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Distortion in those good vibrations

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Abstract

The features that make inner ear hair cells so sensitive to vibrations may also be responsible for the introduction of surprisingly large distortions.

In their unending search for the ultimate stereo electronic components, high-fidelity aficionados eagerly peruse manufacturers' specifications, always hoping for lower, distortion figures. Whether the electronic components are loudspeakers, amplifiers, compact-disk players or digital-tape machines, the goal is the same: components should be 'transparent', delivering only the beauty of the original musical composition and adding no additional sounds of their own. Paradoxically, the human ear, the biological receptor that the electronic stereo components are designed to gratify, generates distortion to an extent that would be unacceptable in electronic equipment. Most astonishingly, it is becoming increasingly clear that this generation of distortion is part and parcel of the very biological apparatus that endows hearing with its marvelous sensitivity and acuity.

That the human auditory system generates distortion of its own has been known since the 18th century. Armed with little scientific apparatus, probably nothing more sophisticated than a violin, the Italian musician Giuseppe Tartini discovered *circa* 1754 that when listening to a pair of tones, humans hear additional tones that are not present in the physical stimulus [1]. These additional tones, whose perceived magnitude can exceed 10% of that of the acoustic stimulus (at least 100 times what is common in high-fidelity equipment), have frequencies that consist of simple combinations of the frequencies of the primary tones. For example, for primary-tone frequencies of f_1 and f_2 , where $f_2 > f_1$, the resulting 'combination', or Tartini, tones, also known as intermodulation-distortion products, will have frequencies of $2f_1 - f_2$, $f_2 - f_1$, $2f_2 - f_1$, $3f_1 - 2f_2$ and so on.

The study of combination tones, first by means of psychophysical measurements in humans and more recently via physiological experiments in the auditory nerve and inner ear of animal subjects, has played a central role in the development of auditory theory. To appreciate why such a 'second order' effect has been deemed worthy of intensive investigation by hearing scientists, it is helpful to keep in mind an overview of the organization of the auditory system. In brief, the auditory system consists of three components: the ear (external, middle and inner), the auditory nerve and the auditory regions of the brain (Fig. 1). Sound impinges upon the external ear and the eardrum, setting in motion ossicles in the middle ear; these, in turn, create pressure fluctuations in the largely fluid-filled inner ear or cochlea, causing a slow displacement wave to propagate along the organ of Corti (the organ of hearing proper) and its substratum, the basilar membrane.

The organ of Corti, the basilar membrane and the cochlear fluids jointly perform a spatial frequency analysis: waves resulting from low-frequency stimulation travel the length of the cochlea and peak toward its apex, whereas waves evoked by high-frequency stimuli reach a peak near the cochlear base and do not propagate further. Thus, each cochlear site is tuned to a single, or 'characteristic' frequency. The displacement of the basilar membrane deflects

the 'hairs', or stereocilia, located at the top of the hair cells of the organ of Corti, causing them to generate electrical receptor potentials that mimic the acoustic stimulus, much like tiny microphones. Finally, the receptor potentials of inner hair cells produce chemically-mediated excitation in the peripheral terminals of cochlear afferent neurons, generating trains of action potentials that travel to the brain via the auditory nerve (Fig. 2).

A century after the discovery of combination tones, the polymath Herman LF Helmholtz dedicated a chapter of his influential book, *On the Sensations of Tone* [2], to this topic, suggesting that the distortion products arise as a result of overloading the eardrum and ossicles of the middle ear with too-intense stimuli. More modern psycho-acoustical findings led Goldstein, in 1967, to dispute Helmholtz's hypothesis and to put forth prescient views of cochlear function that are amazingly in accord with our present knowledge [3]. Firstly, Goldstein emphasized that combination tones are audible even at low stimulus intensities and, more importantly, that their relative audibility (in other words, audibility normalized to stimulus level) remains fairly constant over wide ranges of stimulus intensities. In the case of acoustic overload, the expectation is that combination tones should be inaudible at moderate levels and that their relative audibility should grow as a power function with stimulus intensity. Secondly, based on the strong dependence of combination-tone perception on the frequency separation of the primary tones, Goldstein ruled out the middle ear as the site of origin of distortion products and proposed that they arise in the cochlea, the only sensory structure capable of performing a frequency analysis of acoustic signals. Thirdly, he tentatively pinpointed the site of origin of mechanical distortion products to be the hair cells in the cochlear region most sensitive to the primary tones (blue arrow in Figure 2) and suggested that, upon generation, each mechanical distortion product propagates along the basilar membrane to the site whose characteristic frequency matches its own frequency (hatched area toward apex in Figure 2), where it is detected by other hair cells and signaled to the brain via the auditory nerve. Goldstein's hypothesis was especially daring because, at the time, basilar membrane vibrations were almost universally viewed as linear and uninfluenced by the physiological state of the organ of Corti.

Indirect support for Goldstein's hypothesis came from the study of humans and animals suffering from partial deafness confined to restricted frequency bands [4,5]. For example, when a human subject's ear is stimulated by tones with frequencies in the region of impaired hearing, the subject is unable to hear combination tones with frequencies corresponding to regions of normal hearing [4]. Also consistent with Goldstein's hypothesis was the finding that auditory-nerve fibers [6] and inner hair cells [7] tuned to $2f_1 - f_2$ can respond to a pair of tones, f_1 and f_2 , even when they are unable to respond to either tone in isolation. Perhaps most spectacular, however, was the discovery that the ear responds to pairs of tones by broadcasting distortion-product otoacoustic emissions into the surrounding environment (left arrow in Figure 2) [8]. This discovery established that mechanical distortion products are generated in the inner ear, and provided a tool for testing the role of hair cells in their production. Taking advantage of the fact that the endings of certain neurons of the olivocochlear efferent system synapse with outer, but not inner, hair cells, Mountain [9] then showed that distortion-product otoacoustic emissions can be altered by electrical activation of these neurons, thus demonstrating that the outer hair cells can influence cochlear mechanics.

A tantalizing hint that distortion products might exist in basilar membrane vibrations was suggested in Rhode's seminal discovery [10] of a non-linearity in basilar membrane responses to characteristic-frequency single tones. Working on the squirrel monkey cochlea, Rhode measured compressive input-output functions that, at least to a first approximation, could be described by power laws with exponents less than one. It can be shown mathematically that when the sum of two sinusoids is operated on by such a simple power

law, combination tones arise of necessity and that, as noted by Goldstein in the case of psycho-acoustically measured distortion products, their magnitudes remain more-or-less constant relative to the magnitude of the stimulus. In addition, Rhode showed that this non-linearity was metabolically vulnerable, disappearing upon death or cochlear trauma. Although Rhode's findings were eventually confirmed and extended (reviewed in [11]), nearly two decades elapsed before definitive proof could be obtained for the propagation of mechanical distortion products on the basilar membrane. Two investigations arrived at the conclusion that if $2f_1-f_2$ distortion products exist on the basilar membrane, they are vanishingly small [12,13] and, probably, additional failures to detect mechanical distortion products went unreported. In retrospect, it seems that the long-lasting failure to find basilar membrane correlates of the $2f_1-f_2$ distortion product was due to two main reasons, namely experimenter-induced cochlear trauma and inadequate technology for the recording of submicroscopic displacement or motion.

Finally, in the past few years, investigators in three laboratories have independently used laser interferometry to demonstrate that various distortion products, including those with a frequency equal to $2f_1-f_2$ and $2f_2-f_1$ are indeed present in the vibration of the basilar membranes in guinea pigs, cats and chin chillas [14–18]. In the case of the $2f_1-f_2$ distortion product, the main features of psycho-acoustical observations have appropriate counterparts in the basilar membrane, including the dependence of their audibility on the frequency separation between the primary tones, and on their combined or relative intensities [17]. The mechanical distortion products are physiologically vulnerable, being absent in traumatized cochlea. Most interestingly, it is possible to use acoustic overstimulation to reduce the magnitude of the $2f_1-f_2$ distortion product selectively, while leaving relatively unaffected the response to a single tone with a frequency equal to $2f_1-f_2$. Such selectivity implies that the distortion product travels on the basilar membrane from its site of origin, with a characteristic frequency near f_1 and f_2 , to its site of analysis, with a characteristic frequency equal to $2f_1-f_2$. Surprisingly, it is now doubtful whether basilar-membrane mechanical f_2-f_1 distortion products are large enough to account for their conspicuous psycho-acoustical counterparts [13,18,19].

Which cochlear structure generates the basilar-membrane distortion products? The basilar membrane itself can probably be ruled out because, being largely acellular, it should be insensitive (at least in the short term) to various insults capable of abolishing mechanical non-linearities, including distortion products. The most likely candidates are the outer hair cells, which in isolation exhibit electromotility; in other words, they act like alternating-current motors, changing their length in response to electrical stimulation [20], (reviewed in [21]). Accordingly, cochlear damage that destroys outer hair cells but leaves inner hair cells apparently intact abolishes distortion products in auditory-nerve responses [5]. Activation of the medial olivocochlear efferent system, which innervates outer hair cells exclusively, can alter distortion-product otoacoustic emissions [9]. Furthermore, reduction of the receptor potentials of hair cells (due to death or the effects of ototoxic drugs) drastically degrades the sensitivity of basilar-membrane responses and eliminates its frequency-specific non-linearity [22].

If the outer hair cells are ultimately responsible for the generation of distortion products in basilar-membrane vibrations and in otoacoustic emissions, the mechanism could conceivably be a byproduct of mechanical-to-electrical transduction at the stereocilia, or of electromotility (electrical-to-mechanical transduction) at the lateral cell membrane. Mechanical-to-electrical transduction at the hair cells of both the frog sacculus and the mammalian cochlea is substantially non-linear. The function relating receptor potentials to stereocilia displacement is sigmoidal, saturating at large displacements [23,24]. Most significantly in the generation of distortion products, which can occur at low and moderate

levels, the ‘stiffness’ with which the stereocilia resist displacement is constant for large stimuli but dips to a minimum for small stimuli [25,26].

In a recent paper, Jaramillo *et al.* [27] convincingly show that such low-level transducer non-linearity leads to the generation of mechanical distortion products in frog-sacculus hair cells, reminiscent of those present in basilar-membrane vibration. Even if the electromotility in outer hair cells was fully linear, the non-linearity of forward transduction should cause the responses of the basilar membrane to tone pairs to contain distortion products. In fact, electromotility is non-linear, with a voltage-to-displacement relationship described by a Boltzman function [28,29]. Whether this non-linearity actually leads to significant two-tone distortion is controversial. Under voltage-clamp conditions, the mechanical response of outer hair cells to moderate-level sinusoidal voltages contains little harmonic distortion [28]; presumably, responses to tone pairs would also generate negligible intermodulation distortion. On the other hand, transmembrane electrical stimulation of outer hair cells held in micro-chambers does appear to generate prominent two-tone distortion products [30].

Thus, somewhat paradoxically, both of the mechanisms that endow the sense of hearing with exquisite sensitivity, frequency selectivity and time resolution — stereociliar transduction in hair-cell organs throughout the phylogenetic scale and electromotility in the outer hair cells of the mammalian cochlea — may also be responsible for distorting the auditory sensation.

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Fig. 1.
A schematic diagram of the structure of the human ear.

Fig. 2. Simplified bird's eye view of the mammalian cochlea. The organ of Corti, here represented by three rows of outer hair cells and one row of inner hair cells, rests on the basilar membrane. Acoustic-stimulus frequencies are organized spatially along the basilar membrane, with the basal region responding maximally to high frequencies and the apical region responding mainly to low frequencies. Stimuli consisting of paired tones (f_1 and f_2 , with $f_2 > f_1$) appear to generate mechanical distortion products in the responses of the outer hair cells, which are injected into the local vibration of the basilar membrane (blue arrow). Subsequently, each distortion product propagates (red arrow) toward the cochlear site with appropriate characteristic frequency ($2f_1 - f_2$ in this illustration), where it is detected by the inner hair cells and signaled to the brain via the auditory nerve (green arrow). Distortion products also propagate toward the middle ear, being measurable at the external ear canal as otoacoustic emissions (left red arrow).