The process by which the ear receives air-borne sound waves and transforms them into electrical impulses understandable to the central nervous system has often been compared to a microphone. Today, however, we know that the function of the organ of Corti is much more complex and sophisticated than the most elaborate man-made device. Possibly the most important event in recent auditory research is the recognition of the active processes occurring within the inner ear. Active processes are expressed not only as stimulus-evoked length changes of sensory outer hair cells isolated from the hearing organ (see Ref. 6 for an overview) but also, and more importantly, as mechanical events occurring in the intact auditory system (see Ref. 14 for a review).

Hearing is to a large extent based on a combination of mechanical and electrical events taking place at the periphery of the auditory system: in the organ of Corti within the inner ear. The organ of Corti, resting on the basilar membrane, consists of the sensory inner and outer hair cells and various supporting cells (Fig. 1A). Sound stimuli, i.e., pressure alterations in the air surrounding us, are transmitted via the ear canal and the middle ear ossicles to the cochlea, where the resulting pressure differences across the hearing organ and the basilar membrane elicit a complex vibratory motion. The sound-induced vibrations of the basilar membrane elicit a complex vibratory motion. The sound-induced vibrations of the basilar membrane are mechanically transmitted to the surface of the hearing organ, the reticular lamina, where the interaction with the overlying tectorial membrane causes deflection of the sensory hair bundles. The bending of the sensory hairs affects the transduction channels in the hair bundle region, allowing an ion current to pass through the hair cells, thereby generating receptor potentials. Thus sound causes complex mechanical interactions which in turn elicit electrical variations across the sensory cells. After the mechanoelectrical transduction, the nerve fibers contacting the basal regions of the hair cells are synaptically activated.

The cochlea performs a mechanical frequency analysis, separating the incoming sound signal into its frequency components, which are then processed at different locations along the length of the cochlea. High-frequency sounds are processed at the base of the cochlea, low frequencies at the apex. The better the system can separate the frequencies, the better is the tuning or frequency selectivity. Until quite recently, the basilar membrane was thought to be solely responsible for providing the frequency selectivity of the cochlea, a view that still is expressed in many textbooks. However, recent experiments have demonstrated that the sharp tuning and the great sensitivity of the organ of Corti are intimately linked to the active function of the outer hair cells.

**Poor tuning without the outer hair cells**

The frequency response of the auditory nerve fibers can be illustrated by plotting the sound stimulus level needed to elicit a change in the neural activity as a function of stimulus frequency (Fig. 1B). At the characteristic or best frequency, the sensitivity is greatest. The sharpness of the “tip” region indicates the frequency selectivity of the system. Several experimental studies have demonstrated that the shape of the tuning curve changes drastically when the sensory hair cells are damaged (10). Selective loss of the outer hair cells, for example caused by ototoxic compounds, typically leads to an increased hearing threshold, and,
instead of a sharp tip region, the frequency selectivity (tuning) curve is broadened (dashed line in Fig. 1B). In addition, the location of maximal sensitivity is shifted toward lower frequencies. The frequency selectivity that normally is seen in the responses of the auditory nerve (Fig. 1B) is already established in the mechanical motion pattern at the very periphery of the auditory system. Measurements made at the basilar membrane, on which the hearing organ rests, or directly from the sensory cells show that the mechanical response is as sharply tuned as the neural response (see Ref. 14 for a review). The fundamental role of the outer hair cells in the mechanics of the organ of Corti has been demonstrated using injections of the ototoxic substance furosemide, which within a few minutes drastically affected the motion of the basilar membrane (13). The magnitude of the sound-evoked basilar membrane motion was reduced (by up to 61 dB), and there was a reduction of the sharpness of tuning and a shift of the tip region toward lower frequencies. Thus the changes were qualitatively the same as illustrated in Fig. 1. Similar observations have been made following acoustic overstimulation (15) in which the structural damage, mainly affecting the outer hair cells, caused a significant reduction of the mechanical tuning and a shift of the mechanical sensitivity toward lower frequencies. The changes in the mechanical response indicated a decrease in the overall stiffness of the system following noise trauma, a notion that has been further supported by a recent study showing that the stiffness of individual outer hair cells is reduced after intense noise exposure (5).

It is generally acknowledged that, without the presence of intact outer hair cells, neither the mechanical function of the organ of Corti nor the behavioral sensitivity and selectivity of the auditory system can be maintained. There is, however, less agreement on whether the outer hair cells contribute only passively to the mechanics or play a more active role.

**Outer hair cells are mechanically active**

It was recognized a long time ago that the auditory system could not exhibit its great sensitivity and selectivity if it were only a passive system; something was needed to provide additional energy. For many years, evidence for this notion was missing. However, less than 20 years ago, it was shown that the inner ear was capable of actually producing sound, which readily could be recorded in the auditory canal (8). This clearly demonstrated that the inner ear contained mechanisms not only for recording sound (like a microphone) but also for producing mechanical motion (like a loudspeaker!). It was shown that these otacoustic emissions were biologically vulnerable and could be suppressed by, for example, ototoxic drugs and anoxia, which suggested that the organ of Corti and specifically its sensory cells were the origin. Final support for this hypothesis was presented a few years later by Brownell and co-workers (1) who showed that isolated outer hair cells “contracted” when stimulated electrically.

*…isolated outer hair cells ‘contracted’ when stimulated electrically.*

---

**FIGURE 1.** A: schematic illustration of a cross section of the organ of Corti. Apical poles of the sensory hair cells form, together with supporting cells, a relatively stiff plate, the reticular lamina. Sensory hair bundles (stereocilia) project from the sensory cells toward the tectorial membrane. Cell bodies of inner hair cells are innervated by afferent fibers, whereas outer hair cell innervation is predominantly efferent. White spaces above, below, and within the organ of Corti indicate fluid-filled compartments. Cross section shown illustrates the hearing organ in the apical region of the cochlea; further toward the base, outer hair cells are shorter and the angle between the tectorial membrane and the basilar membrane is less steep. B: neural tuning (frequency selectivity) curves are obtained when the stimulus level needed to evoke a change in the nerve fiber activity is plotted as a function of frequency. At the best frequency of the unit, sensitivity is maximal and the normal tuning curve (solid line) exhibits a sharp “tip.” Much higher stimulus levels are required to elicit a response at frequencies above or below the best frequency. Response at low frequencies may be rather flat (“tail”). When the outer hair cells (OHCs) are severely damaged, sensitivity of the tip region is lost and there is a shift of the best frequency to the left, to lower frequencies (dashed line). SPL, sound pressure level. [Modified from Liberman and Dodds (10).]
ever since, outer hair cell motility (and especially electromotility) has been a main topic of auditory research. The electromotile response is very rapid and can follow stimuli in the kilohertz range, suggesting that the cells could respond to the electric alterations occurring across the organ of Corti during sound stimulation. The actual cellular mechanism is not fully elucidated but appears related to molecular motors associated with the outer hair cell membrane (6). However, from a functional point of view, the most important question is whether the cells can produce mechanical events also in the intact hearing organ, where the motion must be much more restricted due to the mechanical coupling to the supporting cells. Indeed, it has been demonstrated that applying an electrical field across the organ of Corti evokes length changes of the outer hair cells that change the position of the reticular lamina (12). Furthermore, it was found that the mechanical motion of the basilar membrane, caused by electrical stimulation of the hair cells in the living animal, is accompanied by sound emitted into the auditory canal of up to a 40-dB sound pressure level (11).

Sound stimulation elicits a mechanical response

The adequate stimulus for the hearing organ is sound itself or, rather, the hydromechanical events resulting from the sound pressure changes in the inner ear. It was thus of great functional interest when acoustically induced length changes were demonstrated in outer hair cells isolated from the hearing organ (2, 4). When an acoustic stimulus was applied directly to the cell body of isolated outer hair cells, there was an immediate length change (Fig. 2A). The response was highly frequency specific, and a certain cell responded only to a narrow range of frequencies. In the intact cochlea, long outer hair cells are located in the apical regions of the cochlea, which respond to low sound frequencies, whereas shorter cells are found in the basal regions tuned to high frequencies. When acoustic stimulation was applied to isolated cells of different lengths, it was found that long cells responded specifically to low frequencies, whereas short cells responded best to high-frequency tones (Fig. 2B), just as would be predicted from their original location in the cochlea. It was thus demonstrated that, even in the absence of all accessory structures previously thought to contribute significantly to the tuning of the hearing organ, for example, the basilar membrane and the tectorial membrane, the acoustically induced response of the single cells was as sharply tuned as the corresponding neural tuning curves. Therefore, mechanical and neural tuning must be established already at the level of the outer hair cells.

Of possibly great functional significance is that sound stimulation, in addition to producing frequency-following vibratory motion, elicits an active mechanical response manifest as a shift in the position of the basilar membrane and the reticular lamina. This was first reported by LePage (9), who showed that, during the presentation of a tone, there was a sustained baseline shift of the basilar membrane. Later similar findings were
made directly at the reticular lamina, where it was shown that the displacement response was sharply tuned (3). As illustrated in Fig. 3, the response at stimulus frequencies below the best frequency of the specific cochlear location followed the input signal relatively closely (at 220 and 270 Hz). However, at 320 Hz (best frequency), there was, in addition to the frequency-following vibration, a sudden and significant (~1.5 µm) shift in the position of the reticular lamina: a displacement response. At higher frequencies (370 Hz), displacement response could no longer be evoked. [Modified from Brundin et al. (3).]

**Outer hair cells and tuning**

Without functioning outer hair cells, the detection of low-level sounds or the discrimination of tones of neighboring frequencies is severely impaired. However, even in very damaged ears, the organ of Corti still exhibits a residual tuning, which suggests that, in the intact auditory system, at least two components are involved in producing the frequency-selective, highly sensitive response. There is a broadly tuned response that is quite robust and is maintained even after severe damage to the system. This response is largely linked to the passive hydromechanical properties of the inner ear. Superimposed on the passive component is a sharply tuned response that is located at the high-frequency side of the passive response and that is vulnerable to trauma (Fig. 1B).

There is now overwhelming experimental evidence that the sharply tuned component originates from the outer hair cells. Due to its biological origin, this component is considered to be an active response that produces a feedback force interacting with the mechanics of the cochlea to enhance or amplify its response (Fig. 4). The cochlear amplifier appears to function only at relatively low sound pressure levels, which suggests that it plays a role in improving sensitivity near the auditory threshold.

The basis of the cochlear amplifier is often suggested to be the electromotility expressed by the outer hair cells (6). However, although the electrically evoked response of mammalian hair cells can follow the stimulus up to high frequencies, the magnitude of the response does not change in the same frequency-dependent way as either the nerve fiber response or the sound-evoked response (see Figs. 1B and 2B, respectively). In other words, the electromotile response lacks the frequency selectivity required by the auditory system. Therefore, a more likely mechanism for the selectivity and sensitivity of the cochlea is the sharply tuned mechanical response expressed by the outer hair cells during sound stimulation (see Figs. 2 and 3).

Several possible hypotheses can be advanced to explain how the sound-evoked vibratory response and the displacement response are interrelated. One plausible mechanism is directly related to the mechanical properties of the cells. Because the structure of the outer hair cells changes gradually along the length of the cochlea, the mechanical resonant frequency of each cell is likely to vary (see Fig. 2B). Thus, when the frequency of the sound-induced pressure alterations within the cochlea corresponds to the combined cellular resonant frequency, maximal energy is absorbed from the sound pressure wave, and the vibration amplitude of the cochlear structures is greatly enhanced. This is very similar to the hypothesis put forward by Helmholtz (7) in 1863 but with the outer hair cells serving as the individually tuned resonators absorbing the energy (4) rather than, as suggested at the time, the fibers of the basilar membrane. In such a system, the stimulus-evoked active
changes at the level of the outer hair cells (length and/or stiffness changes) would directly affect the mechanical resonance properties and, consequently, the tuning of the organ of Corti. In the purely passive system, sound stimuli cause only a broadly tuned mechanical response (Fig. 4), whereas, in the presence of the cochlear amplifier, the response of the hearing organ exhibits both great sensitivity and selectivity.

The critical role of the outer hair cells for maintaining normal auditory function may seem paradoxical in that <10% of the fibers of the auditory nerve make synaptic contacts with these cells, whereas the fibers innervating the inner hair cells make up the rest. In other words, it is the inner hair cells that convey the “message” from the organ of Corti to higher levels of the auditory system. However, before the incoming signal acts on the inner hair cells, it is processed within the organ of Corti by means of the action of the outer hair cells. The nature of the interaction between the outer and inner hair cells is still largely unknown.

We thank Drs. Joseph Bruton, Per Conradi, Anders Fridberger, and Jan Lännergren for helpful suggestions during the preparation of this review.

This work was supported in part by the Swedish Medical Research Council, Stiftelsen Tysta Skolan, the Swedish Council for Work Life Research, the National Institute of Deafness and other Communication Disorders, and the Emil Capita Foundation.

References