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Review

A Critique of the Critical Cochlea: Hopf—a Bifurcation—Is Better Than None

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Hudspeth AJ, Jülicher F, Martin P. A critique of the critical cochlea: Hopf—a bifurcation—is better than none. *J Neurophysiol* 104: 1219–1229, 2010. First published June 10, 2010; doi:10.1152/jn.00437.2010. The sense of hearing achieves its striking sensitivity, frequency selectivity, and dynamic range through an active process mediated by the inner ear's mechanoreceptive hair cells. Although the active process renders hearing highly nonlinear and produces a wealth of complex behaviors, these various characteristics may be understood as consequences of a simple phenomenon: the Hopf bifurcation. Any critical oscillator operating near this dynamic instability manifests the properties demonstrated for hearing: amplification with a specific form of compressive nonlinearity and frequency tuning whose sharpness depends on the degree of amplification. Critical oscillation also explains spontaneous otoacoustic emissions as well as the spectrum and level dependence of the ear's distortion products. Although this has not been realized, several valuable theories of cochlear function have achieved their success by incorporating critical oscillators.

The technical specifications of the human ear are remarkable. We can hear sounds that evoke mechanical vibrations of magnitudes comparable to those produced by thermal noise (de Vries 1948; Sivian and White 1933). Hearing is so sharply tuned to specific frequencies that trained musicians can distinguish tones differing in frequency by only 0.1% (Spiegel and Watson 1984). Finally, our ears can process sounds over a range of amplitudes encompassing six orders of magnitude, which corresponds to a trillionfold range in stimulus power (Knudsen 1923).

These striking characteristics of our hearing emerge because the ear is not a passive sensory receptor, but possesses an active process that augments audition in three ways (reviewed in Hudspeth 2008; Manley 2000, 2001). First, *amplification* renders hearing several hundred times as sensitive as would be expected for a passive system. The active process next exhibits *tuning* that sharpens our frequency discrimination. Finally, a *compressive nonlinearity* ensures that inputs spanning an enormous range of sound-pressure levels are systematically encoded by a modest range of mechanical vibrations and in turn of receptor potentials and nerve-fiber firing rates. The active process additionally exhibits the striking epiphenomenon of *spontaneous otoacoustic emission*, the production of sound by an ear in the absence of external stimulation. Although considerable attention has been devoted to these properties in mammalian and especially human hearing, the four defining features of the active process are equally characteristic of nonmammalian tetrapods (reviewed in Manley 2001).

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The biophysical basis of the active process is the object of active research—and substantial controversy—at present. It is clear that the active process stems from the action of hair cells, the ear's sensory receptors. In nonmammalian tetrapods, the features of the active process emerge from active motility of the hair cell's mechanoreceptive organelle, the hair bundle (reviewed in Hudspeth 2008; Hudspeth et al. 2000; Martin 2008). Each hair bundle is a cluster of 20–300 actin-filled rods standing erect on a hair cell's apical surface. Deflection of the hair bundle along a particular morphological axis opens transduction channels and thus elicits a depolarizing receptor potential (reviewed in Hudspeth 1989). This response is assisted by active hair-bundle motility, which provides the energy required for amplification (Martin and Hudspeth 1999), implements frequency tuning and compressive nonlinearity (Martin and Hudspeth 2001), and even powers the spontaneous hair-bundle oscillations thought to underlie spontaneous otoacoustic emissions (Martin et al. 2001, 2003).

Active hair-bundle motility contributes to the active process in mammals as well (Chan and Hudspeth 2005a,b; Kennedy et al. 2005, 2006). In addition, these animals display the phenomenon of membrane-based electromotility (reviewed in Ashmore 2008; Dallos et al. 2006; Fettiplace and Hackney 2006). The plasmalemma of each columnar outer hair cell in the mammalian cochlea is packed with the protein prestin (Zheng et al. 2000), a divergent member of the anion-transporter family (Franchini and Elgoyhen 2006). Cellular depolarization causes prestin to undergo a molecular rearrangement such that the membrane's area decreases and the hair cell shortens, whereas hyperpolarization causes lengthening (Ashmore 1987; Brownell et al. 1985). The outer hair cell thus behaves as a piezoelectric actuator whose movements account for electrically evoked otoacoustic emissions (Mellado Lagarde et al. 2008).

Electromotility operates so swiftly that it seems likely to play an important role in the active process (Frank et al. 1999; Gale and Ashmore 1997); moreover, the absence of prestin or severe modification of its range of voltage sensitivity abrogates the active process (Cheatham et al. 2004; Dallos et al. 2008; Gao et al. 2007; Liberman et al. 2002). Electromotility is nearly linear over the physiological range of receptor potentials, however, and displays no frequency tuning; it thus seems unable by itself to account for the properties of the active process. Theoretical studies suggest that electromotility provides amplification of basilar-membrane vibrations by interacting with the micromechanical environment (Nobili et al. 1998; Reichenbach and Hudspeth 2010). Because the proper interplay between electromotility and the mechanical constituents of the cochlear partition relies on assumptions of unproven

validity, however, no model has been accepted as definitive and the mechanism for cochlear amplification remains elusive. It is most probable that active hair-bundle motility and membrane-based electromotility somehow collude to augment hearing in mammals (reviewed in Hudspeth 2008).

The key features of the active process have been recognized as signatures of a particular instability of dynamical systems: the Hopf bifurcation (Camalet et al. 2000; Choe et al. 1998; Eguíluz et al. 2000; reviewed in Duke and Jülicher 2008). A Hopf bifurcation represents an oscillatory instability that occurs abruptly as a quantity describing some component of the system—the control parameter—is varied continuously (reviewed in Strogatz 1994). Because the control parameter attains its critical value at the bifurcation, we may term an active system poised near that point a critical oscillator. Any process whose workings are characterized by a Hopf bifurcation *must* display certain generic properties—properties that are also characteristic of mammalian hearing. Here we provide an introduction to the Hopf bifurcation, review the features of mammalian hearing suggesting that the cochlear active process is based on critical oscillators, and indicate how the ensuing behavior accounts for the ear's extraordinary performance.

The Hopf bifurcation

Consider an active system characterized by a time-dependent observable variable $X(t)$. If the system exhibits a Hopf bifurcation, its behavior abruptly changes from quiescence to spontaneous oscillation as the value of a control parameter C changes. If the control parameter is poised at or near the critical value C_C, the system is a critical oscillator whose generic behavior is described by a dynamic equation, called the normal form, of a complex variable Z

$$\dot{Z} = -(C - C_C - i\omega_C)Z - b|Z|^2Z + \frac{F}{\Lambda} \qquad (1)$$

Here the overdot denotes a temporal derivative. If $X \equiv \mathrm{Re}\,(Z)$ describes the displacement of a mechanical system and F represents a stimulus force, Λ has the units of a friction coefficient. Note that there is no quadratic nonlinearity in the normal form and that the nonlinearity, with a complex coefficient b, is cubic in the variable Z.

The spontaneous behavior of the system can be appreciated by setting $F = 0$. For $C > C_C$, the variable Z displays an exponentially damped oscillation at an angular frequency ω_C until it reaches the stable, quiescent state $Z = 0$ (Fig. 1*A*). In this case, the nonlinear term plays no important role. For $C < C_C$, however, the state $Z = 0$ is unstable: a small perturbation results in an oscillation that grows in magnitude until it reaches a constant value indicative of a limit cycle: $Z = X_0 e^{i\omega_0 t}$. The amplitude X_0 of this oscillation is stabilized by the nonlinear term in the normal form. Except precisely at the bifurcation, the frequency of oscillation ω_0 differs from ω_C. Because of the nonlinear nature of the system, the oscillation also contains higher harmonics that are not described by the normal form.

We next consider the case $C \geq C_C$, in which the system is either nonoscillatory or situated at the bifurcation. Although the response of the nonlinear system includes components at the integer harmonics of the stimulus frequency, we shall consider only the dominant terms associated with the frequency of stimulation. Indeed, when operating at the bifurcation a critical oscillator displays negligible harmonic distortion in response to small stimuli. If the system is subjected to a sinusoidal stimulus $F = \bar{F}e^{i\omega t}$ at frequency ω, the normal form imposes a steady-state response $Z = \bar{X}e^{i\omega t}$ in which the amplitude $\bar{X}$ displays a nonlinear relation to the stimulus amplitude $\bar{F}$

$$\bar{F} = A\bar{X} + B|\bar{X}|^2\bar{X} \qquad (2)$$

The linear component of the response is described by the impedance $A = \Lambda[(C - C_C) + i(\omega - \omega_C)]$ and the nonlinear term by the coefficient $B = \Lambda b$. In the limit of weak stimulation, the system displays a linear sensitivity $\chi = |\bar{X}/\bar{F}| = 1/|A|$. The sensitivity displays a resonance when the critical oscillator is stimulated at its characteristic frequency $\omega = \omega_C$. The width of the resonance in the linear regime is $\Delta\omega_{lin} \cong |C - C_C|$.

At the bifurcation, $C = C_C$ and the critical oscillator displays a striking behavior that cannot occur in a passive system: if the system is stimulated at its characteristic frequency $\omega = \omega_C$, the linear coefficient A vanishes. As a consequence, the response is governed by the nonlinearity. For an increasing amplitude of stimulation, the amplitude $\bar{X}$ displays a compressive growth described by the power law $|\bar{X}| \propto |\bar{F}|^{1/3}$ (Fig. 1*B*). The sensitivity χ therefore varies as $1/|\bar{F}|^{2/3}$, which formally diverges for small stimuli. For a critical oscillator at resonance, there is *no* stimulus weak enough to elicit a linear response. In that sense, a critical oscillator displays an *essential* nonlinearity. In contrast, a passive system always displays linear behavior in response to weak sinusoidal stimuli: $|\bar{X}_{passive}| \propto |\bar{F}|$. This property arises because frictional forces can never disappear

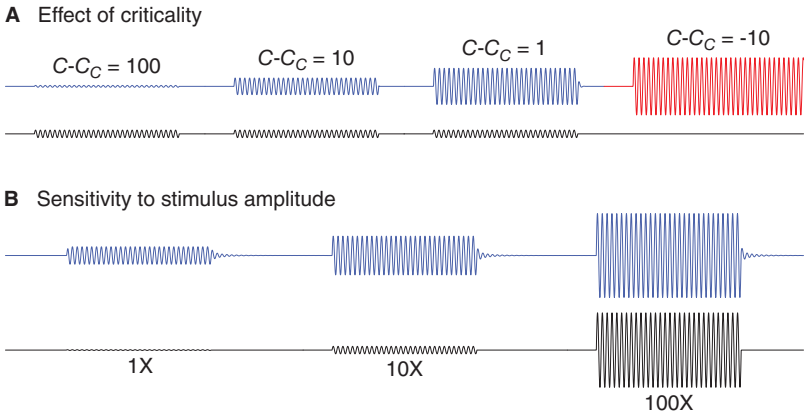

FIG. 1. The behavior of a critical oscillator. *A*: an oscillator whose response is described by *Eq. 1* produces sinusoidal responses (*top traces*) when driven at its characteristic frequency with pulses of sinusoidal stimuli (*bottom traces*). As the difference between the value of the control parameter and the critical value, $C - C_C$, declines from 100 to 10 and then to 1, the response to identical stimuli grows substantially. Finally, when $C - C_C = -10$, the system becomes unstable and undergoes limit-cycle oscillation in the absence of stimulation. *B*: when the oscillator operates near criticality, here with $C - C_C = 0.1$ in each panel, its response exhibits compressive nonlinearity. As the stimulus grows by successive factors of 10, the responses increase by factors of only $10^{1/3}$ or about 2.2.

unless internal sources of energy can be mobilized to produce negative damping. By compensating for the frictional forces, a critical oscillator acts as an active amplifier.

We can define the gain G of the amplificatory process by comparing, for the same stimulus, the response of a critical oscillator to that of an identical system in which the active process is absent: $G = |\bar{X}/\bar{X}_{passive}| \propto 1/|\bar{F}|^{2/3}$. This relation demonstrates that the amplifier is nonlinear and preferentially boosts weak signals. In addition, the sensitivity of a critical oscillator displays nonlinear frequency tuning. When plotted against stimulus frequency at a given force amplitude, the sensitivity displays a peak centered at ω_C and of a width given by $\Delta\omega_{active} \propto |\bar{F}|^{2/3}$ (Fig. 2). Tuning thus becomes increasingly sharp at low levels of stimulation. Note that the peak width and the sensitivity are inversely related; for faint stimuli, the product $\Delta\omega_{active}|\bar{X}|/|\bar{F}|$ is constant. Weak stimuli are therefore detected at resonance both with high sensitivity and with sharp frequency selectivity.

A critical oscillator is ideally suited for the detection of sinusoidal stimuli. By amplifying preferentially weak inputs, this active system naturally displays compressive nonlinearity and provides a large dynamic range of responsiveness. Because nonlinear amplification is strongest at frequencies near the characteristic frequency of the critical oscillator, the system additionally manifests nonlinear frequency tuning. Each critical oscillator is tuned to a specific frequency, so the analysis of complex sound stimuli calls for the operation of an assembly of oscillators with distributed characteristic frequencies.

Psychophysical and physiological characteristics of mammalian hearing

Two experimental approaches have provided most of our insights into the active process of the mammalian inner ear. First, the discipline of auditory psychophysics has characterized the relation between the physical characteristics of acoustic stimuli and the resultant sensory experience. Because psychophysical testing is not invasive, this approach has been widely used on human subjects. The second approach, which has been applied most extensively in guinea pigs, chinchillas, gerbils, mice, and cats, involves various types of neurophysiological recording. Laser interferometry has quantified the mechanical responses of the basilar membrane to acoustic stimulation. Extracellular recordings of cochlear microphonic signals and intracellular measurements of receptor potentials have characterized the responses of hair cells. Finally, recordings of the spiking activity of individual cochlear nerve fibers have provided insight into the signals forwarded to the auditory centers of the brain stem. We shall examine how specific results obtained through these approaches relate to the expectations of the critical-oscillator hypothesis.

Power-law scaling of auditory responses

The vibration of the basilar membrane at its characteristic frequency follows a power-law relation to sound-pressure level in several mammalian species, especially the chinchilla (reviewed in Robles and Ruggero 2001). Although the slopes of the intensity–displacement relations vary, many are near the value of 1/3 anticipated for an active oscillator near a Hopf bifurcation (Ruggero et al. 1997). One should note that the predicted power law pertains at the peak of the basilar membrane's response (Duke and Jülicher 2003), which may shift with changes in stimulus intensity from the usual observation point at the round window. Such a shift, which would be expected to alter the power law measured at that particular position, may account for the fact that some data sets display power-law slopes even below 1/3. Hypercompressive behaviors also emerge in the presence of noise when an oscillator

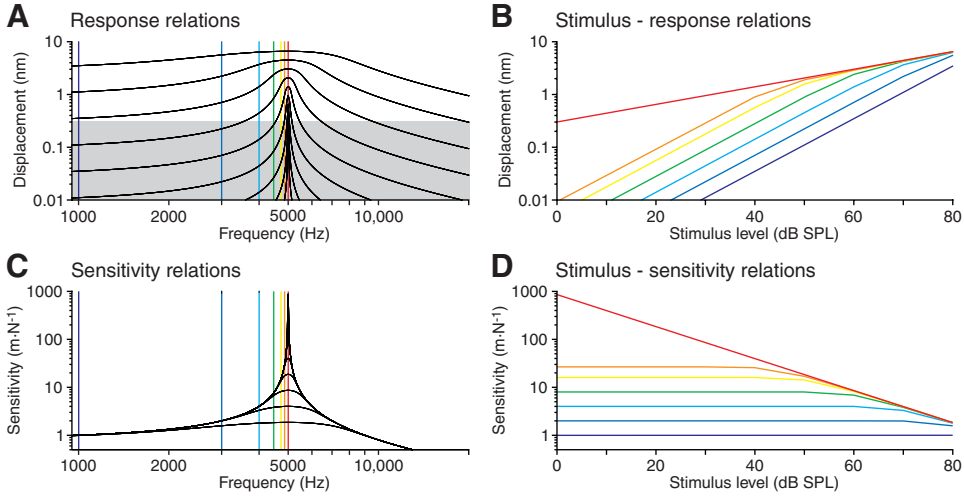

FIG. 2. Characteristics of amplification by a critical oscillator. *A*: a doubly logarithmic plot portrays the magnitude of the oscillator's response as a function of stimulus frequency for a range of stimulus amplitudes. The stimuli vary in 10-dB steps from 0 dB, corresponding to the lowest curve, to 80 dB, the highest. The weakest stimuli produce significant responses only at the characteristic frequency of 5 kHz. As the stimulation becomes stronger, responses become apparent over a wider range of frequencies. The shaded area corresponds to the noise level for hair cells, about 0.3 nm; only responses larger than this elicit neural activity. *B*: plotting the magnitude of the response against the stimulus amplitude demonstrates the compressive nonlinearity of a critical oscillator. The 7 relations correspond to the frequencies marked by the corresponding colored lines in *A*. At the characteristic frequency, the relation (red) displays the slope of 1/3 characteristic of a critical oscillator. At frequencies distant from the characteristic frequency the responses are linear. *C*: the oscillator's sensitivity is determined by dividing its output by its input at each frequency and for each level of stimulation. The sensitivity peaks for the lowest level of stimulation and declines progressively as the forcing becomes stronger. *D*: at the characteristic frequency, a double-logarithmic plot of the sensitivity (red) as a function of the stimulus amplitude shows the characteristic slope of −2/3. The flat relations observed at other frequencies indicate linear responsiveness.

departs from criticality to operate on the oscillatory side of a Hopf bifurcation (Lindner et al. 2009).

In contrast to a deterministic oscillator that operates exactly at a Hopf bifurcation, the basilar membrane's vibration becomes linear for the weakest of stimuli (Robles and Ruggero 2001). A comparable phenomenon is also observed for individual hair bundles in the frog's sacculus whose mechanical responsiveness varies as the 1/3 power of the stimulus amplitude over a tenfold range of stimulus magnitudes, but approaches linearity for nanometer-scale stimuli (Martin and Hudspeth 2001). Both the basilar membrane and the hair bundle are subjected to noise of a magnitude comparable to that of threshold stimuli. By limiting the phase coherence that an active oscillator can achieve, noise imposes a linear regime of responsiveness to faint external signals. The dynamic behavior of a noisy oscillator can still be described by a normal form (*Eq. 2*) but with an effective contribution to the linear coefficient A that remains finite at the characteristic frequency (Jülicher et al. 2009; Lindner et al. 2009). A noisy oscillator thus provides amplification with a gain that reaches a maximal value for low stimuli. This maximal gain is inversely related to noise intensity.

In the frog's sacculus, amplification by active oscillation of a single hair bundle is seriously limited by noise (Nadrowski et al. 2004). It is noteworthy, however, that mechanical coupling between hair bundles, such as occurs through accessory structures such as tectorial and otolithic membranes (Strimbu et al. 2009), increases the phase coherence of spontaneous hair-bundle oscillations, extends the range of the compressive nonlinearity to smaller stimuli, sharpens the frequency selectivity, and enhances the amplification that a noisy oscillator can provide (Barral et al. 2010; Dierkes et al. 2008).

Distortion products

As first noted in the eighteenth century (Tartini 1754, 1767), a person listening to two pure tones can hear not only those frequencies and their integer harmonics, but also other tones originally called *terzi suoni*, or third sounds, and now variously termed distortion products, combination tones, difference tones, or phantom tones. For simultaneous stimulation with a lower frequency ω_1 and a higher frequency ω_2, quadratic distortion products occur at the frequencies $\omega_2 \pm \omega_1$ and cubic products at $2\cdot\omega_2 \pm \omega_1$ and $2\cdot\omega_1 \pm \omega_2$. Additional, higher-order distortion products are also present but fainter. When the ratio $\omega_2/\omega_1 \approx 1.1$, the most prominent difference tone $2\cdot\omega_1 - \omega_2$ is only 15 dB weaker than the primary tones ω_1 and ω_2 (Goldstein 1967; Hall 1972). As a consequence, distortion products have actually been used in musical compositions (Campbell and Greated 2002)! Two-tone distortions have been measured in vivo on the basilar membrane of the mammalian cochlea (Robles et al. 1997). In particular, the distortion product $2\cdot\omega_1 - \omega_2$ displays properties that resemble those measured in human psychoacoustics, which suggests that perceived distortions originate from mechanical nonlinearities of the cochlear partition.

When stimulated strongly enough, almost any mechanical device evidences nonlinearity. In particular, a saturating nonlinearity often occurs when the stimulus becomes so intense that the response can no longer grow proportionally. Nonlinearities of this kind lead to distortions such as the tinny buzzing of an overdriven loudspeaker. In hair cells, the relation between hair-bundle deflection and receptor potential is sigmoidal. Mechanoelectrical transduction thus provides a saturating nonlinearity that would be expected to distort sound-evoked electromotile movements of mammalian outer hair cells (Nobili and Mammano 1996).

Because the gating of transduction channels is directly coupled to tip-link tension, the hair bundle also acts as a nonlinear spring: the displacement–force relation of a hair bundle displays a nonlinear region of reduced slope over the restricted range of deflections that elicit significant receptor currents (Howard and Hudspeth 1988; Martin et al. 2000). As the result of this nonlinear gating compliance, the hair bundle evinces distortion products in response to a stimulus that contains two frequency components (Jaramillo et al. 1993). Because the resting position of the hair bundle lies within the nonlinear region of the force–displacement relation, these distortions are produced at relatively low levels of stimulation. In addition, hair bundles have been shown to contribute significantly to the impedance of the organ of Corti (Chan and Hudspeth 2005b). Nonlinear hair-bundle mechanics thus participates in the production of distortion products that have been measured in vivo, even in prestin-knockout animals lacking electromotility (Liberman et al. 2004).

Any passive device behaves linearly when driven by weak sinusoidal stimuli because frictional forces can never vanish. Even if the relation between the input and output is curved, a sufficiently small input samples a segment of this relation so narrow that it is effectively straight. Distortions thus become negligible for weak stimuli; the response to a stimulus containing multiple frequencies reflects the primary frequencies with high fidelity. Conversely, the higher the intensity $\bar{F}$ of the primaries, the more prominent the distortions should become. For instance, the relative strength $X_{2\cdot\omega_1-\omega_2}/\bar{F}$ of the cubic distortion product at frequency $2\cdot\omega_1 - \omega_2$ is expected to increase as $\bar{F}^2$ until saturation affords no further increase of the distortion amplitude $X_{2\cdot\omega_1-\omega_2}$ (Goldstein 1967).

The nonlinearity underlying cochlear distortion products is extraordinary. First, the cubic distortion product at frequency $2\cdot\omega_1 - \omega_2$ persists even for very weak stimuli. For this reason, the nonlinearity has been termed "essential" (Goldstein 1967). Second, the relation between the perceived cubic distortion product and the intensity of the primary tones is nearly independent of the level of stimulation: as the stimuli become stronger, the distortion product increases at about the same rate so that the relative strength $X_{2\cdot\omega_1-\omega_2}/\bar{F}$ remains almost constant. This behavior is in striking contrast with that expected from a passive nonlinear system but accords with that of an oscillator operating near a Hopf bifurcation (Duke and Jülicher 2008; Jülicher et al. 2001).

As noted earlier, an energy-transducing mechanism allows the impedance of a critical oscillator to become very small for stimulation near the oscillator's characteristic frequency. When stimulated near resonance, a critical oscillator displays a compressive nonlinearity and produces distortion products even in response to vanishingly small stimuli. Within the framework of critical oscillation, prominent distortions appear as an inevitable price to be paid for exquisite sensitivity and sharp frequency selectivity. In agreement with experimental observations (Robles et al. 1997), the spectrum of these distortions displays an exponential hierarchy (Jülicher et al. 2001). The

essential nonlinearity of a critical oscillator holds only near the condition of resonance $\omega_1 \cong \omega_2 \cong \omega_C$ and thus if the frequency separation $\Delta\omega = |\omega_2 - \omega_1|$ is small enough. When stimulated off-resonance at both frequencies, the active oscillator instead behaves like any passive nonlinear system and distortion products plummet for weak inputs. A critical oscillator thus produces distortions whose intensities are inherently dependent on the separation between the primary frequencies.

Critical oscillators and the cochlear traveling wave

An elegant feature of the mammalian ear is the presence of traveling waves on the cochlear partition. Early experimentation on cadavers emphasized the passive contribution of the basilar membrane's mechanical characteristics in determining the shape of the traveling wave and the frequency-dependent characteristic place at which the wave peaks along the cochlea (reviewed in von Békésy 1960). In healthy cochleae, however, it has long been apparent that basilar-membrane responses to sound display tuning properties that cannot be explained by passive mechanical models (de Boer 1983, 1995; Gold 1948; Kim et al. 1980; Lighthill 1991; Shera 2007; Zweig 1991). It has been proposed that the traveling wave is amplified by an active process that pumps energy into the wave as it travels toward the characteristic place. In an attempt to combine wave propagation and the active process, researchers have developed a variety of theoretical models of varying dimensionality and complexity. Although many approaches have focused on a linear limit of cochlear mechanics that may be achieved near threshold, linear descriptions are clearly insufficient to describe the compressive nonlinearity that is essential to cochlear mechanics.

Models in which frequency selectivity emerges from passive resonance of the cochlear partition face an important problem. In these models, the natural frequency ω_0 of each segment is set by the relation $\omega_0 = (\kappa/m)^{1/2}$, in which κ is the stiffness and m is the mass of that segment. The measured range of stiffnesses and masses along the cochlea, however, is such that their ratio spans substantially less than the six orders of magnitude required to account for the 1,000-fold frequency range of hearing in humans and certain other mammals (de La Rochefoucauld and Olson 2007; Naidu and Mountain 1998; but see Emadi et al. 2004).

As detailed in APPENDIX A, the hypothesis of critical oscillation simplifies modeling of the traveling wave. Within this framework, each section of the cochlear partition is considered to operate as a critical oscillator tuned to a specific, tonotopically distributed frequency (Duke and Jülicher 2003; Kern and Stoop 2003; Magnasco 2003). Longitudinal coupling of the oscillators by the cochlear fluids results in an active, nonlinear traveling wave. Each oscillator responds to the local pressure difference across the cochlea according to the generic nonlinear relation (*Eq. 2*). Analyses of basilar-membrane vibration in vivo suggest that the cochlea is locally active and pumps energy into the wave over part of its length (de Boer 1983, 1995; Shera 2007; Zweig 1991). As a consequence of the functional form of their impedance, critical oscillators automatically provide negative damping in the restricted region of the partition where the frequency of the pressure wave is lower than the characteristic frequency of each oscillator (Duke and Jülicher 2008). The oscillators thus pump energy into the wave as it travels from the cochear base toward the apex (Fig. 3). Near the place of resonance, where the wave's frequency matches that of the oscillators, the damping becomes positive, wave energy is dissipated, and the magnitude of basilar-membrane vibration plunges.

The passive physical properties of the cochlear partition help to distribute sound energy along its length. However, the waveform of the traveling wave—and especially the shape of its peak—is determined primarily by the characteristics of the local active process. Each oscillator is expected to recruit up to several tens of neighboring outer hair cells that are mechanically coupled by the tectorial membrane (Barral et al. 2010). The position at which the traveling wave peaks is set by the intrinsic frequency of the critical oscillators that actively resonate at the frequency of the wave. Although this frequency is doubtlessly influenced by the passive stiffness of the cochlear partition, the relation may be steeper than that resulting from a passive spring-mass system, perhaps approximating a linear dependence (Fig. A1). The range of frequencies to which the cochlea can be tuned is therefore broader than would be expected on the basis of passive mechanical properties alone (Duke and Jülicher 2003).

The shapes of tuning curves for mammalian eighth-nerve fibers provide additional support for the idea that tuning by means of the traveling-wave mechanism is supplemented by critical oscillators. At least at high frequencies, each of these relations displays two distinct components, a broadly tuned curve reflecting coarse tonotopy on which is superimposed a sharp notch of much higher sensitivity (Liberman 1978; Temchin et al. 2008). Moreover, the sensitive component representing the contribution of the active process may peak at a frequency below, equal to, or above that of the coarse component reflecting passive mechanical tuning. It appears that critical oscillators accept the sound energy separated crudely by the passive traveling wave and greatly accentuate movement of the cochlear partition at the specific frequencies to which they are responsive.

Spontaneous otoacoustic emissions

Among the most remarkable characteristics of tetrapod ears is their emanation of pure tones in a quiet environment and in

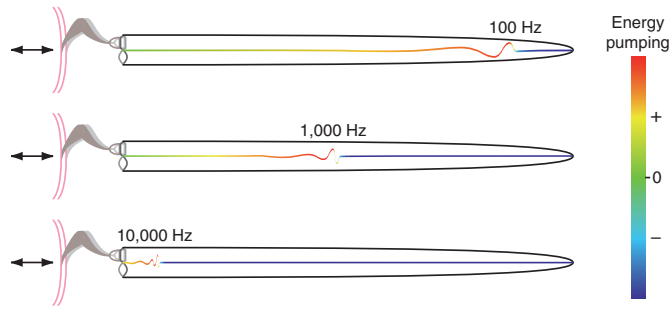

FIG. 3. Locus of energy pumping on the basilar membrane. Each of the 3 diagrams portrays the instantaneous position of the basilar membrane during the propagation of a traveling wave of the indicated frequency. The color scale portrays the extent of energy pumping. The active process grows progressively stronger as the wave approaches the characteristic place, then declines rapidly just before the resonant position associated with the stimulus frequency. If the traveling wave were capable of propagating farther apically than the resonant position, the active process would withdraw energy from it. Note that the amplitude of the traveling wave has been exaggerated about 10^5-fold with respect to the length of the basilar membrane.

the absence of stimulation (reviewed in Probst 1990). Although some spontaneous otoacoustic emissions are clearly pathological, the fact that 70% of human ears emit sounds in a quiet environment indicates that the active phenomenon is generally associated with normal hearing (Zhang and Penner 1998). The statistical features of each spontaneous emission match those of an active oscillator but not those of a sharply tuned, passive filter of noise (Bialek and Wit 1984).

Spontaneous otoacoustic emissions of high intensity have sometimes been related to audiometric anomalies (Ruggero et al. 1984; Zurek 1981). These emissions may reflect the fact that the active process is subject to gain control. As noted earlier, any system subject to a Hopf bifurcation becomes unstable when the control parameter C falls below its critical value C_C. Under normal circumstances, a self-tuning mechanism is expected to maintain criticality to ensure optimal performance and thus to prevent oscillations from growing significantly (Camalet et al. 2000). When perturbed by mechanical or physiological defects within the cochlea, however, this control mechanism may fail, allowing the production of large oscillations.

Active hair-bundle motility probably powers spontaneous otoacoustic emissions in the hearing organs of nonmammalian tetrapods. The hair bundles of reptiles and amphibians exhibit robust spontaneous oscillations in vitro (Crawford and Fettiplace 1985; Howard and Hudspeth 1987; Martin et al. 2003) and the bimodal probability distribution of hair-bundle position (Martin et al. 2001) resembles that observed for sound pressure at the frequency of a spontaneous emission (Bialek and Wit 1984). Although the energy content of spontaneous otoacoustic emissions is so small that only a few hair cells could in principle produce measurable signals (Manley and Gallo 1997), it is probable that larger ensembles participate in the production of robust emissions. In the gecko's ear, for example, clusters of adjacent hair bundles are evidently entrained to oscillate at a common frequency by elastic or viscous coupling; the emission spectrum depends on the number of clusters that can form for a given coupling strength and on the range of characteristic frequencies (Gelfand et al. 2010; Vilfan and Duke 2008). In an intact ear, active hair-bundle oscillations would be expected to direct energy through a tectorial membrane or other accessory structure to the apparatus of the middle ear, culminating in the broadcasting of sound by the tympanum.

Although outer hair cells are thought to drive spontaneous otoacoustic emissions from the mammalian cochlea, uncertainty remains concerning the relative contributions of active hair-bundle motility and prestin-based electromotility, both of which occur in these cells (Chan and Hudspeth 2005a,b; Kennedy et al. 2006). Activation of prestin by an externally imposed voltage can displace the cochlear partition enough to cause electrically evoked otoacoustic emissions (Mellado Lagarde et al. 2008). However, there is no evidence to date that electromotility can by itself display either a Hopf bifurcation or limit-cycle oscillation, so the spontaneous otoacoustic emissions of mammals may require collusion between the two motile processes.

The spontaneous otoacoustic emissions of the mammalian cochlea are not necessarily generated by instabilities of local oscillators, such as those arising from small perturbations in their control parameters. Remarkably, longitudinal coupling to neighbors integrates individual oscillators in a collective mode of basilar-membrane vibration, the active traveling wave. Even though it arises from the coupling of critical oscillators, this wave is a stable phenomenon. Emissions may nevertheless arise globally through the pumping of energy into particular modes of basilar-membrane vibration (Shera 2003). Mechanical fluctuations of the organ of Corti initiate backward- and forward-traveling waves that undergo multiple internal reflections between the stapes and the characteristic place. At some frequencies, these waves interfere constructively, resulting in an active standing wave of sufficiently large magnitude to manifest itself as an emission in the ear canal. This mechanism has been likened to the activity of a laser, in which the dimensions of a resonant cavity select the mode of oscillation in a nonlinear gain medium. It is plausible that an array of critical oscillators—hair cells poised at a Hopf bifurcation—constitutes the mammalian cochlea's gain medium.

Spontaneous activity and phase-locking of nerve fibers

The auditory nerve fibers in the eighth cranial nerve manifest unusually high rates of spontaneous firing in the absence of stimulation. Spontaneous firing, which stems from the release of neurotransmitter by hair cells, has been shown in several nonmammalian species to display preferred interspike intervals that are inversely correlated to the characteristic frequency (Manley 1979). Rhythmic firing can readily be explained by the spontaneous oscillations of membrane potential that have been measured in the hair cells of amphibians and reptiles, including birds, as the result of active hair-bundle motility (Crawford and Fettiplace 1985; Martin et al. 2003) or of electrical resonance in the hair-cell somata (reviewed in Fettiplace and Fuchs 1999). In accordance with the behavior of a critical oscillator, nerve fibers evincing preferred interspike intervals are endowed with sharper tuning and higher sensitivity to external sinusoidal stimuli than fibers with random spiking activity (Klinke et al. 1994).

For rhythmic firing to reflect critical oscillation, the system must operate on the oscillatory side of the Hopf bifurcation, near the critical point. A self-tuning mechanism based on feedback between the magnitude of spontaneous oscillation and the control parameter C would ensure criticality by maintaining the hair cell in a regime of weak spontaneous oscillation (Camalet et al. 2000). The feedback might be mediated by Ca^{2+}, which has been shown to modulate the frequency and amplitude of spontaneous otoacoustic emissions in vivo (Manley et al. 2004) and of hair-bundle oscillations in vitro (Martin et al. 2003; Tinevez et al. 2007), possibly through cAMP-dependent protein phosphorylation (Martin et al. 2003). Although preferred interspike intervals have not been observed in mammals under resting conditions, rhythmic firing of auditory nerve fibers can be evoked by stimulation with noise (Klinke et al. 1994). This observation suggests that the hair cell provides a filter, as expected of a critical oscillator operating on the stable side of the bifurcation.

Depending on its orientation with respect to the hair bundle's axis of sensitivity, a mechanical stimulus can modulate the firing rate in either direction. In birds and mammals, weak sinusoidal inputs do not increase the firing rate of afferent fibers from its resting level. Instead, they partially entrain afferent firing at the frequency of stimulation, resulting in more

regular firing (Johnson 1980; Köppl 1997). Only when stimuli exceed the threshold by 15–20 dB and the neural response has become completely phase-locked does the firing rate increase significantly. The mechanoelectrical-transduction process of an individual hair cell exhibits similar behavior: a threshold stimulus causes noisy spontaneous hair-bundle oscillations to phase-lock to the input, whereas the amplitude of oscillation grows only after the stimulus has increased tenfold (Martin and Hudspeth 2001). When fluctuations are taken into account, the hypothesis of critical oscillation recapitulates the phase-locking behavior of both oscillatory hair bundles and auditory nerve fibers in response to weak stimuli (Camalet et al. 2000).

Relation to alternative models

Because of the technical difficulty in conducting experiments on the mammalian cochlea, theoretical studies have proven especially fruitful in providing insight into the operation of the traveling-wave mechanism and active process. Contributions of this type quantitatively reproduce many of the characteristics of hearing discussed earlier, yet bear no obvious relation to critical oscillators or the Hopf bifurcation. It is revealing to analyze how certain of the well-known models achieve their success.

One valuable model produces realistic responses by constructing an active process that provides negative damping (Mammano and Nobili 1993; Nobili and Mammano 1996). In particular, the authors invoke mechanical resonance of the tectorial membrane to introduce a phase change between basilar-membrane oscillation and hair-bundle deflection. When the action of electromotility is appropriately timed (Markin and Hudspeth 1995), the process adds energy to the basilar membrane's oscillation and thereby enhances sensitivity.

The approach of Mammano and Nobili provides an example of an active model that captures many features of the experimentally observed cochlear response, including robust amplification, sharp frequency selectivity, and compressive nonlinearity. This success stems from combining wave propagation by harmonic oscillators interacting through the cochlear fluids with electromotile feedback that generates negative damping for small stimuli and nonlinear damping for large ones. As demonstrated in APPENDIX B, however, the model in fact represents a specific example of a system operating near a Hopf bifurcation. The generic properties of this unrecognized bifurcation generate the hallmarks of the cochlear amplifier noted by the authors.

An alternative approach to cochlear mechanics is to deduce the local impedance of the organ of Corti from measurements of basilar-membrane vibrations near threshold (de Boer 1983, 1995; Shera 2007; Zweig 1991). Such inverse methods, which do not require a precise a priori knowledge of the interplay between the mechanical constituents of the cochlear partition, have provided strong evidence for negative damping at locations basal to the characteristic place and thus for the operation of a local active process in the cochlea. Zweig (1991) has interpreted the impedance of the organ of Corti as that of a harmonic oscillator with a negative friction coefficient that is combined with a delayed force proportional to velocity. In this formulation, the positions in the complex plane of the zeros of the frequency-dependent impedance control the dynamic responsiveness of the organ of Corti to external stimulation. Although the impedance displays an infinite number of zeros, only the zeros that lie nearest the imaginary axis of the complex plane matter for the long-time response. Notably, it was found that two zeros occur very close to the imaginary axis. Because crossing the imaginary axis constitutes a Hopf bifurcation, this analysis indicates that the relevant segment of the organ of Corti hovers on the brink of criticality.

Conclusions

Despite the power of critical oscillation to explain many cochlear phenomena, the idea has provoked some skepticism in the decade since its introduction. The principal objections seem to stem from consideration of engineering principles. The design of electrical circuits customarily emphasizes *linearity*: for the reproduction of music and other sounds, as well as in the amplification, transmission, and storage of time sequences in general, every effort is made to minimize distortions arising from nonlinearity of the apparatus. Although the proposal of critical oscillation inevitably introduces nonlinearity into our understanding of the ear's operation, that choice is thrust on us: mammalian hearing *is* highly nonlinear, so much so that attention has been directed specifically to the sense's essential nonlinearity.

A second common goal of engineering is *stability*: whenever possible, it is desirable that apparatus be immune from spontaneous oscillation and other instabilities. The ear's behavior offers us little choice but to accept the presence of oscillators within the cochlea, given that spontaneous otoacoustic emissions are ubiquitous. Even though these oscillators operate individually at the brink of instability, however, the mammalian cochlea as a whole is generally stable and reliable. Evolution plays by rules different from those of the best engineers: the least sliver of selective advantage trumps the esthetic and practical considerations of circuit design. The evidence discussed throughout this review suggests that the positive qualities of a critical oscillator–including amplification, frequency tuning, and compressive nonlinearity–have led to the selection of an active process operating at a Hopf bifurcation.

APPENDIX A: ENERGY PUMPING IN THE COCHLEAR TRAVELING WAVE

Using generic properties, we explain here how a one-dimensional array of critical oscillators immersed in fluid gives rise to an active traveling wave with characteristics that accord with observations on the basilar membrane. Each section of the cochlear partition is described by a critical oscillator whose characteristic frequency $\omega_C(x)$ varies tonotopically with its position x on the longitudinal axis of the cochlea. In the limit of a weak sinusoidal stimulus $F(t, x) = \bar{F}e^{i\omega t}$ at a frequency ω that differs sufficiently from $\omega_C(x)$, the relation between the Fourier component $\bar{X}$ of the response $X(t, x) = (1/2\pi) \int \bar{X}(\omega, x)e^{i\omega t}d\omega$ and that of the stimulus is dominated by its linear part (*Eq. 2*). The real part of F may be interpreted as the cross-sectional pressure that sets the partition into motion at position x.

The functional form of the complex impedance $A(\omega, x) = \bar{F}/\bar{X}$ must comply with three constraints. First, because both X and the cross-sectional pressure are real, the complex conjugate $A^*(\omega, x) = A(-\omega, x)$. Decomposing A into real and imaginary parts, $A = A' + iA''$, one finds that A' is an even function of ω, whereas A'' is odd. Second, criticality requires that A vanish at $\omega = \omega_C(x)$: for ω near ω_C, $A \cong \lambda[\omega - \omega_C(x)]$, in which λ is a complex coefficient. Finally, at high frequencies inertia and passive friction must dominate respectively the real

and imaginary parts of the impedance: for $\omega \gg \omega_C(x)$, $A' \cong -m\omega^2 < 0$ and $A'' \cong h\omega > 0$, in which m and h represent respectively a mass and a friction coefficient.

Assuming that each oscillator is characterized by a single frequency $\omega_C(x)$ of spontaneous oscillation, the relation $A(\omega)$ displays only one zero and $A''(\omega)$ crosses the abscissa at $\omega = \omega_C(x)$ with a positive slope (Fig. A1). This property ensures that a critical oscillator provides negative damping ($A'' < 0$) when stimulated at a frequency lower than its characteristic frequency but positive damping beyond. Moreover, because $A''(\omega) = 0$ for $\omega = 0$, the relation $A''(\omega)$ must be nonmonotonic and thus exhibit a frequency at which negative damping is maximal. In contrast, on increasing frequency, $A'(\omega)$ decreases from a positive maximal value $K(x)$ at $\omega = 0$, which represents the passive stiffness of the cochlear partition, to become negative for $\omega > \omega_C(x)$.

A cochlear partition equipped with critical oscillators is automatically endowed with generic properties that have been observed experimentally. The traveling wave originates at the cochlear base, where it first encounters critical oscillators whose characteristic frequencies exceed the frequency of stimulation. Because $A''(\omega, x) < 0$ at these locations, the oscillators pump energy into the wave and thus amplify the vibration of the cochlear partition. This active pumping can oppose or even overcome the effects of viscous dissipation in the moving fluid. The oscillators thus maintain or enhance the mechanical energy carried by the wave. As the wave progresses toward the apex, the frequency mismatch $\omega - \omega_C(x)$ declines. The real part $A'(\omega)$ of the impedance, which controls the speed of propagation of the wave $c(x) \propto A'(x)$ and the local wave vector $q(x) = \omega/c(x)$, decreases correspondingly. As a consequence, the wave slows and its wavelength declines. Because the energy flux is conserved or even enhanced by energy pumping, the wave also grows in magnitude.

As the wave approaches the place where the stimulus frequency matches the characteristic frequency of the local oscillators, energy pumping into the wave diminishes and velocity gradients in the fluid sharpen. In addition, the impedance of the oscillators becomes so small that the nonlinear part of the response, which provides positive damping, asserts itself (*Eq. 2*). Together with the fluid, the oscillators absorb energy from the wave and the magnitude of vibration drops abruptly. The remaining energy of the wave is reflected in a backward traveling wave. At the position $x = x_C$, where $\omega = \omega_C(x_C)$, $A'(\omega)$ and $A''(\omega)$ change sign. Beyond this characteristic place, the wave vector becomes imaginary, indicating that the wave stops propagating. For weak stimuli, the traveling wave peaks at a position only slightly basal to the position of resonance. As the stimulus intensity increases, the crossover between the linear and nonlinear regimes of the oscillator's response occurs at a larger frequency mismatch $\omega - \omega_C(x)$ and the peak of the response accordingly shifts toward more basal positions.

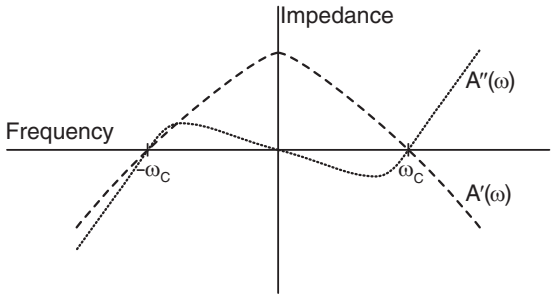

FIG. A1. Schematic representation of the impedance $A(\omega) = A'(\omega) + iA''(\omega)$ of a critical oscillator as a function of the stimulus frequency ω. In the linear limit of cochlear mechanics, the local impedance A of the cochlear partition is defined as the ratio of the Fourier component of the cross-sectional pressure to the Fourier component of the basilar-membrane vibration at the frequency of stimulation. This impedance is a complex number with units of stiffness per unit area. The real or reactive part A' is an even function of ω, whereas the imaginary or dissipative part A'' is odd. Criticality requires that the impedance vanish at $\omega = \pm\omega_C$, in which ω_C is the characteristic frequency of the oscillator. At low frequencies, as A'' approaches zero, $A' > 0$ describes the local stiffness of the cochlear partition. At high frequencies, $A' < 0$ is instead dominated by inertia, whereas $A'' > 0$ reflects dissipation by hydrodynamic friction. These generic constraints ensure that a critical oscillator provides net negative damping ($A'' < 0$)—corresponding to the active pumping of energy *into* the traveling wave—when stimulated below its characteristic frequency, but that it dissipates energy ($A'' > 0$) when stimulated above that frequency. Note that energy pumping peaks at a frequency below ω_C. In principle, an active oscillator may also achieve criticality by opposing damping so that $A'' = 0$ at all frequencies (APPENDIX B). This is the case for the van der Pol oscillator, a standard model for the generation of spontaneous oscillations (Strogatz 1994). However, this singular realization of a critical oscillator does not produce energy pumping.

APPENDIX B: THE MODEL OF MAMMANO AND NOBILI

In a discrete representation of the model of Mammano and Nobili, the basilar membrane is divided into local oscillators $n = 1, 2, \ldots, N$ whose characteristic frequencies are exponentially distributed along the tonotopic axis of the cochlea (Nobili et al. 1998). The membrane's local displacement X_n obeys the dynamic equation of a harmonic oscillator

$$m_n\ddot{X}_n + h_n\dot{X}_n + k_nX_n = F_n \tag{B1}$$

For the nth local oscillator, m_n is the mass, h_n is the friction coefficient, and k_n is the stiffness; the overdots denote temporal derivatives.

The force F_n acting on each local oscillator includes contributions from the motion of the stapes and from hydrodynamic couplings to all the other oscillators, both of which propagate through the fluid. The hydrodynamic interactions are described with Green's functions, an approach that is physically identical to a wave description in a one-dimensional transmission-line model (Shera et al. 2004). The authors also include a shear-resistance term that couples neighboring oscillators; we neglect this term for the sake of simplicity.

To describe the cochlear amplifier, Mammano and Nobili invoke the force $-U_n$ generated by electromotility and acting on each element of the basilar membrane in response to changes in the receptor potentials of the outer hair cells. They further assume that the coupling between the reticular lamina and the basilar membrane is viscoelastic and thus provides a high-pass filter to the electromotile force. Under such circumstances, low-pass filtering of the receptor potentials by hair-cell membranes can in principle be cancelled, yielding an electromotile force that is proportional to the local hair-bundle deflection Y_n. In a fully nonlinear model, the function $U_n(Y_n)$ is sigmoidal; its strongly nonlinear shape reflects the behavior of the transduction current as a function of hair-bundle deflection.

In the simplest version of the model, hair-bundle deflection is directly proportional to basilar-membrane displacement: $Y_n \propto X_n$. However, this situation fails to produce negative damping and thus to compensate for the viscous friction that impedes movements of the basilar membrane. To overcome this problem, the authors invoke harmonic resonance of the tectorial membrane to induce a phase shift between the basilar-membrane motion X_n and the stereociliary deflection Y_n. If the characteristic frequency of the oscillator falls near that of the tectorial-membrane resonance, the hair-bundle deflection behaves as

$$Y_n \cong -\frac{C_n}{\bar{h}_n}\dot{X}_n \tag{B2}$$

in which C_n, with units of mass, represents the coupling between basilar-membrane and hair-bundle movements and $\bar{h}_n$ is the friction coefficient associated with tectorial-membrane movement.

As a consequence of the phase shift between X_n and Y_n, the electromotile feedback generates negative damping. Each element of the basilar membrane thus behaves as a nonlinear oscillator characterized by the relation

$$m_n\ddot{X}_n + h_n\dot{X}_n + k_nX_n + \bar{U}_n(\dot{X}_n) = F_n \quad \text{(B3)}$$

in which $\bar{U}_n(\dot{X}_n) = U_n(-C_n\dot{X}_n/\bar{h}_n)$. We can expand the nonlinear function $\bar{U}_n(\dot{X}_n)$ as a Taylor series in $\dot{X}_n$

$$\bar{U}_n(\dot{X}_n) \cong -h'_n\dot{X}_n + \alpha_n\dot{X}_n^2 + \beta_n\dot{X}_n^3 \quad \text{(B4)}$$

The first term on the right produces negative damping with a coefficient $-h'_n = d\bar{U}_n/d\dot{X}_n < 0$. This procedure reveals that each local oscillator experiences a Hopf bifurcation when the electromotile feedback satisfies the condition $h_n = h'_n$. Because of the nonlinear terms described by the coefficients α_n and β_n, each local oscillator exhibits all the hallmarks of a critical oscillator if poised near the Hopf bifurcation. In particular, the dynamic equation describing this nonlinear oscillator in response to sinusoidal forcing can be brought into the generic form described by *Eq. 2* with

$$A = k_n - m_n\omega^2 + i(h_n - h'_n)\omega \text{ and}$$
$$B = (4\alpha_n^2\omega^4)/[k_n - 4m_n\omega^2 + 2i(h_n - h'_n)\omega] + 3i\beta_n\omega^3 \quad \text{(B5)}$$

At the bifurcation, the basilar membrane displays a compressive nonlinearity that behaves as $X_n \propto F_n^{1/3}$ during stimulation at the characteristic frequency $\omega_C = (k_n/m_n)^{1/2}$. The quadratic nonlinear terms described by the coefficients α_n generate second harmonics in the response. Because the nonlinearity stemming from the force production by the outer hair cells is sigmoidal, the system behaves linearly for large forces that saturate the transduction channels.

In this specific realization of a critical oscillator, the passive damping acting on a section of the cochear partition is canceled precisely by undamping from the electromotile process ($h_n = h'_n$). At the critical point, the imaginary part A'' of the impedance is null for all stimulus frequencies. As shown in APPENDIX A, this situation is singular. Both the real and the imaginary parts of a critical oscillator usually remain finite except at the characteristic frequency. Moreover, contrary to the available evidence (Shera 2007), the active process proposed by Mammano and Nobili does not provide net negative damping within a restricted region of the partition. Although electromotile feedback exactly compensates hydrodynamic friction on the cochlear partition at the critical point, no energy is pumped into the traveling wave.

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