Evidence for basal distortion-product otoacoustic emission components

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Distortion-product otoacoustic emissions (DPOAEs) were measured with traditional DP-grams and level/phase (L/P) maps in rabbits with either normal cochlear function or unique sound-induced cochlear losses that were characterized as either low-frequency or notched configurations. To demonstrate that emission generators distributed basal to the f_2 primary-tone contribute, in general, to DPOAE levels and phases, a high-frequency interference tone (IT) was presented at 1/3 of an octave (oct) above the f_2 primary-tone, and DPOAEs were re-measured as “augmented” DP-grams (ADP-grams) and L/P maps. The vector difference between the control and augmented functions was then computed to derive residual DP-grams (RDP-grams) and L/P maps. The resulting RDP-grams and L/P maps, which described the DPOAEs removed by the IT, supported the notion that basal DPOAE components routinely contribute to the generation of standard measures of DPOAEs. Separate experiments demonstrated that these components could not be attributed to the effects of the 1/3-oct IT on f_2 , or DPOAEs generated by the addition of a third interfering tone. These basal components can “fill in” the lesion estimated by the commonly employed DP-gram. Thus, ADP-grams more accurately reveal the pattern of cochlear damage and may eventually lead to an improved DP-gram procedure. [DOI: 10.1121/1.3353121]

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I. INTRODUCTION

In previous studies of distortion-product otoacoustic emissions (DPOAEs), [Martin *et al.* \(1999, 2003\)](#) described phenomena whereby a third or interference tone (IT) placed slightly less than or more than an octave (oct) above the f_2 primary-tone produced either suppression or enhancement of the DPOAE being measured. Besides rabbits and humans representing the main species for the investigations noted above, these phenomena were also observed in guinea pigs, mice, and gerbils ([Martin *et al.*, 1995, 1999, 2003](#); [Whitehead *et al.*, 1995](#); [Jassir *et al.*, 1996](#); [Jimenez *et al.*, 1996](#); [Mills, 1998](#)).

Such suppression or enhancement phenomena were sensitive to both the f_1 and f_2 primary-tone levels and the f_2/f_1 ratio. The suppression/enhancement effects were also extremely vulnerable to common cochlear traumas such as ototoxicity ([Martin *et al.*, 1999](#)) or noise over-exposure ([Howard *et al.*, 2002, 2003](#)). In these instances, return of suppression/enhancement in response to the high-frequency IT occurred long after apparent recovery of DPOAEs that were presumably generated near the f_2 place on the basilar membrane (BM). Because of the sharp apical cutoff of the traveling wave (TW) of the IT when presented at more than 1 oct above f_2 , there was no obvious mechanism whereby the IT could directly affect the f_2 place to produce the observed suppression/enhancement of DPOAEs. Consequently, to explain these effects, it was postulated ([Martin *et al.*, 1999, 2003](#)) that DPOAE components were generated considerably

basal to f_2 that were either created or removed by the IT, or removed by the cochlear insults. Depending on the phase relationship between these basal components and the f_2 component, either suppression or enhancement of the measured DPOAE could result. At the time, the two notions put forward to explain the generation of basal components involved harmonics of the primaries interacting with the primaries via even-order difference tones, or the IT itself producing components via a complex “catalyst” route ([Fahey *et al.*, 2000](#)). The possibility that the tails of the primary TWs themselves were interacting at frequencies above f_2 and generating significant components was considered and discounted as unlikely. We intend to show convincing evidence below that such basal TW interactions do exist after all and that they generate sizable components that most likely are sufficient to explain the previous findings.

The suggestion that DPOAE components were generated considerably basal to the f_2 region was also consistent with the complex DPOAE onset latencies noted by [Whitehead *et al.* \(1996\)](#) in rabbits, where it appeared that under certain circumstances, two DPOAE components were mixing. In noise-damaged rabbit ears, the presence of a low-frequency “hearing loss” revealed by DP-grams elicited by low-level primary-tones was no longer evident for higher-level primaries thus also inferring that DPOAEs were being generated somewhere else and were masking the damage pattern ([Martin *et al.*, 1998](#)). Moreover, in the presence of higher-level primaries, DPOAE suppression-tuning curves (STCs) of the low-frequency damaged region were observed to tune to the undamaged high-frequency region. Finally, brief high-frequency noise over-exposures ([Stagner *et al.*, 2003](#)) that presumably targeted basal cochlear regions also

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eliminated suppression/enhancements above f_2 . Vector differences between DPOAE STCs obtained before and after such short over-exposures produced residual STCs that tuned toward the higher frequencies above f_2 , where suppression/enhancement was previously observed. It is reasonable to suggest that these STCs were identifying basal DPOAE components that were presumably eliminated by the noise exposure.

More recently, Withnell and Lodde (2006) attempted to directly address the basal DPOAE generation hypothesis in guinea pigs by using amplitude-modulated primary-tones to produce DPOAEs for ten different values of f_2 , and then traumatizing the basal cochlea using intense sounds. The expectation in their study was that if basal DPOAE components existed, then postexposure differences would be observed in the modulated DPOAE responses. However, in their study, correlations between the pre- and postexposure DPOAE responses did not differ significantly. Thus, the authors concluded that in their experiment there was little evidence supporting the notion of a basal locus of DPOAE generation apart from the primary site of generation assumed to be at or slightly basal to the peak f_2 TW. Unfortunately, the Withnell and Lodde (2006) study did not search for the presence of any baseline suppression/enhancement effects in the presence of an IT prior to administering the noise trauma, which would have provided an indication that these extremely vulnerable components were still present in their anesthetized, experimental guinea pig preparation. An even more important weakness of their study was that Withnell and Lodde (2006) did not utilize a vector-difference strategy, whereby both the magnitude and phases of pre- and postexposure DPOAEs were considered. Thus, relatively large basal DPOAE components could be removed following a noise-exposure episode and, depending on the vector relationship of the f_2 and basal components, they might not be apparent. To our knowledge, no other studies have attempted to directly establish the existence of basal DPOAE contributions in laboratory animals.

In humans, a number of studies (e.g., Talmadge *et al.*, 1999; Knight and Kemp, 2000, 2001; Kalluri and Shera, 2001; Konrad-Martin *et al.*, 2001; Dhar *et al.*, 2005) have supported the original suggestion by Kim (1980) that DPOAEs can be considered to consist of a combination of two emission sources. One source referred to as the “generator” or “distortion” component is thought to arise from the nonlinear interactions between the f_1 and f_2 primary-tones, and this constituent travels both apically and basally within the cochlea. When the apically traveling distortion component reaches the lower-sideband $2f_1-f_2$ DPOAE frequency place (f_{dp}) on the BM, some of the energy is reflected basally to produce a second DPOAE source referred to as the reflection component. These two DPOAE components combine to produce the final emission signal recorded in the ear canal. The fine structure observed in human DP-grams is attributed to the interference between the two different DPOAE sources (Talmadge *et al.*, 1999; Kalluri and Shera, 2001; Dhar *et al.*, 2002; Knight and Kemp, 2000; Konrad-Martin *et al.*, 2002). Thus, the prevailing view is that lower-sideband DPOAEs conform to a two-source model with these emissions arising

from two locations associated with distinct mechanisms of generation. The possibility of DPOAE components arising basal to the primary-tones (significantly above f_2) has typically not been addressed in these formulations.

It is important to point out that the majority of the research designed to explore the two-source DPOAE model in humans has been conducted in exceptional subjects having very robust DPOAEs (e.g., Dhar *et al.*, 2005) using low to moderate primary-tone levels (e.g., Kalluri and Shera, 2001; Konrad-Martin *et al.*, 2001). However, at the higher primary-tone levels required to obtain robust $2f_1-f_2$ and $2f_2-f_1$ DPOAEs across a wide range of f_2/f_1 ratios, especially in subjects with various types of sensorineural hearing loss (e.g., Stagner *et al.*, 2007), it might be expected that the larger TW envelopes associated with such conditions would be sufficient to generate DPOAEs significantly basal to f_2 . It should be pointed out that in actuality DPOAE components are presumably generated all along the overlapping TW envelopes basal to the f_2 frequency place. Consequently, there is no clear demarcation between those components generated near the peak of the f_2 TW and those produced basal to this site. In the present studies, basal DPOAE components are operationally defined as those that can be influenced by an IT placed 1/3 oct above f_2 , while those components generated nearer the peak of the f_2 excitation are generally not affected by the IT.

Recently, in human subjects, our laboratory (Martin *et al.*, 2008) assembled DPOAE level/phase (L/P) maps like those developed by Knight and Kemp (2000, 2001) for similar higher primary-tone levels at $L_1=L_2=75$ dB sound pressure level (SPL). The Martin *et al.* (2008) DPOAE L/P maps depicted both horizontal and vertical phase banding that was very similar to that originally described by Knight and Kemp (2000, 2001). In L/P plots, a constant vertical phase band for a given DPOAE frequency presumably indicates a place-fixed source associated with steep phase gradients for constant f_2/f_1 ratio sweeps. In contrast, a constant horizontal phase band for a given f_2/f_1 ratio, as a function of DPOAE frequency, is supposedly indicative of a wave-fixed source associated with shallow phase gradients. The “wave-fixed” and “place-fixed” terms of Knight and Kemp (2000, 2001) can be considered equivalent to, respectively, the “distortion” and “linear-reflection” emissions terminology established by Shera and Guinan (1999).

Knight and Kemp (2001) used inverse fast Fourier transform (IFFT) techniques to reveal the place-fixed (reflection) and wave-fixed (distortion) emission components in isolation on these maps, and found the two components to be widely distributed. Unlike Knight and Kemp (2001), Martin *et al.* (2008) utilized ITs to extract the reflection and distortion components. With this approach, DPOAE L/P maps were obtained with and without an IT placed near f_{dp} to remove the reflection component, and vector differences were computed between the two conditions to reveal the reflection constituent as a “residual,” i.e., the DPOAE components “taken away” by the IT. Contrary to the results of Knight and Kemp (2001), these latter methods extracted a “patchy” reflection-like component at f_{dp} for both $2f_1-f_2$ and $2f_2-f_1$ DPOAEs. Unexpectedly, a significant component with verti-

cal phase banding remained in the condition with the IT present. Further experiments with ITs placed at 1/3 of an octave above f_2 , hereafter referred to as the 1/3-oct IT, showed that the IT removed most of the vertical phase banding for both DPOAEs. The 1/3-oct IT also revealed a significant component with horizontal phase banding at wider ratios for $2f_1$ - f_2 , which is indicative of a distortion source. Based on the results of this study, [Martin et al. \(2008\)](#) proposed that these residual DPOAE components, with either vertical or horizontal phase banding properties, depending on the primary-tone frequency ratio and emission type, were generated basal to the IT-frequency place in humans. These findings challenge the notion that DPOAEs with steep phase gradients necessarily arise through reflection from the f_{dp} , and those with shallow phase gradients arise from distortion near f_2 .

The present report describes similar studies carried out with rabbits as experimental subjects in which DPOAE L/P maps and DP-grams were acquired with and without an IT placed either near the f_{dp} or with a 1/3-oct IT. These rabbits exhibited one normal ear, while the contralateral ear was permanently damaged by exposure to either an intense pure tone or an octave band of noise (OBN). Consequently, one rabbit exhibited a notched-loss DP-gram configuration, while the other showed a low-frequency DP-gram loss pattern, respectively. The presence of these “hearing losses” was corroborated by auditory brainstem evoked responses (ABRs).

A noteworthy outcome was that when the IT was placed near the f_{dp} , unlike humans, rabbits did not have a significant reflection component arising from the f_{dp} that could potentially confound the interpretation of the vertical phase banding that remained in comparable human experiments. With a 1/3-oct IT, large residuals were obtained in normal ears, and in damaged ears these residuals masked the extent of dysfunction estimated by low-level DP-grams and ABR threshold shifts. It was hypothesized that these residuals represent DPOAE components generated basal to the f_2 frequency place. The presence of distinctive DPOAE-loss patterns in combination with the above vector-difference techniques allowed experiments to be performed that produced convincing demonstrations of the existence of basal DPOAE components in rabbits. Based on the similarity of these findings in rabbits to those obtained in humans, it is reasonable to suggest that most animal and human DPOAE measures are, to some extent, contaminated by the presence of these basal DPOAE components. Consequently, an augmented DP-gram procedure, hereafter referred to as the ADP-gram, is proposed in which a 1/3-oct IT is utilized to remove these potentially confounding basal components.

II. METHODS

A. Subjects

Three young female rabbits, two albinos and one pigmented, weighing 3–4 kg, served as experimental subjects. One albino rabbit (RV2) had normal cochlear function in both ears as measured by DP-grams that were compared to our laboratory’s extensive normative database of DPOAEs. This animal was used to illustrate our inability to extract

reflection emissions from rabbit ears by placing an IT near the f_{dp} . The other two rabbits (RV5 and RV12) were selected from a pool of seven noise-exposed rabbits, because of their unique DP-gram loss patterns. Prior to experimental manipulations, the rabbits were determined to have normal DPOAEs in both ears as compared to the laboratory’s database.

All DPOAE testing was performed in a sound-attenuated chamber in unanesthetized rabbits that had been habituated to being confined in a standard Plexiglas rabbit holder. The ABR testing and intense noise exposures (105 dB SPL for 2 h) were carried out while the rabbits were anesthetized by an intramuscular injection of ketamine (50 mg/kg) and xylazine (10 mg/kg), with supplementary doses administered as required. Study protocols were approved by the Institutional Animal Care and Use Committee (IACUC) of the VA Loma Linda Healthcare System.

B. DPOAE measures

All experimental methods utilized were highly similar to those described previously ([Martin et al., 2008](#)). Briefly, DP-grams as a function of the f_2 frequency were measured in 0.1-oct steps, with f_2 ranging from 1.6 to 20.55 kHz, and the f_2/f_1 ratio held constant at 1.25 to assure normal baseline DPOAEs. Equilevel DP-grams were obtained at seven different primary-tone levels in 5-dB steps from $L_1=L_2=45$ –75 dB SPL. In addition, four unequal-level DP-grams were obtained with $L_1, L_2=60, 55; 55, 45; 50, 35$; and 45, 25 dB SPL. Two digital-to-analog (D/A) channels of a digital-signal processing (DSP) board (Digidesign, Audiomedia, Daly City, CA) mounted in a microcomputer (Apple, Macintosh Quadra 700, Cupertino, CA) were used to produce the primary-tones. Two ear-speakers (Etymotic Research, ER-2, Elk Grove Village, IL) were employed to present the primary-tones. A low-noise microphone assembly (Etymotic Research, ER-10A, Elk Grove Village, IL) was used to measure the level of the ear-canal sound pressure. The ear-canal signal was synchronously sampled at 44 100 Hz, and averaged ($n=4$) by an analog-to-digital (A/D) channel of the DSP board to obtain a 4096-point sample. A FFT of the time sample was performed so that the $2f_1$ - f_2 and $2f_2$ - f_1 DPOAEs and associated noise-floor (NF) levels could be measured. The NF was based on the average of $n=8$ frequency bins on either side of the f_{dp} frequency bin, excluding the first bin on either side of the DPOAE frequency. The IT was digitally mixed with f_1 for DP-gram IT measures. The IT was rotated in phase by 90° after each sample, so that when the ear-canal signal was time averaged, the majority of emission components produced by the addition of a third tone were canceled. The ITs were presented on alternate trials to minimize any effects due to efferent or time-dependent changes in the measured DPOAEs. Hereafter, the commonly employed DP-gram with only the f_1 and f_2 primary-tones present is referred to simply as a DP-gram. For DP-grams with a 1/3-oct IT, the term augmented or ADP-gram noted above is used to reflect the improvement achieved by removing DPOAE components generated basal to f_2 . For all equal-level ADP-grams the IT was set to 75 dB SPL. For unequal-level ADP-grams the IT was set to L_1+10 dB for rabbit RV-5 and to L_1

+5 dB for rabbit RV12. A residual DP-gram, hereafter referred to as the RDP-gram, plotted the vector difference between a DP-gram and an ADP-gram; that is, it represented the basal DPOAE components that were eliminated by the presentation of the 1/3-oct IT.

C. DPOAE L/P maps

To create DPOAE L/P maps, DPOAEs were measured in response to primary-tone sweeps at constant f_2/f_1 ratios varying from 1.025 to 1.5 in 0.025 increments. DPOAE frequency steps of ~ 44 Hz were measured from 0.5 to 6.0 kHz, with f_1 ranging from 0.258 to 12.016 kHz, and f_2 from 0.366 to 18.023 kHz. DPOAE L/P maps were based on a 2048-point FFT of the averaged time sample. This procedure produced an array of 5160 points apiece for each DPOAE L/P plot. DPOAE level was then directly plotted using commercial software (Microsoft Excel 2003, v.11.5, Redmond, WA), while phase was corrected for primary-tone phase variation and unwrapped by “looking” in two directions (ratio and frequency) using custom-developed spreadsheet routines before plotting. Final plots were constructed using technical-computing software (MathWorks, MATLAB, v.R2008A, Natick, MA). The resulting DPOAE L/P maps were highly similar to those described by Knight and Kemp (2000, 2001) in which DPOAE magnitude and phase were plotted as a function of the f_2/f_1 ratio and DPOAE frequency. These maps were obtained at the majority of the primary-tone levels used to measure the DP-grams. When the primary-tone levels were unequal, L_1 and L_2 were transposed for the $2f_2-f_1$ DPOAE.

DPOAE L/P maps were produced with and without an IT placed either at 44 Hz below f_{dp} or with a 1/3-oct IT (i.e., 1/3-oct above f_2). However, in one control experiment, the IT was fixed at 8 kHz (see Fig. 6). The ITs were again presented on alternate trials throughout the relevant protocols. To reveal the effects of the IT, vector differences were computed between control DPOAE L/P maps and those collected in the presence of the IT to produce residual DPOAE L/P maps. The magnitude and phase of DPOAE L/P maps in the presence of the IT and the resulting residual maps were plotted identically to the control maps.

D. ABR measures

The ABRs were collected at 1/2-oct intervals from 1.4 to 22.6 kHz for both the exposed and non-exposed ears. Permanent ABR threshold shifts for the experimental ear were calculated as differences from thresholds in the non-exposed ear, and were measured at approximately 8–14 mo postexposure. Eliciting stimuli were 3-ms tonepips with 1-ms rise/fall times that were digitally generated with a commercially available signal-generation device [Tucker Davis Technologies (TDT) System II, SigGen, Alachua, FL] and presented at a rate of 21/s using associated signal-presentation hardware (TDT System II, BioSig, v.3.12, Alachua, FL). Active ABR electrodes were placed at the vertex and mastoid of the test ear, while the hind foot served as the ground. Signals were amplified with a gain of 200 k, and average waveforms were based on $n=260$ stimulus presentations. Tonepips were

decreased in level from 80 to 15 dB SPL in 5-dB steps. Waveforms were subsequently printed out and scored by six blinded observers, to determine thresholds for each test frequency. Threshold was defined as a visually just-detectable response for the ABR’s waveform II. Final ABR thresholds were based on the average of the six-observer threshold determinations.

E. Noise exposure

The majority of data for the present report was obtained from the two noise-exposed rabbits that exhibited either a low-frequency loss (RV5) or a notch-loss (RV12) pattern in their DP-grams. The low-frequency loss was produced by an exposure of RV5’s right ear, while under anesthesia, to a 2-kHz OBN at 110 dB SPL for 2 h. For RV12’s left ear, the exposure was a pure tone at 4.242 kHz (i.e., 1/2 oct below 6 kHz), at 100 dB SPL for 5 min while this rabbit was awake. The contralateral ears served as controls for both rabbits. The postexposure data were collected between approximately 8 and 20 mo postexposure. Consequently, these functional losses can be considered as permanent thresholds shifts (PTSs).

III. RESULTS

A. Steep phase gradient DPOAEs not reflected from the DPOAE frequency place (f_{dp})

In rabbits, as described below, reflection-like emissions associated with vertical phase banding were present, but, unlike as established in humans, none of these emissions originate from the f_{dp} . It appeared that the region of generation for these emissions was basal to f_2 , for the case of the $2f_1-f_2$ DPOAE, and basal to the emission itself for the $2f_2-f_1$ DPOAE. The data presented below support these assertions by first presenting relevant findings for a rabbit with normal cochlear function as confirmed by comparing this animal’s DP-gram levels to the laboratory’s database of rabbit DPOAEs. Then, results are presented for two rabbits exhibiting unique configurations of abnormal DP-grams induced by deliberate exposures to high-intensity sounds.

Figure 1 illustrates detailed DPOAE L/P map examples of normal-hearing rabbit RV2-R. The rows making up this figure show control [Figs. 1(A) and 1(B)], IT [Figs. 1(C) and 1(D)], and residual [Figs. 1(E) and 1(F)] DPOAE L/P maps obtained with primary-tone levels at $L_1, L_2=60, 55$ dB SPL. In the control DPOAE level condition of Fig. 1(A), rabbit RV2-R exhibited robust emissions for both the $2f_1-f_2$ (top half of plot) and $2f_2-f_1$ (bottom half of plot) DPOAEs. In the accompanying phase plot of Fig. 1(B), two types of phase patterns can be appreciated. That is, for the $2f_1-f_2$ DPOAE, horizontal phase banding dominated at wide f_2/f_1 ratios (white arrows above dashed black line at $f_2/f_1=1.25$), while vertical phase banding was apparent at narrow f_2/f_1 ratios (black arrows below dashed black line at $f_2/f_1=1.05$). For the $2f_2-f_1$ DPOAE, the vertical phase banding shown in the lower half of Fig. 1(B) was the rule.

In the IT condition of Figs. 1(C) and 1(D), a 45-dB SPL IT was placed 44 Hz below the f_{dp} . It can be seen that there was no obvious effect on either the level [Fig. 1(C)] or phase

FIG. 1. (Color online) DPOAE L/P maps for a normal rabbit measured at $L_1, L_2 = 60, 55$ dB SPL demonstrating the lack of measurable reflection emissions from f_{dp} . DPOAE L/P maps were collected without [(A) and (B)] and with [(C) and (D)] a 45-dB SPL IT placed near f_{dp} . The vector difference is shown as residual maps [(E) and (F)]. Emission levels as a function of DPOAE frequency are shown in the level plots [(A), (C), and (E)], and their corresponding phases as phase plots [(B), (D), and (F)]. In the control phase condition (B), both horizontal (white arrows at $f_2/f_1 \sim 1.3$) and vertical (black arrows at $f_2/f_1 \sim 1.05$) phase patterns were apparent. In the IT condition [(C) and (D)], there was no obvious effect of the IT 44 Hz below f_{dp} on the DPOAE L/P maps. White arrow on the residual map in (E) points to a small DPOAE component the IT extracted. However, this emission had horizontal phase banding [white arrow in mid-(F)] consistent with a distortion component as opposed to a reflection-based DPOAE. On these DPOAE L/P maps, the black dashed horizontal lines on the level and phase plots demark the $f_2/f_1 = 1.25$ ratio for acquiring commonly measured $2f_1 - f_2$ DP-grams, where horizontal phase banding predominates, and narrow-ratio ($f_2/f_1 = 1.05$) DP-grams where vertical phase banding is most apparent. On all DPOAE L/P maps, data for the $2f_1 - f_2$ and $2f_2 - f_1$ DPOAEs are displayed above and below, respectively, the white dashed horizontal line at $f_2/f_1 = 1.0$ (not labeled). The thin white diagonal dashed lines through the phase plots [(B), (D), and (F)] of this figure represent constant f_2 trajectories beginning at 15 kHz in the top right of each plot and ending at 1 kHz in the lower left region that can be used as a reference for this and other DPOAE L/P maps. See text for complete details of this and other figures.

[Fig. 1(D)] of either the $2f_1 - f_2$ or $2f_2 - f_1$ DPOAE when the IT was presented near the f_{dp} . This observation was confirmed by the small residual (white arrow around $f_2/f_1 = 1.2$) obtained by taking the vector difference between the IT and control L/P conditions in Fig. 1(E). In the corresponding phase plot of Fig. 1(F), this small residual was associated with horizontal phase banding (white arrow at $\sim f_2/f_1 = 1.2$) characteristic of distortion emissions arising from the f_2 place. In fact, in this rabbit, the IT was set to a level just high enough to reveal a measurable DPOAE residual that appeared to come from the f_2 distortion source based on its phase behavior. At slightly lower levels of the IT, no residual could be extracted with ITs near the f_{dp} , even with map re-

gions obtained at twice the frequency resolution and $n=32$ vs the typical $n=4$ time averages. Thus, these findings demonstrate for the rabbit that it is unlikely that reflection components from the f_{dp} could in any way complicate the interpretation of the evidence presented below for basal DPOAE components. Furthermore, in rabbits, there appears to be one region of DPOAE generation from the f_2 place associated with horizontal phase banding, and other DPOAE components arising from sites basal to f_2 , associated with both horizontal and vertical phase banding.

B. Predicting the effects of basal components on DP-grams in damaged ears

If DPOAE components generated basal to f_2 are present in rabbit ears, then specific predictions can be made regarding their effects on DP-grams, or on DPOAE L/P maps obtained from rabbits exhibiting various types of cochlear damage. Such predictions are diagrammed in the cartoon of Fig. 2 for two different hearing loss configurations, i.e., a low- [Fig. 2(A)] and a high-frequency DP-gram loss pattern [Fig. 2(B)] for control (top), IT (middle), and residual (bottom) experimental conditions, with the latter depiction computed by taking the vector difference between the IT and control. Note that the frequency representation in these plots goes from the apex at the left end of the abscissa to the base at the right extent of the abscissa; i.e., frequency is plotted from low to high as is traditional for DP-grams or audiograms.

In Fig. 2(A), the effects of basal DPOAE components on DP-grams for a low-frequency loss pattern are depicted. In the control condition without the IT, line A1 illustrates the low-frequency loss pattern [bold dashed line associated with the lesion (L)]; i.e., outer hair cells (OHCs) are severely damaged, until the loss abruptly returns to normal (N) signified by the dashed vertical line about three-quarters along the abscissa. For line A2 the corresponding DP-gram is at the NF in the region of damaged low-frequency OHCs until the tapered tail of the overlap region of the TWs (crossed hatched pattern in A1) encounters normal OHCs at N. At this point, basal DPOAE components begin to be generated to produce DPOAEs that are measured in the region of the lesion (L), prior to f_2 encountering the beginning of the area of normal OHCs depicted in A1. In other words, the “real” extent of OHC damage is “filled in” by the presence of these basally generated DPOAEs. In the IT condition indicated by lines A3 and A4, a 1/3-oct IT was utilized and the ADP-gram collected. In this situation, the IT removes the basal DPOAE components as shown by the crosshatched area in A3, and the ADP-gram (A4) now more accurately reflects the actual OHC-loss pattern. That is, DPOAEs are not generated until the f_2 peak region reaches the area of normal OHCs. In the residual condition illustrated in A5 and A6, the RDP-gram reveals what the IT “took away;” i.e., the IT eliminated the basal DPOAE components. Since the control DP-gram (A2) in the lesion (L) area consists of DPOAEs generated in the “basal to” f_2 area, the RDP-gram resembles the control DP-gram as it emerges from the loss region.

In contrast to the low-frequency loss pattern of Fig. 2(A), the effects of basal DPOAE components on DP-grams

FIG. 2. (Color online) Cartoon predicting the effects of basal DPOAE-generator components on corresponding DP-grams for ears exhibiting either a low- (A) or high-frequency (B) OHC lesion. Frequency is depicted along the abscissa from low (apex) to high (base) as indicated by the frequency arrow at the bottom of the figure. Dashed line in A1 depicts a hypothetical low-frequency OHC lesion (L) that abruptly returns to normal (N). Dashed line at B1 illustrates the opposite situation where normal function (N) exhibits a precipitous drop at the beginning of the high-frequency OHC lesion (L). A notched-like loss pattern would be expected to resemble a combination of these two situations. In all cases, the presentation of a 1/3-oct IT is assumed to remove DPOAE components generated basal to f_2 (A3, A4, B3, and B4). The residual in both scenarios represents the basal components that were removed (A5, A6, B5, and B6). For the low-frequency loss cartoon, the DP-gram is filled in by basal DPOAE components in A2, with the loss being accurately revealed by the ADP-gram in A4. The RDP-gram of A6 reveals the DPOAEs removed by the IT. For the high-frequency loss counterpart, DP- (B2) and ADP-grams (B4) are relatively unaffected by the presence of basal DPOAE components. However, for the RDP-gram in B6, the loss appears to extend to lower frequencies, because DPOAE components generated basal to f_2 can be envisioned as encountering the loss region first when the primaries are swept from low (apex) to high frequencies (base).

for high-frequency loss patterns are predicted to be much less, and this expectation is diagrammed in Fig. 2(B). In the control situation depicted in B1 and B2, both DPOAE com-

ponents are diminished as the TW overlap region leaves the N OHC region and enters the L area. Because in most circumstances the f_2 components dominate the DP-gram, B2 reveals the abrupt loss pattern as the sharp cutoff of the low-frequency extent of the f_2 components enters the L region. In the IT condition of B3 and B4, since basal components have a minimal impact when the f_2 region is normal, as explained above, the ADP-gram of B4, for the most part, resembles the control DP-gram of B2. In the residual condition diagrammed in B5 and B6, the RDP-gram reflects what the IT took away, that is, the basal DPOAE components. Because basal components leave the N region first, when sweeping from low to high frequencies, the RDP-gram of B6 shows the loss pattern beginning at a lower frequency. This frequency shift of the residual is a key prediction in that it is very difficult to envision any other mechanism besides the existence of basal DPOAE components that could produce this effect.

The consequences of a notched OHC-loss pattern (not shown) can be predicted by combining the effects of the low- and high-frequency loss configurations. Thus, a notched pattern DP-gram will resemble the outcomes shown in Fig. 2(B) for the low-frequency side of the notch, and look like Fig. 2(A) for the high-frequency side of the loss.

C. Evidence for basal components in a normal vs noise-damaged ear: Low-frequency loss DP-grams

For the study findings described below, a paradigm was adopted where the experimental ear of a rabbit was permanently damaged by exposure to an intense noise and the damage allowed to stabilize over time. The corresponding contralateral ear remained normal and consequently could be compared to its noise-damaged counterpart. The DP-gram loss patterns were selected so that the presence of basal DPOAE components generated in the remaining normal OHC area could be appreciated in isolation from those produced near the peak of the f_2 TW. Rabbit RV5 exhibited a low-frequency loss pattern in the DP-gram of the noise-exposed ear, which will be described below. It will be demonstrated that the predictions based on the existence of basal DPOAE components depicted above in Fig. 2(A) were largely fulfilled for this subject.

The open squares of Figs. 3(A)–3(F) illustrate DP-grams for the non-exposed normal ear obtained at about the same time as the DP-grams for the exposed ear in Fig. 4. The ADP-grams (solid circles) were obtained with a 1/3-oct IT. ADP-grams should be composed mainly of near- f_2 components, since the IT serves to remove the DPOAE components generated basal to its frequency place. RDP-grams represented by the solid triangles were computed by taking the vector difference between DP- and ADP-grams. Consequently, they should reflect the basal components that were removed by the IT.

In the normal ear of rabbit RV5-L [Figs. 3(A)–3(F)], the addition of a 1/3-oct IT (solid circles) had no systematic effect on DPOAE levels for the primary-tone levels shown in Figs. 3(A), 3(C), 3(E), and 3(D) as compared to the control DP-grams (open squares). However, for the emissions elicited by the $L_1, L_2=65, 65$ dB SPL [Fig. 3(B)], there was roughly an 8-dB reduction in DPOAE levels, and a some-

FIG. 3. (Color online) Comparison of DP- (open squares), ADP- (solid circles), and RDP-grams (solid triangles) as a function of f_2 for the normal ear of rabbit RV5 showing that basal DPOAE components (RDP-gram) can be extracted in normal ears. Except for the lowest optimal unequal-level primary-tones (F), ADP-gram levels closely tracked DP-grams demonstrating that the 1/3-oct IT had little effect on near- f_2 DPOAE components. In most cases, RDP-gram levels were similar to those of the DP-grams indicating that basal DPOAE components removed by the IT were sizable in this normal ear.

what larger effect for the lowest-level set of primaries at $L_1, L_2=50, 35$ dB SPL [Fig. 3(F)]. The overall outcome suggests that, in general, f_2 components dominated the generation of DPOAEs and, consequently, there was little noticeable effect of the IT. The obvious exception at the lowest primary-tone levels [Fig. 3(F)] where above ~ 3 –4 kHz the IT consistently reduced DPOAE levels might indicate that the basal components were larger than the components from the f_2 region for this condition. This is consistent with previous results (Martin *et al.*, 1999, 2003) that showed STCs for such $L_2 < L_1$ “optimal” levels tuning basal to f_2 .

Figure 4 shows DP-grams from rabbit RV5-R ~ 20 mo following a 2-h exposure to a 110-dB SPL OBN centered at 2 kHz. The DP-gram from the contralateral control ear is plotted as a thin black line, so that comparisons can be made between the normal and noise-exposed conditions. From the plots of Figs. 4(A)–4(F), it is clear that in the experimental

FIG. 4. (Color online) Comparison of DP- (open squares), ADP- (solid circles), and RDP-grams (solid triangles) as a function of f_2 in the low-frequency loss ear of rabbit RV5-R demonstrating that basal DPOAE components caused the high-frequency extent of the presumed OHC loss to be underestimated. Thin black lines plot DPOAE levels for the normal ear (see Fig. 3) for comparison. For this ear, ADP-grams even at relatively high primary-tone levels, e.g., $L_1, L_2=70$ (A) or 65 (B) dB SPL, more closely tracked the lesion pattern revealed by lower-level primaries [e.g., (E)].

ear, the noise exposure produced a complete loss of DPOAEs (open squares) up to ~ 5 –6 kHz as judged by the lowest test levels of Figs. 4(E) and 4(F). However, this was clearly not the case for the highest primary-tone level [Fig. 4(A)], where the remaining DPOAEs were just moderately below the levels of emissions for the control ear (thin line). The effect of the 1/3-oct IT in this damaged ear is shown by the ADP-grams (solid circles). For this ear, the ability of the IT to remove DPOAEs is apparent in all but one of the panels of Figs. 4(A)–4(F) and, unexpectedly, even for the lowest unequal-level condition of Fig. 4(F). These findings imply that DPOAEs generated basal to f_2 at higher primary-tone levels were removed by the IT thus revealing the real DPOAE-loss pattern indicated by the lower primary-tone levels of Figs. 4(E) and 4(F). It appears that even for the lowest unequal-level, primary-tone condition [Fig. 4(F)] basal DPOAE components may play a role in shifting the apparent DP-gram loss pattern to lower frequencies. The residuals (basal components) again were large as in the control ear, and lined up precisely with the DP-gram in the low-

FIG. 5. (Color online) Plots of ADP-gram (solid circles) and ABR threshold (solid squares) differences computed between the normal and noise-exposed ears of rabbit RV5 substantiate the functional losses estimated by the ADP-gram.

frequency loss region, which indicates that the DP-gram was largely composed of basal DPOAE components in this region.

D. Low-frequency loss pattern: Corroboration with ABR

The findings presented so far provide support for the notion that under normal measurement conditions, DP-gram loss patterns can be filled in by DPOAE components generated basal to f_2 . However, up to this point, these claims are based on the assumption that the damage pattern revealed by low-level primaries [Figs. 4(E) and 4(F)] accurately reflects the frequency extent of the cochlear lesion. However, a much stronger case can be made if the DP-gram loss patterns were independently substantiated by a non-OAE measure of auditory function. Figure 5 illustrates an attempt to accomplish this goal by comparing the DP-gram loss pattern in the noise-damaged ear of rabbit RV5-R to the hearing loss estimated by conventional ABR methods. Here, the ABR threshold differences (solid squares) were measured at 9 mo post-noise exposure. These differences were obtained by subtracting the ABR thresholds obtained in the non-exposed normal ear from those measured in the noise-exposed ear. Between 6 and 8 kHz, threshold shifts of around 45 dB abruptly returned toward “normal” as compared to the non-exposed ear.

This ABR threshold-shift pattern is compared to the ADP-gram level differences (solid circles) revealed by a similar subtraction of ADP-grams, which was also computed 9 mo postnoise exposure. Specifically, the ADP-gram level differences were obtained by subtraction of DP-grams obtained with the 1/3-oct IT for both normal and damaged ears like those shown in Figs. 3(A) and 4(A), respectively. It is clear that in the presence of an IT, the damage pattern depicted by the ADP-gram elicited by higher-level primaries at $L_1=L_2=70$ dB SPL closely matched the hearing loss revealed by the ABR, and the lowest-level DP-grams displayed in Figs. 4(E) and 4(F). Furthermore, the higher-level 70-dB SPL primaries produced an ADP-gram with a large signal-to-noise ratio that allowed the evaluation of DPOAE level in the damaged region for f_2 approximately <5 kHz, whereas

the DP-grams at the lower primary levels were completely at the NF in this same frequency region. Since the high-level ADP-gram allowed emissions to be measured above the NF in the damaged region, the emissions could be compared to ABR or other threshold measures having a larger dynamic range. The results shown in Figs. 4 and 5 strongly support the hypothesis that basally generated DPOAEs act to mask the true extent of low-frequency dysfunction, particularly as primary-tone levels are increased, and that such contaminating DPOAE components can be removed by using a 1/3-oct IT.

E. Controlling for the effects of noise damage on cochlear tuning

One alternative explanation or, at least, confounding factor that could contribute to the above findings is that in placing the IT close to f_2 (i.e., 1/3 oct above f_2) the apical spread of the IT’s TW could have “suppressed” the primary-tones. Such suppression, especially at the f_2 place, would decrease DPOAEs, particularly at higher primary-tone levels like those depicted in Fig. 4(A), where $L_1=L_2=70$ dB SPL. This effect could be particularly strong, if the cochlea was “detuned,” for example, by the noise damage.

Figures 6(A) and 6(B) illustrates data from an experiment designed to rule out this possibility. This study was identical to the conditions shown in Fig. 3(B) (normal ear) and Fig. 4(B) (low-frequency loss ear), except that the 75-dB SPL IT (arrow) was fixed at 8 kHz, and the DP-grams with the fixed-IT (solid circles) and without the IT (open squares) were measured. In both ears, the residual was computed between these two conditions (solid triangles). In the normal ear [Fig. 6(A)], it is clear that the 8-kHz IT had little effect on the control DP-gram until the f_1 and f_2 primaries approached the IT, which resulted in an abrupt decrease in DPOAE levels (solid circles) as compared to the DP-gram (open squares) collected without the IT. Above 10 kHz, the effects of the IT were diminished and DPOAE levels approached the control condition. Most importantly, the residual computed as the vector difference between the control and IT conditions increased as the primaries approached the 8-kHz IT. This outcome is exactly what would be predicted if the 8-kHz IT removed more basal DPOAE components as f_2 approached the IT. This experiment demonstrates one strategy for investigating the generation of remote DPOAE components in normal ears. It seems reasonable that the residual reflects the removal of DPOAE components generated basal to f_2 , since it is not clear how the IT could affect frequencies as remote as 1–2 kHz and have little effect on DPOAE levels (solid circles) in this same region.

Figure 6(B) shows the same experiment performed on the noise-damaged ear of the same rabbit that exhibited a low-frequency loss pattern. The DP-gram (thin black line) for the non-exposed control ear [Fig. 6(A)] is shown to make comparisons easier. It can be seen that placing the IT at 8 kHz in a region of normal DPOAEs also reduced emissions in the noise-damaged region, but not as fully as depicted by the ADP-gram [see Fig. 4(B)]. In this study, the 8-kHz IT must have removed DPOAEs that were generated basal to the 8-kHz place, even for f_2 frequencies that were almost 3

FIG. 6. (Color online) Control experiments to rule out the possibility of residuals based on suppression of f_2 components by the IT in a normal ear (A), or residuals due to the increased effects of the IT on f_2 components resulting from changes in cochlear tuning in a noise-damaged ear (B). In the normal ear (A), the suppressive effect of the IT on the DP-gram (solid circles) can be seen when f_2 is at or above 8 kHz. Little or no suppression occurs for this condition below approximately 5 kHz. The existence of the residual (solid triangles) at frequencies almost 3 oct below the IT and the systematic growth of this component as the tails of primary-tone TW envelopes approached the IT strongly support the notion that the residual represents basal DPOAE components removed by the IT. Unlike in the normal ear, in the damaged ear (B), DPOAEs were decreased in the presence of the IT (solid circles vs open squares) at similar low frequencies. Since near- f_2 DPOAE components were presumably absent in this damaged region and the residual magnitude matched the DP-gram, these DPOAEs appeared to be largely composed of basal components removed by the remote 8-kHz IT.

oct below the IT-frequency place, i.e., just above 1 kHz. Above 8 kHz, the predicted suppressive effect of this tone on DPOAEs in the normal region can again be appreciated. In this situation, the residual (solid triangles) tracked the DP-gram in the damaged region indicating that the DPOAE components removed by the IT were responsible for the bulk of the DP-gram in this region. Above the damage region, like in the control ear, the residual was as large as the f_2 component. It should be noted that in the damaged region the residual was almost as large as the one obtained in the control ear. This finding is difficult to explain unless the residual DPOAE components came from someplace else, that is,

FIG. 7. (Color online) DPOAE L/P maps [(A)–(F)] measured at $L_1=L_2=65$ dB SPL showing that the IT in (D) eliminated vertical phase banding present in the control phase map [(B) black arrows near $f_2/f_1=1.0$] for this normal ear of rabbit RV5-L. Note how the 75-dB SPL 1/3-oct IT [(C) and (D)] also removed amplitude notches [(A) white arrow] and phase discontinuities obvious in (B) indicative of the mixing of DPOAE components.

from the region of normal DPOAEs. This experiment was performed at higher primary-tone levels where the effects on f_2 by a 75-dB SPL IT might be expected. However, at lower unequal primary-tone levels, where the IT was often set to 5 or 10 dB above the level of L_1 , this potentially confounding effect would be much less likely. Thus, the effects of the IT in these ADP-grams [e.g., Figs. 4(D) and 4(F)] presumably occurred, because of suppression of the DPOAE components arising 1/3-oct or more above f_2 , and were not due to suppression of DPOAEs generated near the f_2 region on the BM.

F. Evidence for basal components in a normal vs noise-damaged ear: Low-frequency loss DPOAE L/P maps

The above DP-gram findings can be appreciated in more detail by comparing DPOAE L/P maps obtained from the normal and noise-damaged ears of this rabbit. In these maps, DPOAE levels and their associated phases are plotted as a function of the f_2/f_1 ratio and DPOAE frequency for the $2f_1-f_2$ and $2f_2-f_1$ DPOAEs. DPOAE L/P maps obtained with equilevel primaries ($L_1=L_2=65$ dB SPL) for the normal ear of rabbit RV5-L and for its noise-damaged ear (RV5-R) exhibiting a low-frequency DP-gram loss pattern are shown in Figs. 7(A)–7(F) and Figs. 8(A)–8(F), respectively. Figure 7 displays DPOAE levels [Figs. 7(A), 7(C), and 7(E)] and associated phase maps [Figs. 7(B), 7(D), and 7(F)] for the normal ear. In the control L/P map condition of Fig. 7(A), robust

FIG. 8. (Color online) DPOAE L/P maps [(A)–(F)] collected at $L_1=L_2=65$ dB SPL in the low-frequency loss ear of rabbit RV5-R provided evidence consistent with the notion that basal DPOAE components removed by the IT filled in the apical side of the lesion. In (C) (white arrows), the 1/3-oct IT removed essentially all DPOAEs present in (A) (white arrows) below the estimated high-frequency extent of the lesion indicated by the bold dashed line along a 5-kHz constant f_2 trajectory through the map. Also, vertical phase banding and abnormally wide bands in (B) (black arrow near $f_2/f_1=1.0$) are absent in (D). Panel (E) shows the levels of the DPOAE components and their phases (F) that the IT removed.

DPOAE levels were obtained over most of the map's space for the $2f_1-f_2$ DPOAE, and in patchy areas for the $2f_2-f_1$ DPOAEs. The related phase plot of Fig. 7(B) shows that for the $2f_1-f_2$ DPOAEs horizontal-like banding (white arrows) occurred at standard f_2/f_1 ratios (i.e., $f_2/f_1=1.2-1.3$) indicative of distortion emissions (wave-fixed). Additionally, vertical phase banding (black arrows) materialized at f_2/f_1 ratios <1.1 , which is a signature of reflection-like emissions (place-fixed). It should be recalled that as demonstrated above in Fig. 1 these emissions in rabbits are not reflected from the f_{dp} . For the most part, the $2f_2-f_1$ DPOAE was associated with vertical phase bands that appeared to be a continuation of those observed for the $2f_1-f_2$ DPOAEs elicited at narrow f_2/f_1 ratios. These results are typical for normal rabbits at primary-tone levels at and above ~ 60 dB SPL.

In the IT condition [Figs. 7(C) and 7(D)], which corresponds to the ADP-grams of the earlier illustrations, a 75-dB SPL 1/3-oct IT was presented on alternate trials, while the DPOAE L/P map was collected. There were some changes in the $2f_1-f_2$ DPOAE magnitude map of Fig. 7(C) consisting primarily of decreases in level. The abrupt notch in the DPOAE levels visible in the control condition of Fig. 7(A) (white arrow $\sim f_2/f_1=1.3$), presumably caused by cancellation between the f_2 and basal components, was also eliminated by the IT (white arrow in C). The robust $2f_2-f_1$

DPOAE present in the control condition (black arrows in A) was largely removed by the presence of the IT (black arrows in C). In the related phase map of Fig. 7(D), dramatic changes were observed as compared to the control condition of Fig. 7(B) in that essentially all the vertical phase banding for both emissions was absent, and the resulting phase map was composed almost entirely of uniform horizontal bands indicative of distortion (wave-fixed) sources (white arrows), presumably emanating from f_2 .

The residual level map of Fig. 7(E) illustrates sizable regions of large $2f_1-f_2$ DPOAEs that were revealed by the IT, and, indeed, these basal components looked quite similar to the control level map of Fig. 7(A). In the corresponding phase map of Fig. 7(F), it is clear that emissions with both horizontal and vertical phase banding patterns were removed, which again appeared very similar to the control phase map of Fig. 7(B). In summary, in a normal ear, the IT removed both reflection-like and distortion-like emission components, which were presumably generated above f_2 , i.e., basal to the location of the 1/3-oct IT, that appeared to be as large or larger than the emission components generated closer to f_2 . These maps obtained from the normal ear provided a reference against which the noise-damaged ear could be compared.

The DPOAE L/P maps shown in Figs. 8(A)–8(F) were obtained for the noise-damaged ear of rabbit RV5-R at the same primary-tone levels as utilized for the normal ear. The DP-gram for this rabbit, which is shown above in Fig. 4(B), was measured at the same equilevel primaries of $L_1=L_2=65$ dB SPL using our standard f_2/f_1 ratio of 1.25, and corresponded to a horizontal slice through the top half of this map on the ordinate at an f_2/f_1 value of 1.25. These maps provide a comprehensive “panorama” of DPOAE space that further reinforces the notion that basal DPOAE components were acting to “mask” the noise damage in the damaged ear of this rabbit. The top panels [Figs. 8(A) and 8(B)] illustrate control DPOAE L/P maps. The heavy-black dashed line running on a diagonal through these maps demarks the 5-kHz constant- f_2 line at the approximate edge of the lesion revealed by the low-level DP-grams in Figs. 4(E) and 4(F), and reinforced by the ABR threshold shifts illustrated in Fig. 5. In Fig. 8(A), it is obvious that there was a large region of DPOAEs at frequencies below this line (white arrows). In the related phase plot of Fig. 8(B), three obvious phase banding patterns were evident. In the region of normal DPOAEs (white arrow), phase bands were horizontal and narrowly spaced. As the lesion was approached in the apical direction (i.e., toward lower DPOAE frequencies), the phase bands curved to become diagonal for the $2f_1-f_2$, and assumed the normal vertical orientation of place-fixed emissions for the corresponding $2f_2-f_1$ emission. Near the lesion, the phase banding not only showed diagonal curvature, but also the banding became much wider (black arrow around 3.5 kHz), indicative of a shorter group delay computed along an f_2 trajectory through this region of the map. These patterns can be compared to the normal ear of Fig. 7(B), where the very wide phase bands were completely absent in the analogous region.

Figures 8(C) and 8(D) show the DPOAE L/P map mea-

sured with a 75-dB SPL 1/3-oct IT, which is, again, similar to the ADP-grams from earlier figures. In this condition, all of the DPOAEs measurable below the dashed black line in Fig. 8(C) indicating the estimated apical extent of the lesion were eliminated for both DPOAEs (white arrows). In the phase map of Fig. 8(D), all the wide diagonal and vertical phase banding present without the IT were removed, and only narrow, wave-fixed phase banding (white arrow) indicative of distortion emissions with relatively long group delays remained.

The bottom two panels of Figs. 8(E) and 8(F) show the residual obtained by taking the vector difference between the control and IT conditions. As mentioned previously, one interpretation is that these maps represent DPOAEs that the IT took away. It can be seen that the residual levels and phases appeared very similar to the control condition, but that the horizontal phase bands in the normal region tended to be wider (white arrow). The wide phase bands (black arrow at 3.5 kHz) of Fig. 8(B) near the edge of the lesion were also apparent in the residual [Fig. 8(F), black arrow at 3.5 kHz]. The residual appears to represent DPOAE components that were mixing with those remaining in Figs. 8(C) and 8(D) to produce the control maps of Figs. 8(A) and 8(B). DPOAEs apical to the constant $f_2=5$ -kHz line can be explained, if they represent DPOAEs generated basal to the lesion, where DPOAEs were normal in this rabbit. Overall, placing an IT at 1/3 oct above f_2 helped to clearly reveal the real extent of the lesion over the entire DPOAE space for both $2f_1-f_2$ and $2f_2-f_1$ DPOAEs, regardless of the f_2/f_1 ratio.

Overall, this rabbit with a low-frequency loss pattern provided a very compelling case for the existence of basal DPOAE components. In normal rabbit ears, f_2 and basal components are presumably mixing and thus making it more difficult to appreciate the existence of the basal DPOAE-generator components. However, such basal components can be appreciated when the tails of the TWs stimulate a normal cochlear region as the locus of f_2 is within the lesion, but advancing basally, i.e., toward higher frequencies through the map. In the presence of a 1/3-oct IT, generation of these basal components was suppressed, and the real extent of the lesion was revealed. Thus, these findings conform closely to the predictions of Fig. 2(A), which depict the effects of basal DPOAE components with respect to accurately detecting a low-frequency loss DP-gram pattern.

G. Evidence for basal components in a normal vs noise-damaged ear: Notched-loss DP-grams

The above results were not just limited to low-frequency loss configurations in that similar findings were obtained in a rabbit with a permanent noise-induced notch in its DP-gram obtained 19-mo postnoise exposure that was produced by a pure tone at 4.42 kHz at 100 dB SPL for 5 min. DP-grams (open squares), ADP-grams obtained with a 1/3-oct IT (solid circles), and RDP-grams (solid triangles) for rabbit RV12 are depicted in Fig. 9 for the noise-damaged left ear. The corresponding control DP-grams from this rabbit's normal contralateral right ear (thin lines) are plotted on the noise-exposed ear for comparison. Findings for the normal ear of this rabbit were highly similar to those obtained for the nor-

FIG. 9. (Color online) DP-grams for rabbit RV12-L with a notched-loss pattern demonstrating that the ADP-grams (solid circles) again more clearly revealed the notched loss [(e.g., (B) and (D))] tracked by the low-level DP-grams [(E) and (F)]. Note the pronounced effects of the 1/3-oct IT in the unequal-level optimal primary-tone conditions [(D) and (F)]. As predicted in Fig. 2(B), the RDP-grams (solid triangles) dropped in level before the high-frequency extent of the lesion are encountered.

mal ear of rabbit RV5-L (Fig. 3). Consequently, plots of its DP-grams are omitted here. For the noise-damaged ear shown in Fig. 9, the results paralleled those described in Fig. 4, where the IT consistently removed DPOAEs that were “filling in” the DP-gram notch revealed by low-level primaries in Figs. 9(E) and 9(F). What is particularly remarkable is that even at the lowest levels tested [i.e., $L_1, L_2=50, 35$ dB SPL in Fig. 9(F)] it is clear that the apparent extent of the notch was moved from ~ 7 to 10 kHz by the presence of the 1/3-oct IT. Once more, these findings are consistent with basal DPOAE components obscuring the real damage pattern. This notched-loss situation also agrees with the predictions regarding the effects diagrammed in Fig. 2 for basal DPOAEs. Thus, the high-frequency side of the notch behaved like a low-frequency loss [Fig. 2(A)], while the low-frequency side of the notch operated like a high-frequency loss [Fig. 2(B)]. It can be seen that for this notched-loss pattern basal DPOAEs did not appear to affect the DP-gram on the low-frequency side of the lesion in that the ADP-gram

FIG. 10. (Color online) Plots of ADP-gram (solid circles) and ABR threshold (solid squares) differences computed between the normal and noise-exposed ears of rabbit RV12-L corroborating the functional changes estimated by the ADP-gram.

at the low-frequency boundary of the notch, which was measured with the IT present, exactly matched the DP-gram without the IT [Figs. 9(A)–9(F)]. Again, as predicted in Fig. 2(B) (line 6), the RDP-grams showed the loss pattern beginning at a lower frequency. As noted previously, this finding supports a key prediction of the basal-component hypothesis, and such results are difficult to explain by any other mechanism.

H. Notched-loss pattern: Corroboration with ABR

Yet again, the findings presented above provide strong support for the notion that DP-gram loss patterns, such as notches, can be filled in by DPOAE components generated basal to f_2 . Figure 10 corroborates the DPOAE estimates of the frequency extent of the presumed noise-induced notched loss by comparing the ADP-gram pattern (solid circles) for the noise-damaged ear of rabbit RV5-L to hearing loss assessed with ABR measures. The ABR threshold differences (solid squares) obtained by subtracting the thresholds obtained in the non-exposed normal ear from those measured in the noise-exposed ear at 8-mo postexposure are depicted in this plot. The notch assessed by ABR was maximal with a threshold shift of ~ 40 dB at 5.6 kHz. This ABR threshold-shift pattern is compared to the ADP-gram level differences (solid circles) revealed by a subtraction of ADP-grams obtained between the normal and damaged ears. It is clear that the ADP-gram damage pattern elicited with unequal-level primaries of $L_1, L_2 = 60, 55$ dB SPL [Fig. 9(B)] closely matched the hearing loss revealed by ABR, and the lowest-level DP-grams shown in Figs. 9(E) and 9(F). Like the previous low-frequency loss example, the ADP-gram at this higher primary level allowed the DPOAE levels in the notch region to be accurately characterized thus revealing an upwardly sloping loss pattern within the notch proceeding from ~ 6 kHz, which closely matched the ABR threshold-shift pattern. Overall, the DP-gram results shown in Figs. 4 and 9 strongly support the notion that basally generated DPOAE components act to conceal the true extent of a DP-gram loss pattern and, in the case of a notch-like configuration, the extent of the high-frequency side of the damage is obscured, particularly as primary-tone levels are increased. However,

FIG. 11. (Color online) DPOAE L/P maps measured at $L_1, L_2 = 50, 35$ dB SPL from the normal ear of rabbit RV12-R showing that the presence of a 1/3-oct IT set to 50 dB SPL (C) decreased the overall level of DPOAEs, and dramatically removed low-frequency DPOAEs (white arrow) as compared to the control condition (A). The substantial residual (E) demonstrates that even at low optimal unequal primary-tone levels large DPOAE components appear to be generated basal to f_2 . At these less intense primary-tone levels, no $2f_2 - f_1$ DPOAEs were detectable in the lower halves of the DPOAE L/P maps.

these basal DPOAE components can be removed by utilizing a 1/3-oct IT during the acquisition of the DP-gram. This paradigm has been dubbed the augmented or ADP-gram, both because an extra tone was added to the normal two-tone eliciting protocol, and because this makes the DP-gram more accurate for tracking OHC damage patterns at all possible primary-tone levels.

I. Evidence for basal components in a normal vs noise-damaged ear: Notched-loss DPOAE L/P maps

Figures 11 and 12 display the DPOAE L/P maps for the normal and noise-damaged ears for rabbit RV12, respectively, obtained at the lowest optimal primary-tone level measured for this rabbit, i.e., at $L_1, L_2 = 50, 35$ dB SPL. As before, DPOAE L/P maps are shown for the control, IT, and residual conditions for both ears. For the normal ear [Figs. 11(A)–11(F)], several features can be noted. At these levels, no $2f_2 - f_1$ DPOAEs were measurable throughout the map, nor was any vertical phase banding apparent. In the IT condition, the $2f_1 - f_2$ DPOAE levels were substantially reduced and the lowest frequency DPOAEs [white arrow, Fig. 11(C)] were particularly affected. The phase banding in the control L/P map condition of Fig. 11(B) was slightly wider (white arrow) than in the IT condition [white arrow, Fig. 11(D)], which would be consistent with a longer group delay computed

FIG. 12. (Color online) DPOAE L/P maps measured at $L_1, L_2 = 50, 35$ dB SPL for rabbit RV12-L with a notched-like loss pattern demonstrating that the IT (C) removed basal DPOAE components apparent in the control (A) DPOAE L/P condition (white arrow). The IT aligned the DPOAEs with the estimated high-frequency edge at ~ 13 kHz (bold dashed diagonal at upper right) of the lesion (C), an effect similar to that observed for the DP-gram in Fig. 9(F). In (E), the loss detected by the residual extended to lower frequencies below the bold dashed diagonal at 5 kHz, as predicted in Fig. 2 (line B6).

along equal f_2 lines than in the control condition. One explanation of this observation is that the IT removed basal DPOAE components with shorter group delays. The residual DPOAE level [Fig. 11(E)] and phase maps [Fig. 11(F)] indicate that the IT removed large DPOAE components with phase characteristics similar to those seen for the control condition of Figs. 11(A) and 11(B), but with even wider phase bands throughout. Overall, the results for the normal ear of rabbit RV12 at these lower primary-tone levels were very similar to those described for the normal ear of rabbit RV5 shown at higher primary-tone levels in Figs. 7(A)–7(F), with respect to the distortion component (wave-fixed) affected by the IT.

Figure 12 shows DPOAE L/P maps for the noise-damaged ear of this rabbit for the control, IT, and residual conditions, with constant f_2 -frequency lines (dashed black lines) equivalent to the apical and basal extent of the lesion revealed by low-level primaries [e.g., Figs. 9(E) and 9(F)], and especially by ADP-grams and the associated ABR threshold shifts (Fig. 10). In the control condition of Fig. 12(A), a large region of DPOAEs extending below the estimated basal extent of the lesion is apparent (white arrow), and was also associated with abnormally wide phase banding [Fig. 12(B), white arrow] as compared to the normal control ear [Fig. 11(B)]. In the 1/3-oct IT condition of Fig. 12(C),

this DPOAE component (white arrow) was removed by the IT, and the remaining DPOAEs were outside the constant f_2 lines marking the estimated extent of the notch-like loss. In the residual condition of Fig. 12(E), DPOAEs presumably removed by the IT, i.e., basal components, are depicted. Here, as predicted in Fig. 2(B) (line 6), the loss on the low-frequency side of the lesion seemed to extend to lower frequencies, while the DPOAEs on the high-frequency side of the lesion behaved like a low-frequency loss as predicted in Fig. 2(A) (line 6). Thus, the pattern of the combined residuals makes it seem as if the entire notch region shifted to lower frequencies. Phase banding for the residual [Fig. 12(F)] on the high-frequency side of the notch was clearly wider (white arrow) than that shown for the residual at similar DPOAE frequencies in the normal ear. Overall, this rabbit's DPOAE L/P maps behaved as predicted in Fig. 2 and, again, support the notion that basal DPOAE components can partially obscure the frequency extent of noise-induced damage to the cochlea's OHC system as revealed by standard DP-grams, even at low optimal primary-tone levels.

IV. DISCUSSION

The present findings demonstrate the existence of basal DPOAE components in rabbits that can be extracted by an ADP-gram procedure. Recently, Martin *et al.* (2008) observed that an IT placed near f_{dp} during the collection of DPOAE L/P maps in humans revealed a DPOAE component with a steep phase gradient associated with vertical phase banding. Removal of this component also decreased DPOAE fine structure consistent with this constituent being the commonly described reflection source from the f_{dp} (e.g., Shera and Guinan, 1999; Kalluri and Shera, 2001). However, vertical phase banding still remained throughout much of the map. Adding a 1/3-oct IT during the collection of these maps removed almost all of the vertical phase banding, and also uncovered a distortion-like component with horizontal phase structure. These DPOAE components presumably originated basal to f_2 , similar to what was demonstrated in the current study for rabbits.

In humans (Martin *et al.*, 2008), it is possible that these basal-source contributions with steep phase gradients were somehow reflected from the f_{dp} . In the human situation, the 1/3-oct IT may have eliminated the basal component that could in turn travel apically to be subsequently reflected. However, this potentially confounding circumstance cannot account for the observations detailed here for the rabbit, because, in this species, reflection components could not be measured by placing an IT near f_{dp} (see Fig. 1). Any DPOAE-source components that could be extracted near the f_{dp} in rabbits were associated with shallow phase gradients, and horizontal phase banding, which are indicative of a distortion component arising from the f_2 place. Because vertical phase banding was subsequently eliminated by the 1/3-oct IT in DPOAE L/P maps of rabbits, by a simple process of elimination, such findings strongly implicate a basal site as the sole origin for these emissions.

In the two noise-damaged rabbits described here, the existence of basal DPOAE components was much easier to

appreciate, because the nonlinear distortion source attributable to the peak of the TW near f_2 was eliminated over a restricted BM region by noise-induced damage to associated OHCs. With a 1/3-oct IT, a significantly larger area of damage was revealed by both ADP-grams and DPOAE L/P maps in both the low-frequency loss case (see Figs. 4 and 8) and similarly in the notched-loss pattern instance (Figs. 9 and 12). Since near- f_2 components were presumably significantly damaged in both cases, we proposed that the emission components that partially filled in the loss regions were generated by TW interactions basal to f_2 . This hypothesis is consistent with our current understanding of TW-excitation patterns along the BM. Additionally, both ADP- and RDP-grams matched the predictions for the basal components described in Fig. 2.

A remote possibility is that these emission components originated from the region around f_2 that was suppressed by the 1/3-oct IT, either by normal apical spread of excitation to the f_2 place, or because of detuning in a noise-damaged ear. These possibilities were ruled out for the present study by findings from the ear with a low-frequency loss by measuring DP-grams with and without an IT fixed at 8 kHz (see Fig. 6). Results from this 8-kHz IT experiment demonstrated that DPOAEs were decreased almost 3 oct apical to the 8-kHz IT. Since the IT was in a region of presumably normal “hearing” assessed by both low-level DP-grams and ABRs, these emissions must have had their source of generation at or above the 8-kHz place on the BM.

In addition, a pilot study (unpublished observations) was performed in normal rabbit ears in which the effect of a wide range of primary-tone and 1/3-oct IT level combinations were examined to determine the most effective level of the IT for removing basal components for a given primary level. Within this matrix, systematic effects of the IT on ADP- and RDP-grams were observed relative to control DP-grams. If IT levels were set too high with respect to the primaries, ADP-grams were clearly decreased as compared to the control situation, presumably due to suppression of the f_1 and f_2 primary-tones. This effect on ADP-gram levels was mainly observed for unequal-level primaries. However, for the most part, the primary-tone and IT levels used in the present study were within the ranges where the IT had little, if any, effect on ADP-gram levels, since they were chosen based on the results of this pilot study. Although the following equation determined from these preliminary data was not strictly adhered to in the present study, it could possibly serve to calculate appropriate IT levels in rabbits that avoid any suppression effects on the primary-tones:

$$L_{IT} = L_1 + 20 - (L_1 - L_2) \quad \text{with} \quad L_{IT \max} \leq 75 \text{ dB SPL.}$$

In general, for the results described here, levels of the IT were chosen that were intense enough to produce the largest RDP-gram without making the level of the ADP-gram appreciably lower than the control DP-gram. Consequently, suppression of the primaries by the IT is unlikely to account for the present results, which strongly support the presence of basal DPOAE components.

In DPOAE L/P maps from the normal ears of the two noise-damaged rabbits, large emission components were un-

covered by the 1/3-oct IT, presumably generated basal to f_2 (see Figs. 7 and 11). This claim is consistent with RDP-grams revealing basal DPOAE components in normal ears [see Figs. 3(A)–3(F)] that were similar in magnitude to ADP-grams revealing the f_2 source for these rabbits. Under some conditions, particularly for unequal-level primaries as mentioned above [e.g., Fig. 3(F)], the ADP-gram procedure significantly reduced DPOAEs in normal ears. At this time, it is not possible to determine if the 1/3-oct IT had more impact on the f_2 place using unequal-level primary-tone protocols, or if larger basal components were present. Because the ADP-gram was also more effective in removing DPOAEs at these low, unequal levels in damaged ears [Figs. 4(F) and 9(F)], it is tempting to speculate that unequal levels designed to optimize the input to the cochlear nonlinearity (e.g., Whitehead *et al.*, 1995; Kummer *et al.*, 1998) also align the tails of the TWs to produce optimal basal generation. Thus, the commonly observed increase in DPOAE levels for optimal unequal-level primaries may be due in part to enhancement of basal DPOAE components. Also, because there is little phase change in the tails of the TWs, basal DPOAE components would be expected to add in phase to produce relatively large effects.

Although the present findings are based largely on the damaged ears of only two rabbit subjects, it is important to emphasize that these findings help elucidate a collection of phenomena that cannot be easily explained by any other mechanism. For example, DPOAE onset latencies in rabbits and humans often have complex waveforms at their onset that can be explained by the mixing of two DPOAE sources (Whitehead *et al.*, 1996; Martin *et al.*, 1998). Also, mid-frequency DPOAE STCs in noise-damaged ears were shown to tune to high-frequency regions where DPOAEs are normal (Martin *et al.*, 1998), which is consistent with a basal source of emissions. Following temporary threshold-shift (TTS) exposures designed to affect regions above f_2 , vector subtraction of STCs often showed the vector-difference STC pointing to the region where suppression/enhancement above f_2 was previously observed, thus suggesting that DPOAE components were removed by the temporary damage (Stagner *et al.*, 2003). In noise-damaged rabbits, some DPOAEs are often enhanced, particularly $2f_2$ - f_1 emissions and narrow-ratio $2f_1$ - f_2 DPOAEs, as if one DPOAE component that was in cancellation with another was removed by the injury process (e.g., Howard *et al.*, 2003). Finally, in the present study and in other rabbits (not described here), the addition of the 1/3-oct IT often eliminated amplitude notches and conspicuous phase discontinuities in the DPOAE L/P maps, as if interfering DPOAE components were removed [see Fig. 7(A) vs Fig. 7(C), and Fig. 7(B) vs Fig. 7(D)].

It appears that both humans and rabbits exhibit basally generated DPOAEs, and some with phase characteristics previously attributed to reflection from the f_{dp} . Thus, depending on primary-tone levels and species, the commonly accepted two-source model of DPOAE generation may need to be qualified, or at least the contributions from basal DPOAE components should be considered. The observation that DPOAE components with horizontal (distortion source) phase behavior can be generated in the base may not seem

too surprising, if one considers these sources as a summation of DPOAE wavelets generated by basal OHCs in response to stimulation by the f_1 and f_2 primaries. However, some of these DPOAE components assume reflection-like phase characteristics, but are not necessarily reflected from the f_{dp} .

How this reflection-like phase behavior originates basal to the primary-tone place is not clear. DPOAE components arising from the base have vertical phase bands for the $2f_1$ - f_2 DPOAE at narrow f_2/f_1 ratios that are contiguous with the reflection-like phase structure consistently observed for the $2f_2$ - f_1 DPOAE. One possibility is that in these circumstances $2f_2$ - f_1 DPOAE components cannot travel basally past the f_{dp} without being absorbed at their characteristic frequency. Consequently, the phase properties of the measured emission are dominated by basal components in the region just above the $2f_2$ - f_1 DPOAE, which scales with the emission instead of with the primaries, and appears reflection-like as a consequence of this limitation.

The shallow phase gradients associated with regions of horizontal phase banding (wave-fixed or distortion source) in DPOAE L/P maps result, presumably, because of cochlear-scale invariance where TWs have the same number of periods irrespective of frequency. For DPOAEs to reflect this property, their region of generation must also scale geometrically with the TWs. Of course, when this assumption is violated, phase banding will no longer assume the expected horizontal phase pattern. This outcome apparently occurs in normal ears as the cochlear apex is approached thus causing phase bands to assume a diagonal, or nearly vertical trajectory, at optimal ratios for $2f_1$ - f_2 [see Figs. 1(B), 7(B), and 11(B)]. In noise-exposed ears, similar changes in phase behavior were observed [see Fig. 8(B), black arrow], presumably because DPOAEs were coming from relatively constant normal regions above the damaged area, consequently, “forcing” their phase behavior to assume a reflection-like characteristic. Obviously, the generation of upper-sideband DPOAEs (see above) and basal DPOAE components, as well as the mechanisms responsible for their phase behavior, are important problems for further study.

The suggestion that OAEs can be generated basal to the region of maximal excitation on the BM is not new or unique to this study. In the case of stimulus frequency otoacoustic emissions (SFOAEs), Brass and Kemp (1993) utilized an IT to extract this emission as a residual based on the suppression of the SFOAE by the IT. In a simple model, they assumed that saturating nonlinear elements all along the BM contributed to the magnitude of the SFOAE. In modeling the asymmetry observed for suppression of the SFOAE by tones of lower and higher frequency than the probe, they assumed that the SFOAE was in part generated basal to the probe-tone place. Along similar lines, Siegel *et al.* (2005) and Siegel (2006) presented evidence from the chinchilla that ITs presented 1 oct or more above the probe tone used to evoke a SFOAE extracted a component with a shallow phase slope indicating a short delay. Likewise, in a study of transiently evoked SFOAEs in normal and hearing-impaired human ears, Konrad-Martin and Keefe (2005) observed an emission component with a latency that was too short to be considered a reflection constituent from the probe-tone place. One hy-

pothesis these investigators considered to explain their findings was that this component was a source located basal to the tonotopic place of the probe tone. Finally, in a recent simulation of human SFOAEs, Choi *et al.* (2008) identified constituents arising from irregularities in the TW peak region, and a short-latency component from regions basal to the peak.

Evidence also can be found (e.g., Avan *et al.*, 1991, 1995, 1997) for the influence of the cochlear base on transiently evoked otoacoustic emissions (TEOAEs). In guinea pigs, Avan *et al.* (1991) measured TEOAEs after pure-tone exposures that produced compound action potential (CAP) threshold elevations of 10–50 dB. The TEOAEs were significantly decreased by these exposures, although CAP thresholds in the frequency range of guinea pig TEOAEs remained unchanged. Avan *et al.* (1991) concluded that either TEOAEs were more sensitive than CAP thresholds for detecting the low-frequency sound-induced damage, or that TEOAEs contained components that originated from much higher frequency regions. In humans with cochlear damage due to noise trauma or presbycusis, Avan *et al.* (1995) observed significant correlations between TEOAEs and SFOAEs with audiometric thresholds shifts on the order of 1 oct above the OAE frequency thus inferring that these emissions cannot be considered as a purely localized phenomenon. Finally, in a later study, Avan *et al.* (1997) correlated TEOAEs with ultra-high-frequency (UHF) hearing. They discovered that TEOAE magnitude exhibited a significant correlation with the audiometric status of the basal cochlea assessed by UHF hearing, demonstrating once more that changes in the cochlear base can either influence OAEs generated at much lower frequencies, or that TEOAEs contain basally generated sources. Recently, Goodman *et al.* (2009) investigated in humans the relationship between UHF behavioral thresholds and high-frequency TEOAEs, and also reported evidence consistent with the presence of basal distortion components in TEOAEs.

Similar studies in laboratory animals and humans suggest that DPOAEs also have contributions from regions basal to f_2 . In our own laboratory, Arnold *et al.* (1999) demonstrated that 4- to 8-kHz DPOAE levels were significantly correlated with UHF hearing. In this study, UHF hearing significantly and uniquely accounted for about 14% of the variance in DPOAE levels from 4 to 8 kHz. More recently, in a large-scale study of 553 normal-hearing adult males, Dreisbach *et al.* (2008) observed that as UHF hearing thresholds worsened, DPOAE levels decreased at all test frequencies.

Many studies in laboratory animals have also found discrepancies when attempting to relate DPOAEs to hearing loss or to some other functional measure. For example, Harding *et al.* (2002) reported that in noise-damaged chinchillas DPOAE levels recovered postexposure, even in cochlear regions with substantial OHC loss. These investigators also showed that plotting DPOAEs with respect to f_1 rather than f_2 produced the best alignment with cochlear damage confirmed histologically. Overall, Harding *et al.* (2002) concluded that DPOAEs can originate from other cochlear locations, and possibly from the basal 20% of the

cochlea, when this region is intact. Such a conclusion is consistent with the existence of the basal DPOAE components observed in the present study.

The fact that upper-sideband DPOAEs appear to be generated at or above their characteristic place (e.g., [Martin et al., 1987, 1998](#)) also supports the notion of basal mechanisms contributing to DPOAE generation. In rabbits, STCs tune to just above the $2f_2-f_1$ frequency place, and selective TTS episodes demonstrated that this emission was generated basal to f_2 ([Martin et al., 1987](#)). Similar findings were obtained in humans for this upper-sideband DPOAE in that DPOAE STCs tuned to the $2f_2-f_1$ place, $2f_2-f_1$ DPOAEs had significantly shorter onset latencies than did $2f_1-f_2$ emissions, and correlated best when the frequency of the $2f_2-f_1$ DPOAE was aligned with the primary frequencies that generated the $2f_1-f_2$ DPOAE ([Martin et al., 1998](#)). Together, all these findings point to basal generation as the genesis of the upper-sideband $2f_2-f_1$ emission, thus suggesting that other order emission components arise basally as well.

In order for emissions to be generated basal to f_2 in the case of DPOAEs, the two primaries must interact in the non-linearity responsible for emission generation. One approach toward estimating the region over which DPOAEs can be generated basal to f_2 is by determining the separation of the f_1 and f_2 primary-tones that are capable of producing the f_2-f_1 difference-tone emission. [Martin et al. \(2003\)](#) observed in rabbits that robust difference-tone emissions could be measured at f_2/f_1 ratios ranging from 1.25 to 6.75. Unpublished observations in rabbits indicate that the maximum separation between moderate-level primaries that will support the generation of an f_2-f_1 DPOAE is approximately 3 oct. Assuming that the tail of the TW-excitation pattern of f_1 must interact with f_2 to produce f_2-f_1 DPOAEs, then DPOAEs can be generated over a significant distance along the BM, thus representing a finding that is consistent with evidence for basal DPOAE components.

Finally, to be assured that the present findings represent reasonably conclusive evidence for the existence of basal DPOAE components in rabbits, it is important to consider a hypothesis previously proposed by [Fahey et al. \(2000\)](#). These investigators considered the possibility that DPOAE suppression/enhancement phenomena might be based on what they termed as a catalyst mechanism. In this scenario, the addition of the IT produced additional DPOAEs that were responsible for the suppression/enhancement effects originally reported by [Martin et al. \(1999, 2003\)](#). These DPOAEs, depending on their phases, could decrease (i.e., suppress) or increase (i.e., enhance) the DPOAE being measured. Likewise, in the present study, the presentation of the 1/3-oct IT could theoretically produce DPOAEs that might be construed as basal components, if it were not for the unique cochlear damage patterns exhibited by these rabbits.

In fact, in normal ears alone, the possibility of a catalyst route being responsible for the presence of a residual emission is complicated, if not impossible to rule out. For example, in Fig. 7(A), it is difficult to determine if the residual in Fig. 7(E) represents DPOAEs removed by the IT, or DPOAEs somehow created by various catalyst routes. However, the fact that the residual DPOAE [Fig. 7(E)] resembled

the control [Fig. 7(A)] emission, and was not like the IT condition [Fig. 7(C)] argues for the notion that the IT did not produce these DPOAEs. Additionally, the phase maps in the IT condition lack many of the discontinuities and irregularities observed in the control condition elicited without the third tone present. It is difficult to imagine how the creation of new DPOAE components could mix with the control DPOAE to make these phase maps more orderly.

In damaged ears, catalyst effects are much easier to discount as major sources that could be mistaken as basal DPOAE components. First, in the two rabbits described in detail here, the catalyst mechanism would have to “know about” the damage pattern to explain the ability of the IT to more clearly reveal the DPOAE-loss patterns. For example, in Fig. 4(B), the catalyst mechanism must “anticipate” the noise loss observable for the lower-level primaries [Figs. 4(E) and 4(F)] and associated ABR threshold shifts (Fig. 5). Then, it would be necessary for the catalyst mechanism to produce a component of the correct magnitude and phase to cancel the low-frequency DPOAEs in this region, so that the noise-damage pattern could be uncovered. This scenario seems highly unlikely for a mechanism based solely on the properties of a nonlinear system, that is, the generation of additional DPOAE components by the straightforward addition of a third tone. Similar effects can be noted in Figs. 9(A)–9(F) for the notched-loss pattern. In this situation, to make the notch more distinct at higher primary-tone levels, the catalyst mechanism again would have had to detect the loss pattern revealed by lower-level stimulation, and then produce DPOAEs of the correct magnitude and phase to accentuate the notched configuration.

A second argument against the catalyst mechanism that can be appreciated in damaged ears is that the IT should be creating DPOAEs. In the IT magnitude map for the rabbit with the low-frequency loss [Fig. 8(C)], the IT should have been generating DPOAEs; however, DPOAEs were eliminated by the IT (white arrows). The DPOAE L/P maps for this noise-exposed ear also argue against catalyst effects, because the residual magnitudes and phases [Figs. 8(E) and 8(F)] resembled the control condition [Figs. 8(A) and 8(B)]. If the IT created these DPOAEs, then the IT condition should have looked like the residual situation, but this was clearly not the case. Overall, the results obtained in noise-damaged ears cannot reasonably be explained by the creation of new DPOAE components by the addition of a third tone. Consequently, the effects of the IT in the noise-damaged rabbits almost certainly can be ascribed to suppression of DPOAE components generated basal to the f_2 place on their BMs.

V. SUMMARY AND CONCLUSIONS

DPOAE L/P maps in normal rabbit ears were in many respects similar to those obtained in humans ([Martin et al., 2008](#)) in that rabbits often exhibited horizontal phase banding at wide f_2/f_1 ratios (e.g., 1.25) for $2f_1-f_2$ DPOAEs, and vertical-like phase banding at narrow f_2/f_1 ratios (e.g., <1.1) for $2f_1-f_2$ DPOAEs, and for all ratios of $2f_2-f_1$. Vector differences between maps in which a 1/3-oct IT was present or absent allowed the computation of residual DPOAE L/P

maps that described the DPOAEs removed by the IT (i.e., basal components). Results in noise-damaged ears largely ruled out the possibility that DPOAE basal components were mistaken for catalyst products produced by the presence of the third interfering tone. Unlike humans, in rabbits, no significant reflection components were extracted by ITs placed near the f_{dp} . For rabbit DPOAE L/P maps, these findings eliminated the possibility that a reflection mechanism similar to that found in humans contributed to the generation of emissions with a vertical-like phase structure.

Finally, the configurations of residual DPOAEs produced by the 1/3-oct IT were not attributable to any significant effects of the IT on f_2 . Consequently, the patterns of residuals produced with a 1/3-oct IT demonstrated the presence of basal DPOAE components. Additionally, ADP-grams measured in noise-damaged rabbit ears suggest that, especially at higher primary-tone levels, basal DPOAE components fill in the extent of the lesion revealed by DPOAEs evoked by low-level primaries and ABR threshold shifts. These findings have significant implications for both animal and clinical studies of DPOAEs. It is likely that experiments attempting to correlate DPOAEs with various behavioral or functional measures have suffered from the fact that DPOAE components generated basal to f_2 may have complicated the results. Here, we have described an ADP-gram procedure that can be easily applied to DP-grams. In future studies, it will be possible to test the efficacy of this procedure in laboratory models of hearing impairment as well as in clinic patients. In the clinic, the ADP-gram procedure promises to more accurately reveal the precise pattern of cochlear damage, so that relatively high-level primary-tones can be utilized to increase DPOAE signal-to-noise ratios in ears with sensorineural hearing loss.

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NOMENCLATURE

ABR	= Auditory brainstem response
ADP-gram	= Augmented DP-gram obtained with an IT 1/3 oct above f_2
BM	= Basilar membrane
CAP	= Compound action potential
DP-gram	= DPOAE level as a function of the f_2 primary-tone frequencies
DPOAE	= Distortion-product otoacoustic emission
DSP	= Digital signal processor
f_1, f_2	= Lower- and upper-frequency primary-tones, respectively
f_2/f_1	= Ratio describing the frequency separation of f_1 and f_2

f_{dp}	= Distortion-product frequency
FFT	= Fast Fourier transform
IT	= Interference tone
L/P map	= Level/phase map
L_1, L_2	= Levels of f_1 and f_2 , respectively
NF	= Noise floor
OBN	= Octave band of noise
oct	= Octave
OHC	= Outer hair cell
PTS	= Permanent threshold shift
RDP-gram	= Residual DP-gram representing vector difference between DP- and ADP-grams
SFOAE	= Stimulus frequency otoacoustic emission
STC	= Suppression tuning curve
TEOAE	= Transient evoked otoacoustic emission
TTS	= Temporary threshold shift
TW	= Traveling wave
UHF	= Ultra-high frequency

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