requested any donations be sent to African Enterprise www.africanenterprise.com.au

Looking to the future, it would appear from recent email correspondence that the first joint Australian and New Zealand Conference this November in Christchurch is shaping up to be one of the best ever in terms of likely attendance and number of papers. It really is the only opportunity each year to get together with your peers from around the region to share ideas and knowledge.

On a more local stage, the need to have regular get-togethers in your own State at technical meetings is also important so I would encourage you all to support these events by both offering to present and supporting your peers.

Neil Gross

From the Guest Editor

Since the last issue of Acoustics Australia directed at basic mechanisms in 1993, biological research has drawn over a billion of dollars of funding and is poised to make several huge advances. Hearing science has increasingly embraced other disciplines, such as genetics and molecular biology, which at first glance might seem to have little connection with acoustics. Accordingly, the Australian authors were challenged to condense into just a few pages those developments which may soon have application to acousticians and clinicians, i.e. the articles had to relate to sound parameters, signal processing, engineering concepts and auditory psychophysics.

Accordingly the articles are presented in a "top-down" order, from the psychophysics of sound localisation using Head Related Transfer Functions (Carlile). Next, Irvine and colleagues review the concept of plasticity of 'wiring' of the neural connections in the auditory cortex and how that has applicability to the fitting of cochlear implants. Further down the brainstem, Mulders reviews the extensive neural organisation with particular emphasis on the signals which descend to the cochlea to either control the mechanical processing of sound via the outer hair cells, or the excitability of primary neurons carrying the frequency analysis upward.

The next two articles are about the genetics of hearing loss (Dahl and colleagues) and the source of biological energy which drives cochlear processes (Pickles). These authors ask why deafness occurs; and what syndromes relate to malformations of molecular structures which allow ionic currents to flow. The charged ions must be pumped using energy provided by mitochondria. These two papers also contain the basis of mechanisms for characterising individual susceptibility to hearing loss. Basic hearing science now regards the effects of noise trauma as just another of the toxic influences which cause hair cells to die. Hair cell death occurs by two separate processes and, whereas we might once have had a simple mental connection between temporary threshold shift as an indicator for permanent loss, we now have a new branch of science.

Traditionally, reviews of cochlear mechanics discuss how the frequency analysis in terms of tuning curves for each frequency and the important nonlinear processes which occur due to outer hair cell activity. The sixth article (Sen) models two-tone interactions at the mechanical level and explains the upward spread of masking which started out being the basis of mpeg compression technology, but has deep associations with distortion product emissions, combination tones, and critical bands. Increasingly, analysis of cochlear mechanics suggests that the outer hair cells providing the frequency analysis are also involved with regulation. The last article (LePage) reviews direct mechanical evidence for an internal automatic volume control system which optimises cochlear performance during trauma and aging of the ear. The new insights into structure and function lead to some possible explanations of the relation between sound level and duration – Dixon Ward's equal energy relation, and suggest new approaches to hearing loss prevention based on actual mechanisms.

This special issue thus has particular significance because it draws attention to the exciting cross-fertilisation now taking place between the worlds of psychoacoustics and physiological acoustics. The next decade may well reveal precise explanations of well-known psychophysical phenomena and issues of individual susceptibility.

Eric LePage, guest editor

A REVIEW OF MECHANICAL EVIDENCE FOR A SERVO-LOOP IN THE MAMMALIAN COCHLEA

Eric L. LePage
OAEricle Laboratory, Sydney, Australia
PO Box 6025 Narraweena, 2099
ericlepage@oaericle.com.au

The outer hair cells in the cochlea are recognised as the active mechanical elements in the normal operation of the cochlear amplifier. Yet the functions of their two motor mechanisms are still not clear. Increasingly, the outer hair cells are also being implicated the control elements in homeostasis – normal regulation of cochlear activity by the descending neural pathway. This review targets articles with mechanical data and suggests new clues as to structure and function in terms of a mechanical-feedback loop for dc-stabilisation. The literature relevant to such an idea is reviewed and directly leads to clues underlying the notion of a time-intensity trade-off for noise exposure, the cause of Ménière's disease and the upward spread of masking.

INTRODUCTION

The cochlear amplifier

In presenting a modern review of cochlear mechanics it is essential to mention the work of Gold [1] who showed that the cochlea must have an active mechanism to achieve its sharp tuning and high sensitivity. Yet a general recognition that this was the case took 30 years. It came with Kemp's unambiguous evidence [2] of evoked emissions plus the demonstration that low hearing thresholds were necessary to see nonlinear behaviour in the basilar membrane (BM) resonance [3]. Soon after, it was shown that the BM was as sharply tuned as the neural tuning curves [4] and the notion of "cochlear amplifier" was introduced by Hallowell Davis in 1983 [5]. It was an idea with strong intuitive appeal because of widespread take up of hearing aids when the internal amplifier failed with age. Indeed at threshold, the vibrations of the basilar membrane are fractions of a nanometre [4]. Since that time increasingly sensitive sophisticated measurement techniques have been used widely, such as laser interferometry coupled with confocal scanning microscopy to view the motion of the whole organ in three dimensions [6-11].

The weakness of invasive mechanical measurements has been the possibility of adversely damaging these delicate preparations. All the earliest experiments damaged the organ so that it did not show sharp tuning, and from that time [6] no mechanical measurement has been acceptable if there was not simultaneous sharp tuning to prove 'normal physiological operation' [6,12-13]. Yet as we see below, this insistence may have dramatically impeded progress in relating structure to function.

There are, of course, now thousands of publications on otoacoustic emissions, and most of these display correlates of the behaviour discussed and are reviewed elsewhere [14-16].

Special properties of the outer hair cells

The outer hair cells (OHC) are central to providing the gain of the cochlear amplifier. They are now recognised as perhaps the most specialised motor cells in the body for several reasons, not least because they possess not one, but two motor mechanisms (summary Kros [17]). The roles for these motor mechanisms are still the subject of intense debate, but the hair-bundle motor at the apex of the cell is thought responsible for amplification of the audio signals [18], and Hopf bifurcation is proposed to account for the process poised on the verge of instability [19] and how that state is regulated. On the other hand, the somatic motility is due to a cylindrical 'girdle' [20] located just inside the OHC cell membrane binding thousands of motor molecules christened *prestin* [21] to exert efficiently an axial force. The name stems from its own high-frequency electromotility described in piezoelectric terms, but increasingly associated with slow motility [17]. Indeed the latter is well accepted to account for relatively huge length changes [22], which, by virtue of their mechanical coupling in the organ of Corti, are linked back to modify OHC transduction at their stereocilia [23]. While most of the literature is concerned to use this feedback to overcome the effects of damping it is becoming clear that OHC slow motility also regulates the operating point (OP) of stereocilia transduction. What is not being answered specifically is why this stabilisation is needed.

Another remarkable specialisation of the OHC is that they effectively have not just one membrane potential, but two. Viewing both potentials from within the cell, these batteries would seem to be driving current in opposite directions. One steady potential (the endocochlear potential, EP ~+80mV) exists across the cuticular plates at their apex. The "regular" cell resting membrane potential for the lower cell membrane supported below the cuticular plate is of -70 mV relative to the 0 mV of the surrounding perilymph. Having a whole chamber such as the scala media (SM) at a voltage different from the surround is unique in mammalian physiology. Yet its function in holistic terms is unexplained. It clearly has not evolved just to provide a gain of 6 dB. This falls far short of explaining the 50 dB gain of the cochlear amplifier. It is tempting to speculate that the potential across the cuticular plates exists so as to power current flow, or OHC tonic force generation

in both axial directions for the very same reason that an electronic amplifier has positive and negative supply rails. Numerous studies of OHC in isolation show that they can contract or elongate according to the current pulses delivered to them, e.g. [24].

Homeostasis in the cochlea

There has been another line of interest in the mechanics of the labyrinth and this realm is most populated by otologists. In their regular practices they are confronted with patients who, in addition to having hearing problems, also present with a variable set of vestibular symptoms, including positional vertigo and debilitating violent giddy attacks. The literature devoted to these symptoms is as extensive as any other branch of hearing science. It reveals extensive knowledge on fluid dynamics within the cochlea and vestibular apparatus [25,26]. There are two basic fluid compartments – a high-sodium, low-potassium fluid (perilymph), and the reverse (endolymph). Perilymph is derived from the cerebrospinal fluid (CSF, via the cochlear duct) which fills the two outer chambers of the cochlea, *scala vestibuli* (SV), and *scala tympani* (ST), which are connected at the apex via a small hole termed the helicotrema. There are substantial pressure variations in the CSF due to exercise or change in posture. These are transmitted through to the cochlea [27,28], and while they could potentially affect the acoustic signal-processing they are generally discounted because 1) cochlear fluids are primarily water and therefore incompressible, and 2) being low frequency, pressure fluctuations are believed to equalise rapidly across the two chambers and to constitute no pressure differential to stimulate the hair cells.

The reason for inserting homeostasis into a review of cochlear mechanics lies with static pressures in the centre compartment, *scala media* (SM). It is widely recognised that SM can swell large enough to cause serious hearing and vestibular problems, i.e. to affect the OHC transduction operating point. This centre chamber is bordered 'above' by Reissner's membrane, 'below' by the Reticular membrane and the Stria Vascularis lining the outer bony wall. The whole chamber normally only contains a tiny amount of endolymph (~ 1-2 µl) yet this volume may vary by hundreds of percent. When the SM swells to a pathological extent, hearing loss may occur because the pressure displaces the whole sensory apparatus in the direction of ST and constitutes a bias disabling OHC forward transduction [29]. This condition is termed *hydrops*. The morphological evidence appears to be that it does not develop suddenly – it appears as if the pressure drifts upward slowly over many years. The basis for this creep in "pressure set-point" has been described in principle [30,31] without specifically invoking OHC as the control elements (see Fig. 1.C).

It was thought for many years that any excess build-up of endolymph normally drains away via the endocochlear duct, which connects with the vestibular apparatus. It was long supposed that if, for some reason, the flow resistance of endolymphatic sac rises then this would account for the abnormal rise in endolymph pressure. In an important series of articles by Salt and colleagues [25] it has been shown this

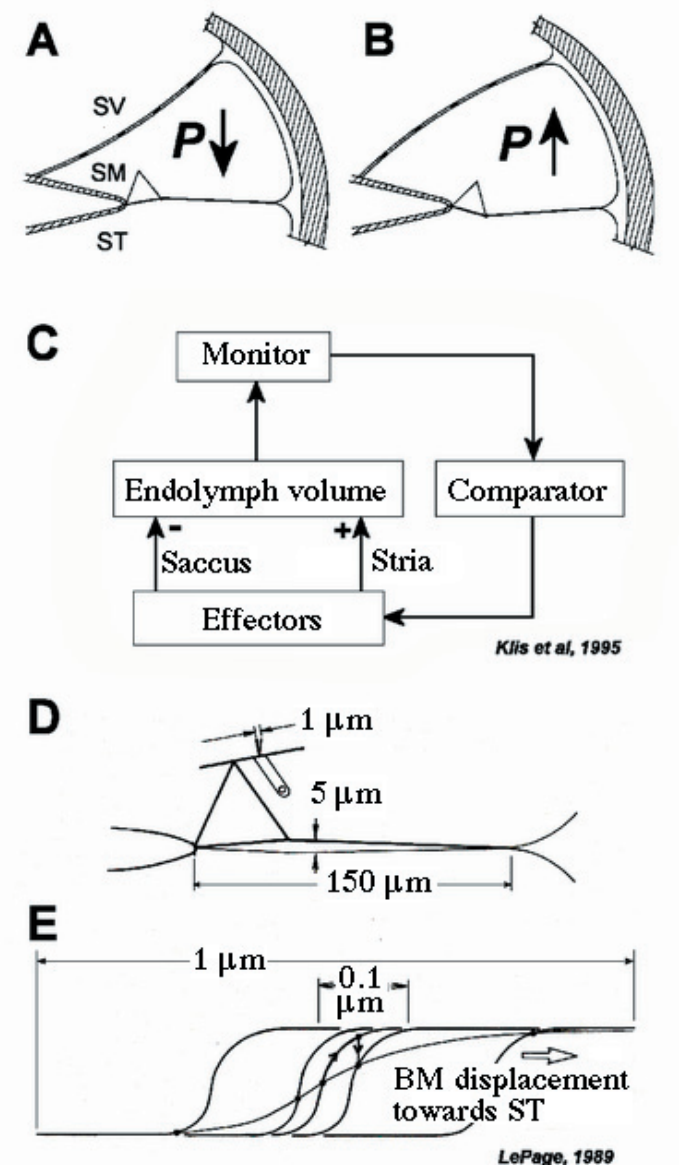


Figure 1. Panels A and B show that the basilar membrane is subjected to transverse movement by change in static pressure in scala media – pressure down will produce excitatory shear of the OHC stereocilia, pressure up will cause suppression. Panel C shows the schematic control system envisaged by Klis (1995) to effect control of endolymph volume. Panels D and E indicate the need for a mechanism to regulate operating point (see text).

theory has no basis. Using tracers, there is no regular flow. Since removal or partial removal of the fluid resistance at the sac has been the basis of surgical procedures to provide relief from patient distress [32], this new finding has resulted in intense interest in looking for alternate causes. The result is considerable interest in the processes of cochlear homeostasis. This has become a very important branch of hearing science and is well summarised in this edition with reviews by Dahl et al [33] and Pickles [34].

At the 5th international conference on Ménière's Disease and Inner ear Homeostasis Disorders in Los Angeles last year, some 187 scientific papers were presented where the overwhelming emphasis was on 1) the genetic and molecular-

biological factors regulating the volume of endolymph under normal circumstances, and 2) how to manage this abnormal condition. The bulk of presentations, and indeed the keynote address [35] dealt with biochemical aspects of transport of potassium ions (K^+) into SM from the stria vascularis. At this time the new candidate explanation is that hydrops is caused by *potassium intoxication* of the endolymph [36] which stemmed from pioneering work of Johnstone and colleagues [37]. The central idea is that K^+ accumulates in SM because, although the ions are recycled in a loop, this current loop is not like a passive electric circuit. These ions need to be actively transported against potential gradients and it would appear that the rate of transport of K^+ out of SM is not perfectly matched to the rate at which the ions are delivered into endolymph [38]. Loud noise exposure results in a rise in K^+ concentration. A couple of presentations only were directed at mechanical correlates. Quadratic distortion products (QDP) are now being added [39] to the battery of tests available to diagnose hydrops. The QDP are the lowest frequency components of the distortion product family and therefore most likely to best represent baseline changes.

Previously mechanical measurements by Flock [40] have observed, in guinea pigs exposed to loud sound, substantial "dc-shifts" in the motion of the Hensen cells (where "dc" is conventional terminology denoting the instantaneous value of the baseline). Flock interpreted these shifts as signifying the presence of hydrops. Since then it has been shown using a two tone suppression algorithm that that baseline pressure changes can be measured directly in the ear canal with an otoacoustic emission probe [41,42].

IMPLICATIONS 1

A fact which seems poorly appreciated is that variations in hydrostatic pressure in this centre compartment are presented *unattenuated* to the OHC. Investigators interested in frequency analysis have largely dismissed this influence 1) because of being outside the frequency range of interest, and 2) because such pressure changes are considered pathological and therefore beyond consideration of mechanisms of cochlear amplification. Pressure variations within SM seem rarely considered as being important or comparable. Yet it is becoming recognised they must be considered because 1) they are graded, i.e. they exist before the condition causes disability, 2) the hearing of sufferers might be compromised, but the mechanisms must cope with pressure variations, 3) the OHC are sensitive to displacement, and 4) the same ion species fundamental to OHC transduction is also responsible for the pressure rise in scala media. These displacements caused by such pressure fluctuations are superimposed on the sound vibrations to cause shear of the OHC stereocilia (see Fig. 1 A, B and D). The implication is that "pathological" issues cannot be ignored while trying to understand the cochlear amplifier. To do so might allow missing important clues.

In order for potassium intoxication to occur there must be a mismatch between the rate at which potassium enters SM and the rate at which it leaves. Flock's work implies that sound evokes a spike of K^+ entering the chamber, which depends on the characteristics of the sound. On the other hand, much recent work suggests that K^+ is being removed from SM at a rate which is determined not by sound but by energy-dependent processes [34]. One might surmise a simple analogy is that of a bilge pump in a boat. While ocean waves splash over the bow of a boat at highly variable rates, the water collecting in the hull is removed at a constant rate. There seems to be general interest in the explanation that the osmolality of SM varies according to the ratio of ions accumulating in endolymph. Although the mechanism by which this happens is far from clear, there is great interest in aquaporins – water flow through pores into the SM and raising the pressure [26,43]. It is postulated that water enters the SM under an osmotic gradient [29]. This means that there is substantial capacity for pressure rise in the SM, which cannot be neglected from the point of view of operation of the OHC and, if it occurs to any extent, cannot be ignored in respect of signal processing.

Evidence for control processes involving the OHC

We learn from the accompanying articles in this special edition, that the auditory system possesses a plethora of control systems (Mulders, [44]) which can modify cochlear sensitivity, the internal protective response. The brainstem can be regarded as a control centre with a host of motor programs to control not only OHC motility, but also the excitability of the primary afferent neurons. The medial olivo-cochlear (MOC) fibres may achieve this by varying the local stiffness of the basilar membrane and the damping of the structure. Efferent effects are produced by changes in OHC membrane potential and changes in slow motility. Because the OHC are so exquisitely sensitive to displacement, modifying the standing K^+ current and responding with force — the MOC must also be involved in cochlear homeostasis.

Mechanical correlates of homeostatic processes: a new look at old data

There are now many reports of cochlear mechanics displaying history-dependent effects. The classic description is that of high sound level exposure producing a temporary perturbation of the mechanical activity, and associated with temporary threshold shift (TTS) [45].

Another frequently studied phenomenon (and one easy to demonstrate psychophysically) is the mechanical bias experiment, which results in an instantaneous loss of hearing sensitivity if the basilar membrane is displaced towards ST [46]. In order to conduct the experiment using acoustic stimuli one needs typically a 25 Hz and >100 dB SPL tone. Such a bias tone will modulate most cochlear measures at acoustic frequencies [47-50].

The history of direct mechanical measurements describing the BM displacement in guinea pigs includes three separate series increasingly focussed on detecting mechanical correlates of homeostasis. These were early studies and at the time published they did not fit in completely with the prevailing travelling wave theory.

This author's experiments began in 1974, when, instead of using the prevailing approach of the time (the Doppler-shift, velocity-sensitive Mössbauer technique), he began using a capacitive probe [51] to measure basilar membrane motion in guinea pig ears by inserting a probe through a hole in

the wall of ST in the basal turn, the tip being brought close to the surface of the BM. Being displacement sensitive, it immediately revealed slow components of the motion never been previously reported. By comparison with the accepted approach, and also well-behaved neural data, the capacitive probe produced displacement data displaying a high degree of variability [50]. These "artifacts" were put down either to 1) the required temporary draining of ST (shown to result in poor neural sensitivity [52,53]), or 2) suspicion that they were due to poor surgical technique. The probe signal was viewed on an oscilloscope in real time, and the immediacy of the baseline variations was impossible to ignore. The output signal of the sensor probe was recorded digitally and averaged synchronously with the stimulus pulses to extract the submicroscopic vibrations. Earliest visual observations formed an indelible impression. In response to sound, even the stimulus clicks used to obtain the impulse response, the basilar membrane moved slowly towards the tip of the probe which was initially located 3 μm distant from the surface. The drifts amounted to micrometres of dc-drift in comparison with nanometres of ac-vibration. Such behaviour was totally inconsistent with the history of studies of cochlear mechanics and models. Nonetheless, the technique and results were accepted insofar as the approach did confirm the story that the basilar membrane motion was nonlinear and first revealed the connection with hearing sensitivity [3,50].

The second set of capacitive probe experiments took place after Brownell had shown OHC length changes *in vitro* amounting to 10 μm [22]. These experiments [54] tested specifically for baseline shifts in basilar membrane motion consistent with OHC length changes which might have been missed with velocity-sensing techniques. The capacitive probe data resulted from low- to medium-threshold preparations in which measurements were made near the round window, from where the summating potential (SP) was recorded on a second channel. To date, only one other report of doing so simultaneously has appeared [11]. They showed not only that there were small baseline shifts in the motion of the BM at the time of the tone burst, but that their polarity reversed systematically, consistent with the polarity changes in the SP. Perhaps more importantly in hindsight, the data were processed to differentiate short-term shifts (during tone bursts) from longer-term baseline shifts. Both measures showed the same polarity for regions away from the characteristic frequency (CF) of the place of measurement. By contrast, at the CF, short term shifts towards SV during the tone bursts were superimposed upon drift towards ST in the longer-term ([54], Fig. 9). The short term excitatory displacements produced a long-term response taking the movement in the direction of lower overall sensitivity – behaviour not dissimilar from what one might expect from a servo-control (automatic gain control) mechanism [54-56].

The third series used a fibre optic technique which did not require draining in the region of the measurement [57]. A small mirror was placed on the basilar membrane to yield an input noise level of the displacement sensor of *ca.* 1 nm. These data did show what appeared to be large tone-produced movements of the basilar membrane – the displacements were of the same order as moving the probe tip 1 μm relative to the BM. The displacement responses also displayed two opposing components of the motion each with different time courses – and occurring at the expected characteristic frequency of the place measured (see Fig 1D). One of the components was physiologically vulnerable to the extent that it disappeared with loss of activity, and could be manipulated by substances known to mimic efferent activity (perfusion of acetylcholine) or interfere with it (strychnine and atropine). The opposing component had a very different time course; after loud tone stimulation it wandered to full scale and stayed there or showed strong hysteresis [58].

Since the publication of those controversial data, two reports have appeared which claim to have adequately repeated these three series of measurements and using a highly displacement-sensitive laser interferometer. No evidence was found for any of the described behaviour at the base of the guinea pig cochlea [13]. However, at the apex, baseline shifts attributable to OHC activity were seen [59]. The preparations were deemed to have high hearing sensitivity, the data free of artifacts. However, it may be significant that the author waited until the preparation "settled down" before obtaining the published data.

SUMMARY 1

A servo-loop is being considered to explain not tuning, but homeostasis. Since the OHC are both detectors and actuators, a new idea surfaces. It is that OHC motor responses may not be triggered invariably by raw sound signals causing vibrations of the basilar membrane, so much as *error-signals* whenever the OHC operating point is displaced. This kind of motor response may not be continuously present but may depend upon "how challenged" are the OHC. This new realisation puts the direct basilar membrane measurements in a totally new light. The outcome of any experiment would then vitally depend upon the expectation that the dc-shifts are an inevitable consequence of acoustic stimulation. Insisting upon low thresholds and sharp tuning may mean that the error-signal is small so no dc-shifts will be seen. If on the other hand the OHC are strongly biased by e.g. draining, their dc-responses may be large which would explain the remarkably large deflections of the basilar membrane [57], particularly if the error signal could not be nulled, these direct measurements support the growing notion of an AGC loop in the mammalian ear, shutting down sensitivity for louder sounds and vice versa.

Why the need for a servo-loop?

It is necessary to consider the exquisite sensitivity of the OHC in comparison to the relatively large displacements they can produce when excited. A 50 to 100 nm stereocilia deflection will produce a full scale electric response (See Fig. 1E). Compared with the micrometre displacements which might result from pressure fluctuations in SM, this deflection is 40 dB smaller. Without any dc-compensation, the OHC transduction will be either off, or saturated most of the time. A servo-loop is necessary to maintain the OHC operating under small signal conditions. The OHC slow motility has the means to hold the operating point close to its most sensitive position (highest

gradient on the transducer curve). An externally applied bias moving the operating point will result in a motor response tending to stabilise the operating point, but resulting in a dc-shift at the same time (Fig. 1E). Any sustained contraction of the OHC will tend to pull the tectorial membrane down upon the inner hair cell stereocilia and excite them generating a receptor potential with both ac and dc components [60]. A full set of speculations about likely changes in hair cell stimulation were invited in a chapter on mechanical triggers of tinnitus [61].

In terms of signal analysis, it seems inescapable that the cochlea must deal with any fluctuations in pressure, but still attempt to deliver a signal to the auditory nerve fibres in which all such fluctuations have been removed leaving only essential details indicating the presence of any frequency component. This means that *at every point along the basilar membrane* these acutely displacement-sensitive hair cells must act so as to 'buck out' the pressure signal. Before the days of highly stable dc amplifiers, such an amplifier was termed a "bootstrap amplifier" – a dc-amplifier which compensated for drift in the input stage. It would make considerable sense of the whole structure if the slow motility of the OHC, acting via the leverage of the arch, can follow whatever is the slow pressure-bias in the system. This further supports the notion of a servo-control system in which the error signal is proportional to the difference between the current transduction operating point, and the absolute position of the bias displacement.

A role for efferent control of OHC motility

There is a 1000:1 variation in stiffness of the basilar membrane along its length. This will produce a large gradation in bias due to any value of hydrostatic pressure which is equally distributed throughout the vessel and is expected to cause larger biases where the basilar membrane is less stiff (Hooke's Law). While the OHC set-points could be "hard-configured" along the length of the cochlea to account for this bias curve versus distance, such an arrangement will not cope with ongoing decline in the numbers of OHC due to noise damage and ageing. The MOC system can thus be conceived to be also providing minor adjustments to the operating point (OP), not just in the short-term, but indeed over life. It follows that there must be a frequency range over which the OHC cannot distinguish between a deflection due to sound or due to a bias.

Control element for a biological servo-control mechanism

What therefore sets the transduction OP for any stimulus condition? A hypothesis [50,54,57] is that, since the OHC generate tonic force as well as amplify at audio-frequencies, there must be two mechanisms working in opposition and the OP is set at which their opposing effects balance. Quite apart from electrical balance, the stability of the operating point for any mechanoreceptor *must* depend upon the collective response of two opposing forces. One force might be passive (or osmotic in origin), the other active. There is growing agreement that multiple processes are interacting [62,63].

Flock's observations are important for a holistic overview of cochlear function. Hydrops may not be such a pathological condition so much as a "runaway stage" of the standard cochlear response to sound. In these terms OHC participation in homeostasis cannot be isolated from OHC participation in tuning. Disruption of any part of the potassium circulation, such as rendering connexons non-functional [33] or downgrading the energy available to these pumps [34] may mean that restoration may take much longer, and maybe even never complete, resulting in a permanent shift in operating point of the hair cells to the point of cell death. As the OHC response weakens there is permanently raised pressure in SM. *In these terms normal hearing is redefined as the capacity of OHC motility (both contraction and elongation) to track displacements caused by potassium intoxication.*

A recent set of studies set out to test the idea in humans using otoacoustic emissions [41,42]. It has been shown that signal-averaging of otoacoustic emission destroys evidence of homeostatic regulation which appears to be contained within the otoacoustic emission signal. This is revealed when the distortion product magnitudes are directly related to measures of static bias. In the two-tone probe/masker experiment the resulting distortion products are related to baseline pressures in the ear canal at the time the second tone is turned on. The result is widespread high correlations between the size of the distortion product and estimates of the current baseline-pressure signal. Moreover, the correlations are pronounced for frequencies which are meaningful in terms of distortion product generation, particularly the behaviour of the QDP [39].

It follows that, after acoustic trauma, it may take many hours of quiet to reset pressure in SM to pre-exposure values. Expressed in other words this describes the recovery function from temporary threshold shift. However, if raised pressure in SM is a normal accumulation which resets away from noise we arrive at the notion of 'Daily Dose' by another approach. If so, there should be existing data which might support the notion of pressure rise being normal. Moreover, if it is normal process, then it should be observable with sub-traumatic exposure; it may even be observable as a diurnal variation in other measures of cochlear mechanics.

Diurnal variation in cochlear mechanics

While otoacoustic emissions are not part of this review, there is one key result which has no explanation from conventional cochlear mechanics. Figure 2 suggests that such a diurnal variation exists in unambiguously cochlear mechanical data. The data shown are for over 300 babies and infants up to 12 months of age. ILO88 apparatus was used to obtain standard click-evoked otoacoustic emissions [16,64] and the waveform reproducibility is plotted versus the time of day. This variable is taken here as representing the incremental work being done by the OHC over the period of 1 click (20 ms). This suggests that the incremental OHC tonus rises slowly as the SM pressure rises. Since only daytime recordings were ever made, the observed trend is unidirectional, but there is a clear increase in the waveform reproducibility of 2.5% / hr from 9am through 6pm. The upward trend is significant ($p<0.01$) for both ears. If this seems a strange result, it nevertheless belongs to a broader class of influences on the mechanics [65].

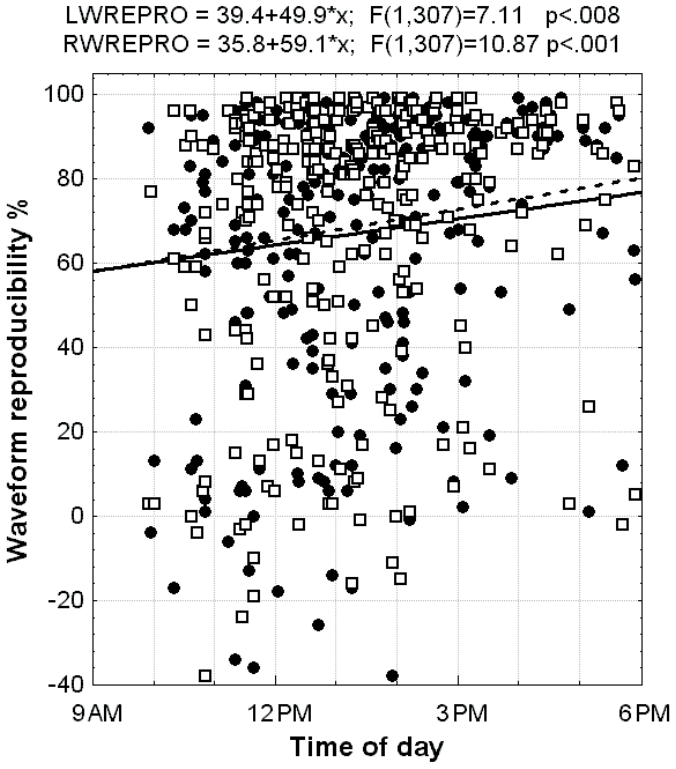


Figure 2. The scatterplot shows the Waveform Reproducibility (%) of standard click-evoked otoacoustic emissions versus the time of day of the measurement for left and right ears (circles and squares respectively) of over 300 neonates and infants up to 12 months of age. The trends which are significant ($p<0.01$) shows that this measure of the activity of the OHC rises over the course of a 9 hour period.

IMPLICATIONS 2

In the past cochlear mechanical studies have almost exclusively focussed upon the origin of the sharp tuning in the cochlea. Increasingly, the issue of cochlear stability is widening the debate, yet there has been a residual selectivity for data which conforms to preconceived notions of tuning so that other prerequisites of energy expenditure have been neglected. The issue of large slow motions of cochlear structures has certainly gained credibility. Nevertheless, the effort has gone towards examining the fine details of the vibration to support the current theories, rather than seriously considering the many systems of the body in which chamber turgor pressure is vital to its normal physiological function. Stability of operating points of the hair cells needs regulation of two opposing forces; one of which is OHC slow motility. It is by no means inconsistent that the other force should be pressure in SM. If it is normally regulated, then it is to be expected that this regulation should occasionally fail.

Ménière's disease

There are many corollaries for this theory, but we have gone some way to explaining the complex set of distressing symptoms of Ménière's disease. Unlike the slow homeostatic drifts, the violent vestibular attacks are certainly sudden, and – with variations on a theme – are generally attributed to rupture of the centre vessel when hydrops becomes too advanced, leaking endolymph into the perilymph spaces with severely toxic effects [66]. In the context here, if a static pressure influences OHC transduction at all, it is of decided interest [67] particularly in respect of acoustic signal processing, because it can be reasonably expected that the ear has evolved so that it loses hearing as a very last resort.

Conceptual problems arising from considering OHC as the only source of force

A second major corollary of the theory is that the long-term baseline shifts in the motion of the basilar membrane may have a time course which is not strongly coupled to timing of the sound stimuli. Any mechanical experiment averaging many responses to improve the signal-to-noise ratio will likely fail to register any longer-term effect. Indeed, the signal may be perceived to be highly noisy; the response deemed to be small, and many repetitions needed to extract the tiny response from the "noise". More importantly, the large basilar membrane shifts observed [57] are likely the result of a large pressure bias due to draining, to which the OHC have responded with a large compensatory push in the reverse direction. Cochlear preparations with low challenges to OHC stabilisation do not capture this effect [6,13]. Unless one designs an experiment to look for much broader-ranging behaviour one will be tempted to interpret the data as noise.

Loss of hearing sensitivity

The third corollary of the theory is that cochlear hearing sensitivity remains normal while the local tonic force capability of the OHC (related to its turgor pressure and somatic motility) can match any basilar membrane displacement-bias due to a slow accumulation of pressure in SM. As the numbers of OHC decline with age and with toxic influences (including accumulated noise exposure), or the individual cells deteriorate [68], the sensory transducer operating point deviates from the point of highest sensitivity and the gain of the cochlear amplifier (proportional to the local slope of the transducer characteristic at the operating point) is reduced.

Audiometric variability

The fourth corollary is an explanation for the huge variability in the outcomes of any experiment. The variability is not only attributable to recent trauma. Audiometric thresholds themselves, under test-retest conditions, vary by ±5 dB for most frequencies, and up to ±27 dB at 6 kHz [69] a variation which clinically is managed rather than ever seriously questioned. Nothing about the process of obtaining a pure tone audiogram or its classic interpretation takes the number of known internal control mechanisms into account. Indeed, *the variability in all ear and hearing experiments (biophysical and psychophysical alike) is invariably so great* that the researcher typically must either 1) select, describe and interpret a representative set of individual responses to any particular experiment, or 2) conduct an analysis of variance, and in so doing effectively (and often implicitly) bypass any consideration of underlying mechanisms.

Basis of the *Equal Energy Rule*

A fifth corollary is that the servo-theory provides a ready basis for explaining the *Equal Energy Rule* [70-72]. *The basis for the explanation provided here is that the absorbed acoustic energy is stored essentially as potential energy in the stiffness of the basilar membrane*, now seen as a spring being stretched by the SM pressure. The higher level the sound, the longer it is present, the more that SM is distended and the higher the stretch applied. The slower process of recovery from temporary threshold shift (TTS) is identified as the removal of potassium, which will occur continuously at a constant rate (explaining the exponential recovery of TTS in terms of a first order differential equation). This model potentially explains 1) the recovery process which occurs away from noise, 2) the basis of the trade-off, 3) the diurnal variation which is implicit in the notion of "daily-noise dose" and 4) dissipation of hydropic pressure before the next industrial work shift.

Cochlear response to noise trauma

A sixth corollary is an explanation of why high-level sound causes discomfort and feelings of "fullness" often mistaken for effusion of the middle ear and accompanied by tinnitus. When sound is externally amplified to make up for loss of internal amplification, a newly appreciated effect will be a bias due to swelling of SM which will invoke a compensation response while any viable outer hair cells remain. Attempts to adjust the spectrum of speech sounds to match hearing losses will not achieve the desired localised effect because the rise in pressure will be distributed and affect adjacent areas. Such a distribution probably underlies the upward spread of masking and the tails of tuning curves as outlined in the article by Sen [73] herein.

What is normal operation of the cochlea?

The key evidence, here re-presented for consideration, is the notion that the 'artifacts' BM displacement recordings were indeed mechanical correlates of homeostatic processes in operation, as previously highlighted in principle by Klis and Smoorenburg [29,31]. Any insights presented here lead to our new definition: "*Normal hearing" is not just the existence of low thresholds, but, more generally, the existence of viable homeostasis mechanisms.* The single factor contributing to homeostasis may well be as Pickles describes in this volume: the availability of energy to drive both the servo-loop and potassium recycling.

SUMMARY 2

Diverse contributions to the recent literature are drawn together to yield a new level of understanding structure and function of the mammalian cochlea. It is that the scala media is a pressure vessel in which acoustic stimulation normally releases potassium ions causing an osmotic pressure rise deflecting the basilar membrane towards the scala tympani creating shear of the OHC stereocilia. The pressure rises because of a mismatch in potassium inflow and removal from scala media by ion pumps. The OHC respond by using their slow motility to track this mechanical bias using the leverage of the arch to stabilise their transduction operating point. Any error-signal at the OHC stereocilia due to changing pressure is thus normally zeroed out. The result is a very efficient mechanism for expanding the dynamic range of the mammalian ear beyond that of the hair cells alone. While the OHC have the capacity to track the pressure bias, hearing will be normal. If the pressure grows too large, or if the OHC are depleted in numbers or de-energised, hearing loss is the result. It follows there should be a diurnal cycle of pressure fluctuation which forms the basis of the so-called Equal Energy Rule describing the level/duration trade-off for loud sound exposure. Preliminary OAE evidence is provided for such a diurnal fluctuation.

ACKNOWLEDGEMENTS

I thank Dr. N.M. Murray particularly and numerous other clinicians for obtaining the neonatal OAE data presented here. I thank all my collaborators and particularly the early formative stimulating interactions with Drs. B.M. Johnstone and Hallowell Davis. I thank the reviewers for their valuable comments.

REFERENCES

1. Gold, T. (1948). Hearing II. The physical basis of the action of the cochlea. Proc. Royal Soc. Lond. B: 135, 492-498.
2. Kemp, D. T. (1978). Stimulated acoustic emissions from within the human auditory system. J Acoust Soc Am 64(5), 1386-91.
3. Le Page, E. L., & Johnstone, B. M. (1980). Nonlinear mechanical behaviour of the basilar membrane in the basal turn of the guinea pig cochlea. Hear Res 2(3-4), 183-9.
4. Sellick, P. M., Patuzzi, R., & Johnstone, B. M. (1982). Measurement of basilar membrane motion in the guinea pig using the Mossbauer technique. J Acoust Soc Am 72(1), 131-41.
5. Davis, H. (1983). An active process in cochlear mechanics. Hear Res 9(1), 79-90.
6. Recio, A., Rich, N. C., Narayan, S. S., & Ruggero, M. A. (1998). Basilar-membrane responses to clicks at the base of the chinchilla cochlea. J Acoust Soc Am 103(4), 1972-89.
7. Nuttall, A. L., Dolan, D. F., & Avinash, G. (1990). Measurements of basilar membrane tuning and distortion with laser Doppler velocimetry. In: Lecture Notes in Biomathematics: Vol. 87. The Mechanics and Biophysics of Hearing (pp. 288-295). New York: Springer-Verlag..
8. Cooper, N. P. (1999). An improved heterodyne laser interferometer for use in studies of cochlear mechanics. J Neurosci Methods 88(1), 93-102.
9. Ren, T., & Nuttall, A. L. (2001). Recording depth of the heterodyne laser interferometer for cochlear vibration measurement. J Acoust Soc Am 109(2), 826-9.
10. Gummer, A. W., Hemmert, W., & Zenner, H.-P. (1993). Resonant tectorial membrane motion in the inner ear: its crucial role in frequency tuning. Proc.Natl.Acad.Sc.USA, 8727-8732.
11. Fridberger, A., de Monvel, J. B., Zheng, J., Hu, N., Zou, Y., Ren, T., & Nuttall, A. (2004). Organ of Corti potentials and the motion of the basilar membrane. J Neurosci 24(45), 10057-63.
12. Robles, L., Ruggero, M. A., & Rich, N. C. (1986). Basilar membrane mechanics at the base of the chinchilla cochlea. I. Input-output functions, tuning curves, and response phases. J Acoust Soc Am 80(5), 1364-74.
13. Cooper, N. P., & Rhode, W. S. (1993). Nonlinear mechanics at the base and apex of the mammalian cochlea: in-vivo observations using a displacement-sensitive laser interferometer. In 5th International symposium on the mechanics of hearing:

Biophysics of Hair Cell Sensory Systems (pp. 249-257). Singapore, New Jersey: World Scientific Publishing.
14. Shera, C. A. (2004). Mechanisms of mammalian otoacoustic emission and their implications for the clinical utility of otoacoustic emissions. Ear Hear 25(2), 86-97.
15. Lonsbury-Martin, B. L., & Martin, G. K. (2003). Otoacoustic emissions. Curr Opin Otolaryngol Head Neck Surg 11(5), 361-6.
16. Kemp, D. T. (2002). Otoacoustic emissions, their origin in cochlear function, and use. Br Med Bull 63, 223-41.
17. Kros, C. (2005). Hearing: aid from hair force. Nature 433(7028), 810-1.
18. Kennedy, H. J., Crawford, A. C., & Fettiplace, R. (2005). Force generation by mammalian hair bundles supports a role in cochlear amplification. Nature 433(7028), 880-3.
19. Nadrowski, B., Martin, P., & Julicher, F. (2004). Active hair-bundle motility harnesses noise to operate near an optimum of mechanosensitivity. Proc Natl Acad Sci U S A 101(33), 12195-200.
20. Brownell, W. E., Spector, A. A., Raphael, R. M., & Popel, A. S. (2001). Micro- and nanomechanics of the cochlear outer hair cell. Annu Rev Biomed Eng 3, 169-94.
21. Zheng, J., Shen, W., He, D. Z., Long, K. B., Madison, L. D., & Dallos, P. (2000). Prestin is the motor protein of cochlear outer hair cells. Nature 405(6783), 149-55.
22. Brownell, W. E., Bader, C. R., Bertrand, D., & de Ribaupierre, Y. (1985). Evoked mechanical responses of isolated cochlear outer hair cells. Science 227(4683), 194-6.
23. Evans, B. N., & Dallos, P. (1993). Stereocilia displacement induced somatic motility of cochlear outer hair cells. Proc Natl Acad Sci U S A 90(18), 8347-51.
24. Santos-Sacchi, J., Kakehata, S., & Takahashi, S. (1998). Effects of membrane potential on the voltage dependence of motility-related charge in outer hair cells of the guinea-pig. J Physiol 510 (Pt 1), 225-35.
25. Salt, A. N. (2001). Regulation of endolymphatic fluid volume. Ann N Y Acad Sci 942, 306-12.
26. Andrews, J. C. (2004). Intralabyrinthine fluid dynamics: Meniere disease. Curr Opin Otolaryngol Head Neck Surg 12(5), 408-12.
27. Buki, B., de Kleine, E., Wit, H. P., & Avan, P. (2002). Detection of intracochlear and intracranial pressure changes with otoacoustic emissions: a gerbil model. Hear Res 167(1-2), 180-91.
28. Marchbanks, R. J., & Reid, A. (1990). Cochlear and cerebrospinal fluid pressure: their inter-relationship and control mechanisms. Br J Audiol 24(3), 179-87.
29. Klis, S. F., & Smoorenburg, G. F. (1994). Osmotically induced pressure difference in the cochlea and its effect on cochlear potentials. Hear Res 75(1-2), 114-20.
30. Salt, A. N. (2006). Low frequency pressure changes may participate in endolymph volume regulation. Proceedings of the 5th International Symposium: Meniere's Disease and Inner Ear Homeostasis Disorders (pp. 27-29). 2100 West Third Street, Los Angeles, CA 90057: House Ear Institute.
31. Klis, S. F. L., & Smoorenburg, G. F. (1995). A comparison of several experimental animal models for Meniere's disease. Meniere's disease: 16th Danavox Symposium (pp. 123-139).
32. Portmann, D. (2006). Why Sac surgery is still our first choice. Proceedings of the 5th International Symposium: Meniere's Disease and Inner Ear Homeostasis Disorders (p. 100). 2100 West Third Street, Los Angeles, CA 90057: House Ear Institute.
33. Dahl, H.-H., Manji, S., de Silva, M., Peverelli, M., & Hildebrand, M. (2006). Genetic aspects of hearing loss. Acoust. Aust., 34, 25-29.
34. Pickles, J. O. (2006). Mitochondria, cell death, and deafness: will it be possible to prevent presbyacusis? Acoust. Aust., 34, 31-36.
35. Petit, C. (2006). Inner ear K^+ homeostasis disorders: what have we learned from the deafness genes? Proceedings of the 5th International Symposium: Meniere's Disease and Inner Ear Homeostasis Disorders (pp. 9-11). 2100 West Third Street, Los Angeles, CA 90057: House Ear Institute.
36. Gibson, W. P. R. (2006). The cause of attacks of vertigo in Meniere's disease: Potassium intoxication theories versus the drainage theory -- electrophysiological investigations. Proceedings of the 5th International Symposium: Meniere's Disease and Inner Ear Homeostasis Disorders (pp. 323-324). 2100 West Third Street, Los Angeles, CA 90057: House Ear Institute.
37. Johnstone, B. M., Patuzzi, R., Syka, J., & Sykova, E. (1989). Stimulus-related potassium changes in the organ of Corti of guinea-pig. J Physiol 408, 77-92.
38. Schulte, B. (2006). Inner ear K^+ recycling pathways. Proceedings of the 5th International Symposium: Meniere's Disease and Inner Ear Homeostasis Disorders (pp. 68-72). 2100 West Third Street, Los Angeles, CA 90057: House Ear Institute.
39. Sirjani, D. B., Salt, A. N., Gill, R. M., & Hale, S. A. (2004). The influence of transducer operating point on distortion generation in the cochlea. J Acoust Soc Am 115(3), 1219-29.
40. Flock, A., & Flock, B. (2000). Hydrops in the cochlea can be induced by sound as well as by static pressure. Hear Res 150(1-2), 175-88.
41. LePage, E. L., Murray, N. M., & Seymour, J. D. (2006). Baseline shifts measured in the human ear canal pressure related to distortion product generation and two tone suppression. Presented at the Mid-winter meeting of the Association for Research in Otolaryngology (pp. Session D4: Inner Ear: Mechanics I, Poster #75).
42. LePage, E. L., Murray, N. M., & Seymour, J. D. (2006). Otoacoustic emission correlates of intracochlear pressure variations in humans: Summating behaviour. Proceedings of the 5th International Symposium: Meniere's Disease and Inner Ear Homeostasis Disorders (pp. 110-111). 2100 West Third Street, Los Angeles, CA 90057: House Ear Institute.
43. Löwenheim, H., Hirt, B., & Zenner, H.-P. (2006). Endolymph regulation and mechanism of hydrops - aquaporins in the inner ear. Proceedings of the 5th International Symposium: Meniere's Disease and Inner Ear Homeostasis Disorders (pp. 42-44). 2100 West Third Street, Los Angeles, CA 90057: House Ear Institute.
44. Mulders, W. H. A. M. (2006). Efferent control of hearing. Acoustics Aust., 34, 19-24.
45. Patuzzi, R. (1998). Exponential onset and recovery of temporary threshold shift after loud sound: evidence for long-term inactivation of mechano-electrical transduction channels. Hear Res 125(1-2), 17-38.
46. Patuzzi, R., Sellick, P. M., & Johnstone, B. M. (1984). The modulation of the sensitivity of the mammalian cochlea by low frequency tones. III. Basilar membrane motion. Hear Res 13(1), 19-27.
47. Bian, L. (2004). Cochlear compression: effects of low-frequency biasing on quadratic distortion product otoacoustic emission. J Acoust Soc Am 116(6), 3559-71.
48. Patuzzi, R., & Moleirinho, A. (1998). Automatic monitoring of mechano-electrical transduction in the guinea pig cochlea. Hear Res 125(1-2), 1-16.
49. Lukashkin, A. N., & Russell, I. J. (2005). Dependence of the DPOAE amplitude pattern on acoustical biasing of the cochlear partition. Hear Res 203(1-2), 45-53.
50. LePage, E. L. (1981). The role of nonlinear mechanical processes in mammalian hearing. Unpublished doctoral dissertation, The University of Western Australia, available at www.oaericle.com.au.

51. LePage, E. L. (1987). The application of a capacitive probe technique for direct observation of electromechanical processes in the guinea pig cochlea. J Acoust Soc Am 82(1), 126-38.
52. Robertson, D. (1974). Cochlear neurons: frequency selectivity altered by perilymph removal. Science 186(4159), 153-5.
53. Patuzzi, R., Sellick, P. M., & Johnstone, B. M. (1982). Cochlear drainage and basilar membrane tuning. J Acoust Soc Am 72(3), 1064-5.
54. LePage, E. L. (1987). Frequency-dependent self-induced bias of the basilar membrane and its potential for controlling sensitivity and tuning in the mammalian cochlea. J Acoust Soc Am 82(1), 139-54.
55. Lyon, R. F. (1990). Automatic gain control in cochlear mechanics. In: Lecture notes in Biomathematics, v. 87. The Mechanics and Biophysics of Hearing (pp. 395-402). New York, Springer-Verlag 1990.
56. van der Heijden, M. (2005). Cochlear gain control. J Acoust Soc Am 117(3 Pt 1), 1223-33.
57. LePage, E. L. (1989). Functional role of the olivo-cochlear bundle: a motor unit control system in the mammalian cochlea. Hear Res 38(3), 177-98.
58. LePage, E. L. (1992). Hysteresis in cochlear mechanics and a model for variability in noise-induced hearing loss. In Noise-Induced Hearing Loss, edited by A. Dancer, D. Henderson, R.J. Salvi , & R.P. Hamernik. Chapter 10 (pp. 106-115). St.Louis : Mosby-Year Book.
59. Cooper, N. P., & Rhode, W. S. (1995). Nonlinear mechanics at the apex of the guinea-pig cochlea. Hear Res 82(2), 225-43.
60. Russell, I. J., & Sellick, P. M. (1978). Intracellular studies of hair cells in the mammalian cochlea. J Physiol 284, 261-90.
61. LePage, E. L. (1995). A model for cochlear origin of subjective tinnitus: excitatory drift in the operating point of inner hair cells. In Jack A. Vernon and Aage R. Moller Mechanisms of Tinnitus (Vol. Chapter 11pp. 115-148). Boston: Allyn and Bacon.
62. Guinan, J. J. Jr, Lin, T., & Cheng, H. (2005). Medial-olivocochlear-efferent inhibition of the first peak of auditory-nerve responses: evidence for a new motion within the cochlea. J Acoust Soc Am 118(4), 2421-33.
63. Cooper, N. P., & Guinan, J. J. Jr. (2003). Separate mechanical processes underlie fast and slow effects of medial olivocochlear efferent activity. J Physiol 548(Pt 1), 307-12.
64. LePage, E. L. and Murray, N. M. Click-evoked otoacoustic emissions: comparing emission strengths with pure tone audiometric thresholds. Aust.J.Audiol. 1993; 15 :9-22.
65. Bell, A. (1992). Circadian and menstrual rhythms in frequency variations of spontaneous otoacoustic emissions from human ears. Hear Res 58(1), 91-100.
66. Zenner, H. P., Reuter, G., Zimmermann, U., Gitter, A. H., Fermin, C., & LePage, E. L. (1994). Transitory endolymph leakage induced hearing loss and tinnitus: depolarization, biphasic shortening and loss of electromotility of outer hair cells. Eur Arch Otorhinolaryngol 251(3), 143-53.
67. Zenner, H. P. (1993). Possible roles of outer hair cell d.c. movements in the cochlea. Br J Audiol 27(2), 73-7.
68. LePage, E. L., Reuter, G., & Zenner, H. P. (1995). A threshold decrease for electrically stimulated motor responses of isolated aging outer hair cells from the pigmented guinea pig. Eur Arch Otorhinolaryngol, 252, 215-221.
69. Macrae, J. H. (1979). An investigation of repeated testing as a means of improving the accuracy of audiometry. NAL Informal Report #64, National Acoustic Laboratories, Sydney.
70. Ward, W. D., Santi, P. A., Duvall, A. J. 3rd, & Turner, C. W. (1981). Total energy and critical intensity concepts in noise damage. Ann Otol Rhinol Laryngol 90(6 Pt 1), 584-90.
71. Clark, W. W., Bohne, B. A., & Boettcher, F. A. (1987). Effect of periodic rest on hearing loss and cochlear damage following exposure to noise. J Acoust Soc Am 82(4), 1253-64.
72. Ahroon, W. A., Hamernik, R. P., & Davis, R. I. (1993). Complex noise exposures: an energy analysis. J Acoust Soc Am 93(2), 997-1006.
73. Sen, D. & Allen, J.B. (2006). Functionality in cochlear micromechanics – As elucidated by upward spread of masking and two-tone suppression. Acoustics Aust., 34, 37-42.