Deriving a Cochlear Transducer Function from Low Frequency Modulated Cochlear Microphonic

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Background & Objectives: Recently, a new method was developed to construct a cochlear transducer function from the summating potential using a low-frequency bias tone. In this study, another method to derive a cochlear transducer function (fTr) from the cochlear microphonic (CM) using the same low frequency modulation technique was introduced and compared to the fTr obtained from the summating potential (SP). Before real experiment, mathematical exploration and computer simulation suggested that the CM magnitude is essentially proportional to the first derivative [fTr(1)] of the fTr. Methods: Two probe tones (6 or 12 kHz) ranging from 70 to 90 dB SPL in 10 dB step and a 25 Hz bias tone with a high level (130 dB SPL) were simultaneously presented to record the CM from an electrode placed on the round window at gerbils. After band-pass filtering to remove the low frequency CM responses, the modulation envelope of the CM was obtained. Results: Results showed that the CM modulation envelope as a function of the bias levels has a shape similar to the fTr(1) as shown in the simulation. Furthermore, when the cochlear transducer function derived from the CM was compared to those obtained from the SP previously described by Choi et al. (2004), there were significant differences between the Boltzmann functions fitted to the CM and SP responses. Discussion & Conclusion: This study showed another method to derive a cochlear transducer function from the cochlear microphonic using a low-frequency bias tone. However, there were differences between cochlear transducer functions derived from CM and SP. The most significant difference was the dynamic range in the cochlear transducer function from the CM greater than those from SP. The cochlear transducer function obtained from the CM was more symmetric than those from the SP. These features in the cochlear transducer function from the CM may reflect the origin of outer hair cells (OHCs). Therefore, the major difference between the cochlear transducer functions obtained from the CM and the SP may result from different contribution of the inner hair cells (IHCs) and OHCs. (Korean Journal of Communication Disorders 2010;15;232-250)

Key words: cochlear microphonic, summating potential, cochlear transducer function, inner hair cells, and outer hair cells.

I. Introduction

Normal hearing requires the presence of a cochlear amplifier for dramatic improvement in hearing sensitivity and frequency selectivity. Two transduction processes are necessary for cochlear amplification. The first process, mechano-electrical transduction (MET) is the transformation of acoustical energy into electrical signal via the ion channels located within the stereocilia at the apex of the
sensory hair cells. Deflections of the stereocilia due to sound-induced vibrations of the cochlear partition open the transduction channels to depolarize the hair cells by allowing the entries of $K^+$ and $Ca^{2+}$ ions (Howard & Hudspeth, 1988; Hudspeth, 1982). The second process is a reverse transduction in which electrical activities within the hair cells can produce mechanical movement of the cell structures to boost the sound-induced vibrations of cochlear partition. In mammals, this mechanical feedback is mediated by the electromotility of the outer hair cells (OHCs) which refers to the changes in OHC lengths in response to variations in the receptor potentials (Brownell et al., 1985). Force production from the conformational change in the OHC lateral membrane is critical for the cochlear amplifier. However, this mechanical feedback is driven by the receptor potential changes generated from the MET. Cochlear MET demonstrates an asymmetrical, and compressive nonlinearity which is often represented by a second order Boltzmann function (Hudspeth, 1982, Fig. 1)

\[
f_{Tr}(x) = \frac{A}{1 + e^{(bx+c)[1 + e^{(dx+e)}]}}, \tag{1}
\]

This function describes a nonlinear cochlear transducer functions $f_{Tr}$ and their first and second derivatives $f_{Tr}'$ and $f_{Tr}''$. The parameter values used to obtain the Boltzmann function and its derivatives are as the following: $A=0.88$, $b=-5$, $c=-0.8$, $d=0.07$, and $e=8$. The outputs were normalized to 1.

<FIG. 1> A second-order Boltzmann function

where $f_{Tr}(x)$ is the hair-cell receptor current, $x$ is the stereociliary displacement, $A$ is the maximal conductance, constants $b$ and $d$ are related to the slope of $f_{Tr}$ or the sensitivity of the transduction, and $c$ and $e$ are constants related to the resting position of the stereocilia. Such a function representing hair cell transduction is also termed a cochlear transducer function ($F_{Tr}$).

In vivo, cochlear MET can be characterized by the cochlear microphonic (CM), which can be recorded at the round window (RW) as a spatial summation of OHC receptor currents from the cochlear base. The cochlear $F_{Tr}$ can be derived from low-frequency evoked CM that is sensitive to changes in cochlear mechanics or hair cell physiology induced by ATP, tetrodotoxin (TTX), transient hypoxia, and endolymphatic hydrops (Bobbin & Salt, 2005; Kirk, Moleirinho & Patuzzi, 1997; Patuzzi, 1995; Sirjani et al., 2004). Since the cochlear transduction processes are highly nonlinear, measuring distortions in the cochlear responses can also be used to obtain the cochlear $F_{Tr}$. With a low-frequency modulation technique, acoustic distortion products, including cubic difference tone ($2f_1-f_2$) and quadratic difference tone ($f_2-f_1$), were used to obtain the cochlear $F_{Tr}$ (Bian, 2004; Bian, Chertoff & Miller, 2002; Lukashkin & Russell, 2005). The cochlear $F_{Tr}$ derived from these methods are associated with the transfer characteristics of the OHCs.

Estimating the functional status of another category of cochlear sensory cells, the inner hair cells (IHCs), would be useful in differentiating inner ear pathology. The summating potential (SP), a dc component in the cochlear electrical response recorded from the round window (RW), is shown to have a major contribution from the IHCs for high frequency inputs presented at moderate levels (Durrant et al., 1998; van Emst, Giguere & Smoorenburg, 1998; Zheng, et al., 1997). Therefore, attempting to derive a cochlear $F_{Tr}$ from the SP may provide an estimate of IHC function. Recently, a cochlear $F_{Tr}$ was constructed from the SP using the low-frequency modulation technique.
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(Choi et al., 2004). The cochlear \( F_{Tr} \) obtained from the SP showed noticeable differences from that derived from the acoustic distortion products (Bian, Chertoff & Miller, 2002). It is speculated that the two kinds of \( F_{Tr} \) could have different physiological origins. However, these different results may also come from the difference in the signals, because one is a dc electrical potential recorded from the RW, the other is an acoustic signal in the ear canal. The purpose of this study was to obtain a cochlear \( F_{Tr} \) from the ac component of the RW potential or the CM. Subsequently, the results obtained from the CM were compared with the \( F_{Tr} \) derived from the SP.

1. Deriving a cochlear \( F_{Tr} \) from the CM

Low-frequency biasing can be used to estimate a cochlear \( f_{Tr} \) because it can modulate the cochlear response by shifting the operating point (OP) and varying the gain of the cochlear transducer. The modulated response is proportional to the proper derivative of the \( F_{Tr} \) depending on the type of response. In response to a pure tone, the CM is an ac potential primarily at the frequency of the stimulus. It can be shown that the variation of the ac component or the CM amplitude relates to the first derivative of a cochlear \( f_{Tr} \). For a nonlinear \( f_{Tr} \), its output can be estimated with a Taylor’s series expansion around an arbitrary OP with a value of \( x_0 \):

\[
f_{Tr}(x) = \sum_{n=0}^{\infty} a_n(x_0) \cdot (x - x_0)^n
\]  

(2)

where \( a_n = f_{Tr}^{(n)}(x_0) / n! \), and \( f_{Tr}^{(n)}(x_0) \) is the nth derivative of \( f_{Tr} \) at \( x_0 \) or the OP which can be varied by a bias tone. If a probe tone \( (x_p = L \cdot \cos \Theta) \) is used as input, the output is determined by the transfer characteristics of the \( f_{Tr} \) at the OP set by the bias tone. Therefore, with a total input of \( x = x_p + x_0 \), the output of the cochlear \( f_{Tr} \) is in the following form

\[
f_{Tr}(x_0) = \sum_{n=0}^{\infty} a_n(x_0) \cdot (L^n \cos^n \Theta)
\]  

(3)

The power spectrum of these related sinusoids can be expanded in a Fourier series

\[
f_{f}(x) = \sum_{n=0}^{\infty} B_n(x_0) \cdot L^n \cos(n \Theta) = \sum_{n=0}^{\infty} B_n(x_0) \cdot L^n \cos(2n \Theta).
\]  

(4)

where the first terms involves only the even multiples of \( \Theta \), the second term indicates the odd multiples of \( \Theta \). \( B_{2n} = a_{2n}(x_0) \cdot (2/2n) \), \( B_{2n-1} = a_{2n-1}(x_0) \cdot (2/2n-1) \), here \((2/2n)\) and \((2/2n-1)\) are binomial coefficients. The CM in response to the probe tone is associated with the fundamental frequency \( \Theta \) that is produced by all the odd components in Eq. (4). Therefore, the amplitude of CM response can be represented by the following series involving the products of \( B_{2n-1} \) and \( L^{2n-1} \):

\[
CM(x_0) = \sum_{n=1}^{\infty} \frac{a_{2n-1}(x_0)(2n-1)}{2^{2n-2}} L^{2n-1}
\]  

(5)

Replacing \( a_{2n-1}(x_0) \) with its original form, the above equation can be expanded as a power series relating to the amplitude of probe tone (\( L \)):

\[
CM(x_0) = f_{Tr}^{(1)}(x_0)L + \frac{1}{8} f_{Tr}^{(3)}(x_0)L^3 + \frac{1}{192} f_{Tr}^{(5)}(x_0)L^5 + \ldots
\]  

(6)

Therefore, the CM amplitude at \( x_0 \) is determined by the first and other odd derivatives of the \( f_{Tr} \). Eq. (6) also indicates that the term of first derivative is predominant when the probe tone level is small \((0 < L < 1)\). In this case, the higher order terms can be neglected when estimating the CM amplitude, i.e.,

\[
CM(x_0) \approx f_{Tr}^{(1)}(x_0)L.
\]  

(7)
Only two cycles of a low frequency bias tone (25 Hz) were shown in the temporal domain (t=0.08 s).

In a whole cycle (t=0.04 s), the label “up” indicates the monotonic increase (t=0.02 s) in bias tone pressure while “down” means the decrease (t=0.02 s). The responses of the bias tone only and a bitonal stimulus consisting of the bias tone and a high frequency probe tone (6 kHz) sent to the Boltzmann function were shown in panels (A) and (B), respectively. These were obtained using the real parameter values as shown in Fig.1. The response of Panel (B) was band pass filtered with center frequency of 6 kHz to obtain the CM in response to only the high frequency probe tone [Panel (C)]. Finally, the CM modulation envelope was obtained [Panel (D)]. Panels (C) and (D) was normalized to 1 for relative comparison. The high correlation coefficient ($r^2=0.99$) between the CM modulation envelope (solid line) and the first derivative (opened circles) indicates that the CM is highly proportional to the first derivative.

*FIG. - 2* First computer simulation deriving a cochlear transducer function from the CM
For fixed $L$, the magnitude of the CM is proportional to the first derivative of the $f_{Tr}$ at the designated OP.

2. Simulation

The relation between the CM and the $f_{Tr}^{(1)}$ in Eq. (7) was explored in two computer simulations. The first simulation describes a method to construct a $F_{Tr}$ from the CM (Fig. 2).

A low frequency bias tone (25 Hz) and a bitonal stimulus consisting of the bias tone and a high frequency probe tone (6 kHz) were sent to the Boltzmann function [Eq. (1)], respectively [panels (A) and (B)]. The response obtained from the bitonal stimulus was band-pass filtered at 6 kHz to obtain the CM whose magnitude was modulated by the bias tone [panel (C)]. The CM modulation envelope was obtained as the magnitude of the analytic signal obtained from a Hilbert transform [panel (D)]. In each panel, the temporal windows labeled “up” and “down” indicate the monotonic increase or decrease in bias tone pressure within one half cycle, respectively. The CM envelope corresponding to the “down” phase of the biasing was flipped to be consistent with the direction of biasing pressure change in the “up” phase. The CM envelopes were curve-fitted to the $f_{Tr}^{(1)}$ using a least-squared method (SigmaPlot version 9.0.1). The correlation coefficient ($r^2$) between the CM envelope and the $f_{Tr}^{(1)}$ was 0.99 suggesting that the CM envelope had a similar shape with the $f_{Tr}^{(1)}$ (Fig. 2).

The second simulation showed the contribution of the first derivative term to the CM relative to a total contribution of the first 20 terms of the series in Eq. (6) at probe tone levels ($L$) ranging from 0.02 Pa (60 dB SPL) to 2 Pa (100 dB SPL).

As shown in panel (A) of Fig. 3, the CM magnitude was mainly determined by the first derivative below 0.6 Pa (90 dB SPL). However, for $L$ above 100 dB SPL, the CM magnitude was affected by the higher-order terms and the contribution of the first derivative declined. Therefore, the simulations confirm that at low $L$, the CM is proportional to the $f_{Tr}^{(1)}$. In addition, the $r^2$ between the CM and the $f_{Tr}^{(1)}$ shown in panel (B) was also affected by probe tone level ($L$). With the $L$ decreasing from 1 to 0.1, the $r^2$ approaches 1. Below 0.6 Pa (90 dB SPL), the coefficient was over 0.95. This is very consistent with the result of panel (A). Both simulations indicate that a cochlear $f_{Tr}$ can be derived from the CM with a small probe tone and a bias tone.
II. Method

1. Animal preparation and data acquisition

Animal preparation, experimental procedure, data acquisition and analysis used in this study were the same as reported previously by Choi et al. (2004). Before the main experiment, compound action potential (CAP) thresholds in response to tone bursts were obtained at frequencies of 1, 2, 4, 8, 16 kHz. The animals showing hearing thresholds below 30 dB SPL across the whole frequency range were included for this study. A total of 8 Mongolian gerbils (Meriones unguiculatus) were used as subjects. Animals were sedated with pentobarbital (64 mg/kg), the right pinna was removed and bulla was opened by a dental drill. A silver wire electrode was placed at the RW niche and a needle electrode inserted into the neck served as ground. A cotton wick was used to absorb the fluid at the RW niche.

Acoustic signals consisting of a probe tone and a bias tone were generated from an array processor (Tucker-Davis Technology, TDT AP2) and downloaded to a 16-bit D/A converter (TDT, DA3-4). The outputs of the D/A were routed to two attenuators (TDT PA4). The probe tone was presented with a probe-tube headphone (Etymotic ER-3A) that was attached to a speculum sealed to the animal’s bony ear canal. The bias tone was sent through a subwoofer (Paradigm Servo-15) to the bony ear canal via a silicon tube. A probe microphone (Etymotic ER-7C) placed approximately 5 mm from the umbo of the tympanic membrane was used for monitoring the signal level.

A probe tone at frequencies of 6 and 12 kHz was presented at levels ranging from 70 to 90 dB SPL in 10-dB increments. The bias tone was presented at 25 Hz with amplitude decreasing from 70 (130 dB SPL) to 0 Pa in 21 steps. Only experimental data at the highest bias level (130 dB SPL) were used for analysis in this paper because it shows saturation of the cochlear transducer function. The duration of the signals was 250ms. Both the probe tone and the bias tone were simultaneously presented. The electrophysiologic responses recorded from the RW electrode were amplified 5000 times through two amplifiers [Stanford (SR560) and Stewart (VBF 10)], low-pass filtered at 16 kHz (54 dB/octave), and digitized at 65.536 kHz (TDT, AD2).

2. Data Analysis

The cochlear responses were analyzed using MATLAB (MathWorks). The RW electrical signal was band-pass filtered with a bandwidth of 200 Hz centered at the probe tone frequencies (6 and 12 kHz) and the CM envelope was obtained with Hilbert transform. Similar to the simulation in the previous section, a least-square curve fitting technique was used to derive the cochlear $F_{Tr}$ from the CM envelopes within half cycle of the bias tone. The accuracy of the curve fitting was assessed by the $r^2$ between the CM envelope and the $f(1)^\nu$. The effect of the probe tone intensity and frequency on the parameter values of the cochlear $F_{Tr}$ and the $r^2$ was analyzed by ANOVA (SPSS 14.0). In addition, we investigated the effect of the CM envelopes corresponding to upward and downward biasing of the bias tone on the parameter values.

It is previously shown that the low-frequency modulated dc component of the electrical response from the RW or the SP is proportional to the second derivative of a cochlear $F_{Tr}$ (Choi et al., 2004). To test if the $F_{Tr}$ obtained from the CM and SP were the same at the same signal condition, a paired samples $t$ test was used to compare the Boltzmann parameters derived from these two types of electrical potentials. A $p$-value less than 0.05 was considered a statistically significant difference.

III. Results

1. CM magnitudes

An example of the CM waveforms evoked by the bias tone at 130 dB SPL and the bitonal stimulus
The cochlear responses to bias tone and bitonal stimulus, the band-pass filtered responses, and the CM modulation envelope are shown. The cochlear responses to the bias tone (25 Hz) with 70 Pa (130 dB SPL) and the bitonal stimulus consisting of the bias tone and a high frequency probe tone (6 dB SPL) with a signal level (70 dB SPL) were shown in panels (A) and (B), respectively. The duration of the signals was 0.25 s. The third cycle out of five biasing cycles, the most stable one, was used for analysis. The labels “up” and “down” correspond to the half up and down part in a cycle of the cochlear biasing response, respectively. The band pass filtered CM with the center frequency of probe tone (6 kHz) and the CM modulation envelope obtained from Hilbert transform were displayed in panels (C) and (D). These data were normalized to 1 for comparison.

<FIG. - 4> Cochlear responses
These functions were obtained from seven or eight animals. Three different levels (90, 80 and 70 dB SPL) of a high frequency probe tone (6 kHz) were shown for both “up” [panels (A), (B), and (C)] and “down” [panels (D), (E), and (F)] parts. The CM envelope at “down” part [panel (D) of Fig. 4] was flipped to show the same direction with that of “up” part. The CM magnitude was normalized to 1.

<FIG. 5> Individual CM-bias functions at 6 kHz
These functions were obtained from eight animals. Three different levels (90, 80 and 70 dB SPL) of a high frequency probe tone (12 kHz) were shown for both “up” [panels (A), (B), and (C)] and “down” [panels (D), (E), and (F)] parts.

<FIG. – 6> Individual CM-bias functions at 12 kHz.
The mean and standard deviation (s.d.) of the five parameters of the $f_{Tr}(x)$ across the animals when the first derivative of $f_{Tr}(x)$ was fit to the CM data and the correlation coefficient ($r^2$) between the CM and the first derivative.

### Table 1: Curve fitting results during “up” part

<table>
<thead>
<tr>
<th>Frequency (kHz)</th>
<th>Mean CM (Up)</th>
<th>Fitted CM (Up)</th>
<th>Mean CM (Down)</th>
<th>Fitted CM (Down)</th>
</tr>
</thead>
<tbody>
<tr>
<td>60</td>
<td>0.60 ± 0.45</td>
<td>0.41 ± 0.36</td>
<td>0.59 ± 0.46</td>
<td>0.39 ± 0.35</td>
</tr>
<tr>
<td>80</td>
<td>0.30 ± 0.24</td>
<td>0.21 ± 0.15</td>
<td>0.29 ± 0.24</td>
<td>0.20 ± 0.15</td>
</tr>
</tbody>
</table>

They were obtained by fitting the mean CM-bias functions to the first derivative using a curve fitting method at 6 kHz [panels (A), (B), and (C)] and 12 kHz [panels (D), (E), and (F)]. Both mean CM and fitted CM were displayed for both “up” and “down” parts. The correlation coefficients ($r^2$) between the CM and $f_{Tr}^{(1)}$ were very high (above 0.96) indicating that the CM are well fitted to $f_{Tr}^{(1)}$. As the results of this curve fitting, the values of the second-order Boltzmann function parameters were obtained and shown at Table 1 and 2.

<FIG. 7> Mean CM-bias functions and curve fitted CM-bias functions for both “up” and “down” parts.
are shown in Fig. 4 (A) and (B), respectively.

In each panel, the CM responses show five biasing cycles with similar amplitude. Among these biasing cycles, only the data within the third cycle (indicated by the dashed lines) were analyzed because the bias tone pressure was most stable during the middle of the signal. Panel (C) illustrates the band-pass filtered CM centered at the probe tone frequency, 6 kHz. The envelope of the filtered CM was obtained from Hilbert transform [panel (D)]. Both the band-pass filtered CM and the envelope were normalized to 1 for comparison between different probe tone levels. After the beginning portion of the signal where the bias tone was delayed due to the silicon tube that guides the sound to the ear canal, the 6 kHz-CM amplitude was large and stable. As the biasing pressure builds up, it can be observed that the magnitude of the band-passed CM varies regularly with the bias tone. During one biasing cycle, the CM magnitude peaked twice and each peak occurred in the middle of the “upward” or “downward” slope of the bias tone (between the dashed lines). When the CM response reaches the extreme in either direction [panels (A) and (B)], the CM amplitude shows a minimum [panels (C) and (D)].

It is noticeable from Fig. 4 (D) that the envelope of the filtered CM within one half biasing cycle (between the dashed lines) is similar to the first derivative of the Boltzmann function shown in Fig. 1. However, the CM envelope during “upward” going bias is a mirror image of the envelope during “downward” biasing with different magnitudes. For a direct comparison in further analysis, the CM envelope for “downward” biasing was flipped so that the direction of biasing became “upward”. At the probe frequency of 6 kHz, each CM modulation envelope from eight animals for both “up” and “down” parts was plotted as a function of the instantaneous bias tone pressure at three different signal levels (70, 80, and 90 dB SPL) [Fig. 5].

These CM-bias functions are generally similar to the bell-shaped first derivative of the Boltzmann function. The vertex of the curve is located around zero Pa bias tone pressure. The slope in the negative sound pressures is steeper than the opposite side and the cochlear $F_T$ is asymmetrical. The shapes of the CM-bias functions also showed a dependency on probe tone level. When the probe level increased, the overall magnitude of the CM envelope is compressed and the peaks of the CMare smoother. This phenomenon also was observed for the probe frequency of 12 kHz (Fig. 6).

### 2. Deriving a Boltzmann function from CM

The CM-bias functions obtained from the experimental animals were fit individually to a function that represents the first derivative of a second-order Boltzmann function using the formula given by Bian et al. (2002). The values of the Boltzmann function parameters were obtained from the best fit. The mean and standard deviation (s.d.) of the cochlear $F_T$ parameters derived for all the animals

| kHz | dB SPL | $|A|$ | $b$ | $c$ | $d$ | $e$ | $r^2$ |
|-----|--------|------|------|------|------|------|------|
| 6   | 90     | 6.90 ± 1.40 | 1.45 ± 0.24 | .47 ± 0.45 | -.82 ± .40 | -.71 ± .40 | .98 ± .00 |
|     | 80     | 4.49 ± 1.00 | 2.54 ± .39  | .75 ± .57  | -1.48 ± .72 | -1.04 ± .45 | .98 ± .00 |
|     | 70     | 4.14 ± .84  | 1.83 ± .59  | .99 ± .35  | -.15 ± .97  | -.02 ± .38  | .98 ± .00 |
| 12  | 90     | 6.24 ± .55  | 1.25 ± .08  | .37 ± .29  | -.90 ± .11  | -.37 ± .25  | .97 ± .00 |
|     | 80     | 4.38 ± .77  | 1.71 ± .32  | 1.13 ± .41  | -.84 ± .32  | -.92 ± .27  | .98 ± .00 |
|     | 70     | 3.05 ± .30  | 1.71 ± .40  | .75 ± .39  | -.01 ± .74  | .25 ± .58  | .99 ± .00 |

Mean ± S.D.

The mean and standard deviation (s.d.) of the five parameters of the $f_T(x)$ across the animals when the first derivative of the $f_T(x)$ was fit to the CM data and the correlation coefficient ($r^2$) between the CM and the first derivative.
These functions were derived from the parameter values obtained from the fitted first derivative at three levels (90, 80 and 70 dB SPL) of two high frequency probe tone (6 and 12 kHz) at both “up” and “down” parts, respectively. The mean data were obtained from averaging the “up” and “down” parts. There were no significant difference among up, down, and mean parts.

<FIG. 8> Second-order Boltzmann functions
under different signal conditions are reported for the “up” and “down” biasing phases (Table 1 and 2).

As indicated in Fig. 7, the first derivatives of the Boltzmann function fit the CM-bias level data very well since the averaged $r^2$ of the fits from all the animals are 0.95 for the two probe tone frequencies and three probe tone levels.

The characteristics of the cochlear $F_{T_{h}}$ under different signal conditions can be implied from examining the Boltzmann parameters obtained from the curve-fitting. Based on post-hoc testing, parameter $A$, the maximal CM magnitude, is probe tone level dependent for the “up” and “down” biasing phases at both 6 and 12 kHz. When the probe tone level rose, the absolute value of $A$ increased. Parameters $b$ and $d$ are the indicators of the slope or sensitivity of the cochlear $F_{T_{h}}$ in the negative and positive sound pressures ranges. When the probe tone level increased, the values of $b$ decreased at only “up” biasing phase while the values of $d$ increased at only “down” biasing phase at 12 kHz. For different signal conditions, values of $b$ and $d$ were positive while those of $d$ were negative. In addition, the absolute values of $b$ were greater than those of $d$. The difference between $b$ and $d$ values is relatively small suggesting that the cochlear $F_{T_{h}}$ is symmetrical. Parameters $c$ and $e$ indicate the off-set or the resting position of the cochlear transducer. Parameter $c$ is level dependent for only the “up” phase at 6 kHz. When the probe tone level increased, the values of $c$ decreased. Values of $c$ were positive while those of $e$ were negative. These off-set parameters seemed to shift to the negative values or in the negative sound pressure direction when probe tone level increased. The probe tone level dependency is more distinct at the “up” phase than the “down” phase at both frequencies.

Cochlear $F_{T_{h}}$ for the “up” and “down” biasing phases can be plotted from the Boltzmann parameters obtained from curve fitting (Fig. 8).

Since there is no significant difference in the cochlear $F_{T_{h}}$ among “up” and “down”, a mean cochlear $F_{T_{h}}$ was obtained by averaging the “up” and “down” phases. The $F_{T_{h}}$ demonstrate a compressive nonlinearity with a steep slope around 0 Pa and saturations beyond ±5 Pa. The overall output or dynamic range of the $F_{T_{h}}$ showed level-dependency. At the lower probe tone frequency (6 kHz), the dynamic range varied from about 1.3 to 1.8 mV within a 20 dB increase in the probe-tone level from 70 to 90 dB SPL. For each probe tone level, the dynamic ranges of the $F_{T_{h}}$ at 12 kHz probe tone frequency were smaller than those at 6 kHz. Although there were the small differences at the shape of the $F_{T_{h}}$ in the positive sound pressure direction, the shapes of the $F_{T_{h}}$ Boltzmann functions at 6 kHz are very similar to those of 12 kHz.

**IV. Discussion and Conclusion**

1. **CM amplitude modulation by bias tone**

The results demonstrate that the CM amplitude can be modulated by a low frequency bias tone. The CM magnitude is minimized when the cochlear partition is shifted to its extreme displacements in either direction by the bias tone. The CM magnitude is largest with the biasing sound pressure crosses zero that corresponds to the middle portion of the $F_{T_{h}}$ where the gain is maximal. This indicates that the modulated CM responses are proportional to the first derivative or the slope of the $F_{T_{h}}$. The modulated CM responses are consistent with the findings of Nieder & Nieder(1968a, 1968b, 1971) who first studied the characteristics of the cochlear transfer function by using the low-frequency modulation technique and displayed double modulation, two peaks of CM amplitudes consisting of “up” and “down” parts, in one bias tone cycle.

In addition, the present study used only the highest intensity (130 dB SPL) of the bias tone that was able to investigate the effects of the “up” and “down” parts on the modulated CM responses. Nieder & Nieder’s (1968b) showed that there are two maxima and two minima per cycle of the low frequency bias tone at higher intensities and one maximum and one minimum per cycle of the bias
tone at lower levels. It is interesting to note that the modulated envelopes for the “up” part are much shaper than those for the “down” part showing smooth bell shaped envelopes. However, there were no statistically significant differences in the modulated CM envelopes between the “up” and “down” parts. This is not consistent with the findings of Nieder & Nieder (1968b) and Bian (2004) showed a hysteresis loop between the “up” and “down” parts. This difference may result from different signal conditions, experimental designs, and analysis methods.

2. Effects of probe tone level

Mathematical theory showed that the probe tone level should be small enough and the computer simulation suggested that when the probe tone level is below 90 dB SPL, the CM and the first derivative of the cochlear transducer function are highly correlated to each other. When the probe tone level of 66 dB SPL was used, Nieder & Nieder (1968a, 1968b) reported smaller and more variable amplitudes of the modulated CM that limit the accurate estimation of the modulated CM. Therefore, the present study used the probe tone levels ranging from 70 to 90 dB SPL. With the increasing probe tone levels, the correlation coefficient at lower probe tone level was slightly smaller than that of the higher levels, which are consistent with the fact that more variability presents at lower probe tone level than at the higher levels.

The experiment results of the present study show that the shape of the CM-bias function is dependent on the probe tone level. As the probe tone level changes, two trends can be observed: changes in the width of the center peak of the CM modulation envelop and the CM modulation depth indicated by the difference between the maximum and minimum. As the probe tone level increases, the strength of the bias tone to modulate the CM response is reduced, which indicates the magnitude reduction is smaller at the maximal biasing. Therefore, the sharpness of the center peak of the CM modulation envelope decreases with probe tone level. This is consistent with the findings of Nieder & Nieder (1968b). This was not observed in the work of Choi et al. (2004) that reported the increasing SP modulation depth for the increasing probe tone level. This difference may be due to the methods to obtain the SP and CM magnitudes. The present study obtained the CM modulation with band-pass filtering by normalizing to 1 whereas the SP magnitude was obtained from subtracting the cochlear response to bias tone alone response from the response to bitonal stimulus without normalization.

3. Cochlear transducer function

Fitting the CM modulation envelop to the first derivative of the Boltzmann function, the parameter values of the $F_{Tr}$ were derived. The Boltzmann parameters are important because they provide a quantitative measure of the cochlear MET. The most prominent effect of these parameters is the dependence of the maximal conductance parameter $A$ on the probe tone level. When the probe level increased, parameter $A$ increases suggesting that the dynamic range (peak-to-peak amplitude) of the $F_{Tr}$ enlarges. This is in agreement with the results of other studies showed that the dynamic range at higher signal levels is greater than that of the lower levels (Patuzzi & Moleirinho, 1998; Bian & Chertoff, 1998; 2001; Bian, Chertoff & Miller, 2002; Choi et al., 2004).

The slope or sensitivity of the Boltzmann function is represented by the parameters, $b$ and $d$. The difference between $b$ and $d$ is 0.95 under all experimental conditions indicating a small asymmetry of the cochlear $F_{Tr}$. It is observed in vivo that the electrical responses from the hair cells show greater nonlinear compression (saturation) in the negative sound pressure direction than in the opposite direction (Cody & Russell, 1987; Dallos & Cheatham, 1989). The positive sound pressure corresponds to the low frequency biasing of the basilar membrane towards scala tympani (ST) resulting in an
increase in opening probability of the stereocilial transduction channels (Patuzzi, 1995). Greater opening probability corresponds to the depolarizing phase of the hair cell transduction. Therefore, the receptor potential of the hair cells generated at the depolarizing phase is greater than the hyperpolarizing phase.

The off-set parameters $c$ and $e$ of the Boltzmann function indicate that the resting position of the transducer or the inflection of the $F_{Tr}$ shift in the negative sound pressure direction at higher signal levels. A change in the resting position may come from difference in a mechanical displacement of the organ of Corti and/or hair bundle or an electrostatic influence at the transduction channel itself (Patuzzi, 1995). In any case, shifting of the resting position or inflection point in the negative sound pressures results in desensitization of the cochlear transducer (Bian, 2004) since the mechanical input without biasing will encounter a smaller gain (slope) on the $F_{Tr}$. These adjustments of the transfer characteristics of the hair cells could result from the adaptation of the transduction channels. Therefore, the parameters of the sensitivity and the resting position could be used to monitor the adaptation processes in the hair cell current production (Howard & Hudspeth, 1988; Crawford, Evans & Fettiplace, 1989).

4. Comparison with cochlear $F_{Tr}$ derived from the SP

The cochlear $F_{Tr}$ obtained from averaging the “up” and “down” biasing phases of the CM-bias-functions were compared to those derived from the SP previously reported by Choi et al. (2004). To compare these curve fitting results, the Boltzmann parameters obtained from the CM and the SP were submitted to a statistical t test. The results showed that there were significant differences between the cochlear transducer functions obtained from the CM and the SP in all parameters except parameter $e$. Using the Boltzmann parameters averaged across the animals, the $F_{Tr}$ derived from the CM and the SP is plotted in Fig. 9 for a direct comparison.

The most significant difference was that the dynamic ranges of the $F_{Tr}$ derived from the CM were about 2 to 10 times greater than those from the SP, even though they shared the same probe-tone-level dependency. The second noticeable difference was in the symmetry of the $F_{Tr}$. The Boltzmann functions obtained from the CM were more symmetric than those from the SP. The symmetry of the $F_{Tr}$ can also be measured by the difference between $b$ and $d$ values with a value of zero indicating the perfect symmetry. The absolute difference of the Boltzmann functions obtained from the CM (mean=0.95 and s.d.±0.65) are smaller than those from the SP (mean=4.23 and s.d.±1.43). This indicates that the Boltzmann function from the CM is more symmetric.

The Boltzmann parameters obtained from the CM modulation envelop and those derived from the SP show significant differences in its dynamic range, the optimal gain, and the symmetry. The cochlear $F_{Tr}$ derived from the CM shows larger dynamic range, greater gain at the inflection point, and more symmetrical than that obtained from the SP. The above differences in the transducer properties are consistent with the measurements from the intracellular ac and dc receptor potentials recorded in vivo from the OHCs and the IHCs (Dallos, 1986; Dallos & Cheatham, 1976; 1991; Cody & Russell, 1987; Russell & Sellick, 1978). Usually, OHCs produce the largest ac receptor potentials than dc components whereas IHCs produce larger dc electrical response with smaller dynamic range. At the base of the cochlea, a dc response in IHC is preponderant while OHCs do not generate a depolarizing dc response as IHCs except at the highest levels. In addition, the IHC receptor potentials are asymmetrical while the OHC receptor potentials are symmetrical (Cody & Russell, 1985; 1987; Russell & Kössl, 1992; Russell, Cody & Richardson, 1986; Russell, Kössl & Richardson, 1992). It seems to suggest that these different characteristics in the derived $F_{Tr}$ are due to the difference in the generator.

Many studies targeting differential damage to
These functions were obtained at three levels (90, 80 and 70 dB SPL) of two high frequency probe tone (6 and 12 kHz). The SP data were obtained from data published in Choi et al., (2004). The mean CM magnitudes from Fig. 7 and 8 were used for comparison with the mean SP magnitudes at each signal condition. Finally, the CM and SP magnitudes were normalized to 0 by subtracting the maximal value for comparison.

inner and outer hair cells showed that the CM generation is mainly dominated by the OHCs (Dallos, 1973; Dallos, 1985; Dallos & Wang, 1974; Dallos, Cheatham & Ferraro, 1974) while the SP is produced by both IHC and OHCs (Dallos, 1973; Dallos & Cheatham, 1991; Davis et al., 1958; Johnstone & Johnstone, 1966). However, recent studies demonstrated that the IHCs are the major source of the SP production (Durrant et al., 1998; van Emst, Klis & Smoorenburg, 1996, 1997; van Emst, Giguere & Smoorenburg, 1998; Zheng et al. 1997). Therefore, the significant difference between the cochlear $F_{77}$, derived from the CM and SP may result from the difference in the relative contribution of the IHCs and the OHCs. To confirm the sources of the SP, it is necessary to investigate
whether some ototoxic drugs damaging either IHCs or OHCs can affect the cochlear transducer functions derived from the CM and SP.

It is possible that the differences in the Fr derived from the CM and SP are due to the different signal processing techniques utilized in the procedures. In the SP approach, the response to the bias tone alone was subtracted out from the bitoneal response and the residue was low-pass filtered to obtain the dc component. This discrepancy in the methodology between the two studies does less likely play a role in the different results in the derived cochlear Fr, because these differences change with probe tone level and frequency. Plus, numerical simulations using these different approaches showed that the derivatives of the Fr can accurately obtained. Therefore, the different transducer characteristics derived from the CM versus the SP are possibly due to the different generating sources.

A cochlear transducer function representing a nonlinear mechano-electrical transduction was constructed from the CM with the low frequency modulation technique and compared to that obtained from the SP. Mathematical expression and numerical simulations showed that the CM modulation envelope is proportional to the first derivative of the nonlinear function when the probe tone level is very small. A physiologic experiment was completed to estimate a cochlear Fr from the CM in response to a bitoneal stimulus consisting of a low frequency bias tone (25 Hz) and a high frequency probe tone (6 or 12 kHz). The experimental results showed that the CM modulation envelope is proportional to the first derivative of the cochlear transducer function as shown in the computer simulation. The CM responses were probe tone level dependent. The cochlear transducer functions obtained from the CM were compared to those constructed from the SP. These were considerable differences in its dynamic range, the optimal gain, and the asymmetry of the cochlear transducer functions fitted to the CM and SP, which may result from different contributions of the IHCs and OHCs. Therefore, this study demonstrates that the CM and SP could be used to evaluate and characterize the different cochlear transducers and further studies are necessary.

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변조된 저주파수 와우전위를 통한 와우변환함수에 관한 연구

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배경 및 목적: 최근 와우의 정원창에서 얻어진 가중전압(summating potential)를 사용하여 와우변환함수(cochlear transducer function)를 도출하는 새로운 방법이 소개되었다. 본 논문은 저주파수 변조기술을 사용하여 와우에서 측정된 와우전위(cochlear microphonic)를 사용하여 와우변환함수를 도출하는 또 다른 하나의 방법을 소개하고 이 방법으로 가용한 가중전압(summating potential)을 사용하여 얻어진 와우변환함수의 일차 미분을 얻을 수 있고 모의실험을 통해 그 일차미분은 와우전위로부터 얻어진 와우변환함수와 비례한다는 것을 알 수 있었다.

방법: 주파수가 6 또는 12 kHz인 70에서 90 dB SPL 까지 10 dB의 크기로 변화하는 두개의 고주파수 음과 주파수가 25 Hz인 높은 강도(130 dB SPL)의 저주파수 음을 동시에 들려주고 실험동물인 gerbils의 정원창(round window)에 놓인 전극으로부터 와우전위를 측정하였다. 낮은 주파수의 와우전위 변동을 제거하기 위하여 대역필터(band-pass filter)를 사용한 후 와우전위 변조 envelope를 얻을 수 있었다. 결과: 미분 수학과 모의실험의 결과는 와우전위의 크기는 와우변환함수의 일차미분에 본질적으로 비례하였다. 실험의 연구결과는 저주파수음의 함수로서 와우전위의 변조 envelope는 모의실험에서 보여진 바와 같이 와우변환함수의 일차 미분과 비슷한 유형을 보이고 있다. 개구자와 왈진은 와우전위로부터 얻어진 와우변환함수를 외전에 가중전위로 결정해서 만드는 것과 비교해 볼 때 두 와우변환함수는 동태적으로 의미있는 차이가 있었다.

논의 및 결론: 본 연구는 변조된 와우전위를 통해서 와우변환함수를 도출할 수 있다는 것을 수학적으로 실험적으로 보이고 있다. 그러나 본 연구에서 얻어진 와우변환함수는 이전의 가중전위에 얻은 와우변환함수와는 의미있는 차이를 보이고 있었다. 가장 의미있는 차이는 와우전위로 얻어진 변조완전환함수의 역동적인 범위(dynamic range)가 가중전위로 얻어진 와우변환함수보다 훨씬 컸고 더욱 더 대칭적이었다. 큰 역동적인 범위와 대칭적인 와우변환함수의 특징은 외유모세포(outer hair cells)에서 얻어진 것과 더욱 더 유사하였다. 따라서 본 연구에서 얻어진 와우변환함수와 가중전위로 얻어진 와우변환함수의 차이는 외주변 변모세포(inner hair cells)와 외유모세포의 상대적인 기여도의 차이에서 기인될 수 있다. 이 연구는 언어청각장애연구, 2010;15;232-250.

핵심어: 와우전위, 가중전압, 와우변환함수, 내유모세포, 외유모세포

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