Spring 2017

Effects of Medial Olivocochlear Auditory Reflex Activation on Cochlear Vibration

Alexandra Redfern

Shawn Goodman
University of Iowa

EFFECTS OF MEDIAL OLIVOCOCHLEAR AUDITORY REFLEX ACTIVATION ON COCHLEAR VIBRATION

by

Alexandra RedfernShawn Goodman

A thesis submitted in partial fulfillment of the requirements
for graduation with Honors in the Speech Pathology and Audiology

_____

Shawn Goodman
Thesis Mentor

Spring 2017

All requirements for graduation with Honors in the
Speech Pathology and Audiology have been completed.

_____

Amanda VanHorne
Speech Pathology and Audiology Honors Advisor

Effects of Medial Olivocochlear Auditory Reflex Activation on Cochlear Vibration

Alexandra N. Redfern

University of Iowa Department of Communication Sciences and Disorders

Abstract

In the cochlea, the basilar membrane (BM) vibrates in response to sound. The BM separates the different frequency components of sound along its length. BM vibration is a combination of passive mechanics and an active "cochlear amplifier." The cochlear amplifier arises from the motion of cochlear outer hair cells, which change their length in response to specific frequencies. This boosts the amplitude of BM vibration, which improves hearing of soft sounds and frequency resolution. The Medial Olivocochlear Reflex (MOCR) is a feedback pathway in the brainstem which, in the presence of background noise, lessens the boost of the cochlear amplifier. MOCR can be indirectly measured using Otoacoustic Emissions (OAEs), which are soft sounds originating in the cochlea as a byproduct of cochlear amplifier activity. Past research suggests that the MOCR alters the magnitude and phase of OAEs and BM vibration. However, the apparent phase change may be a change in frequency. This would suggest that activation of the MOCR changes the resonant frequency of the BM. The present study sought to explore MOCR effects on OAE frequency, magnitude, and phase. The results indicated high variability between subjects, but many subjects showed changes in OAE frequency without changes to OAE phase. This paradigm shift may have implications for reanalysis of past research on this topic.

Effects of Medial Olivocochlear Auditory Reflex Activation on Cochlear Vibration

Basilar Membrane Vibration

When a sound pressure wave reaches the ear, it travels through the air of the ear canal to the eardrum, which is connected to the bones of the middle ear, or the ossicles. When the ossicular chain is set into vibration, it pushes on the oval window of the inner ear, or the cochlea. The cochlea is a spiral shaped, fluid filled-hole in the temporal bone, and it is divided along its length into three separate chambers. Running between two of these chambers is a thin sheet of tissue called the Basilar Membrane, and the BM houses the auditory transduction complex that turns sound waves into neural signals. The BM remains relatively constant in mass along the length of the cochlea, but decreases in stiffness as it moves apically (upward and away from the oval window). When the oval window is pushed by the ossicles, it sets up a pressure wave in the fluids of the cochlea, which displaces the basilar membrane and sets up a traveling wave along it that travels from the base to the apex. The stiffness gradient of the BM creates a gradient of resonant frequencies, such that any place along it has a resonant frequency lower than the basally adjacent place and higher than the apically adjacent place (Pickles, 2013). The resonant frequency at a given place along the BM is known as the characteristic frequency (CF), and place of resonance for a given frequency is called the characteristic place (CP).

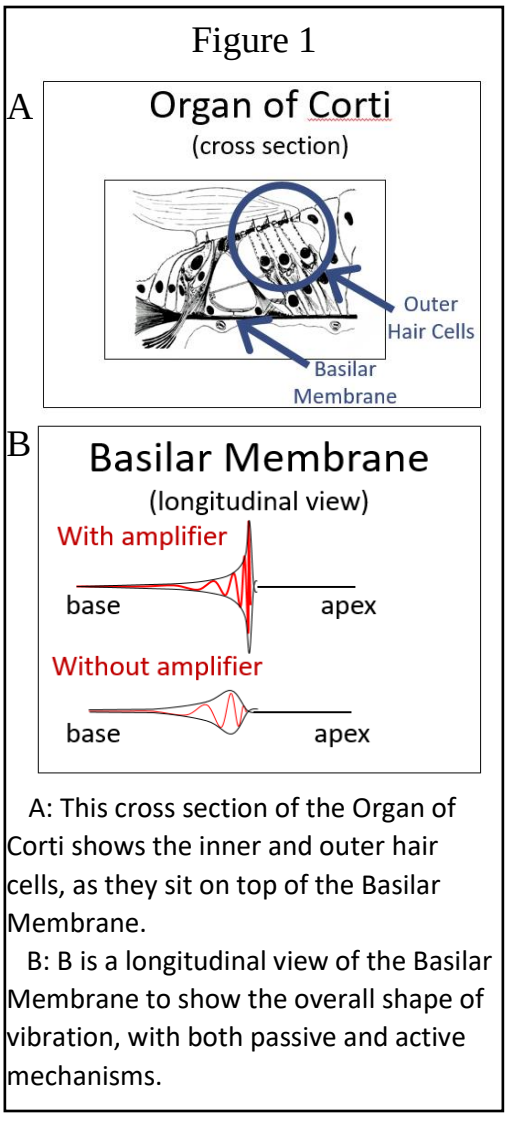
When a traveling wave is set up on the BM, it travels apically from the base toward its CP. As the wave nears its CP, the amplitude of BM vibration increases slowly with increases in intensity. When the wave reaches its CP, the vibration amplitude grows rapidly, peaks, and then quickly dies out just past the peak. This creates the typical shape of BM travelling wave envelopes, with slow growing tails basal to the peak and very short tails just apical to the peak.

Because the stiffness gradient creates this shape without providing any active input to the wave, this effect is referred to as passive mechanics (Pickles, 2013).

Cochlear nonlinearity and active processes.

The passive mechanics of the BM are not the only forces at play when a traveling wave is set up, however. There is also an active amplification process, which is housed within the auditory transduction mechanism on the BM, the Organ of Corti. The Organ of Corti contains both inner and outer hair cells (Figure 1A), which have different functions related to processing sound. Inner hair cells have the function of encoding the traveling waves and sending auditory information up to the brain, whereas outer hair cells have the function of responding to traveling waves and amplifying them. When an outer hair cell is stimulated by a wave of its characteristic frequency, a protein called prestin in its cell walls changes shape, elongating the cell and mechanically increasing the amplitude of the vibration at the outer hair cell's location (the active zone) and just apical to it (Guinan, 2014). This provides a significant and frequency specific boost to the vibration, especially to low-level sounds, and allows for increased sensitivity of softs sounds and increased frequency resolution at all levels. This process of boosting vibration is known as "the cochlear amplifier" (Figure 1B).

Figure 1



A: This cross section of the Organ of Corti shows the inner and outer hair cells, as they sit on top of the Basilar Membrane.

B: B is a longitudinal view of the Basilar Membrane to show the overall shape of vibration, with both passive and active mechanisms.

The MOC Effect

There is a brainstem mediated reflex pathway, which provides a feedback loop for the

auditory system, called the Medial Olivocochlear efferent pathway (MOC). The pathway originates in the olivocochlear bundle, within the superior olive in the brainstem. The medial fibers of this bundle make the MOC pathway, which innervates the outer hair cells (Pickles, 2013). This pathway is activated by broadband signals, or background noise, and its effect is to reduce the gain of the cochlear amplifier. The roles of the MOC reflex are interconnected, but they are to 1) increase the dynamic range of hearing, 2) to improve signal detection in noisy situations, 3) contribute to selective attention, and 4) to reduce acoustic trauma (Guinan, 2014). In noisy situations, or situations that require selective attention, the cochlear amplifier may be saturated by the undesired stimulus, such that desired stimuli cannot be heard above the noise. With MOC activation, the gain of the cochlear amplifier is decreased across the basilar membrane, which allows more room in the amplifier's range for the desired stimulus to be encoded. Although clinical applications of MOC presence have not been confirmed, it is an important system to learn about with hopes of utilizing it in the future, perhaps to detect auditory neuropathies or determining susceptibility to noise induced hearing loss (Goodman, 2013).

Otoacoustic Emissions and Measuring the MOC Reflex

Otoacoustic emissions (OAEs) are a by-product of outer hair cell activity. When a click, or other transient signal, is presented to the ear, the entire basilar membrane is stimulated, and transient evoked OAEs are generated and reflected out of the ear from all along the frequency ranges. When a specific place along the BM generates an emission, the emission comes out at the same frequency and in the same phase as the input that generated it (Pickles, 2013).

The effects of the MOC reflex can be measured by its effects on OAEs. Because OAEs are a result of the interaction of BM vibration and the cochlear amplifier's activity, changes in the OAE waveforms can be interpreted as accurate reflections of BM vibration and amplifier

activity. An important limitation of past studies that have examined non-MOC changes in OAE waveforms is the timing of click presentation. For example, Carvalho et al. 2003 presented clicks to participants' ear at a rate of 33 per second, or one click about every 30 milliseconds. While this is sufficient timing to allow for OAEs to be measured between clicks, this is not enough time to avoid confounding effects of the MOC reflex. The MOC pathway has a longer time delay to turn on and back off than 30 milliseconds, so it is possible that previous studies have activated the MOC reflex with the click stimuli and failed to account for this in their analysis. For research examining MOC effects on OAEs and other OAE related research, therefore, it is important to space the stimulus clicks far enough apart that the MOC is not activated unintentionally.

In the past, studies that have measured MOC related changes have found consistent changes in magnitude and phase of OAEs (Goodman 2013, Mertes & Goodman 2016). While changes in magnitude are to be expected, since the MOC aims to decrease the gain of the cochlear amplifier, which produces OAEs, the changes in phase are not as transparent, and may require further explanation. In fact, past studies have not considered that the MOC could also alter the frequency of the OAE, which could result in apparent phase shifts due to MOC activation that are more accurately accounted for with changes in frequency. The present study aims to explore MOC effects on the phase and magnitude of OAEs, as in past studies, but also to explore changes in OAE frequency, as well.

Research Questions

The research question of the present study is: does activation of the MOC reflex change OAE, magnitude, frequency, phase, or some combination? And, what might this suggest about BM vibration in general and about the process by which MOC activation alters it?

Methods

Participants

Participants in the present study included 30 normal hearing adults between the ages of 21 and 35 (average 24 years). Nineteen (19) were female and 11 were male, and all subjects were recruited from the Iowa City community, including the University of Iowa campus. To participate in the study, subjects were required to present with no suspicion of hearing loss or history of ear surgeries, aside from pressure equalization tubes as a child. In addition, subjects were required to pass a hearing screening, which included otoscopy, tympanometry, and pure tone behavioral audiometry.

Hearing Screening

Otoscopy was performed on all subjects to check for glaring structural anomalies, excessive wax, or other obvious contraindications for further testing. No quantitative values were used to determine typical otoscopy.

The norms used for the peak pressure value in tympanometry were narrower for the present study than most clinical norms, such that only values from -50 to +50 daPa were accepted (normal clinical values -150 to +50 daPa). This narrower range helped to ensure that even very low level OAEs would not be dampened by negative middle ear pressure.

Both otoscopy and tympanometry were performed in the Auditory Physiology Lab in the Wendell Johnson Speech and Hearing Center, outside of the sound booth.

Participants passed the pure tone audiometry screening with responses 15 dBHL, which is also stricter than a typical screening measure (normal hearing screening levels 20dBHL). This helped to ensure that the cochleae tested included healthy, functioning outer hair cells, which

helped to ensure that OAEs would be present in all subjects. Audiometry was done with headphones, in a double-walled, sound-treated booth.

Equipment setup.

For all OAE testing, clicks were presented in one ear and white noise was intermittently presented to the other ear. All stimuli were presented via a personal computer (PC) running custom written MATLAB software (The MathWorks, Inc), connected to sound cards, and power amplifiers. Ear canal pressure recordings were collected in both ears with OAE probe microphone systems connected to the 24-bit sound card. These recordings were later analyzed using custom analysis software written in MATLAB.

Calibrations.

Before each subject, or within the same day of multiple subjects, the equipment was calibrated using cavity recordings of fixed lengths.

Otoacoustic Emission Testing

For all OAE testing, participants were seated and reclined in a recliner in the sound-treated booth. Insert probes were inserted into both ears; the insert to deliver the clicks and to record the OAEs was placed in the left ear, and the insert to deliver noise and silence was placed into the right ear. The cords from the probes were suspended from the ceiling with strings and plastic slinkies to ensure that they did not rub on the subjects' clothing or touch their faces. Each probe was the output of an ER10C box, whose battery voltages were measured before and after testing (9V batteries, replaced if 8.1V or lower).

Once the subjects were comfortably kicked back with insert phones in place, they were instructed to sit as quietly as possible for the duration of the experiment. Subjects were permitted to read quietly to help keep them awake. In addition, after 20 clicks at each level, both with and

without noise, subjects were required to click “continue” on the computer screen to go on to the next round of clicks. This added extra time onto the experiment, but ensured that subjects did not complete the experiment while asleep.

The Stimuli

The goal of the experiment was to examine the effects of contralateral noise on OAEs at 3 different stimulus levels. The hope was to activate the MOC reflex without activating the Middle Ear Muscle Reflex (MEMR), and to only activate the MOC reflex during the noise conditions. Given the suspicion of the authors that previous studies had failed to account for the timing overlap of the MOC pathway and the stimulus presentation, the present study sought to spread out the clicks in time to avoid interference of the MEMR and to avoid unintentional activation of the MOC reflex. For this reason, each subject participated in two experiments. The first experiments presented the clicks and noise much like those of previous studies; with only a 30 msec delay between clicks. In the second session, clicks were presented with a 200 msec pause between each, which allowed plenty of time for any reflexes activated to turn on and back off without interfering with the response to the next click.

The clicks were presented at three levels: 30, 36, and 42 dB sensation level (i.e., 30, 36, or 42 decibels above auditory detection threshold). The contralateral noise was presented at approximately 30 dB SL.

For all intensity levels and for each of the silence and noise conditions, 2,000 clicks were presented to subjects, and OAEs were recorded from the same ear immediately after. This provided enough recordings to average together to drop the noise floor and make analysis possible. The total time for the experiment with more widely spaced clicks was about 55 minutes, and about 10 minutes for the narrowly spaced experiment.

Analysis

All analyses were done on a Windows PC with MATLAB software, using custom written programs by Dr. Shawn Goodman (The MathWorks, Inc.).

Steps of analysis

To analyze the effects of the MOC reflex on OAE frequency, magnitude, and phase, the OAE waveforms were first averaged for each condition in each subject. Only the highest intensity results will be analyzed in this paper; further analysis is needed to determine the interactions of stimulus level and MOC activation in OAEs. The average waveforms were translated into the frequency domain, and a narrow frequency band was selected somewhere within the 1-3kHz range. The waveform was then filtered at the narrow frequency band, and a short time window from the filtered waveform was analyzed for frequency changes. From here, changes in magnitude and phase, due to MOCR, were plotted together on the complex plane.

Results

Analysis of One Subject

Averaged time waveforms.

The first step in the analysis was to average the 2,000 recorded OAE waveforms for each subject in each condition. Figure 2 shows the averaged OAE waveforms for one subject at the highest intensity conditions. The red line shows OAEs recorded with silence in the contralateral ear, and blue line shows OAEs with noise in the contralateral ear. At first glance, the OAEs in silence and noise are very similar, but with decreased magnitude in the noise condition. However, to analyze changes in

Figure 2

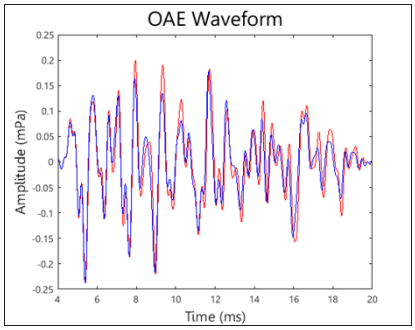


Figure 2: The averaged emission waveforms recorded after 60dB clicks in noise (blue line) and in quiet (red line) for one subject.

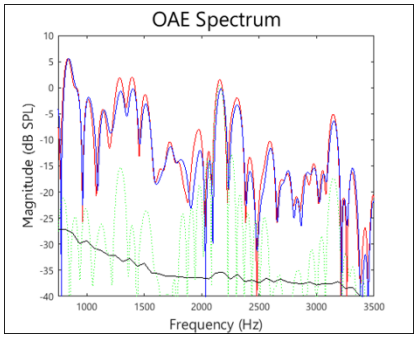
frequency composition, only a narrow band of frequencies is to be chosen. To select the frequency range, the time waveforms were transformed into the frequency domain. Figure 3(A) shows the spectrum of the OAE waveforms. The red line is the spectrum of OAEs recorded with silence in the contralateral ear, and the blue line is the spectrum of OAEs recorded in noise.

Selecting the frequency range.

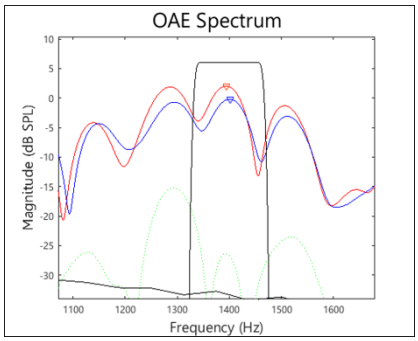
From the total spectrum, a peak in magnitude was selected somewhere in the range of 1-3 kHz. In this case, a peak was selected at around 1400Hz. Figure 3(B) shows a zoomed in view of the peak selected for this subject, and this view shows that the peak appears to shift up in frequency from the silent to the noise condition. For this reason, a filter was crafted that included a narrow band of frequencies around the two peak frequencies. This filter was then applied to the OAE waveforms in time, and the output waveform is shown in figure 4(A). These waveforms look much simpler and less noisy than the original OAE waveforms, as they are dominated by only a few frequencies.

Figure 3

A



B

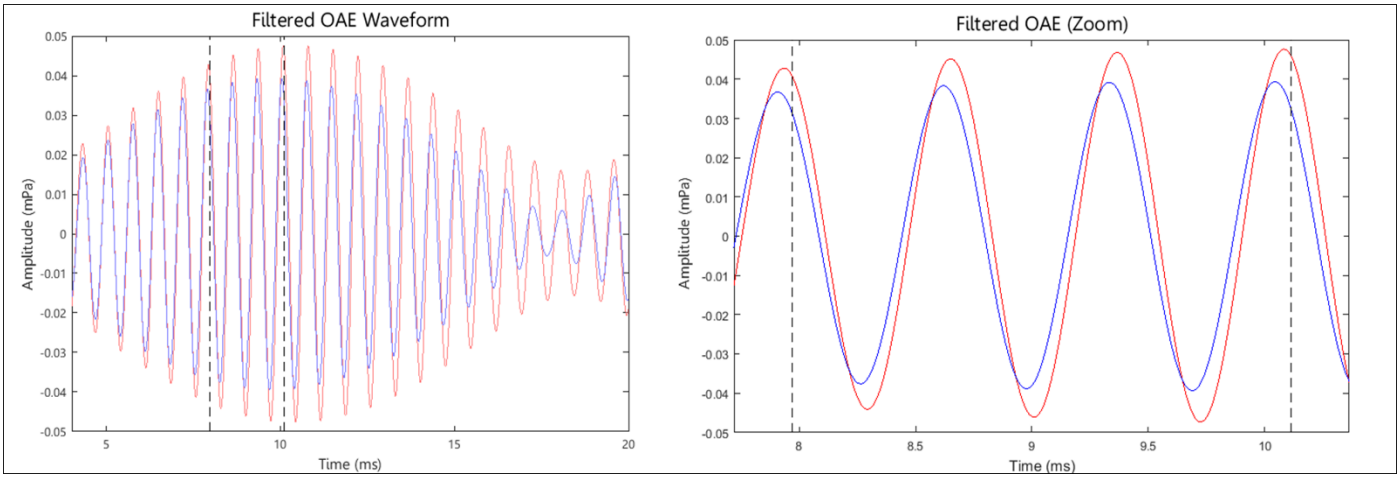


A: The frequency composition spectrum of the emission waveform in fig. 2.
B: The selected frequency range for further analysis. The peaks (red and blue triangles) shift from silence (red) to noise (blue), suggesting a shift in frequency with MOC activation.

Confirming the frequency shift.

To confirm the shift in frequency noted in the OAE spectra, a very short time window was selected from the filtered OAE waveform (figure 4(B)). The time window was selected based on the expected delay of an OAE in that frequency range, to ensure that only changes in frequency of an emission from the selected place on the BM were analyzed. The analysis in the

Figure 4



A: The emission waveforms from fig. 2 was filtered, using the filter crafted in fig. 3(B). The results are waveforms dominated by the two peak frequencies in the spectra of fig. 3.
B: The short time window selected from (A), chosen based on the expected time delay of an emission at the selected frequency range. The noise condition (blue line) is a higher frequency than the silent condition (red line).

short time window revealed, for this subject, a frequency increase of 5Hz from the silent to noise condition (silent frequency: 1394, noise frequency: 1399). There were high levels of variability among subjects for MOC-induced frequency shifts. Many subjects showed increases of frequency of varying magnitudes, while other subjects showed no shifts.

Analyzing magnitude and phase changes.

Past research (Mertes & Goodman 2016) analyzed changes in magnitude and phase of OAEs following MOC activation through a complex plane analysis. In this analysis, phase and magnitude changes are quantified into one complex number. To achieve this, magnitudes and phases for the two waveforms in figure 4(B) were converted to complex numbers ($M\cos(\Phi) + jM\sin(\Phi)$) and divided. This produces a complex ratio, which can be plotted as a single vector on a complex unit circle (fig. 5). In this representation, changes in magnitude are shown by points inside the circle (decreases) or outside the circle (increases), and changes in phase are shown by

Figure 5

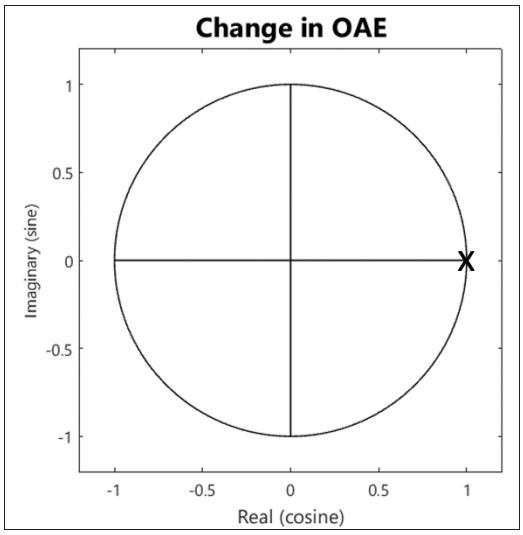


Figure 5: The complex plane used to plot changes in magnitude and phase of OAE's. The x-axis is cosine, or the real part of the vector. The y-axis is sine, or the imaginary part. These axes reflect the following changes:

- No change in magnitude or phase: at point (1,0) along the circle (shown above with "x")
- Decrease in magnitude: x shifted inside the circle (toward the origin)
- Increase in magnitude: x shifted outside the circle (away from the origin)
- Phase lead: x shifted upward around the circle (counterclockwise)
- Phase lag: x shifted downward around the circle (clockwise)

rotations around the circle, where rotations upward reflect a phase lead, and rotations downward reflect a phase lag.

This analysis method was employed in the present study, but it was modified to account for the newly discovered shifts in frequency. Past research assumed that there were no frequency changes in the emissions, which may have resulted in apparently large phase shifts. However, when the frequency of the emission is shifted, there is an expected timing difference, that cannot be accurately described as a phase shift. In the present study, the expected phase shift due to any frequency shifts was determined, and that rotation was removed from the representation. As shown in figure 6, when the expected phase shift is removed, we see no further changes in phase due to MOC activation. The MOC reflex in this subject only changed the frequency of the emission and decreased the magnitude of it; it induced no other changes in phase or timing.

There was significant variability in this analysis across subjects, as well. Some subjects showed no phase changes, while others showed phase leads, and still others showed phase lags.

Subjects showed decreases in magnitude consistently, but of varying levels. Figure 7 shows the complex analysis for two other subjects.

Figure 6

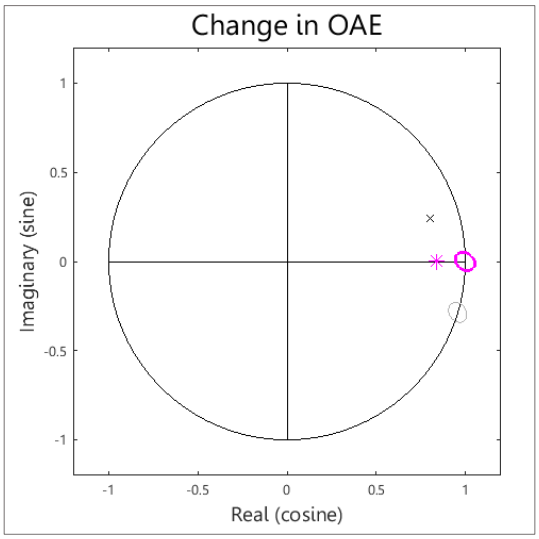


Figure 6: The complex plane analysis for one subject. OAE changes that fall outside of the confidence region (circles) are considered statistically significant MOC effects. The pink asterisk and confidence region account for changes in frequency, while the gray circle and x do not. In this subject, phase was not affected by the MOC once the frequency effect was considered.

Discussion

There have been some previous reports of frequency changes in OAEs due to MOCR; however, these reports have looked at other types of emissions. This is the first study we are aware of that has used transient emissions, and that has simultaneously examined changes in frequency, magnitude, and phase. Although we did not see frequency shifts in all subjects, they were present in many subjects, and frequencies consistently shifted higher in noise for subjects who showed frequency shifts. This suggests that the MOC reflex may act to increase the stiffness of the cochlear amplifier or of the basilar membrane/organ of corti complex, which would increase the resonant frequency of that place. It is not known by what specific mechanism the MOC reflex may achieve this.

Future studies should be sure to account for frequency shifts, especially when analyzing phase shifts. In some subjects, a failure to account for the frequency change would have made phase lags appear to be phase leads, suggesting that previous trends seen in phase shifts may not be entirely accurate.

Overall, the results across subjects raise more questions than they answer. However, these data do support a shift in paradigm and analysis of the MOC reflex to include the

possibility of frequency shifts, and past data may need to be reanalyzed. Further research is needed to fully answer the questions about what the MOC system does and how. Once this system is fully understood, it may become clinically relevant as a test for things like auditory neuropathy or predicting susceptibility to noise-induced hearing loss.

Figure 7

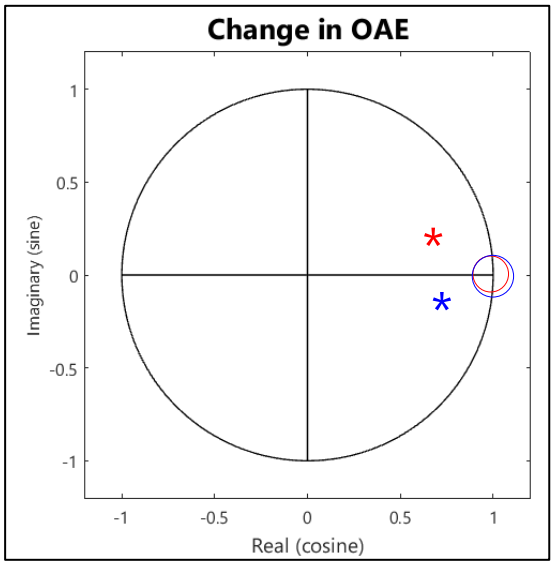


Figure 7: Complex plane analyses for 2 other subjects. The subject in red showed a phase lead, even after the changes in frequency were accounted for. The subject in blue even showed a phase lag after controlling for frequency effects.

References

Carvalho, W., Buki, B., Bonfils, P., & Avan, P. (2003). Effect of click intensity on click-evoked otoacoustic emission waveforms: Implications for the origin of emissions. *Hearing Research, 175* 215-225.

Goodman, S., Mertes, I. B., Lewis, J. D., & Weissbeck, D. K. (2013). Medial olivocochlear-induced transient-evoked otoacoustic emission amplitude shifts in individual subjects. *Journal of the Association for Research in Otolaryngology, 14(6),* 829-842.

Guinan, J.J. (2014). Cochlear mechanics, otoacoustic emissions, and medial olivocochlear efferents: Twenty years of advances and controversies along with areas ripe for new work. In Popper, A. N., & Fay, R.R. (Eds.), *Perspectives on auditory research* (229-246). New York: Springer.

Mertes, I. B. (2014). *Repeatability of medial olivocochlear effects on transient-evoked otoacoustic emissions in normal hearing adults* (Unpublished doctoral dissertation). University of Iowa, Iowa City, Iowa.

Mertes, I. B., Goodman, S. S. (2016). Within- and across-subject variability of repeated measurements of medial olivocochlear-induced changes in transient-evoked otoacoustic emissions. *Ear and Hearing, 37(2),* 72-84.

Pickles, J. O. (2013). *An introduction to the physiology of hearing.* Leiden: Koninklijke Brill NV.