Mechanisms of Mammalian Otoacoustic Emission and their Implications for the Clinical Utility of Otoacoustic Emissions

Christopher A. Shera

We review recent progress in understanding the physical and physiological mechanisms that generate otoacoustic emissions (OAEs). Until recently, the conceptual model underlying the interpretation of OAEs has been an integrated view that regards all OAEs as manifestations of cochlear nonlinearity. However, OAEs appear to arise by at least two fundamentally different mechanisms within the cochlea: nonlinear distortion and linear reflection. These differences in mechanism have be used to construct a new taxonomy for OAEs that identifies OAEs based on their mechanisms of generation rather than the details of their measurement. The mechanism-based taxonomy provides a useful conceptual framework for understanding and interpreting otoacoustic responses. As commonly measured in the clinic, distortion-product and other evoked OAEs comprise a mixtures of emissions produced by both mechanisms. This mixing precludes any fixed correspondence with the conventional, measurement-based nomenclature. We discuss consequences of the taxonomy for the clinical measurement and interpretation of OAEs.

Despite its extraordinary implications, Kemp's discovery that the ear makes sound while listening to sound had difficulty getting published (reviewed in Kemp, 1998). Indeed, the manuscript announcing the discovery was rejected by *Nature* on the grounds that otoacoustic emissions (as these sounds are now called) would doubtless prove of little interest outside the community of clinicians concerned with the diagnosis of hearing impairment. Needless to say, the discovery of otoacoustic emissions (OAEs) sparked a revolution in our understanding of the physical basis of hearing. Ironically, given the reaction by the editors of *Nature*, it has been precisely in the area of clinical utility that the full potential of OAEs has yet to be realized.

As a diagnostic tool, the analysis of OAEs shares with conventional functional imaging techniques the task of reconstructing function from indirect measurements. In contrast to the electromagnetic signals employed by imaging techniques such as functional magnetic resonance imaging, otoacoustic measurements are based on the response of the ear to sound. Acoustic stimuli create hydromechanical waves that travel along the cochlear spiral. Via physical mechanisms still under active investigation, these waves are partially re-emitted back through the middle ear into the ear canal, where they reappear as sound and can be recorded with sensitive, low-noise microphones. The re-emitted sounds carry information back to the ear canal about the mechanisms that generate and shape them. The goal in the clinic is to extract and to utilize the information in these sounds to infer the state of the particular ear that generated them. Yet today, more than a quarter century after their discovery, the clinical use of OAEs is still largely limited to a qualitative normal/abnormal test of cochlear function with roughly half-octave frequency resolution. But OAEs clearly provide the potential for obtaining far more powerful, detailed, and frequency-specific information about the functional status of the inner and middle ears and their feedback control mechanisms. The problem, of course, has been that realizing the potential of OAEs requires first understanding the physical and physiological mechanisms that generate these sounds.

A Mechanism-Based Taxonomy

In both the research laboratory and the clinic, interpretation of measured otoacoustic responses is grounded on an underlying picture of the origin of evoked OAEs. Until recently, the interpretive model guiding the field has been an integrated framework that views all OAEs as manifestations of cochlear mechanical nonlinearity (Allen & Lonsbury-Martin, 1993; Allen & Neely, 1992; Kemp, 1978; Kemp, 1997, 1998; Kemp & Brown, 1983; Patuzzi, 1996; Probst, Lonsbury-Martin, & Martin, 1991). Since all OAEs were understood as arising from the same physical mechanism, it was natural to classify and interpret emissions based on details of the measure-

Eaton-Peabody Laboratory of Auditory Physiology, Massachusetts Eye & Ear Infirmary, and Department of Otology & Laryngology, Harvard Medical School, Boston, Massachusetts
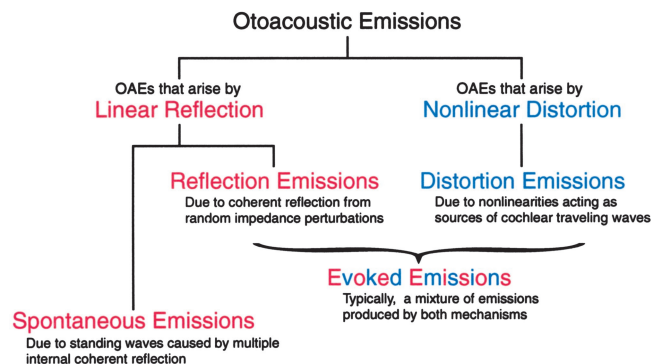
Mechanism-Based Taxonomy for OAEs

Figure 1. Mechanism-based taxonomy for mammalian OAEs. Adapted, with permission, from Shera and Guinan (1999).

ment paradigm.* It is now widely recognized, however, that this integrated view cannot be correct. In particular, OAEs appear to arise by at least two fundamentally different mechanisms. These differences in mechanism have been used to construct a new interpretive framework—a mechanism-based taxonomy or OAE "family tree"—based on underlying emission mechanisms rather than on details of the measurement technique.

The mechanism-based taxonomy, illustrated in Figure 1, identifies two fundamentally different sources of OAEs: distortion source emissions, which arise by nonlinear distortion, and reflection source emissions, which arise through a process equivalent to linear reflection. Outward-traveling waves produced by these two different mechanisms combine to form the emissions commonly measured in the ear canal. Evoked emissions are thus typically mixtures of these two different emission types. The basic experimental distinction between distortion- and reflection source emissions was first noted by Kemp and Brown (1983), who called them "wave-" and "place-fixed" emissions, respectively. Historically, however, wave- and place-fixed emissions were both regarded as originating via mechanical nonlinear-

ity, a supposition both consistent with and reinforced by the integrated view of OAEs. As a result, important implications of the distinction went largely unrecognized. The taxonomy therefore adopts a more mechanistically suggestive nomenclature that emphasizes the fundamental break with the earlier conceptual framework. Before elaborating on the consequences of the taxonomy, we first summarize the argument behind it; a full account can be found elsewhere (Shera & Guinan, 1999).

Two Mechanisms in a Nutshell

Underlying the earlier integrated view of OAEs is a conceptual model that we will call the "nonlinear-distortion model." The recognition of multiple emission mechanisms proceeds from a detailed consideration of this model. It proves especially informative to elaborate the model's predictions for the frequency-dependence of emission phase and to compare those predictions with OAE measurements. Although the nonlinear-distortion model accounts well for pure distortion products,† our analysis shows that it cannot explain SFOAE or TEOAE phase at low levels. The resulting contradiction between the nonlinear-distortion model and experimental data leads us directly to the taxonomy illustrated above. In the following sections we review the kernel of the argument.

The nonlinear-distortion model • Figure 2 provides a schematic illustrating the idea behind the nonlinear-distortion model for the case when the evoking stimulus is a single pure tone (i.e., SFOAEs). In the top panel, the black line shows a snapshot of the traveling wave resulting from this pure-tone stimulus. The wave is shown as a function of distance from the stapes. According to the nonlinear-distortion model, when the cochlear response is nonlinear the traveling wave induces localized distortions in the mechanics, principally about the peak of the traveling-wave envelope. For example, nonlinearities in the mechanisms of force production by outer hair cells can induce distortions in the effective stiffness of the cochlear partition (Brownell, 1990). These nonlinear distortions act, in effect, as sources of traveling-wave energy at the stimulus frequency and its harmonics. For simplicity, the figure shows these distortions idealized as point sources located near the region of maximum displacement. The gray line shows how the traveling wave, and with it the region of induced mechanical distortion, shifts along the cochlear partition when the stimulus frequency is increased.

---

*The conventional, measurement-based nomenclature uses "transiently-evoked emissions" (TEOAEs) to denote OAEs evoked by transient acoustic stimuli such as clicks or tone bursts whose durations are less than corresponding OAE latencies; TEOAEs are often separated from the stimulus using time windowing of the measured ear-canal pressure waveform. "Distortion-product emissions" (DPOAEs) are evoked at combination-tone frequencies by two or more pure tones; they are most readily separated from the stimulus tones by Fourier analysis. Finally, "stimulus-frequency emissions" (SFOAEs) are evoked at the stimulus frequency, usually by a single pure tone. Conceptually, at least, SFOAEs are the most difficult OAEs to measure because they occur both simultaneously with and at the same frequency as the stimulus; they are typically measured by exploiting their nonlinear growth with sound intensity and/or their suppression by nearby tones.

---

†By "pure distortion products" we mean DPOAEs that are uncontaminated by reflection source OAEs. See the discussion of OAE source-type mixing in the "Mixing and Unmixing" section.
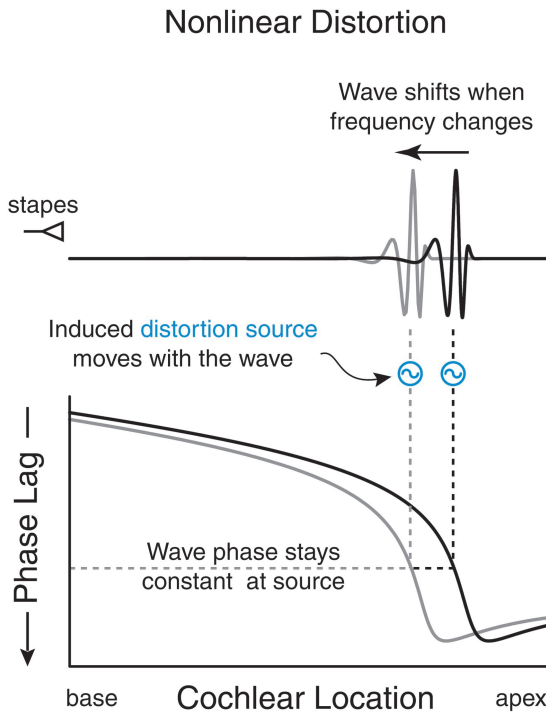
Nonlinear Distortion

Figure 2. Schematic diagram illustrating the idea behind the nonlinear-distortion model for a single pure-tone stimulus such as that used to evoke SFOAEs. The figure shows a snapshot of the traveling wave (black line, top) and the corresponding phase lag (bottom) versus distance from the stapes. Because of nonlinearities in the mechanics, the traveling wave induces distortion sources that create outward-traveling waves. For simplicity, these distributed distortion sources are represented using a single point source located at the peak of the wave envelope (⊘). Since the distortion source is induced by the wave itself, the phase of the wave at the source remains constant as the frequency is increased (gray lines) and the wave pattern shifts basally along the partition (←). To make the wave visible on the graph, the amplitude of the traveling wave has been hugely exaggerated relative to the size of the stapes. Adapted, with permission, from Kalluri and Shera (2001, Fig. 2).

According to the integrated view, both SFOAEs and DPOAEs arise through nonlinear distortion (Kemp, 1998; Patuzzi, 1996). For example, if the two waves shown in the figure are present simultaneously (so that the gray line corresponds to the f_2, or higher frequency wave, and the solid line to the f_1, or lower frequency wave), intermodulation distortion occurs in the region of wave overlap, principally near the peak of the f_2 wave. The region of intermodulation distortion acts as a source of waves (e.g., at the frequency $2f_1 - f_2$) traveling away from the source region in both directions. When the cochlear map is exponential, so that an octave corresponds to a constant distance along the basilar membrane, sweeping the primaries with the frequency ratio f_2/f_1 held fixed simply translates the stimulus wave pattern (and thus the region of induced nonlinear distortion) along the cochlear partition. Stimuli such as this, in which the corresponding wave pattern translates along the partition, are known as "frequency-scaled stimuli."‡

It proves helpful to consider the frequency-dependence of emission phase. In the nonlinear-distortion model, the relative emission phase is a simple sum of two components: (1) a phase shift due to wave-travel to and from the site of stimulus re-emission, plus (2) any phase shift due to the nonlinear re-emission process itself. How do these component phase shifts vary with frequency?

For frequency-scaled stimuli, compelling arguments suggest that each of these two components, and hence their sum, must be approximately constant, independent of frequency (Shera & Guinan, 1999). Central to the argument is the recognition that sources of nonlinear distortion are induced by—and hence, move with—the wave when the frequency is varied (Kemp & Brown, 1983; Strube, 1989; Zweig & Shera 1995). As a consequence, the total phase lag experienced by the traveling wave as it propagates inward from the stapes to the region of largest distortion near the peak of the wave is approximately independent of the frequency of the wave (Fig. 2, bottom). This frequency-independence of the phase lag follows immediately from the approximate local scaling symmetry (Zweig, 1976) manifest by basilar-membrane transfer functions (Rhode, 1971) and neural tuning curves (Kiang & Moxon, 1974; Liberman, 1978). When the cochlear frequency position map is logarithmic, scaling symmetry implies that traveling-wave envelopes are locally "shift-similar," with the number of wavelengths in the traveling wave nearly independent of frequency. Compared with a higher frequency wave, a wave of somewhat lower frequency travels further along the cochlea and requires a longer time to reach its peak. But both waves travel the same number of wavelengths, and their total phase accumulation is therefore the same. Similar arguments grounded in local scaling symmetry also constrain phase shifts introduced by the nonlinear re-emission process itself as well as those arising from the subsequent outward travel of the emitted wave (Shera & Guinan, 1999). According to the nonlinear-distortion model, frequency-scaled OAE phase must therefore be independent of frequency.

Our analysis of the nonlinear-distortion model can be tested experimentally by measuring DPOAE

---

‡Examples of frequency-scaled stimuli are two-tone sweeps with the ratio f_2/f_1 held fixed, i.e., measurement of the so-called "DP-gram," and single-tone sweeps, i.e., the measurement of SFOAEs. Note that a pure-tone sweep can be thought of as a two-tone sweep in the limit that $f_2/f_1 \to 1$.
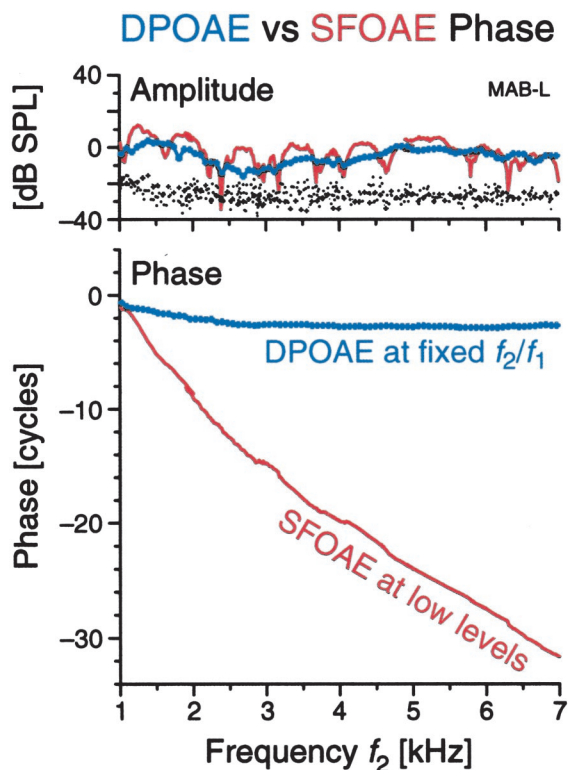
DPOAE vs SFOAE Phase

Figure 3. DPOAE versus SFOAE phase. The blue lines show the amplitude and phase of the human $2f_1 - f_2$ DPOAE measured at fixed $f_2/f_1 = 1.2$ with primary levels $(L_1, L_2) = (50, 40)$ dB SPL. To obtain a nearly pure distortion source OAE, the DPOAE was measured in the presence of a 55-dB SPL suppressor tone with frequency near $2f_1 - f_2$. Shown for comparison (red lines) are measurements in the same subject of the SFOAE measured at a probe level of 40 dB SPL. The dots in the upper panel show the approximate measurement noise floor. Adapted, with permission, from Shera and Guinan (1999, Fig. 9).

phase using frequency-scaled stimuli (e.g., by fixing the primary-frequency ratio f_2/f_1, as in the standard distortion-product audiogram). In this case, the generation mechanism is known to be a frequency-scaled nonlinear distortion, so the nonlinear-distortion model applies.§ The model predicts a constant phase—what do we find experimentally? The answer is shown by the blue lines in Figure 3 (see also Kemp & Brown, 1983). The figure shows the amplitude (top panel) and phase in cycles (bottom panel) of the $2f_1 - f_2$ DPOAE as a function of frequency. The ratio f_2/f_1 was fixed at the value 1.2 during the sweep. Just as predicted, the emission phase is

---

§The nonlinear-distortion model applies to pure distortion products, and the argument is therefore complicated somewhat by the OAE mixing discussed in the "Mixing and Unmixing" section. To isolate the emission generated by nonlinear distortion, the DPOAEs shown in Figure 3 were measured in the presence of an additional suppressor tone, as described in the discussion of DPOAE source unmixing.

essentially independent of frequency, varying by less than half a cycle over the nearly three-octave range of the figure. Thus, the nonlinear-distortion model correctly predicts the constant phase of emissions generated by frequency-scaled nonlinear distortion.

But what about stimulus-frequency OAEs? According to the earlier view, SFOAEs are also generated by frequency-scaled nonlinear distortion (Kemp, 1998; Patuzzi, 1996), and thus SFOAE phase must also be constant. But is it? Again, the answer is shown in Figure 3 (Kemp & Brown, 1983; Shera & Zweig, 1993a; Wilson, 1980; Zwicker & Schloth, 1984), where the amplitude and phase of the SFOAE measured in the same subject at low stimulus levels are shown by the red lines. Whereas the DPOAE phase is roughly constant (consistent with an origin in nonlinear distortion), the SFOAE phase varies by more than 30 cycles over the same frequency range. Furthermore, TEOAEs manifest the same rapid phase rotation found for SFOAEs. Thus, although the nonlinear-distortion model accounts for pure distortion products, it predicts a constant SFOAE (and TEOAE) phase, in striking contradiction with experiment. We conclude that pure DPOAEs and low-level SFOAEs and TEOAEs must arise by fundamentally different mechanisms. This fundamental distinction in source mechanism forms the basis of the taxonomy illustrated in Figure 1.

The origin of reflection source OAEs • The integrated view was half right; it accounts for the existence and properties of distortion source OAEs. But how do reflection source OAEs originate? To understand our answer to this question, recall that the (mistaken) prediction of constant SFOAE and TEOAE phase hinges on the essential feature of the nonlinear distortion model that the emission sources are induced by the traveling wave, as illustrated in Figure 2. The resulting contradiction with experiment suggests that rather than being induced by the wave, the perturbations that reflect the traveling wave may instead constitute pre-existing irregularities in cochlear mechanics. For example, spatial variations in hair cell number and geometry (Bredberg, 1968; Engström, Ades, & Andersson, 1966; Lonsbury-Martin, Martin, Probst, & Coats, 1988; Wright, 1984)—or perturbations not so visible in the anatomy, such as variations in OHC forces due to random, cell-to-cell variations in the number of OHC motor proteins—presumably produce corresponding micromechanical impedance perturbations that act, in effect, to partially reflect the traveling wave. Figure 4 argues that the outward-traveling waves resulting from such perturbations have phases that vary rapidly with frequency, in qualitative agreement with SFOAE phase and in marked contrast to
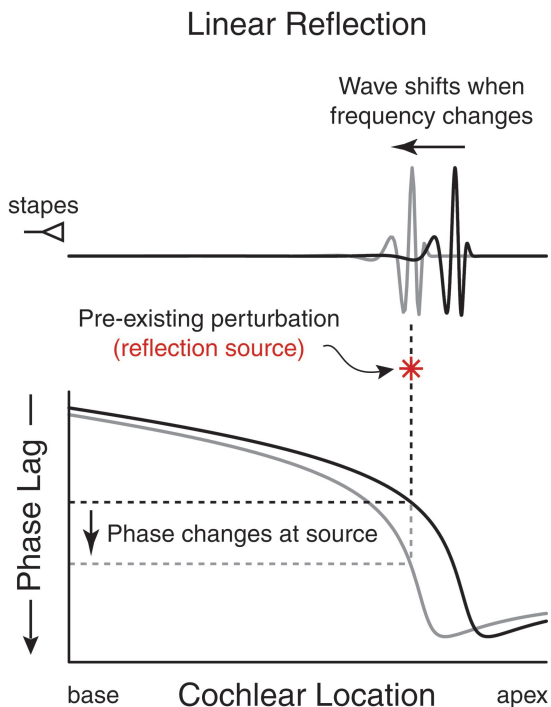
Linear Reflection

Figure 4. Analog of Fig. 2 for a reflection source. Because pre-existing mechanical perturbations (*) are fixed in space, the phase of the traveling wave incident on a perturbation, and thus the phase of the resulting scattered wave, varies rapidly with stimulus frequency. For simplicity, the figure shows only a single perturbation; mechanical perturbations are thought to be densely and randomly distributed along the cochlear partition. As a rule, wavelets scattered by perturbations located near the peak of the traveling wave have much larger amplitudes than those scattered elsewhere (for the case of the single perturbation shown here, the amplitude of the back-scattered wave will be much larger for the higher-frequency stimulus wave shown in gray than for the stimulus wave shown in black). Adapted, with permission, from Kalluri and Shera (2001, Fig. 2).

emissions created by nonlinear distortion (Fig. 2). Indeed, we have shown that the known properties of reflection source OAEs can be accounted for by supposing that they arise through an essentially linear process: coherent wave scattering off random perturbations in the mechanics (Shera & Zweig, 1993b; Talmadge, Tubis, Long, & Piskorski, 1998; Zweig & Shera, 1995).‖

Does the conclusion that SFOAEs and TEOAEs arise through linear reflection at low stimulus levels conflict with the well-known level dependence of these emissions, which exhibit a nonlinear growth in amplitude at all but the lowest sound levels? No. Nonlinear growth does not imply that the outward-traveling waves themselves arise by a nonlinear process. Rather, we argue that the nonlinear growth

‖For a quasi-historical and somewhat less technical review, see Shera (2003b) and the discussion reprinted after the text.

should be understood as a consequence of the level-dependent amplification of inward- and outward-traveling waves. Although the propagation of traveling wave energy along the basilar membrane is a nonlinear function of sound level, the physical mechanisms responsible for reversing the direction of that propagation (i.e., coherent reflection from perturbations in the mechanics) are thought to be essentially linear.

Note that the mechanism-based taxonomy groups spontaneous emissions (SOAEs) within the subset of emissions that arise by linear reflection. SOAEs are commonly thought to result from the autonomous mechanical oscillation of cellular or subcellular constituents of the ear's amplifier (Gold, 1948; Martin & Hudspeth, 2001). However, the properties of mammalian SOAEs strongly suggest that they are actually amplitude-stabilized cochlear standing waves that originate as continuously self-evoking SFOAEs (Shera, 2003a). In other words, SOAEs result from a process of multiple internal reflection of traveling-wave energy initiated either by sounds from the environment or by physiological noise. In the standing-wave model of SOAEs, first proposed by Kemp (1979a; 1979b) and subsequently elaborated in models of evoked otoacoustic emissions (Allen, Shaw, & Kimberley, 1995; Shera & Guinan, 1999; Talmadge & Tubis, 1993; Talmadge et al., 1998; Zweig, 1991; Zweig & Shera, 1995; Zwicker & Peisl, 1990), SOAE frequencies are determined not by local cellular properties, such as hair-bundle geometry and adaptation or transduction kinetics, but by nonlocal characteristics of cochlear mechanics such as round-trip, traveling-wave phase shifts and the impedance mismatch at the basal boundary with the middle ear. When it produces SOAEs, the cochlea is acting as a biological, hydromechanical analog of a laser oscillator (Shera, 2003a).

Mixing and Unmixing

The taxonomy predicts that OAEs are typically mixtures of emissions generated by the two different mechanisms. The generation of DPOAEs at the frequency $2f_1 - f_2$ provides an example of this mixing (Knight & Kemp, 2001; Konrad-Martin, Neely, Keefe, Dorn, & Gorga, 2001; Mauermann, Uppenkamp, van Hengel, & Kollmeier, 1999; Shera & Guinan, 1999; Talmadge, Long, Tubis & Dhar, 1999). According to the model underlying the taxonomy, intermodulation distortion sources, located in the overlap region of the primary traveling waves, create wave energy at the frequency $2f_1 - f_2$ that travels in both directions (outward and inward). Whereas the outward-traveling wave appears in the ear canal as a distortion source OAE, the inward-
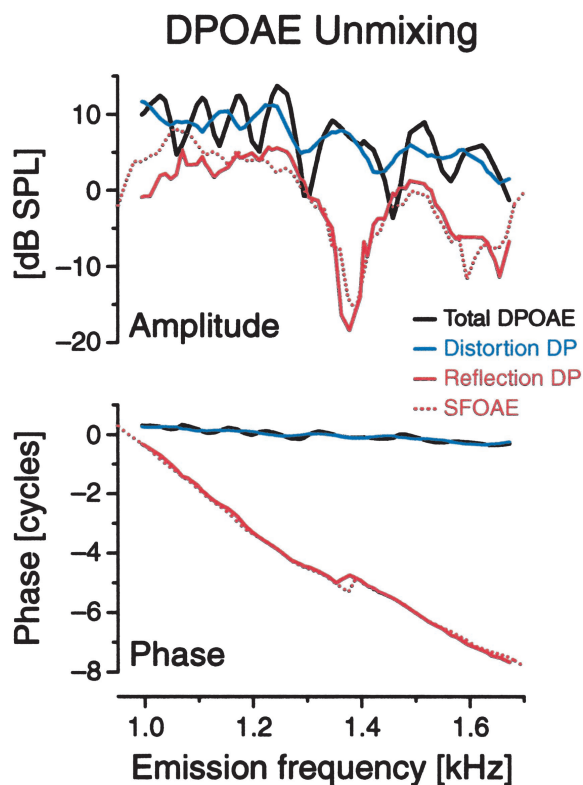
Figure 5. Distortion-product source unmixing. The figure shows the amplitude (top) and phase (bottom) of the total $2f_1 - f_2$ DPOAE (black lines) along with the distortion source (blue lines) and reflection source (red lines) components obtained using suppression-based unmixing in a human subject. DPOAE stimulus parameters: $(L_1, L_2) = (60, 45)$ dB SPL; $f_2/f_1 = 1.2$. For comparison, the dotted red lines show the SFOAE measured in the same subject at a probe level of 40 dB SPL. To make the SFOAE and DPOAE stimulus conditions more comparable, the SFOAE was measured in the presence of an additional tone at the same frequency and level as the f_1 primary used to evoke the DPOAE. Adapted, with permission, from Kalluri and Shera (2001, Figs. 3 and 5, subject no. 1).

traveling wave propagates apically to its characteristic place where it is partially reflected by nearby impedance perturbations. This reflection creates a second outward traveling wave that appears in the ear canal as a reflection source OAE. According to the model, these two components (distortion and reflection source) combine to form the total DPOAE measured in the ear canal.

We have tested this prediction by unmixing the total $2f_1 - f_2$ DPOAE into its constituent components (Kalluri & Shera, 2001). Typical experimental results from a human subject are shown in Figure 5. The black lines show the total DPOAE; emission components obtained by unmixing are shown in color (solid lines). The unmixing procedure isolates the distortion source OAE using a third stimulus tone with frequency near the distortion-product frequency to suppress amplification of the reflection source wavelets that scatter back from their characteristic place (Heitmann, Waldman, Schnitzler, Plinkert, & Zenner, 1998; Kemp & Brown, 1983). As shown in the figure, the total DPOAE unmixes into components whose phase slopes are consistent with the mechanisms of generation predicted by the model. The amplitude characteristics of the two components, e.g., the existence of deep spectral notches in the reflection source component, such as that visible in the figure near 1.4 kHz, are also consistent with model predictions (Kalluri & Shera, 2001; Zweig & Shera, 1995). Finally, the reflection source component closely matches the SFOAE (dotted red lines) evoked at the same frequency under comparable stimulus conditions.

Similar results are found in other subjects, demonstrating that DPOAEs typically comprise a mixture of emissions that arise by two fundamentally different mechanisms within the cochlea. The interference pattern caused by this mixing is known as DPOAE fine structure (Kalluri & Shera, 2001; Mauermann et al., 1999; Talmadge et al., 1999). The phenomenon of OAE source mixing is not, of course, restricted to DPOAEs. For example, although evidently arising largely by linear reflection at low stimulus levels, TEOAEs and SFOAEs measured at higher levels appear to contain significant energy from distortion source waves created by nonlinear distortion, at least in guinea pigs (Goodman, Withnell, & Shera, 2003b; Talmadge, Tubis, Long, & Tong, 2000; Withnell & Yates, 1998a; Yates & Withnell, 1999).

Implications for the Clinical Utility of OAEs

The OAE taxonomy provides a mechanism-based alternative to the conventional classification scheme, which groups emissions based on the stimuli used to evoke them. On some distant planet where all OAEs arise via the same physical mechanism, the conventional measurement-based nomenclature would be both natural and maximally informative, since the various OAE classes (e.g., TEOAEs and DPOAEs) would differ from one another only insofar as different stimuli were used to elicit them. But here on Earth, multiple generation mechanisms are at work, and OAEs from the various branches of the family tree carry different information back to the ear canal. By explicitly recognizing and formalizing these differences, the mechanism-based taxonomy provides an improved interpretive framework that promises to enhance the future clinical utility of OAEs in several important ways.

Extending the etiological specificity of OAE tests • First and foremost, the taxonomy implies that not all OAEs are created equal. Although both reflection and distortion source OAEs share a common dependence on propagation pathways from the cochlea to the ear canal, and are therefore sensitive to modifications of that pathway (e.g., to middle-ear pathology or to reductions in cochlear amplification caused by damage to outer hair cells), their respective mechanisms of generation—and hence their dependence on underlying parameters of cochlear mechanics—remain fundamentally distinct.

To illustrate, note that distortion source OAEs depend on the form and strength of cochlear nonlinearities. For example, a major source of distortion in the cochlea is the nonlinear relation between the displacement of the ciliary bundle and the voltage inside the hair cell. This function, known as the hair cell's displacement voltage transduction function, is an important determinant of the amount of force produced by outer hair cells, and its nonlinear form can therefore have significant mechanical effects. The relation is nonlinear because at extreme excitatory displacements (i.e., displacements towards the tallest stereocilia) all the transduction channels are open, so that displacing the bundle further in the same direction produces no change in the current flowing into the cell (Hudspeth & Corey, 1977); a similar situation occurs at the opposite extreme, where all the channels are closed. The operating point of this nonlinear function defines the point on the curve about which the cell operates when input displacements are small. Models indicate that the amount of distortion produced by any given stimulus depends sensitively on precisely where along the curve the operating point resides (Lukashkin, Lukashkina, & Russell, 2002; Weiss & Leong, 1985). To maintain sensitivity to small displacements, the operating point is controlled by homeostatic processes within the cell, including the mechanisms of hair-bundle adaptation (for a review, see Eatock, 2000). If these mechanisms are disturbed in some way (e.g., as the result of over-stimulation or pathology) then the operating point can shift and produce large changes in the distortion, and thus the distortion source OAEs, generated within the cochlea.

The generation of reflection source OAEs, by contrast, does not depend directly on cochlear nonlinearities. Rather, reflection source OAEs are sensitive to the size and spatial arrangement of micromechanical impedance perturbations located near the peak of the traveling wave (Talmadge et al., 1998; Zweig & Shera, 1995). In addition, because they are generated near the traveling wave peak, reflection source OAEs evoked by low-level stimuli are quite sensitive to small changes in the gain of the cochlear amplifier.¶

Although interpretation may not always be straightforward, the taxonomy thus provides a conceptual framework for understanding and exploring observations, such as species differences in relative emission amplitude and the dissociations among OAE measures often observed in response to aspirin, quinine, and other ototoxic drugs (Martin, Lonsbury-Martin, Probst, & Coats, 1988; McFadden & Pasanen, 1994; Wier, Pasanen, & McFadden, 1988), that remain largely uninterpretable if all OAEs are regarded as sharing a common origin in nonlinear distortion (Shera & Guinan, 1999). For example, Martin et al. (1988) found that although SFOAEs and SOAEs are abolished by aspirin administration, DPOAEs can remain almost unchanged. These findings suggest that aspirin may reduce the gain of the cochlear amplifier while maintaining, or even enhancing, the nonlinearities responsible for generating distortion source OAEs. How might this happen? As one possibility, aspirin could shift the operating point of the OHC transduction function discussed above. Since shifts in the operating point can change the amount of mechanical distortion and the net gain of the cochlear amplifier in opposite directions, the amplitudes of reflection- and distortion source OAEs need manifest no simple relationship, even though both emission types depend on the integrity of the OHCs. Thus, when differences in their mechanisms of generation are properly taken into account, the observation that the different emission types can appear decoupled by certain experimental manipulations and/or pathologies is no longer surprising.

As a consequence of their different origins, reflection and distortion source OAEs presumably manifest different dependencies on cochlear pathologies. Unfortunately, it is still too early to know the significance of these differences for clinical practice. The relative utilities of the various stimulus paradigms represented in the conventional measurement-based classification (e.g., TEOAEs versus DPOAEs) have been well examined. As we now appreciate in retrospect, however, these studies gen-

---

¶Although the distortion source component of DPOAEs arises near the peak of the f_2 traveling wave, the level of the f_2 stimulus used to produce DPOAEs is often substantially greater than that used to evoke reflection source emissions like SFOAEs. At these higher intensities, the gain provided by the cochlear amplifier is substantially reduced. In addition, suppressive effects arising from the nearby tone at f_1 can reduce the amplifier gain at f_2 still further. In such circumstances, distortion source OAEs are expected to be considerably less sensitive to the gain of the cochlear amplifier.

erally blurred the distinction between emission-source mechanisms by using stimulus conditions that failed to control for OAE mixing. As a result, relatively little is known about the different utilities of reflection- and distortion source OAEs. Since the amplitudes of both OAE types share a common, first-order dependence on cochlear amplification, differences between the two may eventually prove unimportant for routine clinical screening. In other applications, however, the bottom line may be very different. For example, because of their expected sensitivity to small changes in amplification, reflection source OAEs may prove to be the emission of choice when using OAEs to monitor cochlear status over time (e.g., in applications designed to detect the onset of ototoxicity and/or noise-induced hearing loss). In the future, clinical measurement and separation of both types of evoked emissions will presumably be needed to maximize the power and specificity of OAEs as noninvasive probes of cochlear function.

Improving the power of existing OAE tests • The taxonomy implies that uncontrolled mixing may be a substantial source of intra- and intersubject variability in current OAE measurements. Consider, for example, the interpretation of DPOAE responses. As usually measured, DPOAEs are mixtures of emissions originating from at least two different regions of the cochlea (i.e., the distortion source region near the f_2 place and the reflection source region near the distortion-product place); this spatial blurring compromises the frequency selectivity of DPOAE measurements (Heitmann et al., 1998). In addition, the emission components from the two regions evidently arise by fundamentally different mechanisms (nonlinear distortion and linear reflection), compromising the etiological specificity of the measurement (Kalluri & Shera, 2001). Furthermore, because of their different mechanisms of generation, the two emission types have different dependencies on stimulus parameters such as frequency and level. The relative mix of emissions from the two sources, and thus the amplitude and phase of the total DPOAE, can therefore vary in complicated ways (Fig. 5), substantially increasing the variability of measured OAE responses.

For these reasons, the taxonomy suggests that existing DPOAE-based diagnostic and screening tests can be improved by using OAE unmixing to reduce variability across subjects. Current clinical tests compare DPOAE measurements at audiometric frequencies with normative data to infer the likelihood of impaired OHC function (for a review, see Gorga, Neely, & Dorn, 2002). The ability of these tests to discriminate degrees of impairment depends on the response variance across subjects (e.g., on the range of responses classified as "normal"). As illustrated in Figure 5, the uncontrolled mixing of distortion- and reflection source OAEs increases the variability of DPOAE measurements across frequency by as much as ± 10 dB in normal-hearing subjects. Since in any given subject the peaks and valleys of DPOAE microstructure are arrayed at random with respect to standard audiometric test frequencies, this intra-subject variability across frequency immediately creates a corresponding inter-subject variability at audiometric frequencies that increases the variance in the normative data. By substantially reducing intra-subject variability across frequency, DPOAE-source unmixing can alleviate this problem and improve the power of existing OAE-based tests (for further discussion, see Shaffer et al., 2003).

Strategies for unmixing • Although the blue and the red may be convenient for distinguishing them on paper, the different types of OAEs do not appear color-coded in the ear canal. Fortunately, however, a variety of techniques are available for at least partially isolating the two types of emissions, and these methods are now beginning to appear in commercial OAE measurement systems. For example, reflection source OAEs can be studied in isolation using stimulus frequency or transient emissions evoked by sufficiently low-level stimuli using methods that do not cancel the low-level linear components of the response (Kemp & Chum, 1980; Shera & Zweig, 1993a). And in DPOAE measurements, the distortion and reflection source components can often be separated by exploiting the spatial separation of the regions of nonlinear distortion and linear reflection within the cochlea. In this technique, an additional tone is presented to selectively suppress the reflection source component of the response (Heitmann et al., 1998; Kemp & Brown, 1983). As discussed above, the DPOAE components shown in Figure 5 were obtained in just this way. Alternatively, the reflection and distortion source components of DPOAEs can be separated based on their onset latency, either directly in the time domain (Talmadge et al., 1999; Whitehead, Stagner, McCoy, & Lonsbury-Martin, 1996) or with appropriate signal processing (Kalluri & Shera, 2001; Knight & Kemp, 2001; Konrad-Martin et al., 2001; Stover, Neely, & Gorga, 1996). Although not all unmixing methods have been compared, those that have (i.e., suppression and Fourier-based time windowing) generally yield similar components (Kalluri & Shera, 2001).

Testing and Extending the Taxonomy

Although elucidating the basic physical mechanisms responsible for mammalian otoacoustic emis-

sions represents an important step toward realizing the potential of OAE-based diagnostics, many unanswered questions remain. For example, the taxonomy illustrated in Figure 1 describes only the two principal branches of the OAE family tree. Are there sub-branches with theoretical or practical significance? Evidence from rodents and rabbits suggests that distortion source OAEs may be divisible into subsets comprising an active, or low-level, component and a passive, or high-level, component that interact to produce characteristic amplitude "notches" at moderate to high sound levels (Mills & Rubel, 1994; Norton & Rubel, 1990; Whitehead, 1998; Whitehead, Lonsbury-Martin, & Martin, 1992a, 1992b; Whitehead, Stagner, McCoy, Lonsbury-Martin, & Martin, 1995). The differential physiological vulnerability of these possible distortion source components has been interpreted as suggesting that they arise from different sources of nonlinearity within the cochlea. For example, the active component may result from nonlinearities associated with the OHC transduction function that only become manifest mechanically through the action of OHC somatic motility, whereas the passive component may result from nonlinearities that arise directly in the mechanics, such as a nonlinear mechanical stiffness in the stereocilia. The case for distortion source subtypes remains open, however, since many qualitatively similar effects can be produced by a single, asymmetric saturating nonlinearity (Lukashkin et al., 2002; Weiss & Leong, 1985; Withnell & Yates, 1998b).

Along similar lines, Kemp (2002) has hypothesized the existence of two subsets of reflection source OAEs based on whether the relevant impedance perturbations occur in the passive mechanics (Type B) or in the physiologically vulnerable active mechanics (Type A).# At the moment, these subsets remain only plausible theoretical possibilities; understanding whether they and/or other possible subsets of reflection source OAEs can be distinguished experimentally remains an important open question.

Also waiting to be established are the taxonomy's limits of validity across stimulus intensity. Based on measurements and models valid at low-to-moderate sound levels, the taxonomy may need modification in other intensity regimes. For example, at higher sound levels the two emission sources may begin to mix in ways more complicated than simple linear summation (e.g., the strength of the micromechani-

cal impedance perturbations may depend on the local amplitude of basilar-membrane vibration). Ultimately, the distinction between the two mechanisms, experimentally clear at low sound levels, may lose operational significance at high intensities. In this regard, we are reminded of the dialectic described by Levins and Lewontin (1985): "A necessary step in theoretical work is to make distinctions. But whenever we divide something into mutually exclusive and jointly all-encompassing categories, it turns out on further examination that these opposites interpenetrate."

Conclusion

The mechanism-based taxonomy identifies two fundamentally different emission-source mechanisms. Distortion source OAEs require cochlear nonlinearity, but not mechanical irregularity; they would not occur in an idealized linear cochlea or at stimulus intensities sufficiently low that the cochlear amplifier operates in its linear regime. By contrast, reflection source OAEs require mechanical irregularity but not nonlinearity; they would not occur in a mechanically smooth cochlea in which the effective impedance of the organ of Corti changes smoothly with position. Since actual cochleae are, to varying degrees, both nonlinear and mechanically irregular, both mechanisms generally operate to produce outward-traveling waves that mix to form the emissions measured in the ear canal.

The mechanism-based taxonomy implies that the information carried back to the ear canal by OAEs is richer than previously supposed. Although OAEs are currently employed in the clinic only as an assay of OHC function, important factors other than cochlear amplification are involved in their generation, and these factors differ among the different emission types. OAE tests of the future will exploit this additional information in at least two ways. First, future tests will increase the power of OAE measurements by reducing their variance. Improved tests will systematically subtract out the various confounding influences on OAEs to obtain measures more closely related to the specific aspects of auditory function they aim to assess. In addition to multiple OAE generation mechanisms, other important influences on OAEs that can and should be controlled for in future OAE-based diagnostic and screening tests include frequency- and subject-dependent variations in middle-ear transmittance and reflectance (Feeney, Grant, & Marryott, 2003; Keefe, Gorga, Neely, Zhao, & Vohr, 2003a; Keefe, Zhao, Neely, Gorga, & Vohr, 2003b) and variations in OAE amplitudes resulting from efferent feedback to the middle and inner ears (Guinan, Backus, Lilaonitkul, & Aharonson, 2003; Maison & Liber-

---

#Kemp (2002) inadvertently misinterprets the taxonomy when he equates "OAE source type B" with reflection source OAEs; because both involve mechanical impedance perturbations, both "A" and "B" types are reflection source subsets.

man, 2000). Second, rather than merely discarding the wealth of subtracted information, future tests will use it to extend the diagnostic ability of OAE measurements beyond their current exclusive focus on cochlear amplification.

The challenge, of course, is that none of the information carried by OAEs comes color-coded in the ear canal. The mixing of the two emission types confounds an understanding of their individual characteristics and clouds the assessment of their different utilities as clinical diagnostic and screening aids. It is the task of research to determine how best to unscramble the information carried by OAEs and make it useful in the clinic. Mitigating the interpretive difficulties as much as possible by focusing on the different emission types measured separately, rather than in confounding combination, represents an attractive strategy for optimizing the power of OAE measurements. Within its range of application, the mechanism-based taxonomy thus highlights the importance, both theoretical and practical, of further characterizing the properties of each emission type (and related subsets), understanding the factors that control their mixing, and determining their individual correlations with cochlear pathology. These and other developments based on continued progress in our understanding of the mechanisms of emission generation will improve the power and specificity of OAEs as noninvasive probes of cochlear function.

REFERENCES

Allen, J. B., & Lonsbury-Martin, B. L. (1993). Otoacoustic emissions. *Journal of the Acoustical Society of America*, *93*, 568–569.

Allen, J. B., & Neely, S. T. (1992). Micromechanical models of the cochlea. *Physics Today*, *45*, 40–47.

Allen, J. B., Shaw, G., & Kimberley, B. P. (1995). Characterization of the nonlinear ear canal impedance at low sound levels. *Journal of the Association for Research in Otolaryngology Abs*, *18*, 797.

Bredberg, G. (1968). Cellular patterns and nerve supply of the human organ of Corti. *Acta Otolaryngolica*, *236*(Suppl.), 1–135.

Brownell, W. E. (1990). Outer hair cell electromotility and otoacoustic emissions. *Ear and Hearing*, *11*, 82–92.

Eatock, R. A. (2000). Adaptation in hair cells. *Annual Review of Neuroscience*, *23*, 285–314.

Engström, H., Ades, H. W., & Andersson, A. (1966). *Structural Pattern of the Organ of Corti*. Williams and Wilkins, Baltimore.

Feeney, M. P., Grant, I. L., & Marryott, L. (2003). Wideband energy reflectance measurements in adults with middle-ear disorders. *Journal of Speech, Language, and Hearing Research*, *46*, 901–911.

Gold, T. (1948). Hearing. II. The physical basis of the action of the cochlea. *Proceedings of the Royal Society of London. Series B*, *135*, 492–498.

Goodman, S. S., Withnell, R. H., & Shera, C. A. (2003). The origin of SFOAE microstructure in the guinea pig. *Hearing Research*, *183*, 1–17.

Gorga, M. P., Neely, S. T., & Dorn, P. A. (2002). Distortion product otoacoustic emissions in relation to hearing loss. In Robinette, M. S. and Glattke, T. J. (Eds.), *Otoacoustic Emissions: Clinical Applications, 2nd Edition* (pages 243–272). Thieme, New York.

Guinan, J. J., Backus, B. C., Lilaonitkul, W., & Aharonson, V. (2003). Medial olivocochlear efferent reflex in humans: Otoacoustic emission (OAE) measurement issues and the advantages of stimulus frequency OAEs. *Journal of the Association for Research in Otolaryngology*, *4*, 521–540.

Heitmann, J., Waldman, B., Schnitzler, H. U., Plinkert, P. K., & Zenner, H.-P. (1998). Suppression of distortion product otoacoustic emissions (DPOAE) near $2f_1-f_2$ removes DP-gram fine structure–Evidence for a secondary generator. *Journal of the Acoustical Society of America*, *103*, 1527–1531.

Hudspeth, A. J., & Corey, D. P. (1977). Sensitivity, polarity, and conductance change in the response of vertebrate hair cells to controlled mechanical stimuli. *Proceedings of the National Academy of Sciences of the United States of America*, *74*, 2407–2411.

Kalluri, R., & Shera, C. A. (2001). Distortion-product source unmixing: A test of the two-mechanism model for DPOAE generation. *Journal of the Acoustical Society of America*, *109*, 622–637.

Keefe, D. H., Gorga, M. P., Neely, S. T., Zhao, F., & Vohr, B. R. (2003a). Ear-canal acoustic admittance and reflectance measurements in human neonates. II. Predictions of middle-ear in dysfunction and sensorineural hearing loss. *Journal of the Acoustical Society of America*, *113*, 407–422.

Keefe, D. H., Zhao, F., Neely, S. T., Gorga, M. P., & Vohr, B. R. (2003b). Ear-canal acoustic admittance and reflectance effects in human neonates. I. Predictions of otoacoustic emission and auditory brainstem responses. *Journal of the Acoustical Society of America*, *113*, 389–406.

Kemp, D. T. (1978). Stimulated acoustic emissions from within the human auditory system. *Journal of the Acoustical Society of America*, *64*, 1386–1391.

Kemp, D. T. (1979a). Evidence of mechanical nonlinearity and frequency selective wave amplification in the cochlea. *Archives of Otorhinolaryngology*, *224*, 37–45.

Kemp, D. T. (1979b). The evoked cochlear mechanical response and the auditory microstructure–Evidence for a new element in cochlear mechanics. *Scandinavian Audiology*, *9*(Suppl.), 35–47.

Kemp, D. T. (1997). Otoacoustic emissions in perspective. In Robinette, M. S. and Glattke, T. J. (Eds.), *Otoacoustic Emissions: Clinical Applications* (pp. 1–21). New York, Thieme.

Kemp, D. T. (1998). Otoacoustic emissions: Distorted echoes of the cochlea's travelling wave. In Berlin, C. I. (Ed.), *Otoacoustic Emissions: Basic Science and Clinical Applications* (pp. 1–59). San Diego, Singular Publishing Group.

Kemp, D. T. (2002). Exploring cochlear status with otoacoustic emissions: The potential for new clinical applications. In Robinette, M. S. and Glattke, T. J. (Eds.), *Otoacoustic Emissions:*

Clinical Applications, 2nd Edition (pp. 1–47). New York, Thieme.

Kemp, D. T., & Brown, A. M. (1983). An integrated view of cochlear mechanical nonlinearities observable from the ear canal. In de Boer, E. and Viergever, M. A. (Eds.), *Mechanics of Hearing* (pp. 75–82). Martinus Nijhoff, The Hague.

Kemp, D. T., & Chum, R. A. (1980). Observations on the generator mechanism of stimulus frequency acoustic emissions–Two tone suppression. In Brink, G. V. D. and Bilsen, F. A. (Eds.), *Psychophysical Physiological and Behavioural Studies in Hearing* (pp. 34–42). Delft, Delft University Press.

Kiang, N. Y. S., & Moxon, E. C. (1974). Tails of tuning curves of auditory-nerve fibers. *Journal of the Acoustical Society of America*, *55*, 620–630.

Knight, R. D., & Kemp, D. T. (2001). Wave and place fixed DPOAE maps of the human ear. *Journal of the Acoustical Society of America*, *109*, 1513–1525.

Konrad-Martin, D., Neely, S. T., Keefe, D. H., Dorn, P. A., & Gorga, M. P. (2001). Sources of distortion product otoacoustic emissions revealed by suppression experiments and inverse fast Fourier transforms in normal ears. *Journal of the Acoustical Society of America*, *109*, 2862–2869.

Levins, R. & Lewontin, R. C. (1985). *The Dialectical Biologist.* Cambridge, Harvard University Press.

Liberman, M. C. (1978). Auditory-nerve response from cats raised in a low-noise chamber. *Journal of the Acoustical Society of America*, *63*, 442–455.

Lonsbury-Martin, B. L., Martin, G. K., Probst, R., & Coats, A. C. (1988). Spontaneous otoacoustic emissions in the nonhuman primate. II. Cochlear anatomy. *Hearing Research*, *33*, 69–94.

Lukashkin, A. N., Lukashkina, V. A., & Russell, I. J. (2002). One source for distortion product otoacoustic emissions generated by low- and high-level primaries. *Journal of the Acoustical Society of America*, *111*, 2740–2748.

Maison, S. F., & Liberman, M. C. (2000). Predicting vulnerability to acoustic injury with a noninvasive assay of olivocochlear reflex strength. *Journal of Neuroscience*, *20*, 4701–4707.

Martin, G. K., Lonsbury-Martin, B. L., Probst, R., & Coats, A. C. (1988). Spontaneous otoacoustic emissions in the nonhuman primate. I. Basic features and relations to other emissions. *Hearing Research*, *33*, 49–68.

Martin, P., & Hudspeth, A. J. (2001). Compressive nonlinearity in the hair bundles active response to mechanical stimulation. *Proceedings of the National Academy of Sciences of the United States of America*, *98*, 14386–14391.

Mauermann, M., Uppenkamp, S., van Hengel, P. W. J., & Kollmeier, B. (1999). Evidence for the distortion product frequency place as a source of distortion product otoacoustic emission (DPOAE) fine structure in humans. I. Fine structure and higher-order DPOAE as a function of the frequency ratio f_2/f_1. *Journal of the Acoustical Society of America*, *106*, 3473–3483.

McFadden, D., & Pasanen, E. G. (1994). Otoacoustic emissions and quinine sulfate. *Journal of the Acoustical Society of America*, *95*, 3460–3474.

Mills, D. M., & Rubel, E. W. (1994). Variation of distortion product otoacoustic emissions with furosemide injection. *Hearing Research*, *77*, 183–199.

Norton, S. J., & Rubel, E. W. (1990). Active and passive adp components in mammalian and avian ears. In Dallos, P., Geisler, C. D., Matthews, J. W., Ruggero, M. A., and Steele, C. R. (Eds.), *Mechanics and Biophysics of Hearing* (pp. 219–226). Berlin, Springer-Verlag.

Patuzzi, R. (1996). Cochlear micromechanics and macromechanics. In Dallos, P., Popper, A. N., and Fay, R. R. (Eds.), *The Cochlea* (pp. 186–257). New York, Springer-Verlag.

Probst, R., Lonsbury-Martin, B. L., & Martin, G. K. (1991). A review of otoacoustic emissions. *Journal of the Acoustical Society of America*, *89*, 2027–2067.

Rhode, W. S. (1971). Observations of the vibration of the basilar membrane in squirrel monkeys using the Mössbauer technique. *Journal of the Acoustical Society of America*, *49*, 1218–1231.

Shaffer, L. A., Withnell, R. H., Dhar, S., Lilly, D. J., Goodman, S. S., & Harmon, K. M. (2003). Sources and mechanisms of DPOAE generation: Implications for the prediction of auditory sensitivity. *Ear and Hearing*, *24*, 367–379.

Shera, C. A. (2003a). Mammalian spontaneous otoacoustic emissions are amplitude-stabilized cochlear standing waves. *Journal of the Acoustical Society of America*, *114*, 244–262.

Shera, C. A. (2003b). Wave interference in the generation of reflection- and distortion-source emissions. In Gummer, A. W. (Ed.), *Biophysics of the Cochlea: From Molecules to Models* (pp. 439–453). Singapore, World Scientific.

Shera, C. A., & Guinan, J. J. (1999). Evoked otoacoustic emissions arise by two fundamentally different mechanisms: A taxonomy for mammalian OAEs. *Journal of the Acoustical Society of America*, *105*, 782–798.

Shera, C. A., & Zweig, G. (1993a). Noninvasive measurement of the cochlear traveling-wave ratio. *Journal of the Acoustical Society of America*, *93*, 3333–3352.

Shera, C. A., & Zweig, G. (1993b). Order from chaos: Resolving the paradox of periodicity in evoked otoacoustic emission. In Duifhuis, H., Horst, J. W., van Dijk, P., and van Netten, S. M. (Eds.), *Biophysics of Hair Cell Sensory Systems* (pp. 54–63). Singapore, World Scientific.

Stover, L. J., Neely, S. T., & Gorga, M. P. (1996). Latency and multiple sources of distortion product otoacoustic emissions. *Journal of the Acoustical Society of America*, *99*, 1016–1024.

Strube, H. W. (1989). Evoked otoacoustic emissions as cochlear Bragg reflections. *Hearing Research*, *38*, 35–45.

Talmadge, C. L., Long, G. R., Tubis, A., & Dhar, S. (1999). Experimental confirmation of the two-source interference model for the fine structure of distortion product otoacoustic emissions. *Journal of the Acoustical Society of America*, *105*, 275–292.

Talmadge, C. L., & Tubis, A. (1993). On modeling the connection between spontaneous and evoked otoacoustic emissions. In Duifhuis, H., Horst, J. W., van Dijk, P., and van Netten, S. M. (Eds.), *Biophysics of Hair Cell Sensory Systems* (pp. 25–32). Singapore, World Scientific.

Talmadge, C. L., Tubis, A., Long, G. R., & Piskorski, P. (1998). Modeling otoacoustic emission and hearing threshold fine structures. *Journal of the Acoustical Society of America*, *104*, 1517–1543.

Talmadge, C. L., Tubis, A., Long, G. R., & Tong, C. (2000). Modeling the combined effects of basilar membrane nonlinearity and roughness on stimulus frequency otoacoustic emission fine structure. *Journal of the Acoustical Society of America*, *108*, 2911–2932.

Weiss, T. F., & Leong, R. (1985). A model for signal transmission in an ear having hair cells with free-standing stereocilia. IV. Mechanoelectric transduction stage. *Hearing Research*, *20*, 175–195.

Whitehead, M. L. (1998). Species differences of distortion-product otoacoustic emissions: Comment on "Interpretation of distortion product otoacoustic emission measurements. I. Two stimulus tones" [J. Acoust. Soc. Am. 102, 413–429 (1997)]. *Journal of the Acoustical Society of America*, *103*, 2740–2742.

Whitehead, M. L., Lonsbury-Martin, B. L., & Martin, G. K. (1992a). Evidence for two discrete sources of $2f_1 - f_2$ distortion-product otoacoustic emission in rabbit: I. Differential dependence on stimulus parameters. *Journal of the Acoustical Society of America*, *91*, 1587–1607.

Whitehead, M. L., Lonsbury-Martin, B. L., & Martin, G. K. (1992b). Evidence for two discrete sources of $2f_1 - f_2$ distortion-product otoacoustic emission in rabbit: II. Differential physiological vulnerability. *Journal of the Acoustical Society of America*, *92*, 2662–2682.

Whitehead, M. L., Stagner, B. B., Martin, G. K., & Lonsbury-Martin, B. L. (1996). Visualization of the onset of distortion-product otoacoustic emissions and measurement of their latency. *Journal of the Acoustical Society of America*, *100*, 1663–1679.

Whitehead, M. L., Stagner, B. B., McCoy, M. J., Lonsbury-Martin, B. L., & Martin, G. K. (1995). Dependence of distortion-product otoacoustic emissions on primary levels in normal and impaired ears. II. Asymmetry in L_1, L_2 space *Journal of the Acoustical Society of America*, *97*, 2359–2377.

Wier, C. C., Pasanen, E. G., & McFadden, D. (1988). Partial dissociation of spontaneous otoacoustic emissions and distortion products during aspirin use in humans. *Journal of the Acoustical Society of America*, *84*, 230–237.

Wilson, J. P. (1980). Evidence for a cochlear origin for acoustic re-emissions, threshold fine-structure and tonal tinnitus. *Hearing Research*, *2*, 233–252.

Withnell, R. H., & Yates, G. K. (1998a). Enhancement of the transient-evoked otoacoustic emission produced by the addition of a pure tone in the guinea pig. *Journal of the Acoustical Society of America*, *104*, 344–349.

Withnell, R. H., & Yates, G. K. (1998b). Onset of basilar membrane non-linearity reected in cubic distortion tone input-output functions. *Hearing Research*, *123*, 87–96.

Wright, A. A. (1984). Dimensions of the cochlear stereocilia in man and in guinea pig. *Hearing Research*, *13*, 89–98.

Yates, G. K., & Withnell, R. H. (1999). The role of intermodulation distortion in transient-evoked otoacoustic emissions. *Hearing Research*, *136*, 49–64.

Zweig, G. (1976). Basilar membrane motion. In *Cold Spring Harbor Symposia on Quantitative Biology, Volume XL*, pp. 619–633. Cold Spring Harbor, Cold Spring Harbor Laboratory.

Zweig, G. (1991). Finding the impedance of the organ of Corti. *Journal of the Acoustical Society of America*, *89*, 1229–1254.

Zweig, G., & Shera, C. A. (1995). The origin of periodicity in the spectrum of evoked otoacoustic emissions. *Journal of the Acoustical Society of America*, *98*, 2018–2047.

Zwicker, E., & Peisl, W. (1990). Cochlear preprocessing in analog models, in digital models and in human inner ear. *Hearing Research*, *44*, 209–216.

Zwicker, E., & Schloth, E. (1984). Interrelation of different oto-acoustic emissions. *Journal of the Acoustical Society of America*, *75*, 1148–1154.