The use of distortion product otoacoustic emission suppression as an estimate of response growth

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Distortion product otoacoustic emission (DPOAE) levels in response to primary pairs ($f_2=2$ or 4 kHz, L_2 ranging from 20 to 60 dB SPL, $L_1=0.4L_2+39$ dB) were measured with and without suppressor tones (f_3), which varied from 1 octave below to $\frac{1}{2}$ octave above f_2, in normal-hearing subjects. Suppressor level (L_3) varied from -5 to 85 dB SPL. DPOAE levels were converted into decrements by subtracting the level in the presence of the suppressor from the level in the absence of a suppressor. DPOAE decrement vs L_3 functions showed steeper slopes when $f_3<f_2$ and shallower slopes when $f_3>f_2$. This pattern is similar to other measurements of response growth, such as direct measures of basilar-membrane motion, single-unit rate-level functions, suppression of basilar-membrane motion, and discharge-rate suppression from lower animals. As L_2 increased, the L_3 necessary to maintain 3 dB of suppression increased at a rate of about 1 dB/dB when f_3 was approximately equal to f_2, but increased more slowly when $f_3<f_2$. Functions relating L_3 to L_2 in order to maintain a constant 3-dB reduction in DPOAE level were compared for $f_3<f_2$ and for $f_3\approx f_2$ in order to derive an estimate related to ''cochlear-amplifier gain.'' These results were consistent with the view that ''cochlear gain'' is greater at lower input levels, decreasing as level increases. © *2002 Acoustical Society of America.* [DOI: 10.1121/1.1426372]

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I. INTRODUCTION

Distortion product otoacoustic emissions (DPOAEs) are elicited when two pure tones, slightly different in frequency, are presented to the ear. They are low-level signals, produced within the cochlea, that propagate in the reverse direction through the middle ear and into the ear canal, where they can be measured with a microphone. These responses are generated by normal nonlinear mechanisms within the cochlea that are associated with outer hair cell (OHC) function. These nonlinear mechanisms are thought to provide amplification for low-level stimuli, in order to enhance the absolute sensitivity and sharp frequency selectivity that are characteristics of normal auditory function. These normal nonlinear mechanisms also provide compression as level increases, thus enabling the ear to encode stimulus level over a wide dynamic range. As a result of this association, it is common clinical practice to assume that the observation of DPOAEs would be consistent with normal nonlinear function and, therefore, normal hearing. Their absence would be consistent with the presence of cochlear (OHC-based) hearing loss, assuming that middle-ear function is normal. Of course, this view is simplistic in that it ignores the fact that DPOAEs do not completely disappear once any degree of hearing loss exists; rather, DPOAE level decreases as threshold increases, even though this relationship is variable (see below).

These observations have led to the use of DPOAEs as tools for identifying the presence of cochlear hearing loss, both as part of universal newborn hearing screening programs and as part of more general clinical applications. Much of the focus of previous work regarding the clinical utility of DPOAEs has been directed toward understanding the relation between these measures and auditory sensitivity (e.g., Martin *et al.*, 1990; Gorga *et al.*, 1993, 1996, 1997, 1999, 2000; Kim *et al.*, 1996; Dorn *et al.*, 1999). These efforts have been designed mainly to make dichotomous decisions in which, based on DPOAE findings, an ear is labeled as normal or impaired (as defined by pure-tone audiometric tests). As a result of these studies, it is now known that DPOAEs can identify the presence of hearing loss accurately at mid- and high frequencies, but are less accurate predictors of auditory status for lower frequencies. These frequency effects appear to be related to noise levels, which increase as frequency decreases. In addition, DPOAEs produce the fewest errors in diagnosis when moderate-level stimuli are used to elicit the response (Stover *et al.*, 1996; Whitehead *et al.*, 1992).

In other studies, DPOAE level or signal-to-noise ratio (SNR) have been correlated with audiometric threshold (Martin *et al.*, 1990; Probst and Hauser, 1990; Gorga *et al.*, 1997, 2002; Kimberley *et al.*, 1997; Kummer *et al.*, 1998; Janssen *et al.*, 1998), even within the range of hearing that is typically considered normal (Dorn *et al.*, 1998; Kummer *et al.*, 1998). Although there is some debate over the strength of the relationship (see Harris and Probst, 1997, for a review), these data showed that DPOAE level (or SNR) decreased as pure-tone thresholds increased up to thresholds of about 50–60 dB HL. For greater losses, no relation was observed because DPOAEs typically are absent. Still other studies have shown that DPOAE threshold (defined as some SNR) increases as audiometric threshold increases (Martin *et al.*, 1990; Gorga *et al.*, 1996; Dorn *et al.*, 2001).

In all of the above efforts, the primary focus was to determine the extent to which DPOAEs could be used to

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dichotomously predict auditory status as normal or impaired, or to estimate the degree of threshold elevation. This approach is consistent with the view that DPOAEs are a by-product of normal nonlinear cochlear behavior that resides in the OHC system. Since this nonlinear behavior probably is tied to normal threshold sensitivity (see Dallos *et al.*, 1980, for a review), damage to the OHCs results in the loss of nonlinear behavior and threshold elevation. A reduction or loss of DPOAEs is one manifestation of these changes to normal nonlinear function. In addition to threshold elevation, other changes occur as a consequence of damage to OHCs, including reduced frequency selectivity (e.g., Kiang *et al.*, 1976; Dallos and Harris, 1978; Liberman and Dodds, 1984) and reduction or elimination of suppression and intermodulation distortion (e.g., Dallos *et al.*, 1980; Kim, 1980). The slopes of functions relating cochlear responses to stimulus level (i.e., response growth) apparently depend on cochlear integrity as well. For example, the slopes of single-unit rate versus level functions, whole-nerve action potential (AP) masking functions, and basilar-membrane velocity versus level functions increase as a consequence of permanent or reversible cochlear insult (Evans, 1974; Sewell, 1984; Gorga and Abbas, 1981a, b; Ruggero and Rich, 1991). The majority of studies examining changes in frequency selectivity and increased response growth was conducted in animals. Still, all of these effects appear to be consequences of damage to the same underlying, nonlinear system.

The purpose of the present study is to determine whether DPOAE measurements can provide estimates of suprathreshold response properties in humans that are at least qualitatively similar to physiological measurements made in lower animals. Specifically, we were interested in knowing whether measures of response growth, derived from DPOAE suppression measurements, share similar characteristics with other measures of response growth, such as single-unit rate vs level functions. While DPOAE input/output functions also provide a measure of cochlear response growth, DPOAE suppression experiments have several advantages, in that they provide an opportunity to derive a measure of response growth for different frequencies at a fixed place along the cochlea. It is already known that DPOAE suppression tuning curves provide estimates of frequency selectivity and are useful in determining the generator site for DPOAEs (e.g., Brown and Kemp, 1984; Martin *et al.*, 1987; Abdala *et al.*, 1996). Data from some of these same studies, as well as others (Harris *et al.*, 1992; Kummer *et al.*, 1995; Abdala, 1998, 2001), reveal that DPOAE level varies with suppressor level, following trends that would be expected from more direct studies of suppression (Abbas and Sachs, 1976; Costalupes *et al.*, 1987; Delgutte, 1990; Ruggero *et al.*, 1992) and/or other measures of response growth, including rate vs level functions as a function of frequency for a fixed characteristic frequency (CF) or place (CP). We intend to extend that work by determining if DPOAE suppression can be used to describe response growth in much the same way decrements have been used in single-unit studies (Smith, 1977, 1979; Smith and Zwislocki, 1975; Harris, 1979; Harris and Dallos, 1979), in measurements of the whole-nerve AP (Abbas and Gorga, 1981; Gorga and Abbas, 1981a, b), and in auditory brainstem response (ABR) measurements (Gorga *et al.*, 1983) from lower animals. These data will be collected for a range of primary levels, with the additional goal of demonstrating changes in response growth and tuning as a consequence of stimulus level.

Furthermore, it has been proposed that the differences between the tip and the tail of a DPOAE suppression tuning curve provides an estimate that is related to the ''gain of the cochlear amplifier'' (e.g., Mills, 1998; Pienkowski and Kunov, 2001). As a final aspect of the present study, we will use a similar approach to provide this estimate as a function of primary level.

II. METHODS

A. Subjects

Thirteen young adults with normal hearing served as subjects for this study. All 13 subjects participated in studies in which $f_2 = 4$ kHz, while six of these subjects also participated in studies in which $f_2 = 2$ kHz. Each subject had thresholds of 20 dB HL (ANSI, 1996) or better for the octave- and half-octave frequencies from 0.25 to 8 kHz. In addition, each subject had normal middle-ear function on each day in which DPOAE data were collected. Normal middle-ear function was defined as a normal 226-Hz tympanogram. Approximately 15 h of data-collection time, divided among 7 to 9 sessions, was required at each f_2 for each subject, thus introducing the possibility of variation in probe placement across test sessions (see the description of calibration below).

B. Stimuli

All stimuli were produced by custom-designed software (EMAV, Neely and Liu, 1993) that controlled a soundcard (Fiji, Turtle Beach) housed in a PC. Separate channels of the soundcard were used to produce f_1 and f_2. The channel producing the lower-level primary frequency (f_2) was also used to produce a suppressor tone (f_3). These signals were delivered to the ear with an Etymotic ER-10C probe–microphone system that had been modified to remove 20 dB of internal attenuation on the sound-delivery side. This probe system includes two transducers for signal delivery and one microphone for recording signals in the ear canal.

Data were collected with f_2 frequencies of either 2 or 4 kHz. The ratio between primary frequencies (f_2/f_1) was approximately 1.25. For each set of suppression measurements at each f_2, the level of f_2 (L_2) was fixed at one of three levels (40, 50, 60 dB SPL for $f_2 = 2$ kHz) or one of five levels (20, 30, 40, 50, 60 dB SPL for $f_2 = 4$ kHz). Measurements for lower L_2 levels were not possible on a routine basis at 2 kHz, due to the increased variability observed at this frequency (see Figs. 3, 5, and 7 below). For each L_2, the level of f_1 (L_1) was set according to the equation, $L_1 = 0.4L_2 + 39$ dB (Janssen *et al.*, 1998). This approach results in the largest DPOAE level in subjects with normal hearing (Whitehead *et al.*, 1995; Kummer *et al.*, 1998, 2000; Janssen *et al.*, 1998). In the context of the present measurements, it may be helpful to think of each set of primary tones as a probe that elicits responses from the f_2 place, much the same

way as probe tones are viewed during psychoacoustic or physiologic masking experiments. The suppressor tone (f_3) varied from about 1 octave below to approximately $\frac{1}{2}$ octave above f_2, with 16 f_3 frequencies for each L_2. The level of the suppressor tone (L_3) was varied from -5 to 80 or 85 dB SPL in 5-dB steps. For each f_2, L_2 combination, there were 336 conditions, including control conditions in which no suppressor was presented.

C. Procedures

Prior to each data-collection session, signal levels were calibrated in the ear canal, using the emission probe microphone. These levels subsequently were used to produce the specified levels for f_1, f_2, and f_3. There are other calibration techniques that might produce more reliable levels at the eardrum by avoiding problems such as standing waves (Siegel, 1994, 2002; Neely and Gorga, 1998). We have opted for the simpler approach in which the emission probe is used to measure SPL because of its ease of implementation.

For each stimulus condition, data were collected into two buffers. The contents of these buffers were summed, and the summed energy in the $2f_1-f_2$ frequency bin was used to estimate DPOAE level. The contents of the two buffers were subtracted in order to derive an estimate of noise level in the $2f_1-f_2$ frequency bin. This approach was followed in order to avoid problems associated with using the energy in several bins adjacent to $2f_1-f_2$, which would occur when f_3 frequencies are used that are close to f_2. By using the subtraction technique to estimate noise level, it was possible to place suppressor tones closer to f_2 than would ordinarily be possible if noise levels were estimated as the average energy in frequency bins surrounding f_2.

During data collection, measurement-based stopping rules were used, in which a run was terminated if the noise floor was below -25 dB SPL or after 32 s of artifact-free averaging, whichever occurred first. This stopping rule resulted in reliable estimates of DPOAE level for essentially all quiet conditions, where the mean signal-to-noise ratio (SNR) ranged from about 20 dB ($L_2=20$ dB SPL for $f_2=4$ kHz; $L_2=40$ dB SPL when $f_2=2$ kHz) to 35 dB or greater ($L_2=60$ dB SPL for both f_2 frequencies). These SNRs represent the effective range over which changes in DPOAE level could be measured as a result of the presence of the suppressor.

For each f_2, L_2 combination, a series of runs was conducted, in which f_3 was fixed at each of 16 frequencies. Figure 1 provides a summary of the stimulus paradigm. In this example, $f_2=4$ kHz, $f_1=3.2$ kHz, and L_2 and L_1 were fixed at 40 and 55 dB SPL, respectively. DPOAE levels (in response to each fixed f_2, L_2 combination) were measured while L_3 was varied over its entire range, thus producing a function in which DPOAE level was related to L_3 for each f_3. In each of these intensity series, the initial condition was a control condition, in which no suppressor was presented. The final condition in each series of f_3 frequencies also was a control condition. The DPOAE level from each experimental condition (i.e., each f_3, L_3 combination) was subtracted from the average DPOAE level from the two closest control conditions preceding and following the experimental condition. This process allowed us to convert DPOAE level changes due to the suppressor into a decrement (or amount of suppression) in dB. These DPOAE decrements were then plotted as a function of L_3, resulting in a series of 16 decrement vs L_3 functions for each f_2, L_2 combination. Decrements were chosen, based on previous neural work, in which it was shown that decrements in either single-unit discharge rate (e.g., Smith, 1979), whole-nerve APs (Abbas and Gorga, 1981), or ABR amplitudes (Gorga *et al.*, 1983) could be used as indirect measures of response to a masker. In addition, they represent the amount of suppression in dB. Finally, they partially control for differences in absolute response levels across subjects. In the present experiment, decrements are used to describe response growth to f_3 at the f_2 place.

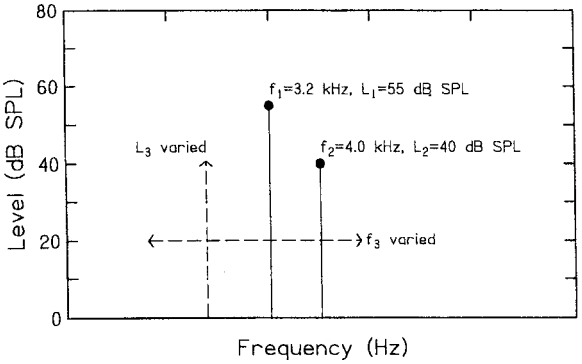

FIG. 1. Stimulus paradigm. In this example, $f_2=4$ kHz, $f_1=3.2$ kHz, $L_1=55$ dB SPL, and $L_2=40$ dB SPL. For each primary frequency and primary level combination, each of 16 f_3 frequencies was selected, its level was varied, and the DPOAE level elicited by the primaries was measured.

III. RESULTS

Implicit in experiments associated with DPOAE suppression measurements is the view that the two primary tones are used as probes or signals that are represented at a fixed cochlear place associated with f_2, and that holding the primary levels constant results in a constant response at this place. The repeatability of DPOAE levels for quiet conditions (no suppressor) would support this view for both f_2 frequencies. While the mean levels for control conditions varied across subjects, these levels were stable within each subject. When averaged across all subjects, the highest mean of the standard deviations (across subjects) for control conditions was 1.6 dB, which occurred when $f_2=2$ kHz and $L_2=40$ dB SPL. For all other f_2, L_2 combinations, the mean standard deviations for control conditions were about 1 dB. Thus, a relatively constant response was achieved for the control conditions in all subjects at both f_2 frequencies and at all L_2 levels.

A. DPOAE decrement vs suppressor level functions

Figure 2 shows individual and median decrement vs L_3 functions for the 16 f_3 frequencies surrounding an f_2 of 4 kHz. Medians were chosen here as the measure of central tendency in order to reduce the influence of outliers. In actuality, however, there was little difference between mean and median functions. In this example, L_2 was presented at 40 dB SPL. The panel in which $f_3=4.1$ kHz represents the

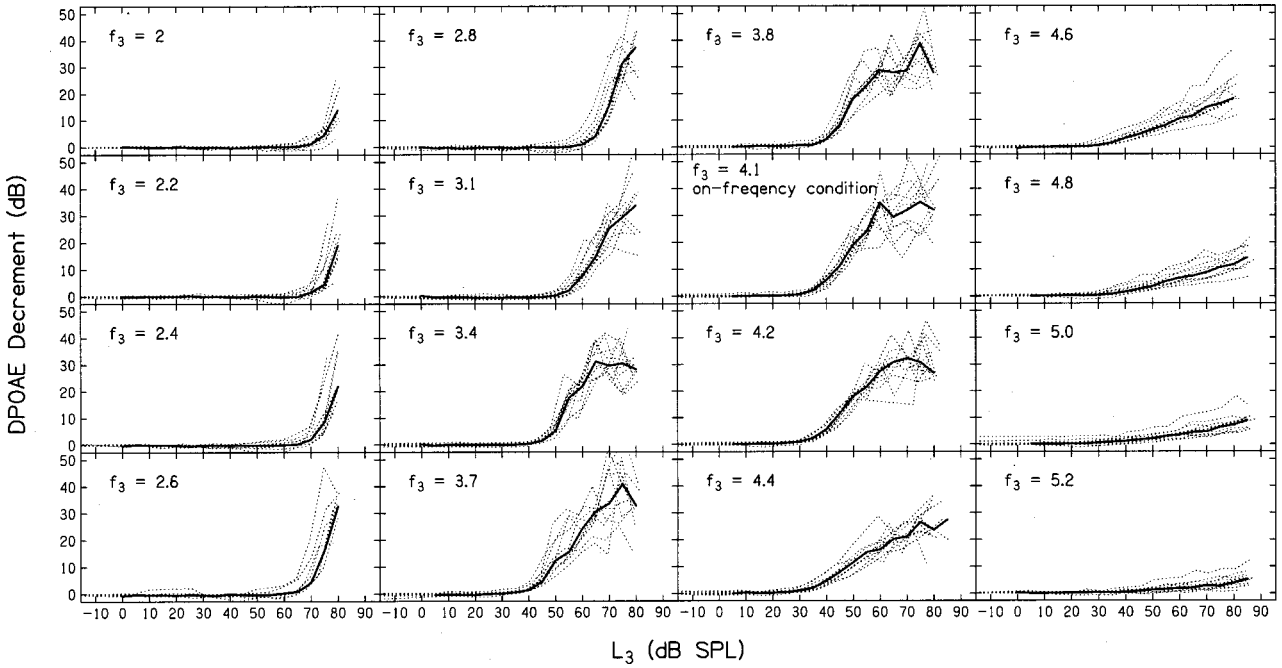

FIG. 2. Individual (dashed lines) and median (solid lines) DPOAE decrements as a function of L_3, with $f_2=4$ kHz and $L_2=40$ dB SPL. Within each panel, data are shown for a different suppressor frequency, f_3, which is noted within each panel.

condition in which f_3 frequency was closest to f_2. This condition ($f_3=4.1$ kHz) can be viewed as the on-frequency condition, when suppressor and probe frequencies are nearly equivalent. In the interest of space, individual data will be shown only for the case when $L_2=40$ dB SPL, although similar trends were observed for both lower and higher L_2 levels. Within each panel, the heavy line represents median data and the thin lines represent data from individual subjects. The apparent increase in variability when the decrement functions "saturate" (most evident when f_3 was between 3.4 and 4.2 kHz) is due to the fact that the response to the primary ($f_2=4$ kHz, $L_2=40$ dB SPL) has been decremented into the noise floor. Thus, the apparent variability on the saturated portion of these functions is actually due to the inherent variability in the noise.

Several trends may be observed in Fig. 2. First, the median decrement functions provide reasonable descriptions of the data from individual subjects, especially over the range of L_3 levels in which the decrement is increasing. Second, the lowest suppression threshold, defined as the lowest level

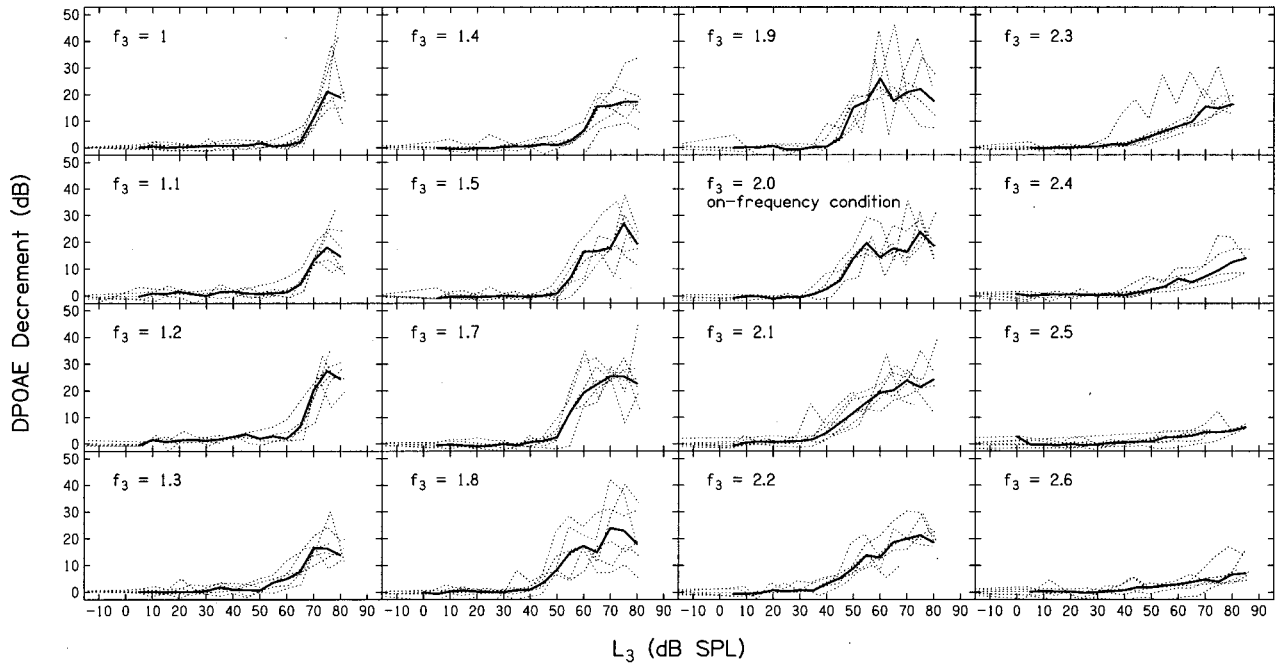

FIG. 3. Following the same convention used in Fig. 2, individual and median DPOAE decrements as a function of L_3, with $f_2=2$ kHz, $L_2=40$ dB SPL, and $L_3=55$ dB SPL.

at which the DPOAE level is first reduced by the suppressor, occurs for f_3 frequencies close to f_2. Thus, the onset of suppression occurs at the lowest level when $f_3=4.2$ kHz. Higher L_3 levels were required when f_3 moved away from this frequency. Third, the slopes of the decrement vs L_3 functions are frequency dependent. The steepest slopes occur for f_3 frequencies well below f_2. This trend is apparent in the left column of Fig. 2, in which f_3 was between about $\frac{1}{2}$ and 1 octave below f_2. As frequency increases, the slope decreases, with the most shallow slopes occurring for f_3 frequencies higher than f_2 (most evident in the right column of Fig. 2). Although previous DPOAE studies have not reported suppression data in this form, these frequency-dependent trends were evident in previous data as well (e.g., Kemp and Brown, 1983; Abdala, 1998, 2001; Kummer *et al.*, 1995).

Figure 3 shows decrement vs L_3 functions when $f_2=2$ kHz and $L_2=40$ dB SPL, following the format that was used in Fig. 2. The trends evident in Fig. 2 can also be seen here, although the data were less orderly compared to data when $f_2=4$ kHz. One difference between decrement functions at 2 kHz and those at 4 kHz was observed for low-frequency suppressors. The median functions in the left column of Fig. 3 (f_3 frequencies between $\frac{1}{2}$ and 1 octave below f_2) were characterized by a saturating portion at higher L_3 levels. This pattern was not observed for similar f_3, f_2 relationships when $f_2=4$ kHz (left column, Fig. 2). We cannot explain these differences in response patterns. We initially attributed the less-orderly results when $f_2=2$ kHz to the increased noise levels associated with measurements at this frequency. Evidence in support of this view was provided by the fact that longer averaging times were needed at 2 kHz. However, invoking increased noise levels to account for the differences in results is inadequate, since the stopping rules resulted in similar noise levels across f_2 frequencies. On the other hand, there are similarities in results across f_2 frequencies. For example, the median provided a reasonable description of individual data, there was increased variability at the saturating portion of the functions (representing the variability inherent in the noise), and the slopes of the decrement functions depended on the relation between f_3 and f_2. This latter observation was apparent on the high-frequency side of f_2 (right column of Fig. 3). The low-frequency effects were less clear at this f_2, compared to 4 kHz.

Figure 4 shows median DPOAE decrements as a function of L_3 when $f_2=4$ kHz and L_2 was at each of five different levels, ranging from 20 dB SPL (top panel) to 60 dB SPL (bottom panel). Data for f_3 frequencies less than f_2 are shown in the left column, while data for f_3 frequencies higher than f_2 are shown in the right column. Within each panel, the heavy line represents data for the condition in which f_3 was the closest to f_2 among the f_3 frequencies represented in the panel. The thin lines moving towards the right side of each panel represent data for other f_3 frequencies; the further the lines move towards the right side, the greater the difference in frequency between f_3 and f_2.

Several trends are obvious in this representation of the data. The lowest suppression thresholds are evident for f_3 frequencies close to f_2. For example, an L_3 of about 15 dB SPL when f_3 was either 4.1 or 4.2 kHz began to suppress the response when $L_2=20$ dB SPL (left-most lines, top panel, right column). As f_3 increased, the level that just began to suppress the response increased. The same trends were evident for f_3 frequencies lower than f_2. Second, decrement (suppression) threshold increased with L_2. This can be seen in the systematic migration of the decrement functions towards the right as L_2 increased down each column. Third, the slope of the decrement vs L_3 function depended on the relationship between f_3 and f_2 as they had in the data summarized in Fig. 2. As in Fig. 2, the high-level portion of some of these functions should not be viewed as evidence of saturation; rather, these portions of the function represent the case when the response to the primary tones was suppressed into the noise floor.

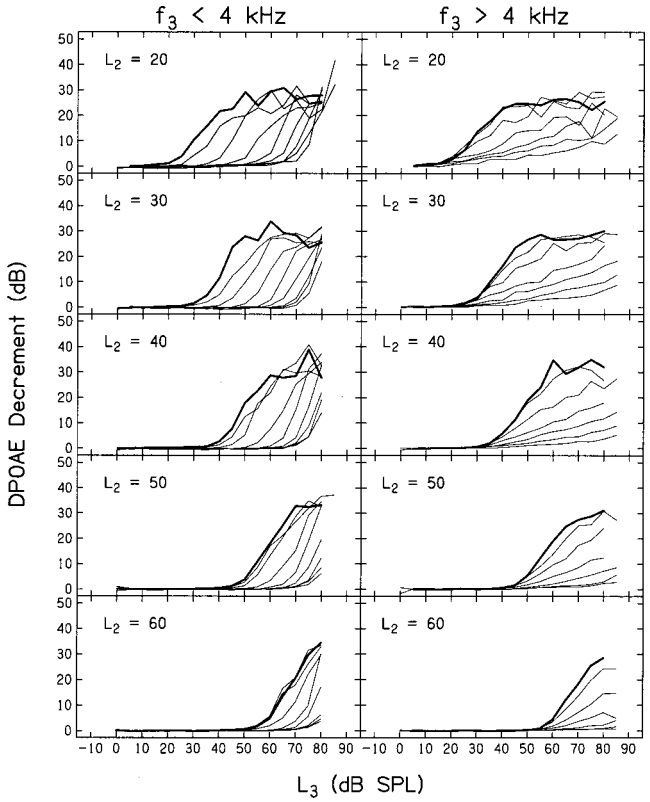

FIG. 4. Median DPOAE decrement vs L_3 functions for f_3 frequencies less than f_2 (left column) and for f_3 frequencies greater than f_2 (right column), when $f_2=4$ kHz. Within each panel, the parameter is f_3, with the heavy line representing data for the f_3 closest to f_2. The level of f_2 (L_2) varies within each column from 20 dB SPL (top panel) to 60 dB SPL (bottom panel).

In similar fashion, Fig. 5 represents median decrement vs L_3 data when $f_2=2$ kHz, following the format used in Fig. 4. Note here, however, that data are shown only for the cases when $L_2=40$, 50, or 60 dB SPL. Once again, the lowest suppression thresholds were observed when f_3 was close to f_2, and migrated to higher L_3 levels as L_2 increased (the progression down each column in the figure). In addition, the slopes of these functions were steepest for f_3 frequencies on the low side of f_2, decreasing as f_3 increases, much like the results that were observed when $f_2=4$ kHz. However, the orderly progression of these decrement functions relative to f_3, both in terms of threshold and in terms of slopes, were not as evident when $f_2=2$ kHz compared to the observation when $f_2=4$ kHz, especially for f_3 frequencies less than f_2.

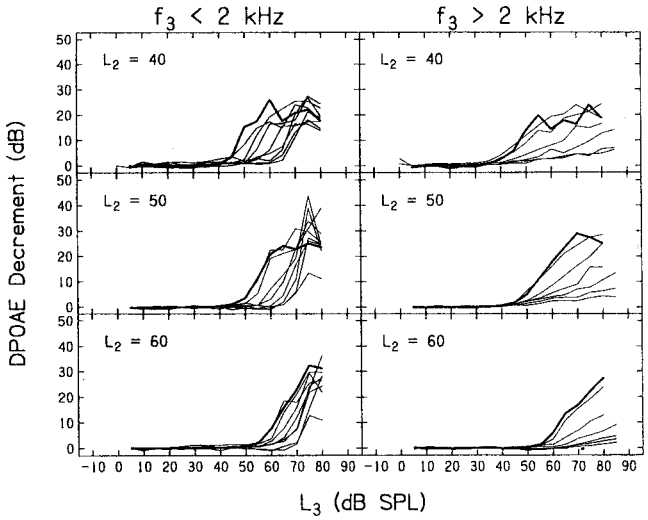

FIG. 5. Following the convention used in Fig. 4, median decrement vs L_3 functions when $f_2=2$ kHz.

B. Suppression tuning curves and slopes of decrement functions

Figure 6 shows median DPOAE suppression thresholds (top row) and slopes of the DPOAE decrement vs L_3 functions (bottom row) as a function of f_3 when $f_2=4$ kHz. Each column represents data for a different L_2. For the purposes of these tuning curves, suppression threshold was defined as the L_3 that resulted in a 3-dB reduction in DPOAE level from what was measured when the primaries were presented in the absence of a suppressor. This ''threshold'' was chosen because it could be estimated reliably, while it represents the level at which f_3 just begins to affect the response to the primary tones. This suppression threshold, however, was not estimated visually from decrement vs L_3 functions. Instead, the median decrement vs L_3 functions for each f_3 were transformed by the following equation:

$$D=10\log(10^{\mathrm{decr}/10}-1), \tag{1}$$

and fit by a linear regression of D onto L_3. Lines were fit only to the range, $-5<D<20$. Each of these linear equations was then solved for the L_3 that resulted in a 3-dB decrement. According to the above equation, $D=0$ when decr$=3$ dB. The same linear regressions were used to provide slope estimates for the decrement functions.

The DPOAE suppression tuning curves shown in Fig. 6 have the lowest threshold when f_3 was close to f_2. This observation is not new, as it was evident in other studies that measured DPOAE suppression tuning curves for the $2f_1-f_2$ DPOAE (Martin *et al.*, 1987, 1999; Harris *et al.*, 1992; Cianfrone *et al.*, 1994; Kummer *et al.*, 1995; Abdala *et al.*, 1996; Abdala, 1998, 2001). As f_3 moved away from f_2, the level necessary to reduce the response by 3 dB increased. The rate at which this increase occurred was more rapid on the high-frequency side of the tuning curve, compared to the low-frequency side. Although difficult to see in this representation, there was a slight shift in the frequency for which the lowest suppression threshold was observed, moving towards lower f_3 frequencies as L_2 was increased. Although variable, the slopes of the decrement functions generally decreased as f_3 increased. The steepest slopes were observed when f_3 was

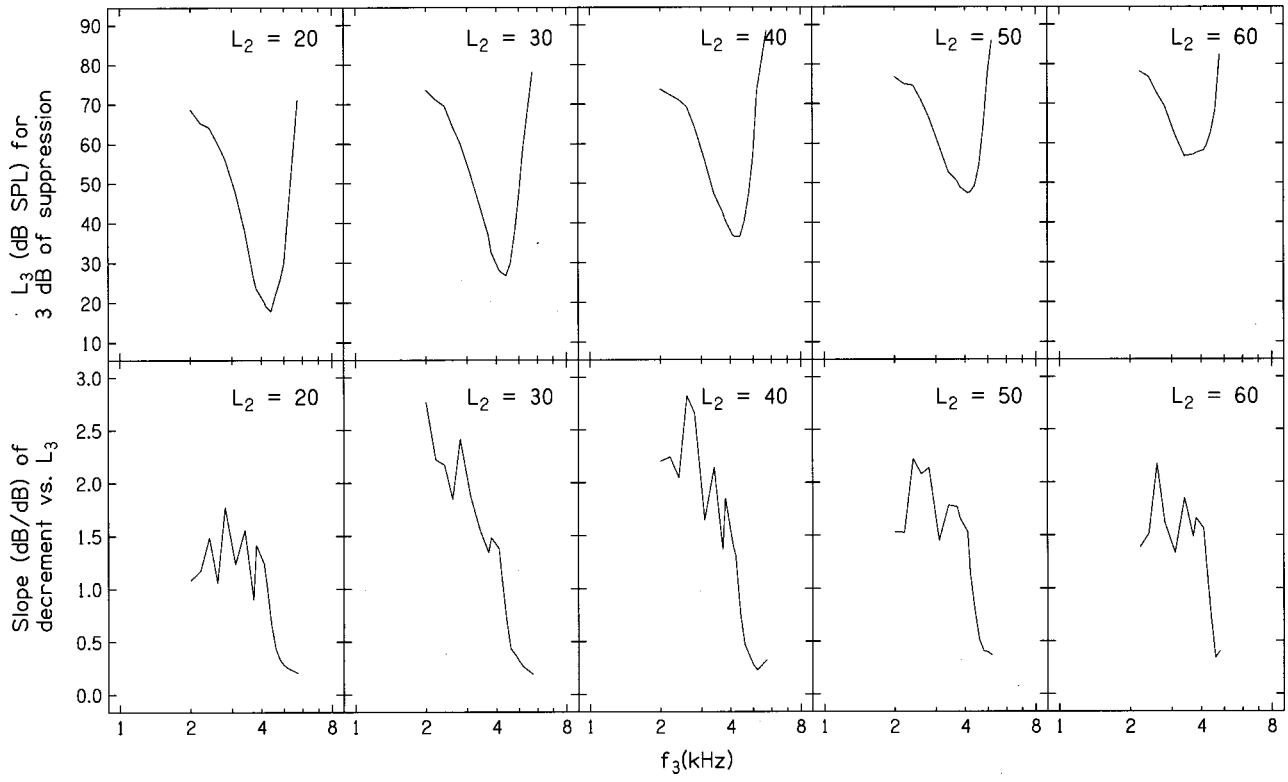

FIG. 6. Top: Suppressor level (L_3) as a function of suppressor frequency (f_3) that resulted in a 3-dB reduction in the DPOAE level elicited when the primaries were presented in quiet. Each of these DPOAE suppression tuning curves represents data for a different L_2. Bottom: Slopes of the decrement vs L_3 functions as a function of f_3. Each panel represents data for a different L_2.

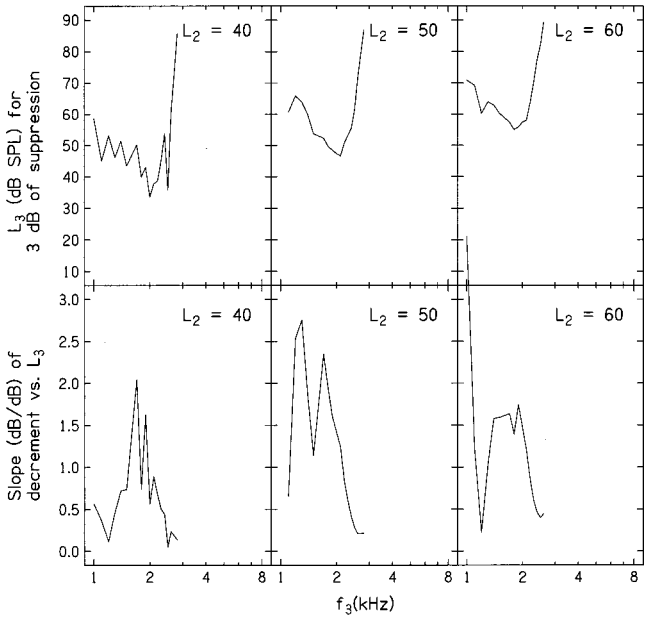

FIG. 7. Following the convention used in Fig. 6, DPOAE suppression tuning curves (top row) and slopes of DPOAE decrement vs L_3 functions (bottom row) for $f_2=2$ kHz.

about an octave below f_2, decreasing as f_3 increased. The shallowest slopes were observed for the highest f_3 frequencies relative to f_2. In most cases, there was a rapid transition between steep and shallow slopes as f_3 frequencies moved from below f_2 toward f_3 frequencies above f_2.

In comparison with previous DPOAE suppression data, Abdala (1998) reports a slope of between 1.2 and 1.4 dB/dB for low-frequency suppressors when $f_2=3$ kHz and $L_2=50$ dB SPL, and Kummer *et al.* (1995) show slopes between 1.5 and 2.0 dB/dB for low-frequency suppressors when $f_2=4$ kHz and $L_2=40$ dB SPL. In the present study, the slopes for low-frequency suppressors ranged from 1.5 to 2.5 dB/dB when $L_2=40$ dB SPL and from 1.5 to 2.0 dB/dB when $L_2=50$ dB SPL (see Fig. 6). For high-frequency suppressors relative to $f2$, all three studies reported rapid decreases in slope to values much less than 1 dB/dB.

Figure 7 displays equivalent DPOAE suppression tuning curves and slopes of decrement vs L_3 functions when $f_2=2$ kHz. Note that data are only shown for primary levels (L_2 levels) of 40, 50, and 60 dB SPL. This primary-level limitation is not thought to reflect fundamental differences in cochlear response properties at 2 kHz, compared to 4 kHz. As stated earlier, however, we cannot invoke differences in noise levels to account for differences in response patterns between 2 and 4 kHz because the measurement-based stopping rules resulted in near-equivalent noise levels across f_2 frequencies.

Some of the trends evident at 4 kHz were also present here. The lowest suppression threshold was observed for f_3 frequencies close to f_2. Higher thresholds were observed as f_3 moved away from f_2. Still, the pattern was more irregular at 2 kHz, compared to 4 kHz, especially when $L_2=40$ dB SPL. The low-frequency side of the suppression tuning curve for this condition was not monotonic. On the other hand, the two higher-level tuning curves at 2 kHz were similar in form

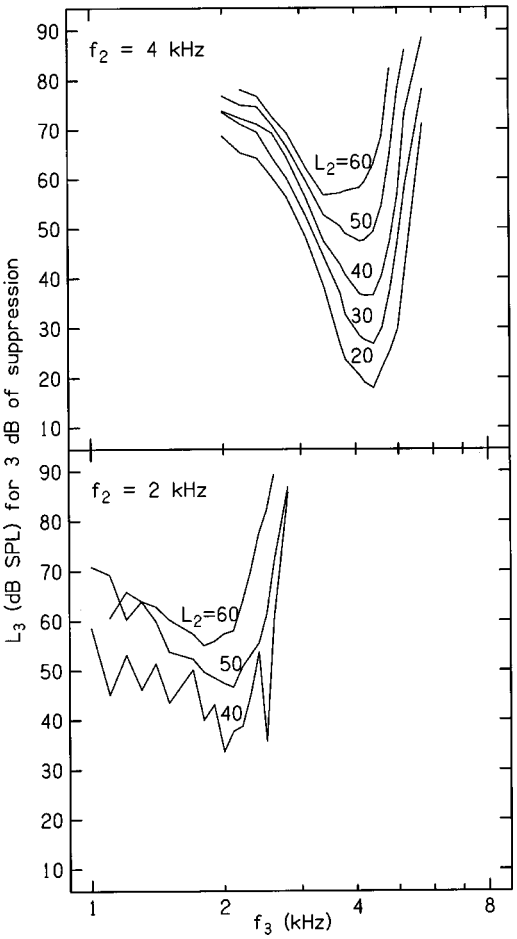

FIG. 8. The tuning curves from Figs. 6 and 7 are reproduced here. Top: $f_2=4$ kHz; bottom: $f_2=2$ kHz. Within each panel, the parameter is L_2.

to those observed at 4 kHz for similar L_2 levels. In addition, the most sensitive thresholds at 2 kHz occurred when f_3 was close to f_2, and the relation between L_2 and L_3 at these points was similar at 2 and 4 kHz.

The slopes of the decrement vs L_3 functions were less orderly when $f_2=2$ kHz compared to the case when $f_2=4$ kHz. While a rapid decrease in slope was observed as f_3 moved from just below f_2 towards higher frequencies, irregular slope patterns were observed on the low-frequency side of the functions relating slope to f_3. Thus, the data at 2 kHz showed the same frequency dependence that was evident at 4 kHz, but mainly for f_3 frequencies approximately equal to or higher than f_2. It is difficult to see any systematic relationship between slope and f_3 for f_3 frequencies $<f_2$.

Figure 8 reproduces the tuning curves from Figs. 6 and 7. The tuning curves at 4 and 2 kHz are shown in the top and bottom panels, respectively. The parameter within each panel is L_2. The slight migration of the tip towards lower f_3 frequencies as L_2 was increased can be seen in this representation of the data. In addition, 3 dB of suppression occurred when L_3 was roughly equal to L_2 for f_3 frequencies close to f_2. Similar trends were evident in other data, even though differences in the definition of ''threshold'' existed across studies (e.g., Harris *et al.*, 1992; Cianfrone *et al.*, 1994; Kummer *et al.*, 1995; Abdala *et al.*, 1996; Abdala, 1998, 2001; Pienkowski and Kunov, 2001). Note also that there

TABLE I. Q_{10}, slope of low-frequency segment (LF slope), and slope of high-frequency segment (HF slope) of suppression tuning curves. Data are provided from several previous studies, as well as from the present study. In addition to some differences in stimulus conditions, differences also existed across studies in how some of these estimates were obtained.

Study	f_2 (kHz)	L_2 (dB SPL)	Q_{10}	LF slope (dB/oct)	HF slope (dB/oct)
Harris *et al.* (1992)	4.0	40	2.97	38.9	128.3
Cianfrone *et al.* (1994)	3.3	62	2.24	25 to 35	100 to 115
Kummer *et al.* (1995)	3.975	40	3.5	43	234
Abdala *et al.* (1996)	3.0	50	3.2	39.5	82
Abdala (1998)	3.0	50	3.3	37	125
Abdala (2001)	3.0	45	3.5		
		65	2.5		
Present study	4.0	20	3.5	59	67
		30	3.4	52	89
		40	2.9	42	89
		50	2.7	37	82
		60	2.0	37	38

was a near-linear increase in suppression threshold with L_2 when f_3 was close to f_2. That is, the shift in L_3 necessary to result in a 3-dB reduction in DPOAE level was about 10 dB for every 10-dB increase in L_2. In contrast, the level necessary to reduce the response by 3 dB increased more slowly when f_3 was about an octave lower than f_2. This can be seen in the small range of L_3 levels on the low-frequency tail of the tuning curve, compared to the spacing when f_3 was approximately equal to f_2, at least when $f_2=4$ kHz.

In general, there were fewer data when $f_2=2$ kHz and there were aspects of the data at this f_2 frequency that were difficult to explain. Having said this, it is not our contention that cochlear function fundamentally differs between the 2-kHz and the 4-kHz places. Rather, we do not understand the reasons underlying the differences in the present measurements at these two frequencies. As a consequence of differences in variability, the limited range of L_2 levels, and the smaller number of subjects on whom data were available, we are less confident in our observations at 2 kHz compared to 4 kHz. Thus, the remainder of this paper will focus on the results at 4 kHz, where more data were available and less variability was evident.

A quadratic function was fit to three points on the tuning curves, including the point with the lowest threshold and one point on either side of this frequency. The minimum of the quadratic function was taken as the best frequency (the frequency for which suppression threshold was lowest). Based on these fits, the best frequency systematically decreased from 4.3 kHz when $L_2=20$ dB SPL to 3.5 kHz for $L_2=60$ dB SPL. That is, the best frequency decreased from 0.11 octaves above to 0.18 octaves below f_2 as L_2 increased from 20 to 60 dB SPL. At 3 kHz, Abdala (2001) observed a downward shift of about 0.07 octaves as L_2 increased from 45 to 65 dB SPL.

Table I provides a summary of tuning-curve characteristics from the present study and compares these estimates to similar estimates from previous DPOAE suppression tuning-curve studies. Stimulus conditions were chosen from these previous studies that were close to the stimulus conditions used presently. However, there was some variation in terms of f_2,L_2, the definition of suppression threshold, the range of f_3 frequencies, and the procedures used to estimate low- and high-frequency slopes of the tuning curves, which could affect agreement across studies. In the present study, low- and high-frequency slopes were determined by fitting the points on the tuning curve between the best frequency (defined by the quadratic function) and the point 20 dB above the threshold at the best frequency.

There is good agreement across studies in terms of Q_{10} (best frequency divided by the bandwidth at 10 dB above best threshold) and in the low-frequency slope of suppression tuning curves. There is less agreement in estimates of high-frequency slope, with the present values being on the low end of these estimates. This difference may relate to the way these slope estimates were derived. In general, however, there is good agreement among studies in terms of these three descriptions of tuning-curve shape. From the present data, it can be seen that, as expected, Q_{10}, and low- and high-frequency slopes decrease as L_2 increases. To the extent that these measures represent the frequency dispersion along the cochlea, that dispersion increases as stimulus level increases.

C. Growth of suppression as a function of L_2

Figure 9(A) plots the L_3 necessary for a 3-dB reduction in DPOAE level as a function of L_2 when $f_2=4$ kHz. The parameter in this figure is f_3, with solid lines representing data for f_3 frequencies $<$ f_2, and dotted lines representing data for f_3 frequencies $>$ f_2. These plots represent the amount by which the suppressor level (L_3) had to be increased as the signal level (L_2) was increased in order to maintain a constant amount of suppression (3 dB). Starting from the lower-left corner of this figure, the four dotted lines clustered together represent conditions in which f_3 was slightly higher than f_2. Data for progressively higher f_3 frequencies are represented by the dotted lines moving up this panel. In a similar fashion, the lowest solid lines represent data for f_3 frequencies that were close to but slightly lower than f_2. Data for progressively lower f_3 frequencies are represented by the solid lines moving up the panel. The lowest L_3 levels and the most linear (dB/dB) functions were ob-

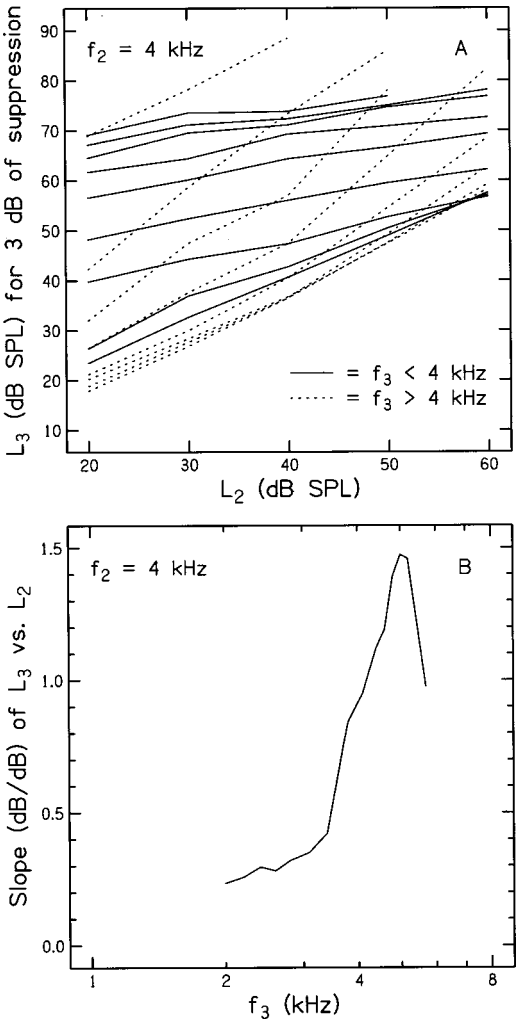

FIG. 9. Top: L_3 to produce a 3-dB reduction in DPOAE level as a function of L_2 for $f_2=4$ kHz. The parameter is f_3, with f_3 frequencies $<f_2$ shown as solid lines and f_3 frequencies $>f_2$ shown as dotted lines. Bottom: Slopes of the L_3 vs L_2 functions (top panel) as a function of f_3 frequency.

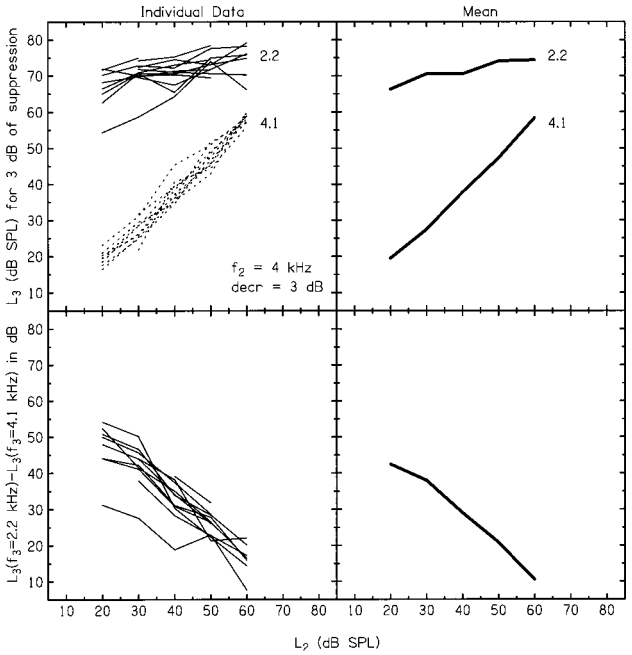

FIG. 10. Top row: L_3 necessary to produce a 3-dB reduction in DPOAE level as a function of L_2, when $f_2=4$ kHz. The parameter is f_3 frequency, as indicated within each panel. The left panel shows data for individual subjects, while the right panel shows mean data. Bottom: Gain as a function of L_2 for individual subjects (left panel) and averaged across subjects (right panel). Gain was defined as the difference in dB between the L_3 necessary to achieve a 3-dB reduction in DPOAE level when $f_3=2.2$ kHz and when $f_3=4.1$ kHz.

served for f_3 frequencies close to f_2, which can be likened to on-frequency conditions. In contrast, higher L_3 levels were needed to achieve a 3-dB reduction in DPOAE level when f_3 was higher than f_2; however, the L_3 level required to maintain a constant amount of suppression increased more rapidly, compared to the on-frequency case. When f_3 was less than f_2, higher L_3 levels also were needed. In these cases, however, the L_3 level necessary to maintain a constant 3-dB reduction in DPOAE level increased more slowly as L_2 increased. The data shown in Fig. 9(A) are the same as the tuning-curve data shown in the top panel of Fig. 8. Here, however, the effects of level for individual suppressor frequencies are more clearly shown.

Figure 9(B) plots the slope of the L_3 vs L_2 functions shown in Fig. 9(A). The slope is shallow at low f_3 frequencies relative to f_2. As f_3 approaches f_2, the slope increases rapidly, with a slope close to 1 dB/dB when f_3 and f_2 frequencies are approximately equal. As f_3 is increased further, the slope also increases. However, estimates of slope for f_3 frequencies above 5 kHz may not be reliable because they are based on fewer points. For some of these frequencies, the suppression criterion of 3 dB could be achieved only for low L_2 levels [see the top dotted line in Fig. 9(A)]. There is a transition in this slope function, such that the slopes are shallow and remain relatively constant at low f_3 frequencies, and then change abruptly and increase rapidly as f_3 increases further. The significance of this abrupt transition, which occurred at about 3.5 kHz, is unknown.

D. Tip-to-tail differences vs L_2

The top row of Fig. 10 plots the L_3 necessary to produce a 3-dB decrement as a function of L_2 for a frequency close to f_2 (4.1 kHz, dashed lines) and for a low frequency (2.2 kHz, solid lines) relative to f_2. Individual lines in the upper left-hand panel represent data from individual subjects. The lines in the right-hand panel represent means of the data shown on the left. The data shown here are equivalent to the data shown in Fig. 9(A). The representations in this figure differ from those shown in the previous figure, however, in that individual and mean data are presented for only two f_3 frequencies. Note that as L_2 increases, the level necessary to reduce the response by 3 dB also increases. However, the increase is more rapid when f_3 is close to f_2, compared to when f_3 is much lower than f_2. This is another representation of the changes in tip-to-tail differences that were evident in the tuning curves of Fig. 6, in which there were greater shifts in the tip versus the tail of the tuning curves as L_2 increased.

It can be argued that the ''cochlear amplifier'' for a specific place along the BM is active when that place is driven by its CF. Furthermore, it can be argued that the cochlear

amplifier is less active when a specific place along the BM is driven by a frequency much lower than the CF for that place (e.g., Mills, 1998; Pienkowski and Kunov, 2001). Thus, a comparison of the ''threshold'' suppressor levels for a low-frequency suppressor vs a suppressor close to f_2 (i.e., the tip-to-tail difference) should provide an estimate that is related to the ''gain'' provided by the cochlear amplifier. These estimates are presented in the bottom row of panels in Fig. 10. The method used to obtain the present estimates of threshold differed slightly from the one described above in that $D=0$ was determined by linear interpolation instead of linear regression. The lines shown in the lower-left panel were derived by subtracting the L_3 for $f_3=4.1$ kHz from the L_3 for $f_3=2.2$ kHz, as a function of L_2. Each line represents the results for an individual subject. The line in the lower-right panel represents the mean of these data. As L_2 increases, the dB difference to maintain a constant response (3 dB of suppression) at the f_2 place decreases, going from about 45 dB when $L_2=20$ dB SPL down to 10 dB when $L_2=60$ dB SPL.

IV. DISCUSSION

We assume that the decrement in DPOAE level as a result of the suppressor (i.e., amount of suppression) is a measure of response to the suppressor at the f_2 place. That is, decrements provide indirect measures of response properties for a fixed cochlear place as a function of the frequency and level of the suppressor. In many ways, therefore, the assumptions associated with DPOAE suppression paradigms are similar to those made whenever physiological or psychophysical masking experiments are performed. Thus, one might view the present fixed-frequency, fixed-level primaries and the variable-frequency and variable-level suppressors the way one would view probes and maskers in masking or suppression studies. This framework might be useful as one considers the context within which the work reported here is interpreted.

As noted above, response patterns were not identical at 2 and 4 kHz. These differences in findings cannot be attributed to differences in noise level, because the measurement-based stopping rules resulted in near-equivalent noise levels for both f_2 frequencies. Control conditions were equally stable as well, thus suggesting that differences in response patterns were not the result of greater variability in DPOAE levels when $f_2=2$ kHz. Others have reported differences in DPOAEs from 2 kHz compared to 4 kHz. For example, He and Schmiedt (1993) noted that greater fine structure was evident in DPOAEs surrounding 2 kHz compared to 4 kHz. Konrad-Martin *et al.* (2001) reported data that revealed greater relative contributions to the ear-canal DPOAE from the reflection source (relative to the intermodulation source) at 2 kHz (compared to 4 kHz), an observation that is consistent with the greater fine structure noted by He and Schmiedt. The source(s) of these differences, and how they might influence the present results, are not known. For the purposes of simplicity, the discussion to follow will focus on results obtained when $f_2=4$ kHz. We remain perplexed, however, by the results when $f_2=2$ kHz, especially in view of the orderly behavior that was observed at 4 kHz.

A. DPOAE decrements as measures of response growth

Although previous studies reported DPOAE level (as opposed to DPOAE decrement) as a function of L_3 for a range of suppressor frequencies (e.g., Kemp and Brown, 1983; Kummer *et al.*, 1995; Abdala, 1998, 2001), the present results were similar to those reported previously. For example, Kummer *et al.* (1995) used an f_2 of 3.975 kHz an L_2 of 40 dB SPL, and an L_1 of 55 dB SPL, stimulus conditions that were nearly identical to one set of conditions in the present study. While we observed slightly steeper slopes for low-frequency suppressors, the overall pattern in their data [their Fig. 2(c)] was the same as we observed (present Fig. 6). Across all studies, changes in DPOAE level occurred more rapidly with suppressor level when the suppressor frequency was below f_2, with more gradual changes in DPOAE level when f_3 was greater than f_2.

Our preference for converting these data to decrements relates to the ease with which such conversions permit comparisons between DPOAE data and data derived from other measurements of cochlear response growth. In this form, these functions share many characteristics with other measures of response growth, including direct measurements from the BM, single-unit rate-level functions, whole-nerve AP decrement vs masker-level functions, and ABR decrement vs masker-level functions. For example, the suppressor levels at which threshold suppressive effects were observed depended on the relationship between f_3 and f_2. Assuming that DPOAE decrements describe the representation of f_3 at the f_2 place, then this relationship reflects how different frequencies are represented at a fixed place along the cochlea in much the same way as is evident in other measures of auditory function.

The slopes of these DPOAE decrement functions also share similarities with other measures of response growth. For example, the slopes of single-unit rate-level functions depend on the relationship between driver frequency and an individual fiber's CF (e.g., Sachs and Abbas, 1974). For driver frequencies much lower than CF, the slope of the rate-level function was steep, compared to the slopes when driver frequencies were higher than CF. Sachs and Abbas compared their single-unit data to the Mössbauer measurements of cochlear mechanics made by Rhode (1971). While Rhode's 1971 measurements were not as sensitive as more recent measures of cochlear mechanical responses, Sachs and Abbas were able to relate the two different measures. More recently, other direct measurements of BM motion have demonstrated a relationship between the slope of I/O functions and frequency for a fixed place along the cochlea (Ruggero and Rich, 1991; Ruggero *et al.*, 1997). These more recent data showed that when a particular place was driven at its CF, the slope of the I/O function was less steep compared to the case when the same place was driven at frequencies lower than CF. The present data, at least qualitatively, show the same systematic relationship between the slopes of the decrement vs L_3 functions and suppressor frequency, at least at 4 kHz. These observations are consistent with previous single-unit data (Sachs and Abbas, 1974; Schmiedt and Zwislocki, 1980), AP data in which the response to a probe

was reduced by a masker (e.g., Abbas and Gorga, 1981), and direct BM measurements of response growth (Ruggero and Rich, 1991). Thus, it would appear that DPOAE decrement vs L_3 functions can be used as an indirect estimate of cochlear response growth as a function of frequency for a specific cochlear place. Quantitative comparisons, however, are not possible between the present data (in dB/dB) and either single-unit data (in spikes/s/dB) or basilar-membrane (in velocity/dB) measurements of response growth.

It may be possible, however, to compare the present results to previous single-unit (Abbas and Sachs, 1976; Costalupes *et al.*, 1987; Delgutte, 1990) and basilar-membrane (Ruggero *et al.*, 1992) recordings of suppression. As a general rule, the trends evident in the present results are consistent with the findings in these previous studies, including the dependence of slope on the relationship between suppressor frequency and best frequency (single-unit and basilar-membrane measurements) or f_2 (DPOAE suppression measurements). In some of these cases, however, direct comparisons are not possible because of differences in the ways suppression was measured. For example, Abbas and Sachs (1976) described the amount of suppression as a fractional response, relative to the discharge rate when the suppressor was not present. In those cases where more direct comparisons are possible, the present data are not in exact agreement with findings from lower animals. For example, Ruggero *et al.* (1992) observed slopes in the range from 0.65 to 1.42 dB/dB (mean = 0.97 dB/dB) for suppressors below best frequency and slopes of 0.28 to 0.48 dB/dB (mean = 0.36 dB/dB) for suppressors higher than the best frequency. The reduced slope of suppression observed for the basilar-membrane measurements may indicate reduced sensitivity of the animal preparation as a consequence of opening the cochlea. Alternatively, the differences in slope estimates may be due to fundamental differences between basilar-membrane suppression and DPOAE suppression. Delgutte (1990) observed slopes of about 2 dB/dB for suppressor frequencies 1 octave lower than CF and slopes of about 0.25 dB/dB for suppressors about $\frac{1}{4}$ octave above CF, but shallower slopes when differences in suppressive effects as a function of CF were taken into account. For one fiber with a CF close to the present f_2 (see Fig. 7, Delgutte, 1990), suppression grew with a slope less than 1.5 dB/dB for a suppressor 1 octave below CF.

B. Suppression tuning curves

The tuning curves described in this paper are similar in form to other measures of peripheral tuning, especially previously described DPOAE suppression tuning curves (e.g., Kemp and Brown, 1983; Abdala, 1998, 2001; Abdala *et al.*, 1996; Brown and Kemp, 1984; Harris *et al.*, 1992; Martin *et al.*, 1987, 1999; Kummer *et al.*, 1995; Cianfrone *et al.*, 1994). These DPOAE suppression tuning curves can be viewed as estimates of level as a function of frequency that results in a constant response (3 dB of suppression in the present study) at the f_2 place. While the data were more variable when $f_2 = 2$ kHz, the present results showed the expected pattern in which the lowest suppressor levels were needed when f_3 and f_2 frequencies were similar, with greater suppressor levels needed as f_3 moved away from f_2.

The most sensitive suppressor frequency shifted slightly towards lower frequencies as primary levels were increased (Fig. 8). Another way of stating this finding is that, for a given place, the frequency that is maximally represented at that place might change with level, an observation that has been made by others using more direct measurements of cochlear responses (e.g., Rhode and Recio, 2000). For example, Ruggero *et al.* (1997) observed about a 0.32-octave downward shift in best frequency as level changed from 10 or 20 dB SPL to 60 dB SPL. We observed a shift of about 0.30 octave (4.3 to about 3.5 kHz) over a similar range of levels. Thus, a basal spread of excitation is evident in cochlear mechanical responses, whether measured directly in animals or indirectly in humans.

C. Growth of suppression

In the data summarized in Fig. 9(A), an alternate approach was taken to describe response growth. Here, the suppressor (masker) level necessary to maintain a constant response was plotted as a function of L_2 (probe level). In this representation, it is evident that lower suppressor levels (L_3) were needed when f_3 was close to f_2, compared to when it was nearly an octave below f_2. For the on-frequency case, L_3 and L_2 were related linearly, such that it was necessary to increase L_3 by 10 dB for every 10-dB increase in L_2. In contrast, much smaller increases in L_3 were needed when f_3 was lower than f_2. Thus, the slopes of functions relating L_3 to L_2 [Fig. 9(B)] were 1 for conditions in which f_3 was approximately equal to f_2 and less than 1 for conditions in which f_3 was less than f_2. This means that the response to the suppressor (f_3) grew more rapidly than the response to the probe (f_2) at the f_2 place when $f_3 < f_2$.

D. Compression ratio in normal ears

The summary in Fig. 10 might provide an estimate of the amount of compression for the on-frequency condition. When $f_3 \approx f_2$, both suppressor and probe are processed through the same input–output (I/O) function. Even though the I/O function is compressive, functions relating L_3 to L_2 grow linearly because they are treated similarly by the nonlinearity. In contrast, the response to a low-frequency suppressor at the f_2 place is less affected by the compressive nonlinearity, and probably grows more linearly. Thus, the slope of the function relating L_3 to L_2 for $f_3 = 2.2$ kHz (top row, Fig. 10) describes the interaction between responses to a stimulus that grows compressively at the f_2 place and one that grows linearly at the same place. In the present case, this slope estimate was 0.26 dB/dB, which compares favorably with values obtained from DPOAE I/O functions in normal-hearing humans (Dorn *et al.*, 2001), where the slope was 0.24 dB/dB, and is in the range of values (0.2 to 0.5 dB/dB) reported by Ruggero *et al.* (1997) for direct measurements from the chinchilla. The estimates from humans suggest that the normal ear compresses the input signal by a factor of about 4 from near-threshold levels to 60–70 dB SPL.

E. Indirect estimates of "gain"

While some have argued that the cochlear amplifier may have a "gain" of 1 (Allen and Fahey, 1992), others suggest that the mechanical responses of the cochlea are such that the displacements at any place are increased when that place is driven at its CF. Regardless of whether gain is provided by the cochlear amplifier, the fact remains that responses from normal cochleae are fundamentally different when a specific place is driven with an on-frequency stimulus, compared to responses when the same place is driven by a lower frequency. For example, Ruggero and Rich (1991) measured lower mechanical thresholds to a 9-kHz tone at a basal cochlear place, compared to the threshold for a 1-kHz tone at the same place. In addition, the I/O function for the 9-kHz tone was characterized by compression for moderate stimulus levels, whereas no compression was observed when the driver frequency was 1 kHz. Thus, the slope of the I/O function was steeper at 1 kHz. Furthermore, the I/O function at 9 kHz showed an elevated threshold and increased slope (approximating the slope at 1 kHz) when the animal was treated with furosemide. However, threshold and slope of the I/O function did not change at 1 kHz following furosemide administration.

Similar differences between on-frequency and low-frequency responses for a fixed cochlear place have been observed by others. For example, single-unit frequency threshold curves (FTCs) are characterized by low thresholds for CF tones, with increasing thresholds as driver frequency moves away from CF. Typically, these FTCs are characterized by a tail or low-frequency region, in which thresholds are elevated (relative to threshold at CF), but remain relatively constant. When OHC damage is sustained, thresholds for frequencies close to CF are elevated, with little or no change in the thresholds on the low-frequency tails of the FTC (e.g., Kiang *et al.*, 1976; Liberman and Dodds, 1984; Dallos and Harris, 1978). Stated differently, damage to the OHCs, which are thought to be closely related to cochlear-amplifier function, affected on-frequency responses more than low-frequency responses. Furthermore, Ruggero *et al.* (1997) compared premortem and postmortem velocity-vs-level functions, taking the difference between these conditions as a measure of gain (see their Fig. 16), on the assumption that the cochlear amplifier was functional prior to death, and disabled following death. This procedure resulted in gain estimates of 54 or 69 dB.

Taken together, these data suggest that a measure related to cochlear-amplifier gain may be obtained by comparing responses for on-frequency and low-frequency stimuli. In a sense, these two stimulus conditions may be viewed as including one in which the cochlear amplifier is active (on-frequency) and one in which it is not (low-frequency). Indeed, Mills (1998) took this approach in an effort to estimate cochlear-amplifier gain in gerbils. He compared tips and tails of DPOAE suppression tuning curves to derive gain estimates, choosing the intersection between the steeply sloped initial low-frequency portion and the more distant, low-frequency shallow-sloped tail of the tuning curve to define the low-frequency condition. More recently, Pienkowski and Kunov (2001) took a similar approach in humans. They showed that this estimate of gain decreased as threshold increased (even within the range of "normal hearing"), but studied only one primary level ($L_1 = 60$ dB SPL and $L_2 = 40$ dB SPL).

In the data from the present study, a sharp break on the low-frequency side of the DPOAE suppression tuning curves was not apparent. Furthermore, completely flat low-frequency tails were not observed. As a consequence, we used the lowest f_3 for which suppression was observed for a wide range of L_2 levels in the majority of subjects ($f_3 = 2.2$ kHz). The responses observed when $f_3 = 2.2$ kHz were viewed as responses that were not influenced by the cochlear amplifier at the place where $f_2 = 4$ kHz is represented (see Fig. 10). This approach results in a slightly larger estimate of gain compared to some of the other definitions that have been used, but the differences are small because the low-frequency tail has a shallow slope. We recognize the indirect nature of our overall approach, in addition to its limitations related to the somewhat arbitrary nature with which this frequency was selected. However, the decision to use the response to a low frequency relative to f_2 is not entirely arbitrary, given previous direct measurements of BM motion, single-unit FTCs, and DPOAE suppression data. Finally, we assumed that the cochlear amplifier was active for responses when f_3 approximated f_2 ($f_3 = 4.1$ kHz).

A comparison of suppression thresholds when $f_3 = 2.2$ kHz and $f_3 = 4.1$ kHz, therefore, was taken as an indirect estimate related to cochlear-amplifier gain. Examining these threshold differences for a range of L_2 levels provided an estimate that demonstrated that gain decreased as level increased (see Fig. 10). Depending on the appropriateness of the assumptions underlying this approach, these data provide an estimate related to cochlear-amplifier gain as a function of level in humans.

In an effort to compare the present results to more direct mechanical measurements, data reported by Ruggero *et al.* (1997) were used to estimate the dB difference between velocity-level functions at CF (10 kHz) and at a frequency (5 or 6 kHz) one octave below CF (see their Fig. 7). This approach to the mechanical data yielded gain estimates ranging from about 37 dB at 20 dB SPL to about 10 dB at 60 dB SPL, values that are close to the present, indirect estimates in humans.

In spite of the agreement between direct and indirect measures, there are other concerns with the conclusions from this study, beyond those associated with the underlying assumptions leading to estimates of gain. As noted earlier, response patterns were not as orderly at 2 kHz, compared to 4 kHz. We assume that cochlear function at the places where these two frequencies are represented is similar. Furthermore, the measurement-based stopping rules helped to equate noise levels for the two f_2 frequencies. Therefore, explanations that account for the differences in responses are not obvious. Furthermore, the present measurements require the use of a complex stimulus paradigm, with two tones serving as a probe signal, and a third tone serving as the suppressor. Opportunities exist for the generation of multiple distortion products and mutual suppression, both among stimulus tones and perhaps even among multiple distortion products.

F. Potential clinical significance

The inherent problems associated with paradigms like the one used here are unavoidable because direct measurements of BM motion and/or single-unit recordings are not possible in humans. While AP and/or ABR measurements are possible, both require a greater investment in recording time compared to DPOAEs, related to problems associated with the SNR for these neural measurements in humans. Averages including many samples, taking several minutes or longer, might be needed for one data point on an ABR decrement vs masker level function. While the SNR for AP measurements can be improved by placing an electrode either on the tympanic membrane or transtympanically on the promontory, such approaches are not routinely feasible in humans, including patients seen in the clinic. On the other hand, a single DPOAE decrement vs suppressor-level function can be obtained in 5–10 min or less, especially when $f_2 = 4$ kHz, a frequency for which the noise levels typically are low. This time could be shortened further if suppressor level were incremented in steps larger than 5 dB. To the extent that these DPOAE decrement functions provide an estimate of cochlear response growth at a specific place, the present data (as well as the data from others) suggest that objective estimates of response growth are possible in humans.

Furthermore, despite the complexity of the stimulus paradigm and the assumptions in the interpretation of these data, the similarity with previous data from lower animals suggest that estimates related to cochlear-amplifier gain are possible in humans. The work of Pienkowski and Kunov (2001) suggests that it might be feasible to design a paradigm that could be used to make similar estimates in patients whose hearing losses do not to completely eliminate the DPOAE. If successful under laboratory conditions, there may be clinical applications to these measurements. For example, these data may lead to a more quantitative approach to developing signal-processing schemes when fitting amplification (such as selecting a compression ratio), especially for infants and young children with hearing loss.

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Abbas, P. J., and Gorga, M. P. (**1981**). "AP responses in forward-masking paradigms and their relationship to responses of auditory-nerve fibers," J. Acoust. Soc. Am. **69**, 492–499.

Abbas, P. J., and Sachs, M. B. (**1976**). "Two-tone suppression in auditory-nerve fibers: Extension of a stimulus-response relationship," J. Acoust. Soc. Am. **59**, 112–122.

Abdala, C. (**1998**). "A developmental study of distortion product otoacoustic emission ($2f_1-f_2$) suppression in humans," Hear. Res. **121**, 125–138.

Abdala, C. (**2001**). "Maturation of the human cochlear amplifier: Distortion product otoacoustic emission suppression tuning curves recorded at low and high primary levels," J. Acoust. Soc. Am. **110**, 1465–1476.

Abdala, C., Sininger, Y. S., Ekelid, M., and Zeng, F-G. (**1996**). "Distortion product otoacoustic emission suppression tuning curves in human adults and neonates," Hear. Res. **98**, 38–53.

Allen, J. B., and Fahey, P. F. (**1992**). "Using acoustic distortion products to measure cochlear amplifier gain on the basilar membrane," J. Acoust. Soc. Am. **92**, 178–188.

ANSI (**1996**). ANSI S3.6-1996, "Specifications for Audiometers" (American National Standards Institute, New York).

Brown, A. M., and Kemp, D. T. (**1984**). "Suppressibility of the $2f_1-f_2$ stimulated acoustic emissions in gerbil and man," Hear. Res. **13**, 29–37.

Cianfrone, G., Altissimi, G., Cerevellini, M., Musacchio, A., and Turchetta, R. (**1994**). "Suppression tuning characteristics of $2f_1-f_2$ distortion product otoacoustic emissions," Br. J. Audiol. **28**, 205–212.

Costalupes, J. A., Rich, N. C., and Ruggero, M. A. (**1987**). "Effects of excitatory and nonexcitatory tones on two-tone rate suppression in auditory-nerve fibers," Hear. Res. **26**, 155–164.

Dallos, P. J., and Harris, D. M. (**1978**). "Properties of auditory-nerve responses in the absence of outer hair cells," J. Neurophysiol. **41**, 365–383.

Dallos, P. J., Harris, D. M., Relkin, E., and Cheatham, M. A. (**1980**). "Two-tone suppression and intermodulation distortion in the cochlea: Effect of outer hair cell lesions," in *Psychophysical, Physiological and Behavioral Studies of Hearing*, edited by G. van den Brink and F. A. Bilsen (Delft University Press, Delft, The Netherlands), pp. 242–252.

Delgutte, B. (**1990**). "Two-tone rate suppression in auditory-nerve fibers: Dependence on suppressor frequency and level," Hear. Res. **49**, 225–246.

Dorn, P. A., Konrad-Martin, D., Neely, S. T., Keefe, D. H., Cyr, E., and Gorga, M. P. (**2001**). "Distortion product otoacoustic emission input/output functions in normal-hearing and hearing-impaired human ears," J. Acoust. Soc. Am. (in press).

Dorn, P. A., Piskorski, P., Gorga, M. P., Neely, S. T., and Keefe, D. H. (**1999**). "Predicting audiometric status from distortion product otoacoustic emissions using multivariate analyses," Ear Hear. **20**, 149–163.

Dorn, P. A., Piskorski, P., Keefe, D. H., Neely, S. T., and Gorga, M. P. (**1998**). "On the existence of an age/threshold/frequency interaction in distortion product otoacoustic emissions," J. Acoust. Soc. Am. **104**, 964–971.

Evans, E. F. (**1974**). "Auditory frequency selectivity and the cochlear nerve," in *Facts and Models in Hearing*, edited by E. Zwicker and E. Terhardt (Springer, New York), pp. 118–129.

Gorga, M. P., and Abbas, P. J. (**1981a**). "AP measurements of short-term adaptation in normal and in acoustically traumatized ears," J. Acoust. Soc. Am. **70**, 1310–1321.

Gorga, M. P., and Abbas, P. J. (**1981b**). "Forward-masking AP tuning curves in normal and in acoustically traumatized ears," J. Acoust. Soc. Am. **70**, 1322–1330.

Gorga, M. P., McGee, J., Walsh, E. J., Javel, E., and Farley, G. R. (**1983**). "ABR measurements in the cat using a forward-masking paradigm," J. Acoust. Soc. Am. **73**, 256–261.

Gorga, M. P., Neely, S. T., Bergman, B. M., Beauchaine, K. L., Kaminski, J. R., Peters, J., and Jesteadt, W. (**1993**). "Otoacoustic emissions from normal-hearing and hearing-impaired subjects: Distortion product responses," J. Acoust. Soc. Am. **93**, 2050–2060.

Gorga, M. P., Stover, L. J., and Neely, S. T. (**1996**). "The use of cumulative distributions to determine critical values and levels of confidence for clinical distortion product otoacoustic emission measurements," J. Acoust. Soc. Am. **100**, 968–977.

Gorga, M. P., Neely, S. T., and Dorn, P. A. (**1999**). "DPOAE test performance for *a priori* criteria and for multifrequency audiometric standards," Ear Hear. **20**, 345–362.

Gorga, M. P., Neely, S. T., and Dorn, P. A. (**2002**). "Distortion product otoacoustic emissions in relation to hearing loss," in *Otoacoustic Emissions: Clinical Applications*, 2nd ed., edited by M. S. Robinette and T. J. Glattke (Thieme Medical, New York), pp. 243–272.

Gorga, M. P., Neely, S. T., Ohlrich, B., Hoover, B., Redner, J., and Peters, J. (**1997**). "From laboratory to clinic: A large scale study of distortion product otoacoustic emissions in ears with normal hearing and ears with hearing loss," Ear Hear. **18**, 440–455.

Gorga, M. P., Nelson, K., Davis, T., Dorn, P. A., and Neely, S. T. (**2000**). "Distortion product otoacoustic emission test performance when both $2f_1-f_2$ and $2f_2-f_1$ are used to predict auditory status," J. Acoust. Soc. Am. **107**, 2128–2135.

Harris, D. M. (**1979**). "Action potential suppression, tuning curves and thresholds: Comparison with single fiber data," Hear. Res. **1**, 133–154.

Harris, D. M., and Dallos, P. J. (**1979**). "Forward masking of auditory nerve fiber responses," J. Neurophysiol. **42**, 1083–1107.

Harris, F. P., and Probst, R. (**1997**). "Otoacoustic emissions and audiometric outcomes," in *Otoacoustic Emissions: Clinical Applications*, edited by M.

S. Robinette and T. J. Glattke (Thieme, New York), pp. 151–180.
Harris, F. P., Probst, R., and Xu, L. (**1992**). ''Suppression of the 2 f_1-f_2 otoacoustic emission in humans,'' Hear. Res. **64**, 133–141.
He, N-j., and Schmiedt, R. A. (**1993**). ''Fine structure of the 2 $f1-f2$ acoustic distortion product: Changes with primary levels,'' J. Acoust. Soc. Am. **94**, 2659–2669.
Janssen, T., Kummer, P., and Arnold, W. (**1998**). ''Growth behavior of the 2 f_1-f_2 distortion product otoacoustic emission in tinnitus,'' J. Acoust. Soc. Am. **103**, 3418–3430.
Kemp, D. T., and Brown, A. M. (**1983**). ''A comparison of mechanical nonlinearities in the cochleae of man and gerbil from ear canal measurements,'' in *Hearing: Physiological Basis and Psychophysics*, edited by R. Klinke and R. Hartman (Springer, Berlin), pp. 82–88.
Kiang, N. Y-S., Liberman, M. C., and Levine, R. A. (**1976**). ''Auditory-nerve activity in cats exposed to ototoxic drugs and high-intensity sounds,'' Ann. Otol. Rhinol. Laryngol. **85**, 752–768.
Kim, D. O. (**1980**). ''Cochlear mechanics: Implications of electrophysiological and acoustical observations,'' Hear. Res. **2**, 297–317.
Kim, D. O., Paparello, J., Jung, M. D., Smursynski, J., and Sun, X. (**1996**). ''Distortion product otoacoustic emission test of sensorineural hearing loss: Performance regarding sensitivity, specificity, and receiver operating characteristics,'' Acta Otolaryngol. (Stockh) **116**, 3–11.
Kimberley, B. P., Brown, D. K., and Allen, J. B. (**1997**). ''Distortion product emissions and sensorineural hearing loss,'' in *Otoacoustic Emissions: Clinical Applications*, edited by M. S. Robinette and T. J. Glattke (Thieme, New York), pp. 181–204.
Konrad-Martin, D., Neely, S. T., Keefe, D. H., Dorn, P. A., and Gorga, M. P. (**2001**). ''Multiple sources of distortion product otoacoustic emissions revealed by suppression experiments and inverse fast Fourier transforms,'' J. Acoust. Soc. Am. **109**, 2862–2879.
Kummer, P., Janssen, T., and Arnold, W. (**1995**). ''Suppression tuning characteristics of the 2 f_1-f_2 distortion-product otoacoustic emission in humans,'' J. Acoust. Soc. Am. **98**, 197–210.
Kummer, P., Janssen, T., and Arnold, W. (**1998**). ''The level and growth behavior of the 2 f_1-f_2 distortion product otoacoustic emission and its relationship to auditory sensitivity in normal hearing and cochlear hearing loss,'' J. Acoust. Soc. Am. **103**, 3431–3444.
Kummer, P., Janssen, T., Hulin, P., and Arnold, W. (**2000**). ''Optimal $L1-L2$ primary tone level separation remains independent of test frequency in humans,'' Hear. Res. **146**, 47–56.
Liberman, M. C., and Dodds, L. W. (**1984**). ''Single-neuron labeling and chronic cochlear pathology. III. Stereocilia damage and alterations of threshold tuning curves,'' Hear. Res. **16**, 55–74.
Martin, G. K., Lonsbury-Martin, B. L., Probst, R., Scheinin, S. A., and Coats, A. C. (**1987**). ''Acoustic distortion products in rabbit ear canal. II. Sites of origin revealed by suppression contours and pure-tone exposures,'' Hear. Res. **28**, 191–208.
Martin, G. K., Ohlms, L. A., Franklin, D. J., Harris, F. P., and Lonsbury-Martin, B. L. (**1990**). ''Distortion product emissions in humans. III. Influence of sensorineural hearing loss,'' Ann. Otol. Rhinol. Laryngol. Suppl. **147**, 30–42.
Martin, G. K., Stagner, B. B., Jassir, D., Telischi, F. F., and Lonsbury-Martin, B. L. (**1999**). ''Suppression and enhancement of distortion-product otoacoustic emissions by interference tones above f_2. I. Basic findings in rabbits,'' Hear. Res. **136**, 105–123.
Mills, D. M. (**1998**). ''Interpretation of distortion product otoacoustic emission measurements. II. Estimating tuning characteristics using three stimulus tones,'' J. Acoust. Soc. Am. **103**, 507–523.
Neely, S. T., and Gorga, M. P. (**1998**). ''Comparison between intensity and pressure as measures of sound level in the ear canal,'' J. Acoust. Soc. Am. **104**, 2925–2934.
Neely, S. T., and Liu, Z. (**1993**). EMAV: Otoacoustic emission averager, Tech. Memo No. 17 (Boys Town National Research Hospital, Omaha, NE).
Pienkowski, M., and Kunov, H. (**2001**). ''Suppression of distortion product otoacoustic emissions and hearing thresholds,'' J. Acoust. Soc. Am. **109**, 1496–1502.
Probst, R., and Hauser, R. (**1990**). ''Distortion product otoacoustic emissions in normal and hearing-impaired ears,'' Am. J. Otol. **11**, 236–243.
Rhode, W. S. (**1971**). ''Observations of the vibration of the basilar membrane in squirrel monkey using the Mossbauer technique,'' J. Acoust. Soc. Am. **49**, 1218–1231.
Rhode, W. S., and Recio, A. (**2000**). ''Study of mechanical motions in the basal region of the chinchilla cochlea,'' J. Acoust. Soc. Am. **107**, 3317–3332.
Ruggero, M. A., and Rich, N. C. (**1991**). ''Furosemide alters organ of cortin mechanics: Evidence for feedback of outer hair cells upon the basilar membrane,'' J. Neuro. **11**, 1057–1067.
Ruggero, M. A., Rich, N. C., Recio, A., Narayan, S. S., and Robles, L. (**1997**). ''Basilar-membrane responses to tones at the base of the chinchilla cochlea,'' J. Acoust. Soc. Am. **101**, 2151–2163.
Ruggero, M. A., Robles, L., and Rich, N. C. (**1992**). ''Two-tone suppression in the basilar membrane of the cochlea: Mechanical basis of auditory-nerve rate suppression,'' J. Neurophysiol. **68**, 1087–1099.
Sachs, M. B., and Abbas, P. J. (**1974**). ''Rate versus level functions for auditory-nerve fibers in cats: Tone-burst responses,'' J. Acoust. Soc. Am. **56**, 1835–1847.
Schmiedt, R. A., and Zwislocki, J. J. (**1980**). ''Effects of hair cell lesions on responses of cochlear nerve fibers. II. Single- and two-tone intensity functions in relation to tuning curves,'' J. Neurophysiol. **43**, 1390–1405.
Sewell, W. F. (**1984**). ''Furosemide selectively reduces one component in rate-level functions from auditory-nerve fibers,'' Hear. Res. **15**, 69–72.
Siegel, J. H. (**1994**). ''Ear-canal standing waves and high-frequency sound calibration using otoacoustic emission probes,'' J. Acoust. Soc. Am. **95**, 2589–2597.
Siegel, J. H. (**2002**). ''Calibrating otoacoustic emission probes,'' in *Otoacoustic Emissions: Clinical Applications*, 2nd ed., edited by M. S. Robinette and T. J. Glattke (Thieme Medical, New York), pp. 416–441.
Smith, R. L. (**1977**). ''Short-term adaptation in single auditory-nerve fibers: Some poststimulatory effects,'' J. Neurophysiol. **40**, 1098–1112.
Smith, R. L. (**1979**). ''Adaptation, saturation and physiological masking in single auditory-nerve fibers,'' J. Acoust. Soc. Am. **65**, 166–178.
Smith, R. L., and Zwislocki, J. J. (**1975**). ''Short-term adaptation and incremental responses of single auditory-nerve fibers,'' Biol. Cybern. **17**, 169–182.
Stover, L., Gorga, M. P., Neely, S. T., and Montoya, D. (**1996**). ''Towards optimizing the clinical utility of distortion product otoacoustic emission measurements,'' J. Acoust. Soc. Am. **100**, 956–967.
Whitehead, M. L., Lonsbury-Martin, B. L., and Martin, G. K. (**1992**). ''Evidence for two discrete sources of 2 f_1-f_2 distortion product otoacoustic emissions in rabbit. II. Differential physiological vulnerability,'' J. Acoust. Soc. Am. **92**, 2662–2682.
Whitehead, M. L., McCoy, M. J., Lonsbury-Martin, B. L., and Martin, G. K. (**1995**). ''Dependence of distortion product otoacoustic emissions on primary levels in normal and impaired ears. I. Effects of decreasing L_2 below L_1,'' J. Acoust. Soc. Am. **97**, 2346–2358.