

MEDIAL-OLIVOCOCHLEAR-EFFERENT EFFECTS ON BASILAR-MEMBRANE AND AUDITORY-NERVE RESPONSES TO CLICKS: EVIDENCE FOR A NEW MOTION WITHIN THE COCHLEA

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We recorded guinea-pig, basilar-membrane (BM) motion, and cat, single auditory-nerve-fiber (AN) responses to clicks, with and without electrical stimulation of medial-olivocochlear (MOC) efferents. In both BM and AN responses, MOC stimulation inhibited almost completely at low click levels. However at moderate-to-high click levels, MOC inhibition was small on the first half cycle and built up over many cycles in BM click responses, but was large on the first half cycle and negligible in the second cycle in AN click responses. The data support the hypothesis that OHCs produce or influence a motion which bends inner-hair-cell stereocilia and can be inhibited by MOC efferents, a motion that is present through most, or all, of the cochlea, but that is not apparent in basal-turn BM motion. These data, from normally-working cochleas, highlight the need to shift the conceptual paradigm for cochlear mechanics to one in which the classic BM traveling wave is not the only motion that excites AN fibers.

1 Introduction

Medial olivocochlear (MOC) efferents synapse directly on outer hair cells (OHCs) and provide a way to reversibly change OHC properties without opening or damaging the cochlea. MOC effects have not been previously studied on basilar membrane (BM) or single auditory-nerve (AN) fiber click responses. Results at these levels shows a surprising difference in the inhibition of the first response peak, a difference that has important implications for cochlear mechanics.

2 Methods

Experiments were performed on deeply anesthetized animals in accordance with local, NIH, UK and US guidelines. BM motion was measured in the first turn of guinea-pig and chinchilla cochleae as in [1]. Single AN-fiber responses were monitored in cats, and recovered probability post-stimulus-time (rpPST) histograms

were calculated as in [2]. Compound action potentials (CAPs) were recorded from a silver round-window electrode, and CAP audiograms were used to monitor cochlear condition. MOC efferents were stimulated via a bipolar electrode at the floor of the fourth ventricle using a paradigm that selected the efferent fast effect [1,3]. Controls were done to insure that the results were not due to middle-ear-muscle contractions.

3 Results

The most salient MOC effects on BM click responses were:

1. The biggest inhibition of BM click responses was at low sound levels.
2. The inhibition was near zero on the first half-cycle of the response and grew over many cycles to nearly full inhibition.
3. The final growth to full inhibition began later at higher click levels.
4. MOC stimulation produced a small phase advance early in the response.

Points one and two can be seen in Fig. 1, left. Results similar to these were found in three guinea pigs with good thresholds and six other animals with poorer thresholds including one chinchilla.

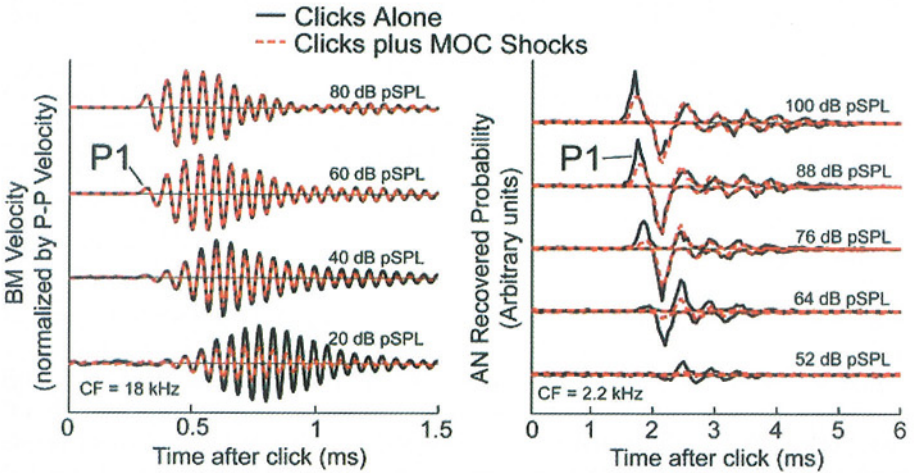


Figure 1. MOC effects on click responses in BM motion (Left) and AN firing (Right). Right: compound histograms with the rPST from rarefaction plotted upwards and from condensation plotted downwards.

In AN click responses, MOC stimulation inhibited [3]:

1. The whole response at low sound levels,
2. The decaying part of the response at all sound levels (in most fibers), and
3. The first peak of the response at moderate to high sound levels. The “first peak” is the peak with the shortest latency across all sound levels; the earliest peak at low sound levels is *not* the “first peak”. Above 100 dB pSPL, some responses showed a reversal of the click polarity which produced the first peak [2]. In these cases, there

was inhibition of the first peak at levels below the reversal, but little MOC effect at levels above the reversal. Points 1 and 3 can be seen in Fig. 1, right.

We quantified AN inhibition by counting spikes in the peaks with and without MOC stimulation for sound levels 75-100 dB pSPL and fibers with CFs <4-6 kHz (where individual peaks could be seen). For CFs > 4-6 kHz, we compared responses with and without MOC stimulation in two abutting, 0.2 ms windows starting at the onset of the click response. The resulting data are shown in Fig. 2A-D with loess-fit [4] trend lines superimposed in Fig. 2E. The data in Fig. 2 show that for CFs < ~8 kHz, MOC stimulation inhibited rarefaction peak 1 significantly more (t-test, $P < 0.01$) than rarefaction or condensation peak 2.

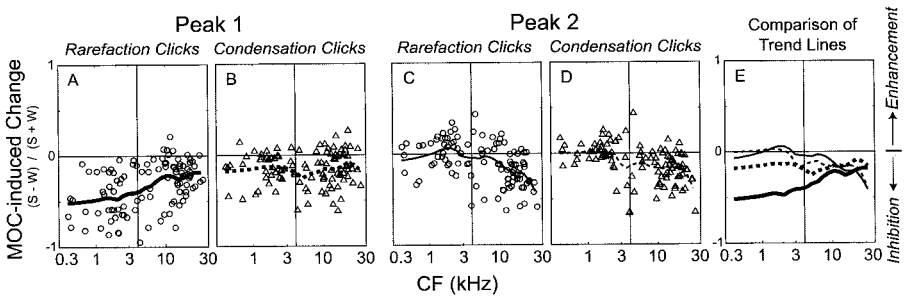


Figure 2. MOC-induced changes in the first and second click-response peaks. A-D: changes from individual fibers. E: Loess-fit [4] curves from A-D. “MOC-induced change” is the rpPST peak amplitude with MOC shocks, S, minus the rpPST peak amplitude without shocks, W, normalized by their sum, $S+W$. For each fiber, rarefaction and condensation responses were considered separately, the response was segmented into peaks, responses from levels 75-100 dB pSPL were averaged, the average number of spikes in each peak was computed, and the MOC-induced change was calculated from these averages. Points from 104 fibers from 10 cats. Vertical lines mark 4 kHz. (adapted from [3]).

4 Discussion

The lack of MOC inhibition of the first peak of BM responses to clicks fits with current conceptions of mammalian cochlear mechanics, but the inhibition of the AN first peak does not. The usual view [5] is that all motion of the organ of Corti is produced by the BM traveling wave which mimics BM motion in the basal turn and extends throughout the cochlea (although it is recognized that the classic traveling wave does not explain some phenomena in the apical turn, e.g. downward glides [6]). However, MOC inhibition of the AN click-response first peak cannot be explained by inhibition of the first peak of the classic traveling wave because, as shown by basal BM responses, the classic traveling wave first peak receives little or no cochlear amplification, and is little changed by MOC stimulation or by death [7-9]. Thus, the strong MOC inhibition of the AN first peak must be due to inhibition of something other than a classic traveling wave that extends throughout the cochlea.

Possible hypotheses are that MOC inhibition of the AN first peak is due to: (H1) Electrical coupling from OHCs to IHCs via local extracellular fields (i.e. by cochlear microphonic). (H2) Efferent synapses on IHCs or AN fibers (i.e. Lateral Efferents). (H3) MOC-induced hyperpolarization of OHCs causing OHC lengthening which changes the coupling of BM motion to IHC stereocilia. (H4) Inhibition of the BM first peak, and that BM motion in the middle and apical turns is substantially different from the classic traveling wave. (H5) Motion of structures or fluid that bends IHC stereocilia and is in addition to motion of the classic traveling wave. (This second motion may, or may not, be seen at the basilar membrane). H1-H3 each has specific reasons for rejection, and a potent argument against all three is that they do not explain how the efferent stimulation can inhibit the first click-response peak without also inhibiting the later peaks. H4 and H5 differ in that H5 considers that there are two superimposed modes of motions in the organ-of-Corti, the classic traveling wave and a new motion, and H4 considers that there is only one motion, the motion of the BM which drives all other motions. For H4 to explain the data, BM motion in the middle and apex of the cochlea would have to look quite different from the classic traveling wave; it would have to have a substantial first peak that is not passive but is dependent in a strong way on OHCs. Against this is the slow base-to-apex variation of cochlear dimensions & physical properties, plus a wealth of models, that indicate that the a traveling wave that is not drastically different from the classic wave should be present throughout the cochlea. While we cannot rule out H2, we think it more likely that the classic BM traveling wave does exist throughout the cochlea, and that MOC inhibition of the first peak of some other motion explains the inhibition of the AN first peak.

Considering the above, our working hypothesis is that MOC inhibition of the AN first peak is due to an OHC-dependent motion of structures or fluid that bends IHC stereocilia and is separate from motion of the classic traveling wave. To account for strong AN first-peak inhibition, there must normally be an OHC-dependent motion of structures and/or fluid that bends IHC stereocilia and produces the AN initial peak (ANIP), and this ANIP motion must be reduced by MOC activation. The ANIP motion could come from OHC stereocilia motility or OHC somatic motility as long as MOC efferents can inhibit the motion. Presumably, the ANIP motion is the first part of a vibrational response mode that continues past the first peak. However, the lack of MOC inhibition of the second AN click-response cycle (Fig. 2) suggests that the ANIP motion decays quickly so that by the second cycle it is less than the little-inhibited motion that evokes the second AN peak, presumably motion due to the classic traveling wave.

A variety of previous data provide evidence for cochlear motion that is separate from, or in addition to, the motion of the classic traveling wave: (1) In the apex, two group delays in AN responses and cochlear motion have been reported many times [10-15]. Although an artifactual “fast wave” from opening the cochlea can contaminate apical mechanical measurements [13], Zinn and coworkers [14] found that computationally removing the fast wave still left response dips and multiple

group delays. Furthermore, in intact cochleae, AN responses show tuning curves (TCs) with multi-lobed shapes [16] and different group delays in each lobe [11]. These data provide evidence from intact cochleae that two interacting drives with different group delays excite apical AN fibers (These data provide perhaps the best reason for choosing H5 over H4). (2) The previously-anomalous phenomenon of downward glides in the apex may be explained by the interaction of two motions, a first-arriving, above-CF wave and a later-arriving CF wave [17]. (3) Interference of two motions may explain many observations of cancellations and phase reversals in AN and BM responses (reviewed in [18]). Although all of the phenomena just cited indicate the presence of two cochlear motions, these two motions do not necessarily correspond to the ANIP motion and the classic traveling wave.

The ANIP motion appears to extend through most the cochlea. MOC inhibition of the ANIP motion is evident, for CFs up to 8-10 kHz, as inhibition of the AN click-response first peak (Fig. 2). For fibers with CFs > 5 kHz, additional evidence comes from inhibition of short-latency, tail-frequency tone responses [3, 19]. The dividing line between supposed basal and apical patterns of BM motion is often thought to be ~1 kHz, the region where click-response glides change from upward to downward [17,21] and tuning-curve “tails” change from below CF to above CF [11]. There are, however, almost no motion measurements in living cochleae with good thresholds between the basal turn and the apex on which to base a judgment of the dividing line. It seems plausible that the classic traveling wave and the ANIP motion are both present throughout the cochlea, perhaps with their relative strengths changing from base to apex. In this view, the classic traveling wave is dominant in the base and the ANIP motion gains in prominence going toward the apex.

4.1 What is the origin of the ANIP motion?

Since the ANIP motion is not apparent in the classic traveling wave and is inhibited by MOC efferents that synapse on OHCs, it appears to be due to OHCs, or at least is strongly influenced by OHCs. It seems possible that the ANIP motion is due to an active, energy consuming process and may be, in some sense, an amplified motion. Even though we have quantified the AN first-peak inhibition only at moderate to high sound levels, it may be present at low sound levels, especially in the apex. Which mechanisms in OHCs produce and/or modify the ANIP motion are unknown. Nonetheless, it is useful to elaborate some hypothetical mechanisms by which the ANIP motion might be produced and to consider their consequences. To fit the data, the mechanism should excite AN fibers early enough to produce the first click-response peak in the middle and apex of the cochlea and to produce the short-group-delay tone response in the base, and should be inhibited by MOC efferents without changing the first peak of the basal-turn BM response.

4.1.1 Possible ANIP source: OHC fluid pumping

One hypothesis for the origin of the ANIP motion is OHC “fluid pumping”. Sound-frequency electrical stimulation in an excised gerbil cochlea causes OHC

contractions which squeeze the cochlear partition producing sound-frequency fluid motion along the tunnel of Corti, i.e. OHCs act as fluid pumps [21]. OHC squeezing of the organ of Corti has also been reported in guinea pigs [22] and may be the origin of phase differences between BM arcuate- and pectinate-zone motions [23-26]. With this hypothesis, pressure differences across the cochlear partition produce the classic traveling wave, and pressure differences inside to outside the organ of Corti produce the ANIP motion which is a squeezing wave in which the walls of the organ of Corti expand and contract. Presumably, the pressure difference inside to outside the organ of Corti produces a large ANIP motion at the reticular lamina but not at the BM because the first peak is primarily from below-CF energy (where stiffness dominates) and the effective stiffness of the reticular lamina is much less than that of the BM [27]. Thus, the ANIP motion should be much greater at the reticular lamina (and presumably, at IHC stereocilia and in AN firing) than at the BM. Finally, the ANIP motion might have a shorter delay than the classic traveling wave because tunnel fluid motion extends ahead of OHC contractions [21].

4.1.2 Possible ANIP source: Stereocilia motility

Another possible source of the ANIP motion is stereocilia motility. One appeal of this mechanism is that an OHC stereocilia twitch could be readily coupled from OHC stereocilia to IHC stereocilia by the tectorial membrane without requiring intervening BM motion. In this hypothesis, the ANIP motion is the motion of the tectorial membrane and/or nearby fluid that bends IHC stereocilia. For calcium-mediated stereocilia motility [28, 29], a drawback of this hypothesis is the lack of a clear mechanism by which MOC synapses affect this motion. Although this stereocilia motility is influenced by membrane voltage, MOC synapses hyperpolarize OHCs which would be expected to increase calcium-mediated OHC stereocilia motility, not inhibit it. On the other hand, if the stereocilia motility was mediated by Prestin [30], then the OHC hyperpolarization could inhibit it.

4.1.3 Possible ANIP source: Direct acoustic coupling to OHCs

Yet another mechanism that might produce the ANIP motion is direct acoustic coupling from the forward cochlear pressure wave. Ren [31] and Ruggero [32] have suggested that mammalian OAEs may be generated by organ-of-Corti motion that is coupled back to stapes motion by fast fluid-pressure waves. Any cochlear process that couples organ-of-Corti motion to fluid pressure waves is likely to be reciprocal, which would imply that normal (forward) cochlear pressure waves may directly produce motion of the organ of Corti. To account for the ANIP motion, such motion, or the amplification of this motion, must be affected by OHCs. This mechanism has the advantage that it readily explains how the ANIP motion can produce a response peak that starts before the lowest-frequency part of the traveling wave. However, it is difficult to account for the long delays of the ANIP motion in the apex of the cochlea if the classic traveling wave is bypassed completely.

As can be noted from the above, a question related to the origin of the ANIP motion is how the ANIP motion travels along the cochlea. Is the ANIP motion a second wave along the cochlea, a separate vibrational mode excited by the classic traveling wave, or a vibrational mode excited directly by the fast cochlear pressure wave (e.g. due to OHC pressure sensitivity)? An important constraint is that the latency of the click-response first peak changes over ~ 2.5 ms from the base to the apex [2], but this does not separate the hypotheses. Since the ANIP response is clearly first in the apex (Figs. 1-2), it seems unlikely that the ANIP response is a separate vibrational mode excited by the classic traveling wave. As the above hypotheses point out, there are many possible ways by which the ANIP motion may be produced and determining which one is correct, or if more than one, requires additional data. Whatever mechanisms are involved, the presence of the OHC-generated ANIP motion early in the response puts it at a time that could influence, shape, or be a first step in cochlear amplification.

4.2 Effects of the ANIP motion on signal coding

Excitation of AN fibers by the ANIP motion seems likely to have a different frequency filter than the classic traveling wave, but does not appear to sharpen the response and produce an old-style “second filter”. Our click results suggest that the ANIP motion has an important influence on neural responses at moderate-to-high sound levels (Figs. 1-2). For tones, a component of the AN response due to ANIP motion was not evident at threshold at the base of the cochlea [33], but an ANIP response may be evident at higher sound levels in the base, and perhaps at low sound levels in the apex.

MOC inhibition of the AN first peak can be expected to have behavioral consequences. Medial efferents improve the detection of transient sounds in background noise and provide protection from sound trauma. MOC inhibition of the ANIP response may be involved in both of these, as well as in any MOC effect at moderate to high sound levels.

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Comments and Discussion

Santos-Sacchi: Why is there expected to be a causal link between the first peak of the BM response and that first peak of the neural response? Can't it be that not all initial cycles of the click BM response sufficiently excite the IHC?

Answer: The expected causal link between the first peak of the BM response and the first peak of the AN response comes about from the hypothesis that BM motion drives the motion of the rest of the organ of Corti. The first AN peak, as we defined it, is not present at low sound levels, presumably because the amplitude of the BM first peak is too small, as you suggest. However, the first peak of the BM response to clicks grows linearly and becomes very large at high sound levels where it might be expected to be producing the first peak of the AN response. It seems worth noting that there is evidence for more than one drive that excites AN fibers at the time of the first peak. Lin and Guinan (2000) found that the polarity that excited the first AN peak reversed at click levels above 100 dB pSPL. We found that MOC stimulation inhibited the AN first peak at levels below this reversal but not above the reversal. Presumably, the ANIP motion saturates and some other motion (perhaps one due directly to the first peak of the classic traveling wave) becomes bigger at high levels and this other motion is not inhibited by MOC efferents.

Ruggero: I think that your interpretation of the effects of electrical stimulation of the medial olivocochlear system on the responses to clicks of the basilar membrane and auditory nerve fibers is flawed in two respects. 1) The first flaw arises from comparing responses to clicks of the basilar membrane at the base of the cochlea and of auditory-nerve fibers recorded largely at apical locations. Contrary to your implicit assumption, the first peak of basilar-membrane responses to clicks differs fundamentally between basal and apical regions of the cochlea. At the base, the first peak of the basilar-membrane response grows linearly as a function of click intensity and grows at increasingly compressive rates over a time course of a few hundreds of microseconds (for a characteristic-frequency period of 100 microseconds at the 10-kHz place) [Recio et al., *JASA*, 1998]. In contrast, at the apex of the cochlea the first basilar-membrane response peak exhibits pronounced compressive nonlinearity [Cooper and Rhode, *Auditory Neuroscience*, 1996]. To the extent that (compressive) nonlinearity is a marker for an influence of outer hair cells on the vibrations of the basilar membrane/organ of Corti complex, it is not at all surprising that at the apex, stimulation of the medial olivocochlear system (whose terminals synapse on outer hair cells) reduces the magnitude of the first peaks of responses to clicks both for basilar-membrane vibrations and post-stimulus-time histograms for auditory-nerve fibers. [The latter has not been

demonstrated yet; I suggest it will be eventually demonstrated.] Similarly, at the base, the first peaks of neither basilar-membrane responses nor of auditory-nerve post-stimulus-time histograms should be affected by stimulation of the medial olivocochlear system. post-stimulus-time histogram largely free of neural recovery effects, such as refractory periods and adaptation. I disagree. Such analysis is successful only when the driven discharge is fully adapted and does not exceed, say, 1 spike per several periods of oscillation in responses to individual clicks (so that, on average, the probability of spike occurrence is unaffected by the occurrence of previous spikes). When such conditions do not hold, a spike triggered by the first peak of the basilar-membrane response will cause later peaks of the post-stimulus time histogram to be relatively attenuated vis-à-vis the corresponding peaks in the underlying basilar-membrane ringing. In other words, the “recovered probability” analysis exaggerates the magnitude of the first peak, especially for responses to more intense clicks.

Now I summarize my own interpretation of your data. Both at the base and at the apex, auditory-nerve fiber responses follow more or less faithfully the corresponding vibrations of the basilar membrane/organ of Corti complex [see review by Robles and Ruggero, *Physiological Reviews*, 2001]. The reason why the correspondence between mechanical and neural responses appears to differ between base and apex is because the appropriate comparisons (neural base vs. mechanical base, neural apex vs. mechanical apex) have not yet been carried out. In other words, at any one place of the cochlea, basilar-membrane and auditory-nerve responses to clicks correspond strictly to each other.

Finally, I do not deny that inner hair cells are stimulated by basilar-membrane vibrations via two distinct pathways. This has been most clearly demonstrated in the chinchilla cochlea: auditory-nerve fiber responses to tones exhibit peak splitting, Nelson’s notches and 180-degree phase shifts which have no basilar-membrane counterpart [Ruggero et al., *PNAS*, 2000].

Answer: First I respond to Point 2 regarding “recovered probability”. Your question incorrectly assumes that we were using low-rate clicks. If we had used such clicks, then at high click levels for every click there would be a spike in the first peak and the result would be no recovered probability for 3 ms after that peak (i.e., 0/0), not a distorted histogram such as you suggest. Also note that recovered probability histograms always reduce the relative size of the first peak, not increase it as you state. Our methods avoided such problems by using high-rate clicks which (in addition to giving data at a faster rate) produce adaptation in the auditory-nerve response so that there was not always a spike in the first peak and spikes occurred at peaks throughout the response. Under these conditions, recovered probability removes the bulk of the effects of refractoriness and short-term adaptation (Gray, 1967. *Biophysical J.* 7, 759-777).

Now I reply to point 1 and the related last two paragraphs of Ruggero's comment. We did not, as your comment asserts, assume that the first peak of the basilar membrane (BM) response to clicks is the same in basal and apical regions of the cochlea. What we asserted is that if the classic BM traveling wave (which is a theoretical construct from basal-turn measurements) is assumed to extend throughout the cochlea, then MOC inhibition of the classic traveling wave response to clicks cannot account for the inhibition of the first click-response peak at the auditory nerve (AN). After ruling out some possible explanations we focused on two possible hypotheses, H4 and H5, both of which allowed there to be a difference in BM motion from the base to apex. There are a few relevant measurements of BM click responses from frequency regions lower than the 15-20 kHz region of most of our BM click data. The one chinchilla in which we measured MOC effects on BM click responses and found negligible first peak inhibition had a best frequency of ~8.5 kHz. In addition, measurements of click responses from the apical turn of the chinchilla (see Cooper, 2003), showed a mild compressive growth of click responses that is about the same on the first four peaks of the response, which suggests that efferent suppression of cochlear amplifier gain would produce a small suppression that would be similar in the first four peaks. So these data, from a similar CF region but a different species (and without efferent effects), suggest that strong efferent suppression of the first peak but not the second peak of the AN response will not be accounted for by an inhibition of BM motion.

The problem is that your comments miss the point we are trying to make. Our point is not about the correspondence, or lack thereof, between BM motion and auditory nerve (AN) firing, it is about the underlying motions of the organ of Corti that produce the motions of the BM and the motion of inner-hair-cell stereocilia which drive AN firing. We hypothesize that there are two motions throughout most (perhaps all) of the cochlea, the motion of the classic traveling wave (or a modest modification of it) and a second motion, the ANIP motion. This ANIP motion may, or may not, move the basilar membrane in the middle and apex of the cochlea. We argued that hypothesis 5 (that there are two underlying vibration patterns that produce the motions) is preferred over hypothesis 4 (that there is only one underlying vibrational pattern and it changes dramatically from base to apex) because it allows us to keep the classical traveling wave throughout the cochlea, as a large body of theory suggests. Another reason (not emphasized in my talk) for preferring hypothesis 5 over 4 is that the two motions hypothesis is much better at explaining the AN tuning curves with two lobes and different group delays in each lobe.

Cooper, N.P., 2003. Compression in the Peripheral Auditory System. In: Bacon, S.P., Fay, R., Popper, A.N., (Eds.), *Compression: From Cochlea to Cochlear Implants*. Springer Verlag, New York.

Siegel: It would be helpful if you would clarify what you mean by the “classical” traveling wave. The feature most commonly associated with the traveling wave is the increasing phase lag with distance from the base for tonal stimuli and this is clearly evident in auditory nerve recordings. Isn’t it likely that the differences in tuning curve shape and click response between the base and apex are a function of macromechanics rather than micromechanics? This is suggested by the observation of nonlinear basilar membrane mechanics throughout the response area in the apex (Cooper and Rhode, 1997). Wouldn’t it be likely that MOC effects would be observed in the first peak of the transient response of the basilar membrane as well?

Answer: I have used the term “classical traveling wave” to mean the translation and scaling to positions throughout the cochlea of the traveling wave measured from basilar-membrane (BM) motion in the cochlear base. This is what is commonly done when people think about BM motion anywhere in the cochlea, except perhaps in the apex. In the cochlear base, we found no MOC inhibition of the first peak of the BM response to clicks, which is consistent with previous data showing almost linear growth of this peak. In the apex, all peaks of the BM click response have slightly nonlinear growth (Cooper and Rhode, 1997). Thus, presuming that nonlinear growth indicates an amplified response, we expect these peaks, including the BM first and second peaks, to be slightly inhibited by MOC stimulation. In contrast, we have found that AN click responses from the apex and middle of the cochlea show strong inhibition of the first peak and little or no inhibition of the second peak. Thus, the MOC inhibition of early peaks in the AN click response from the apex and middle of the cochlea has a different pattern than the nonlinearity seen in BM motion at either the apex or the base.

Your question regarding cochlear micromechanics versus macromechanics reveals a weakness in the application of this terminology to the current situation. If our hypothesis 5 is correct and cochlear motion is a combination of a classical traveling wave and a second wave, with each producing some BM motion (BMm) and some IHC stereocilia bending (IHCsb), but with the two waves having very different ratios of IHCsb to BMm (i.e., each wave has its own macromechanical pattern and its own micromechanical pattern), then different MOC effects might be seen in BM motion and AN firing simply by changing the relative strengths of the two waves from base to apex without any difference in the MOC effect on each wave. In this case, asking whether the change is in macromechanics or micromechanics does not have the same interpretation that it would if there were just one cochlear motion. Thus, if cochlear motion is the sum of two vibrational modes, past ways of attributing effects to macromechanics versus to micromechanics need revision.

Chadwick: Comment: Any candidate for the ANIP response must take into account the increase of the response from base to apex. I would like to suggest that curvature increase from base to apex be considered as a possibility for the mechanism.

van der Heijden: Phase curves and group delay are very different in the apex and in the base. Auditory-nerve data [1,2] show a gradual change from what you call a “classical traveling wave” in the base to a patterning in the apex that is very different: high-frequency tails in tuning curves, anomalous dispersion, and downward FM glides in impulse responses. So we know it is incorrect to extrapolate high-CF behavior to low-CF regions. The transition of the behavior from base to apex is gradual and, moreover, does not show a “competition” or interference between separate response components. So there seems to be little need to postulate any novel modes of vibration from your neural data.

References:

1. Pfeiffer RR and Molnar CE (1970). *Science* 176, 16-14-1616.
2. van der Heijden M and Joris, PX (2003). *J. Neurosci* 93, 201-209.

Answer: I agree that AN data show a gradual change in response properties from the base to the apex. There are no comparable BM measurements that extend throughout the cochlea, but nonetheless, BM measurements from the base are routinely extrapolated to hold for the rest of the cochlea. Sometimes it is acknowledged that mechanical measurements in the apex are different from the base, but then the apex/base dividing line is typically put near 700 Hz (below which glides are anomalously downward) or 1 kHz (where TC tails change from below to above the tips). However, the smoothly changing AN data (e.g. our Fig. 2) suggest that it may be incorrect to extrapolate high-CF mechanical data from the base even to the middle of the cochlea.

A point on which I disagree with Marcel’s comment is in the presence of interference patterns in AN data. We have already published several examples of interference patterns in AN click responses (see Lin and Guinan, 2000); also see Ruggero et al. (PNAS 97:11744) and my reply to Joe Santos-Sacchi’s comment. Furthermore, your own data shows examples of AN TCs with two lobes and different group delays in each lobe. Thus, I think there is ample evidence for interference between separate response components.