

Individual cochlear delay estimated with otoacoustic emissions and auditory brainstem measurements

GILLES PIGASSE, JAMES M. HARTE AND TORSTEN DAU

Centre for Applied Hearing Research, Ørsted•DTU, Technical University of Denmark, DK-2800 Lyngby, Denmark

Methods to estimate cochlear delay in humans have been traditionally based on either phase-derived group delays from otoacoustic emissions (OAE) or derived-band auditory brainstem responses (ABR). There has been a large variability in these cochlear delay estimates, when averaged across a number of subjects. This study aims to assess the degree of inter-subject variability, by focusing on the methods for deriving both OAE and ABR based estimates. The robustness of the measures will be demonstrated via repeat recordings and the associated intra-subject variability.

Tone-burst evoked OAEs (TBOAEs) and tone-burst evoked ABRs (TBABRs) are used to estimate cochlear delay. The ambiguity in time domain OAE onset, for these narrowband stimuli, is analysed by taking advantage of their compressive growth function. This is done by separating the nonlinear components of cochlear origin from the linear reflection in the time domain. The observed latencies as a function of frequency are qualitatively similar across subjects. For the individual subjects, the delay at each tone-burst frequency is reproducible. However, there remains an ambiguity regarding the true onset point of the OAE. For the TBABR data, one limiting factor appears to be the fixed choice of the neural delay. Attempts are made to understand this in the individuals tested.

The difference in inter-subject variability between TBOAE and TBABR is apparent at low frequencies. The assumption that OAE delay is twice the basilar membrane delay, as implied by the theory of coherent reflection (Zweig and Shera, 1995), does not appear to hold for the entire frequency range. Theoretical implications of these findings on the transmission of the travelling wave are discussed.

INTRODUCTION

Inside the inner ear, the cochlea transforms a mechanical signal coming from the stapes into an electrical signal in the auditory-nerve fibres. The tonotopic organization of the cochlea is such that highest frequencies are processed at the base of the basilar membrane (BM) and the lowest frequencies at the apex. This difference in location induces a time difference between the processing of high and low frequencies. This intrinsic relation between frequency and travel time in the cochlea defines the cochlear delay (τ_{BM}) and can provide knowledge about specific regions of the inner ear. For example hearing disorders related with the cochlea can be diagnosed. Since measuring the motion of the BM in living human is not possible, the measurement of the cochlear delay requires indirect techniques such as otoacoustic emissions (OAEs) or auditory brainstem responses (ABRs).

One of the aims of the present study is to compare the estimates of the cochlear delay obtained with both techniques. The comparison of the two estimates can provide information about the robustness of these techniques and also about the generation mechanism of the OAE. The exact place where this phenomenon occurs still remains a matter of discussion. The most commonly accepted theory is known as coherent reflection filtering (CRF) (Zweig and Shera, 1995). It stipulates that a backward travelling wave is created at the site of the basilar membrane whose characteristic frequency (CF) is close to the stimulus frequency. Therefore, the travel time for the OAEs (τ_{OAE}) is made of the inward travelling-wave latency (from the onset to the CF place on the BM, τ_{BM}) and the backward travelling-wave latency (from the CF place to the ear canal). Therefore τ_{OAE} corresponds to the round trip in the cochlea giving $\tau_{\text{OAE}}=2 \tau_{\text{BM}}$. The backward travelling wave is due to micro inhomogeneous perturbations on the BM. It seems that this generation mechanism does not work in the same way at low frequencies. It is suggested that it is due to the change in the filter shape and might be related to the gradual deviation from the scaling symmetry towards low frequency (Zweig and Shera, 1995). The present study aims to highlight this difference between low and high frequencies. Moreover, OAE and ABR measurements provide estimates of the BM delay from different pathways. For ABR, the neural response to the stimulus is recorded whereas only the BM activity is recorded in the case of OAE. The present study compares the estimate τ_{BM} from ABR to τ_{OAE} .

A particularity of the present study is to consider each subject individually. Indeed, the great majority of studies that deal with human physiological data average the results across “normal hearing” subjects. The label “normal hearing” is usually based on a rather brief audiogram (only few frequencies tested). Moreover, people having similar audiogram can have different cochleae (length, state, see Ulehlova *et al.*, 1987). The present study analyses the reproducibility of OAE and ABR for the same subjects and also investigates the inter-subject variability.

METHODS

The OAE and ABR experiments were run separately with the same 11 adult subjects. There were 2 females and 9 males, all having pure-tone threshold better than 15 dB HL in the range of frequencies from 250 to 8000 Hz. Although gender has been shown to have a small effect on ABR (Don *et al.* 1993), the present studies focuses more on intra-subject results and do not aim to compare subject with each other.

The recordings were repeated three times on three different days. The stimuli used were clicks (100 μ s) and tone-bursts (.5, .75, 1, 1.5, 2, 3, 4, 6, 8 kHz) of different duration (10ms at 500Hz to 1.25ms at 8kHz), similar as in the study of Norton and Neely (1987). The durations of the tone-bursts represent a compromise between having a narrow frequency spectrum and maintaining a similar duration in time across the stimuli. The stimuli were played at 66 dB peSPL and the repetition rate was 25/s for OAE and 24.5/s for ABR. The main differences from the Norton and Neely study was a broader frequency range ([.5 8] vs. [.5 2] kHz) and a focus on the OAE generation mechanism.

The OAEs were recorded with the ER-10B microphone, placed in the ear canal, while

the ABR were recorded with electrodes positioned on the forehead, the vertex and the two mastoids. The recorded signals were stored on a disk for off-line analysis. The main problem encountered when analyzing OAE in the time domain is to separate the stimulus from the response. An OAE response is made up of two components: a linear response corresponding to the stimulus reflections in the ear canal (EC) and middle ear, and a non-linear component generated in the inner ear (the actual OAEs). The separation method uses the nonlinear property of the OAEs: a filter estimate of the EC is obtained from click-evoked OAE at two different levels; the stimuli are then convolved with this filter estimate and finally the tone-burst evoked OAEs are compared with the convolved signal (Pigasse *et al.*, 2006). The latency of the OAE is then defined as the time between the stimulus onset and the peak of the burst attributed to the OAE.

ABR waveforms consist of a series of peaks among which the prominent one is wave V. Wave V is assigned to the highest peak followed by a rapid drop and its latency is the time between the stimulus onset and this peak. It is assumed that the latency of the wave V is the sum of the estimated cochlear delay (τ_{fwd}), the synaptic delay ($\tau_{synaptic}$) and the neural delay (τ_{neural}):

$$\tau_{wave\ V} = \tau_{fwd} + \tau_{synaptic} + \tau_{neural} \quad (Eq.1)$$

The synaptic delay represents the time between the hair cells activation and the auditory nerves, it is assumed to be constant and amounts to 1 ms (Kim and Molnar, 1979). The neural delay corresponds to the delay between the auditory nerve and the site of the auditory pathway generating wave V; it can be estimated as the interval between wave I and wave V (Don and Eggermont, 1978). An estimate of the cochlear delay from the ABR measurements (τ_{fwd}) is given by:

$$\tau_{fwd} = \tau_{wave\ V} - \tau_{synaptic} - \tau_{neural} \quad (Eq.2)$$

This estimate of the forward latency can then be multiplied by 2 in order to compare it with τ_{OAE} , as implied by the CRF theory.

RESULTS

As expected, both OAE (left panel) and wave-V latencies (right panel) decrease with increasing frequencies, shown in Fig. 1.

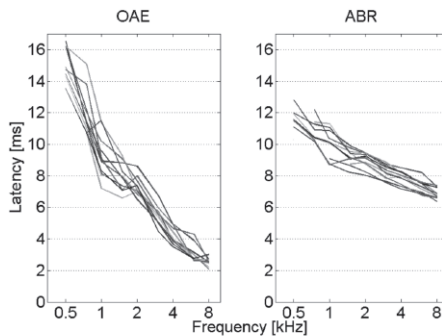


Fig. 1: Latencies of wave V and of OAE for 11 subjects.

Intra-subject variability

Each curve plotted in Fig.1 represents one subject; the standard deviations were omitted for clarity. Instead, the mean and the standard deviation (in brackets) of the intra-subject variability for OAE and ABR are shown in table 1. With both methods, the variability is rather small. For example, at 1 kHz, the averaged intra-subject variability is only 0.33 ms for the OAE latency which is small compared to the average latency τ_{OAE} of around 9.2 ms. The standard deviation of 0.21 ms indicates that the values vary around the mean and they stay of the same order. For ABR, $\tau_{wave V}$ is about 11 ms and the averaged standard deviation is 0.27 ms. The good reproducibility of the data reflects that both techniques are reliable. ABR recordings are more sensitive to noise at low frequencies than OAE recordings, as reflected in the intra-subject variability. Therefore, at these low frequencies, the detection of wave V is more ambiguous for ABR than the detection of the burst for OAE. Another observation is that the intra-subject variability does not seem to be frequency dependent.

Frequencies [kHz]	.5	.75	1	1.5	2	3	4	6	8
OAE	0.37 [0.34]	0.25 [0.29]	0.33 [0.21]	0.29 [0.22]	0.27 [0.30]	0.25 [0.19]	0.19 [0.16]	0.26 [0.28]	0.14 [0.13]
ABR	0.53 [0.47]	0.18 [0.19]	0.27 [0.26]	0.38 [0.33]	0.15 [0.15]	0.22 [0.15]	0.22 [0.08]	0.16 [0.12]	0.18 [0.16]

Table 1: Mean and standard deviations [.] of the intra-subject variability for ABR and OAE latencies, in ms.

Inter-subject variability

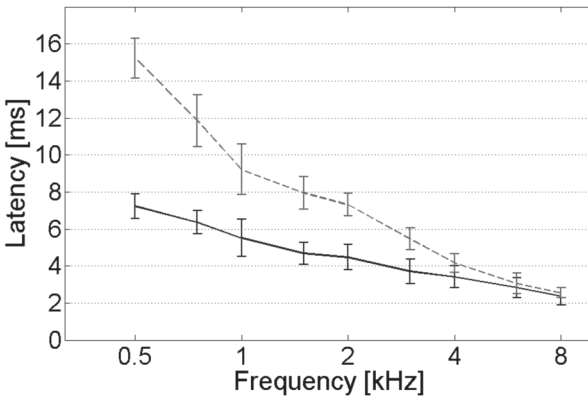


Fig. 2: Mean of the OAE latencies, τ_{OAE} (dashed line), and mean latencies for the forward travelling wave (solid line, τ_{fwd} from ABR data) calculated with eq. 2.. The inter-subject variability is indicated with the error bars (± 1 Std)

Figure 2 presents the mean latencies calculated across all 11 subjects. The dashed line

represents the OAE latency, τ_{OAE} , and the solid line shows τ_{fwd} , which has been calculated from the wave-V latency, as indicated in Eq. 2. The inter-subject variability is shown by the error bars. Between 0.5 and 1 kHz the variability of the OAE is larger than the variability of the ABR data. This difference between OAE and ABR was also observed by Neely *et al.* (1988) and could be due to a greater difficulty of detecting the OAE bursts compared to detecting the wave V. Although ABR and OAE are repeatable for each subject, it seems that their variability does not follow the same trend. There is an apparent decrease of inter-subject variability with increasing frequency for OAEs but nothing similar for ABRs. This suggests that differences between subjects occur at a cochlear level rather than at a neuronal stage. Subjects can indeed present different inhomogeneities along their basilar membrane affecting variably the backward travelling wave, they can also have distinctive cochlear filtering properties as well as a different threshold across the audible frequency range (Don *et al.*, 1994). These are some possible sources of inter-subject variability for OAE delays.

DISCUSSION AND CONCLUSION

For tone-burst stimuli, the travelling wave on the BM peaks at the characteristic place. OAE generation is affected by the outer hair cells and is a by product of the amplification they provide to the forward travelling wave. The exact place where this takes place remains unclear. The CRF theory suggests that the OAE latency is twice the forward latency. This can be examined here with the results obtained in the present study.

Figure 3 shows the OAE latency (τ_{OAE}) and two times the estimated forward latency from the ABR recordings ($2\tau_{\text{fwd}}$), plotted on loglog axes. Neely *et al.* (1988) interpreted similar latency estimates to those presented here in terms of a formula proportional to the frequency raise to some negative power less than unity (i.e. $\tau \propto f^{-\alpha}$, where $\alpha < 1$). This power law encompasses the logarithmic mapping of latency to frequency. Plotting the latency data on loglog axes means that any such power law will be observed as a straight line with slope $-\alpha$. This can be seen in Fig. 3 with the dashed curve representing mean latency for the OAE data (τ_{OAE}), and the solid curve the derived ABR latency ($2\tau_{\text{fwd}}$). Under the CRF theory the slopes for τ_{OAE} and $2\tau_{\text{fwd}}$ should be the same. In order to compare this, a two-way analysis of variance (ANOVA) was carried out to examine the effect of independent factors on the BM latency estimate and slope. The independent factors are the frequency ($n=9$) and the measurement technique ($n=2$, ABR or OAE). The null hypothesis is: "The slope of $2\tau_{\text{fwd}}$ and τ_{OAE} are identical". Results are declared significant if the p-value is less than 0.05 and this would cast doubt on the null hypothesis.

Nine out of the 11 subjects tested presented a significant difference between the two variables. An example for a single subject of this analysis and slope fitting is shown in the left panel of figure 4. If the experimental data are split into two regions before and after a break point at 2 kHz, and the ANOVA test carried out again, then the difference is no longer significant at lower frequencies (see Fig. 4, right panel). Ten subjects present no statistical difference between τ_{OAE} and $2\tau_{\text{fwd}}$ at low frequencies ($f < 2\text{kHz}$) and six out of eleven for the higher frequencies.

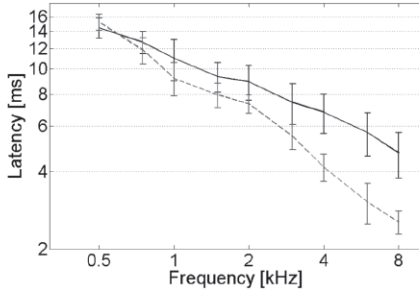


Fig. 3: Mean of the OAE latencies, τ_{OAE} , dashed line. Mean latencies for the forward travelling wave (solid line, τ_{fwd} from ABR data) multiplied by two as suggested by the CRF theory. The inter-subject variability is indicated with the error bars ($\pm 1\text{Std}$).

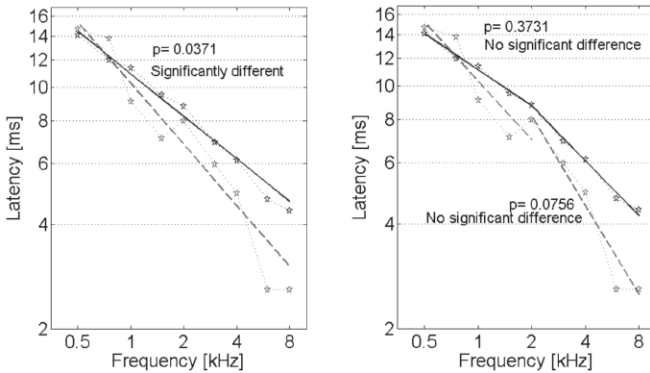


Fig. 4: Comparison between τ_{OAE} (dashed curve) and $2\tau_{\text{fwd}}$ (solid curve) for subject 9. The data points are also plotted (\diamond) and are linked together by a dotted line. The two solid lines represent the best fit to the data. The value of p , from the ANOVA test is indicated, $p > 0.05$ means that the estimates given by OAE and ABR measurements evolve in the same way. The left figure shows a fitting to the entire data set and the right figure shows a separate fitting for frequencies below and above 2 kHz.

These results suggest that there might be different behaviour at low and high frequencies, as also observed in previous studies (see Narayan 1991, Robles and Ruggero 2001 and Siegel *et al.* 2005). Is there a mechanical property of the BM or of the cochlea that could explain the different reaction between high and low frequencies? It has been shown that the scaling symmetry does not hold over the entire frequency range. This results in a change in the excitation pattern shape. If the BM is excited over a larger area, then – according to CRF theory - it is more likely that the OAE generators (wherever they precisely are) will cancel each other’s contribution to the backward travelling wave. The consequence of such cancellation would be a less detectable waveform and a waveform rising from a more basal area (lower latency) might be wrongly assigned to the OAE burst.

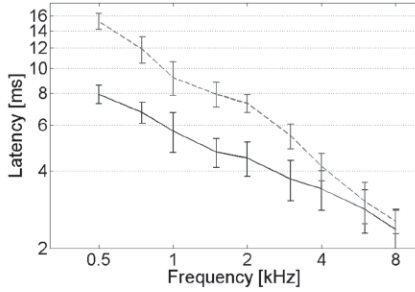


Fig. 5: Comparison between τ_{OAE} (dashed line) and $\tau_{BM} + \tau_{BMfront}$ (solid line). After about 4 kHz the slope of the two curves do not statistically differ, meaning that the prediction suggested by the signal-front hypothesis holds at these high frequencies.

It should moreover be noted that the breaking of the curve is more pronounced for the OAE curve than for the τ_{fwd} one (Fig.3, right panel). The divergence of the two curves at high frequencies can be an effect of the active mechanism on the BM. It could be that, due to the difference in filter shapes, the OAEs are actually generated in a region basal to the CF place. Since the synchronization of the neural population occurs at the CF place, ABRs latencies are therefore not deviated as much as the OAEs latencies.

An alternative to the CRF theory is the signal-front hypothesis (hypothesis IA of Ruggero, 2004). This suggests $\tau_{OAE} = \tau_{BM} + \tau_{BMfront}$, where the signal front delay, $\tau_{BMfront}$, represents the time between the stimulus onset and the start of the BM oscillations. An estimate of $\tau_{BMfront}$ made from human cadavers is given by Ruggero (2007). Figure 5 shows the averaged τ_{OAE} plotted against τ_{fwd} (averaged from ABR measurements) + $\tau_{BMfront}$ (Ruggero, 2007) on loglog axes. Similar ANOVA tests as discussed above were carried out (not shown here), where no statistical difference between the slopes above 4 kHz was observed for any subject. Below this the signal-front hypothesis tends to under predict the τ_{OAE} .

This analysis here suggests that the CRF theory holds at low frequency ($f < 2\text{kHz}$), this reinforces the prediction for the OAE delay being twice the delay of the forward travelling wave, $\tau_{OAE} = 2\tau_{fwd}$, below 2kHz only. The signal-front hypothesis holds for high frequencies ($f > 4\text{kHz}$) confirming the idea of a fast backward travelling wave. This seems to reflect a difference in the generation mechanisms of the OAE between the base and the apex of the cochlea. The present results are in contradiction with previous studies that showed a deviation from $\tau_{OAE} = 2\tau_{BM}$ at low frequencies (Siegel *et al.*, 2005, Shera and Guinan 2003). The differences in the experiments could, to some extent, explain this variation. On the one hand, data are collected from animals comparing stimulus frequency OAE with BM vibration or auditory-nerve fibres, which requires surgical invasion that can lead to cochlear fluid leakage and dramatic changes of the BM properties. On the other hand the recordings of TBABR and TBOAE on humans are non invasive and more indirect. More generally, the discrepancy of the results highlights the difficulty of predicting the exact behaviour of the cochlea.

SUMMARY

No invasive measurements on living human cochlea have been reported so far. Any attempt to describe the behaviour of the cochlea is based on psychophysical data in humans or in vivo measurement in animals. Measuring ABR and OAE offer the opportunity to remotely record the activity of the cochlea. The present study showed that both measurements are reliable and are good indicator for the BM mechanics. This study also brings proofs about a possible change in the cochlear processing above and below 2 kHz. The results support the CRF theory ($\tau_{\text{OAE}}=2 \tau_{\text{BM}}$) at frequencies less than 2 kHz, while they are more in line with the signal front hypothesis ($\tau_{\text{OAE}}= \tau_{\text{BM}}+ \tau_{\text{BMFront}}$) at high frequencies (> 4 kHz). The present study focuses more on the OAE generation mechanism and further work would be needed to model the ABR generation process.

REFERENCES

- Zweig, G., and Shera, C. (1995). "The origin of periodicity in the spectrum of evoked otoacoustic emissions," *J. Acoust. Soc. Am.*, 98, 2018-2047.
- Ulehlová, L., Voldrich, L., and Janisch, R. (1987). "Correlative study of sensory cell density and cochlear length in humans," *Hear Res*, 28, 149-151.
- Pigasse, G., Harte, J. M., and Dau, T. (2006). "Individual cochlear delays measured with tone-burst-evoked otoacoustic emissions," XXVIIIth International Congress of Audiology, Innsbruck 3-7 September 2006.
- Don, M., Ponton, C. W., Eggermont, J. J., and Masuda, A. (1993). "Gender differences in cochlear response time: an explanation for gender amplitude differences in the unmasked auditory brain-stem response," *J Acoust Soc Am*, 94, 2135-2148.
- Norton, S., and Neely, S. (1987). "Tone-burst-evoked otoacoustic emissions from normal-hearing subjects," *J. Acoust. Soc. Am.*, 81, 1860-72.
- Greenwood, D. (1990). "A cochlear frequency-position function for several species-29 years later," *J. Acoust. Soc. Am.*, 87, 2592-2605.
- Kim, D. O., and Molnar, C. E. (1979). "A population study of cochlear nerve fibers: comparison of spatial distributions of average-rate and phase-locking measures of responses to single tones," *J Neurophysiol*, 42, 16-30.
- Don, M., and Eggermont, J. J. (1978). "Analysis of the click-evoked brainstem potentials in man using high-pass noise masking," *J. Acoust. Soc. Am.*, 63, 1084-1092.
- Neely, S., Norton, S., Gorga, M., and Jesteadt, W. (1988). "Latency of auditory brainstem responses and otoacoustic emissions using tone-burst stimuli," *J. Acoust. Soc. Am.*, 83, 652-6.
- Don, M., Ponton, C. W., Eggermont, J. J., and Masuda, A. (1994). "Auditory brainstem response (ABR) peak amplitude variability reflects individual differences in cochlear response time," *J Acoust Soc Am*, 96, 3476-3491.
- von Békésy, G. (1960). "Experiments in Hearing," McGraw Hill, New York
- Siegel, J. H., Cerka, A. J., Recio-Spinoso, A., Temchin, A. N., Van Dijk, P., and Ruggero, M. A. (2005). "Delays of stimulus-frequency otoacoustic emissions and cochlear vibrations contradict the theory of coherent reflection filtering," *J. Acoust. Soc. Am.*, 118, 2434-2443.

- Narayan, S. S. (1991). "Comparison of latencies of N1 and transient evoked otoacoustic emissions: An evaluation of reverse travel in the cochlea," Purdue University.
- Robles, L., and Ruggero, M. A. (2001). "Mechanics of the mammalian cochlea," *Physiol Rev*, **81**, 1305-1352.
- Ruggero, M. A. (2004). "Comparison of group delays of $2f(1)-f(2)$ distortion product otoacoustic emissions and cochlear travel," *ARLO*, **4**, 143-147.
- Ruggero, M. A. (2007). personal communication.
- Shera, C. A., and Guinan, J. J. (2003), "Stimulus-frequency-emission group delay: A test of coherent reflection filtering and a window on cochlear tuning," *J. Acoust. Soc. Am.*, **113**, 2762-2772.

