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Nonlinearity in Intracochlear Pressure

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Abstract
Nonlinearity exists in intracochlear pressure responses close to the cochlea's sensory tissue. Its characteristics are much like those of basilar membrane motion nonlinearity. Here several aspects of the pressure nonlinearity in the base of the gerbil cochlea are illustrated.

Introduction

The cochlea's sensory tissue responds nonlinearly to sound stimuli. The site of the nonlinearity is likely the mechanoelectrical transducer of the outer hair cell. Nonlinearity in basilar membrane (BM) motion was discovered by Rhode [1] and has been explored by several experimental groups since then (reviewed in Cooper [2] and Robles and Ruggero [3]). Nonlinearity has been most thoroughly characterized in the cochlear base and appears to behave similarly in the middle turns of the cochlea, whereas in the apex the character of the nonlinearity is different. In response to single tones, cochlear nonlinearity boosts the response to low- and moderate-level tones over a limited frequency range close to the best frequency (BF). Therefore, in the simplest terms, the cochlea's nonlinear mechanics serves to extend the range of hearing to levels that are substantially lower than would be detectable to a linear cochlea. The nonlinear mechanics has other effects as well; in particular, it generates frequency components that are not present in the stimulus. For single-tone stimuli, these components are the harmonics and for more complex stimuli (two tones and beyond), the response includes a family of tones composed of combinations of the stimulus frequencies. When they are detected as cochlear emissions, these distortion products (DPs) can be used clinically to gauge cochlear condition. Cochlear nonlinearity is susceptible to acoustic trauma, chemical agents and aging. Because of this fragility, it is an experimental challenge to develop a preparation with which intracochlear nonlinearity can be directly observed.

The cochlear fluid carries the mechanical energy of an acoustical stimulus throughout the cochlea as a wave. The compressional wave (fast) propagates at a speed similar to that of sound in water (approx. 1,500 m/s) and nearly instantaneously fills the cochlea. The pressure difference wave (slow) propagates much more slowly than the compressional wave because it depends on interactions between the fluid pressure differences and the relatively flexible mechanical elements of the cochlear partition; this is the cochlear traveling wave. Whereas the fast-wave pressure is nearly unchanging in space, the slow-wave pressure varies substantially spatially (theoretical descriptions of fast and slow waves are found in Lighthill [4] and Peterson and Bogert [5]). From basic fluid mechanics, the pressure gradient (spatial derivative) is approximately proportional to fluid acceleration. At the BM, the fluid moves with the BM, and the pressure gradient there is a measure of BM acceleration. Close to the BM, at frequencies through the BF peak, the slow-wave component of pressure dominates the fast wave and somewhat above the peak the fast wave is dominant. At frequencies

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through the BF we have observed that the pressure and pressure gradient at the BM have similar tuning. Aspects of BM motion that result from cochlear nonlinearity (nonlinear scaling, harmonics, DPs) also appear in the pressure in the vicinity of the BM. Knowledge of the detailed character of the pressure, and its relationship to BM velocity, is useful for understanding both active and passive cochlear mechanics.

Intracochlear pressure has been measured in guinea pig [6–10], cat [11–13] and human temporal bone [14–16] as well as in gerbil (our studies). In most of the studies, the pressure measurements were made close to the wall of the cochlea and their primary objective was to probe middle ear transmission. Cochlear nonlinearity close to the BM was not detected in intracochlear pressure until the studies of Olson [17] in gerbil, which used a specially constructed pressure sensor that could be positioned close to the sensory tissue. Nonlinear scaling of single-tone responses, harmonics, and two-tone DPs in the intracochlear pressure close to the BM have been described and analyzed since then [18–21]. Here, we show examples of these responses from a single experiment in which the nonlinearity was particularly robust.

Methods

Measurements were made in deeply anesthetized gerbils by inserting specialized pressure sensors into the cochlear scalae through small holes that were hand-drilled through the bony wall of the cochlea. Measurements in the scala tympani were made in the first turn of the cochlea at a location close to the BM. The pressure sensor approached the BM in micrometer steps until it touched (creating a noisy output signal), and then was retracted to a distance of 20 μm from the BM. Figure 1 illustrates the approach. The pressure in the ear canal (EC) was also measured simultaneously (with a probe tube Bruel and Kjaer microphone), and served as a reference.

The pressure sensor consists of a glass capillary with inner and outer diameters of 100/170 or 75/150 μm, tipped with a gold-coated polymer diaphragm. Light from a light-emitting diode is delivered via a fiber optic threaded into the capillary, and reflects from the diaphragm. The amount of light returning to the fiber optic for transmission to a photodetector varies linearly with the pressure-induced motion of the diaphragm [22]. The sensors are calibrated individually both in air (at room and body temperature, using a speaker) and in water (using a dynamic shaker, Bruel and Kjaer model 4290) and the air/water sensitivities are usually within a few decibels of each other. The sensitivity is flat (within 3 or 4 dB) up to at least 40 kHz, usually at a level of approx. –30 dBV/80 dB SPL. Water calibrations are performed before and after experiments and it is not uncommon for the sensitivity of a sensor to change by up to 6–10 dB, apparently due to subtle shifts in the fragile membrane. These changes are not frequency dependent. The noise level is set by shot noise at the photodetector at a level of approx. –60 dBV. The sensors operate linearly and do not introduce distortion. The presence of the sensor close to the BM might perturb cochlear mechanics. The perturbation was shown to be small but sometimes measurable as small changes in the compound action potential response [19].

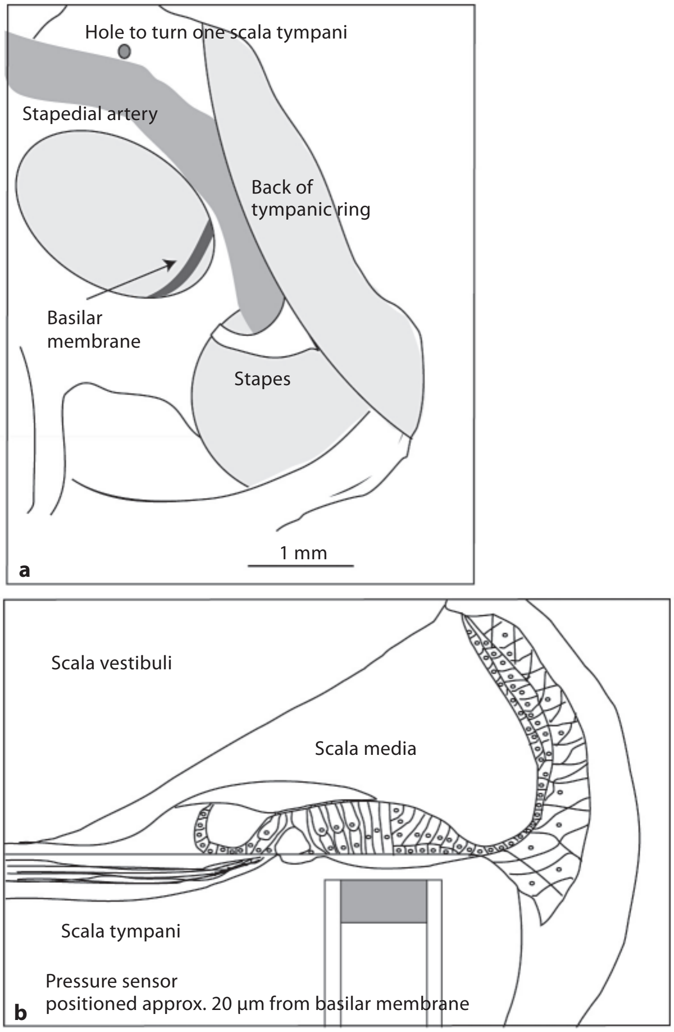

Fig. 1. Experimental approach. **a** View of the basal cochlea after opening the bulla. **b** Sensor positioned close to the BM in turn one.

Results and Discussions

The illustrations of intracochlear pressure nonlinearity were based on the observations from one animal, and were measured with a sensor 20 μm from the BM at a longitudinal location with a BF of 21 kHz.

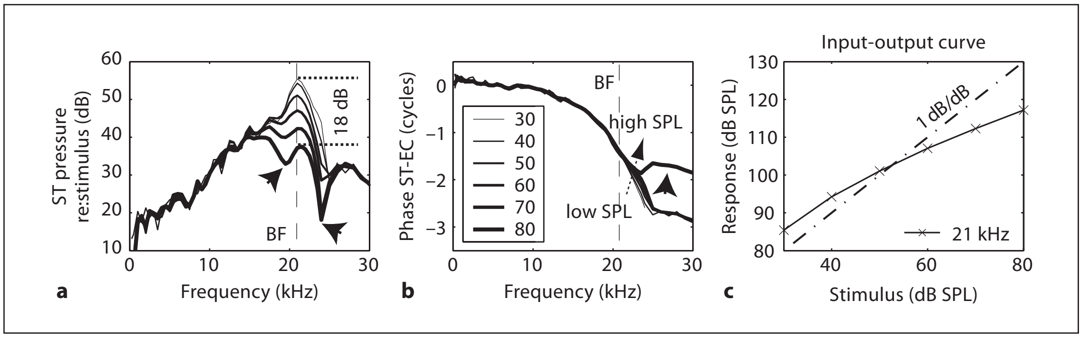

Fig. 2. Pressure measured close to the BM in the scala tympani (ST). **a** Gain (pressure amplitude normalized by stimulus level in the EC). **b** Phases (relative to EC pressure). The stimuli were single tones of 30–80 dB SPL, from 0.5 to 30 kHz. Dashed line indicates the BF position. **c** Input-output curve derived from data in **a** for stimuli at the BF (21 kHz).

Responses to Single Tones

Amplitude and Phase as a Function of Stimulus Frequency

The frequency and level dependence of intracochlear pressure responses to single tones of 30–80 dB SPL is illustrated in figure 2. The gain (response amplitude normalized by the stimulus level) versus frequency is shown in figure 2a. The gain was sharply tuned at the BF at low sound pressure levels and broadly tuned at higher sound pressure levels. At frequencies below 15 kHz and above 25 kHz, the responses scaled linearly, thus gain curves overlaid each other. At frequencies between 15 and 25 kHz, the gain increased progressively with decreasing sound pressure levels, which indicates the action of a compressive nonlinearity. The compressive nonlinearity can also be illustrated via an input-output function and this is shown for a BF stimulus in figure 2c. The pressure responses increased by 32 dB for a 50-dB increase in sound pressure level. The curve shows a growth of 0.5 dB/dB for stimulus levels between 60 and 80 dB SPL. The observed degree of compression is similar to that of BM motion, but not as great as the most highly compressive BM motion results in the literature. The disparity could be due to differences in cochlear condition, but is likely in part due to an intrinsic difference in pressure and motion nonlinearity stemming from nonlinearity in the mechanical impedance of the cochlear partition. In the future, simultaneous measurements of pressure and motion (extending those undertaken in Olson [17, 19]) will further explore this issue. The phase of the responses showed an increasing phase lag as a function of increasing stimulus frequency (relative to the EC pressure phases, fig. 2b). This phase accumulation is the signature of the cochlear traveling wave. Comparing the phase responses at different levels, they remained nearly the same up to the BF, but decreased systematically as the levels decreased at frequencies above BF. This level dependence might be due to, for example, level-dependent changes in damping, or level-dependent variation in the relative sizes of the fast-wave and slow-wave pressures. The notches at 19 and 24 kHz with 70 and 80 dB SPL are evidence of a cancellation of fast and slow waves (arrows in fig. 2a). The phase plateau (arrowhead in fig. 2b) is due to the fast wave dominating the intracochlear responses; the plateau occurs at lower frequencies at higher stimulus levels due to the slow wave's compressive scaling.

Harmonics

As to be expected, the large degree of compressive nonlinearity was accompanied by harmonic distortion. Harmonic distortion was physiologically vulnerable, appeared in cochleae in good condition, and decreased or disappeared with deterioration of the cochlea and after death. In figure 3a–d, harmonic distortion was clear in the fast Fourier transform spectra of pressure responses to single-tone stimulation at the BF. The 2nd harmonic component was clearly above the noise for the 50 dB SPL stimuli, at a level that was approx. 28 dB less than the fundamental component. With increasing stimulus level, the harmonic components increased and more components were observed. The harmonics were level and frequency dependent (solid lines in fig. 3e–f; dotted lines show the responses of the fundamental component). At stimulus levels of 50 dB SPL, the 2nd harmonic emerged from the noise at stimulus frequencies close to the BF. The

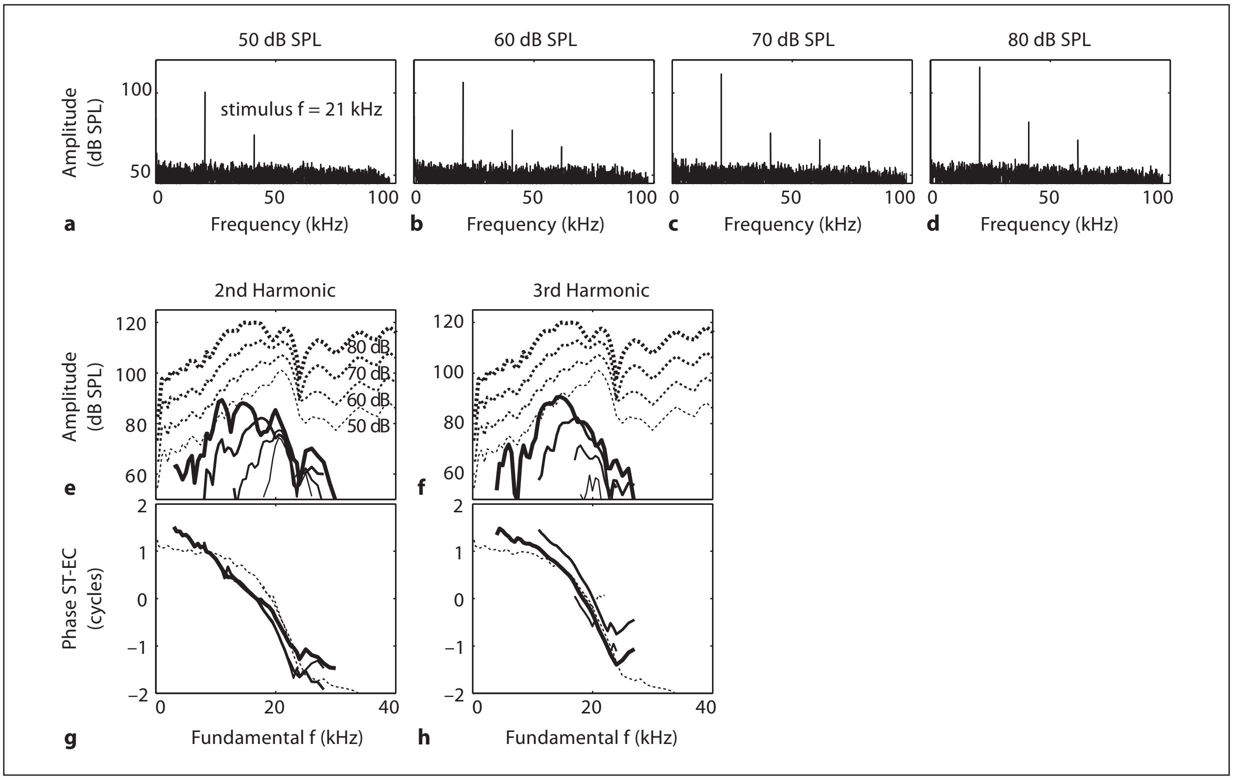

Fig. 3. Harmonic distortion in intracochlear pressure responses to single-tone stimuli. **a–d** Fast Fourier transform spectra at BF (approx. 21 kHz). **e**, **f** Amplitudes of the fundamental component and harmonics as a function of stimulus frequency. **g**, **h** Phases as a function of stimulus frequency (fundamental relative to EC phase, 2nd harmonics relative to 2× fundamental EC phase; 3rd harmonics relative to 3× fundamental EC phase). Dotted lines show the fundamental component responses of 50 to 80 dB SPL; solid lines show harmonics, dotted lines show fundamental.

peaks of the 2nd and 3rd harmonics shifted towards the lower frequencies and became more broadly tuned with increasing stimulus level. The phase versus frequency relationship of the harmonics is plotted in figure 3g, h. The slope of the phase-frequency curve is a measure of the delay time for the stimulus to arrive at the measurement position. At stimulus frequencies around BF, the slopes of the harmonics' phase-frequency curves were similar to those of the fundamental component. This observation – that the harmonics arrived at the observation point with the same delay as the fundamental component – means that the harmonic distortion was generated locally. At stimulus frequencies well below the local BF, the harmonic delays were often longer than the fundamental delays (phases steeper). The increased delay would occur if the harmonics were generated basal to the measurement position and traveled forward to it as independent traveling waves, and would also arise if they were generated apical of the measurement position and traveled backward to it. Further analysis of harmonic distortion is found in Cooper [23] and Olson [20].

Responses to Two Tones

With two-tone stimuli, cochlear nonlinearity gives rise to DPs that appear at combinations of the primary frequencies, $f_1 - n(f_2 - f_1)$, $f_2 + n(f_2 - f_1)$ where n is a positive integer. Figure 4a shows a family of DPs generated by two equal-intensity tones of 80 dB SPL with f_2/f_1 equal to 1.05 and f_2 = BF. The amplitude and phase of the $2f_2 - f_1$ and $2f_1 - f_2$ DPs are plotted in figure 4b–i. The frequency ratio f_2/f_1 was fixed at 1.05 or 1.25. Figure 4b–e shows the amplitude of the DPs, plotted versus their own frequencies, at primary levels of 60, 70 and 80 dB SPL (solid lines). The primary f_2 responses – illustrating single-tone tuning – are included as dotted lines. The tuning of the DPs is expected to reflect both the tuning of the

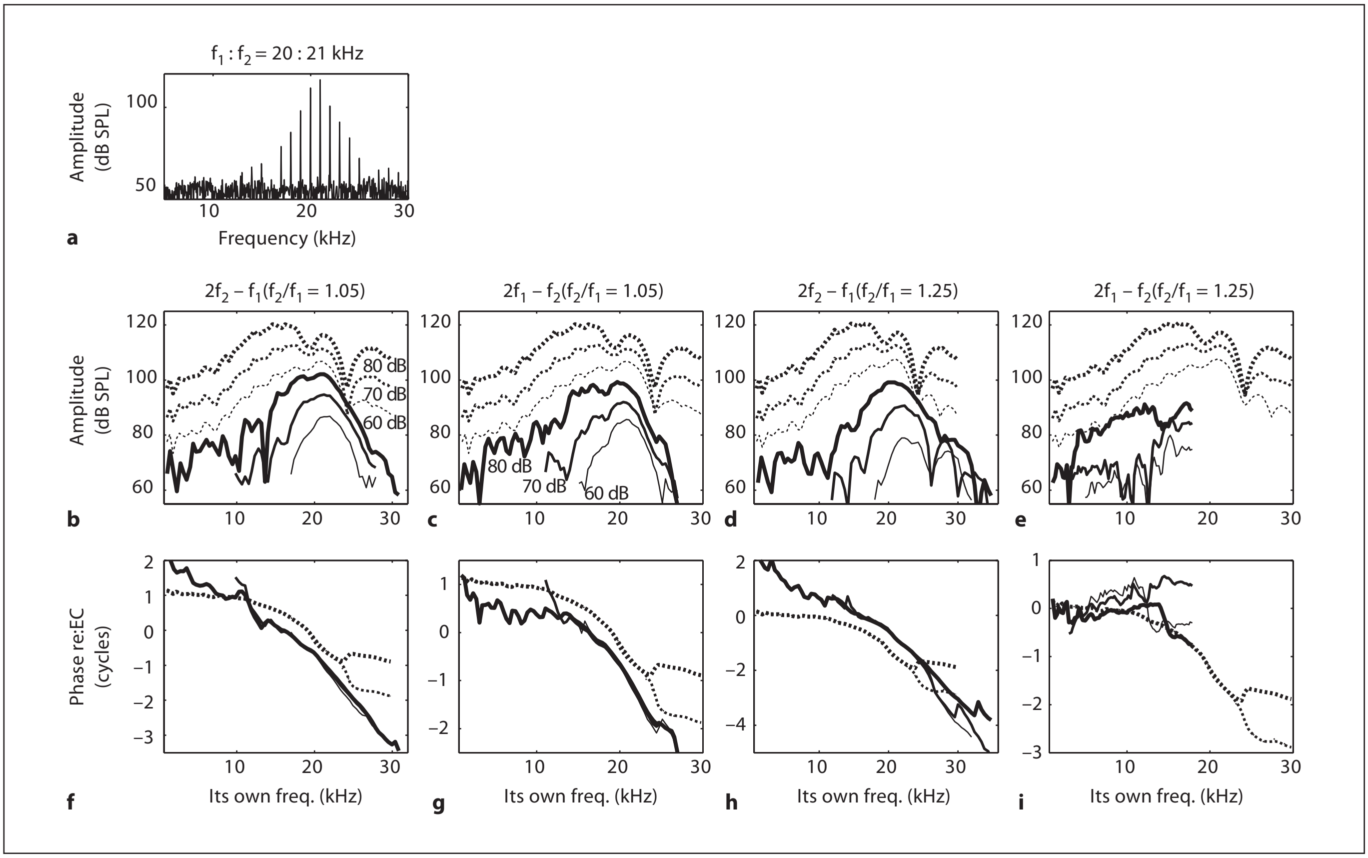

Fig. 4. Intracochlear pressure two-tone distortion. **a** Examples of fast Fourier transform spectral responses to two equal-intensity tones of 80 dB SPL, $f_2/f_1 = 1.05$, showing the rich family of DPs generated. **b–e** $2f_1 - f_2$ and $2f_2 - f_1$ tuning at f_2/f_1 ratio of 1.05 and 1.25 (solid lines, $L_1 = L_2 = 60$, 70 and 80 dB SPL); f_2 primary responses at sound pressure levels of 60, 70 and 80 dB are plotted as dotted lines. **f–i** DP phases relative to EC f_1 and f_2 phases (solid lines); f_2 primary phases relative to EC f_2 phases are plotted as dotted lines.

primaries and the subsequent cochlear filtering of the DPs themselves. Figure 4f–i shows the phases of the DPs relative to EC f_1 and f_2 phases (solid lines). The primary f_2 phases are also plotted to illustrate the single-tone phase accumulation. With an f_2/f_1 ratio of 1.05 (low ratio), the responses at frequencies in the broad vicinity of the BF were tuned quite similarly to the primaries. In addition, their phases showed a similar group delay to that of the primary (fig. 4f–g) with the half-cycle vertical offset that is the expected result of the action of a compressive nonlinearity (discussed further in Dong and Olson [21]). All this suggests that the DPs measured around the BF were dominated by a locally generated component. In contrast, the responses at frequencies some distance from the BF show behavior that is less primary-like and relatively complex. At frequencies below 15 kHz, the behavior was often suggestive of a contribution to the DPs that was produced further apical and was traveling backwards when it was detected at our sensor position – for example, the notches and wiggles and relatively steep phase (long delay) of the $2f_2 - f_1$ component at low frequencies. The results at both ratios suggest contributions to the DPs from both a locally and apically generated component. The notches above BF in $2f_2 - f_1$, ratio 1.25 (fig. 4d), are less easily explained as being due to this type of interference since the DP frequencies were above the local BF. Notches like this have been measured in BM motion in response to electrical stimulation above BF [24]. For the 1.25 ratio, the $2f_1 - f_2$ DP phase was relatively flat with frequency – in fact, its slope was positive. Therefore, it seems to be dominated by a component that in the framework developed by Knight and Kemp [25] and Shera and Guinan [26] and others would be called a wave-fixed/generator component, traveling backwards from apical generation sites. (In this theory, the wave-fixed component has a flat phase response.)

Finally, the tuning of the $2f_2 - f_1$ is slightly offset in frequency compared to the primaries in figure 4b: the low-frequency slope is steeper; the high-frequency slope is less steep than with single-tone tuning. In contrast, the $2f_1 - f_2$ tuning in figure 4c is relatively primary-like. The contrast between low- and high-side DP tuning reinforces the observation from perceptual studies that low-side DPs cause a single-tone-like cochlear response, whereas high-side DPs do not [27, 28]. (This observation could only be made for the low ratio. The $2f_1 - f_2$ data are limited to relatively low frequencies at the high ratio because very high f_2 frequencies are needed to generate high-frequency $2f_1 - f_2$ DPs at the large f_2/f_1 ratio. At very high f_2 frequencies, nonlinearity typically was small due to the fragility of the extreme base.)

In summary, intracochlear pressure responses measured close to the BM in the basal turn of gerbil were nonlinear. The nonlinearity included the compressive growth to single-tone stimuli in the vicinity of the BF and the production of harmonics and, in the case of two-tone stimuli, DPs. The harmonics and DPs, once present, were filtered by the cochlea's mechanics. Therefore, the local response at a particular harmonic or DP frequency was shaped by three processes: the cochlear-mechanical filtering of the primary or primaries, the distortion generation process and the cochlear-mechanical filtering of the DP or harmonic. The harmonics and DPs also appeared to travel within the cochlea. For stimulus frequencies well below the local BF, backward traveling components sometimes appeared to be dominant in the measured responses.

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