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Hair cell mechano–transduction: Its influence on the gross mechanical characteristics of a hair cell sense organ

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Abstract

The complex mechanical behaviour of a hair cell bundle appears to be a direct consequence of the gating forces on the individual transduction channels. The mechanical molecular interactions involved in transduction channel gating, therefore, also bear a reciprocal influence, via the hair bundles, on the mechanical properties of accessory structures driving them. This allows for the possibility to investigate, under in vivo conditions, the mechanical gating machinery of ion channels via the dynamics of accessory structures. We have performed such studies on the lateral line organ of fish and were thus able to relate the mechanics of elementary molecular events to the macroscopical dynamics of an intact organ. © 1997 Elsevier Science B.V.

Keywords: Hair cells; Mechano–electrical transduction; Hair bundle micromechanics; Tectorial structure mechanics; Mechanical tuning; Lateral line

1. Introduction

Hair cells perform the primary mechano–transduction in a wide class of vertebrate mechano–receptive organs varying from the mammalian sense organs of hearing and balance (cochlea and vestibular organ, respectively) to the water motion detecting lateral line organ of fishes and amphibians. Hair cells possess a characteristic organelle, the hair bundle. It consists of several tens of stereocilia, hair like extrusions of the apical cell membrane, that pivot around their base when a force is applied to their tips (see Fig. 1). In most organs this force is applied via an accessory structure, bathed in a fluid. Depending on an organ's combined mechanics and hydrodynamics, it is sensitive to a specific aspect of (particle) motion. In the cochlea, it is the sound pressure of air, while for instance in some lateral line organs, it is the velocity of the water surrounding the animal that is detected.

Physiologically relevant deflections of the accessory structures and the hair bundles attached to it, may range from atomic dimensions up to micrometers. Such deflections are transduced with high fidelity into membrane receptor potentials and coded into action potential patterns that are transported to the brain for further analysis.

In contrast to photo- and olfactory reception, the molecular basis of the first steps in mechano–reception is poorly understood. The engaging machinery of the transduction channel that transfers the deflection of a hair bundle into a force opening the channel

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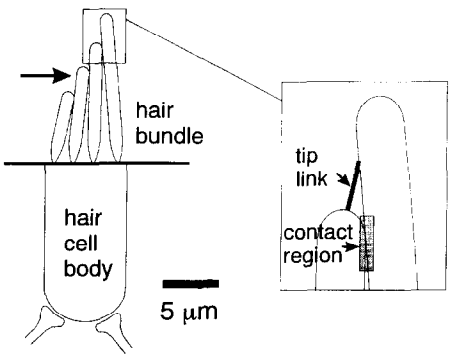

Fig. 1. Hair cell features (schematic) and possible sites of the transduction apparatus (inset). The hair bundle has a stair-case like organization depicted here by only four stereocilia. Usually a tenfold or more are present. Most hair cells also possess a kinocilium (not shown here). Forces applied to the hair bundle in the excitatory direction, shown with the long arrow, deflect hair bundles and stretch the tip links between shorter and longer stereocilia. Such forces will also result in a shearing motion in the contact region between stereocilia, as indicated. Both locations are in a suitable position to host the transduction channels. Hair cells possess afferent as well as efferent innervation, so that information can be send to, and received from the central nervous system.

is still unknown. The molecular identity of the transduction channel and its precise location in the cell's membrane have not yet been identified. There is, however, firm evidence limiting the channel's site to a region somewhere near the tips of the stereocilia [1–4]. Candidates at that location are the tip links, tiny strands connecting the individual stereociliar tips, which will be elongated during hair bundle deflection [5]. Alternatively, the channels may be associated with membrane structures located somewhere in the contact region between individual stereocilia [6] where shearing motion will be produced under these conditions (Fig. 1, enlarged inset).

Most of the current knowledge of the first steps in mechano–electrical transduction has been obtained from studies on isolated hair cell preparations. Since hair cells in an intact system interact mechanically via their hair bundles with accessory structures of the sensory organ in which they are embedded, it is important to study mechano–electrical transduction under in vivo conditions. In the present contribution, such studies on the lateral line hair cell system are discussed together with some of the relevant biophysical properties of hair cells.

2. Hair cell embedding

The mechanosensory tasks performed by hair cell organs are diverse. Related to this, hair cell systems can be categorized with respect to their degree of embedding in the organ in at least three classes (see Fig. 2).

(1) In some hair cell organs (Fig. 2a), like for instance in the ears of certain lizard species, hair bundles are freestanding [7]. This means that they are only surrounded by fluid and driven by its flow with respect to the epithelial layer in which their cell bodies are anchored. Most likely, also cochlear inner hair cells have freestanding hair bundles thus receiving their stimulus via fluid flow in the subtectorial gap.

(2) In a more common class (Fig. 2b), hair cells are embedded in an epithelial layer, usually called macula, with their hair bundles connected to an accessory or tectorial structure. This structure is fluid driven and thus acts as an intermediate to transfer fluid motion to hair bundle motion. Tectorial structures may have densities close to that of the surrounding fluid, as for instance in the fluid motion detecting cupulae of the vestibular system of mammals and the lateral line system of fishes. Alternatively, they may have a different density, usually higher than the surrounding fluid, giving them acceleration sensitivity as occurs in sacculae of mammals and other vertebrates.

(3) A more complicated embedding (Fig. 2c) is found in the mammalian cochlea where outer hair

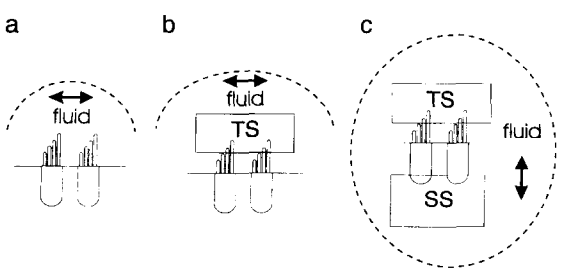

Fig. 2. Categorization of degree of hair cell embedding. Hair cells may be: (a) directly driven by fluid forces acting on freestanding hair bundles, or (b) indirectly driven via a tectorial structure (TS), or (c) driven as a result of a combination of fluid driven motion of a tectorial structure (TS) and a hair cell supporting structure (SS), as takes place in the mammalian cochlea.

cells are not only excited via a tectorial membrane connecting the hair bundles, but where the structure supporting the hair cell bodies, the basilar membrane, is also moving. The mammalian cochlea, in this respect, is the architecturally most intricate hair cell organ providing its owner with the most powerful hardware known, to unravel the information present in complex sounds.

It has been recognized during the past decade that the dynamic characteristics of the driving tectorial- and supporting structures (classes 2 and 3) are predominantly derived from the mechanical properties of the hair cells and the hair bundles. The coupling of hair cells via their cell bodies and bundles to those structures is thus mechanically more significant than other coupling structures that usually are also present (but not shown in Fig. 2). From the point of view of signal transmission this is not surprising. This way, the information present in fluid motion is probably most efficiently propagated into the detector, the hair cell. On the other hand, it implies that the mechanical properties of the hair bundles (class 2), and also cell bodies in the case of the cochlea (class 3), may have a controlling impact on the overall mechanical filtering characteristics of the complete hydromechanical system.

Especially with respect to cochlear mechanics, this has led to an intensive research effort to determine the (active) properties of the specialized outer hair cell bodies and their enhancing effect on cochlear mechanical frequency selectivity [8]. The gradients of hair cell properties along the cochlear length and variations in the tectorial and embedding structures associated with it, make the investigation of the interaction of cochlear hair cell properties with the fluid and the other complicated structures a difficult task.

The effect of hair bundle mechanics on macromechanical functioning, although present in almost all hair cell systems, has received much less attention. We have taken the approach to study the influence of hair bundle mechanics on the gross mechanical characteristics of the lateral line organ of fish. The canal lateral line organ is morphologically a relatively simple system (c.f. Fig. 2b). In the ruffe (*Acerina cernua* L.), for instance, water motion around the animal is transmitted via hydrodynamic windows [9] to the supraorbital canal fluid, thus exciting fairly

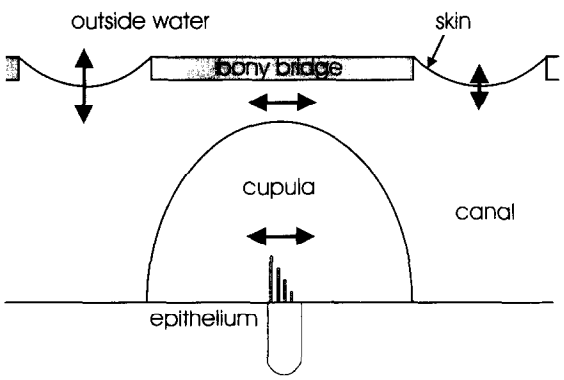

Fig. 3. The supraorbital lateral line canal system of ruffe (*Acerina cernua* L.; schematic). Water motion outside the fish evokes pressure differences of the canal fluid across the length of the canal below a bony bridge. A cupula (∅≈ 600 μm) responds with a motion that deflects the hair cell bundles penetrating into the cupular base. Usually several thousands of hair cells underlie a cupula. Here, only one is shown with its size exaggerated. Cupula plus hair cells make up a functional unit called neuromast, of which several are located in the canal.

rigid hemispherical cupulae that each stimulate a few thousand of hair cells (Fig. 3). The accessibility of the organ permits the use of noninvasive techniques to measure submicrometer motion of the cupula and hair bundles under in vivo conditions [10]. In addition, it is possible to apply theoretical models with a limited number of degrees of freedom.

Hair cells in the lateral line organ are ontogenetically related to hair cells of the inner ear [11] and exhibit a comparable mechano-sensitivity [12]. Morphological and electrophysiological studies on the lateral line organ [13–17] indicate that the hair cells underlying a cupula differ only in their morphological orientation in the macula and thus are expected to share similar mechanical and electrical properties.

3. Hair cells

3.1. Electrical properties

Most of the knowledge on the electrical properties of hair cells has been obtained from lower vertebrates [18,19], although more recently, using new techniques, also cochlear hair cells have been investigated in more detail [20].

The transduction channels are located somewhere

at the apical hair cell membrane [1–4] and face a high K^+ concentration. Hair cells show resting membrane potentials more negative than −50 mV [21,22,12]. When the transduction channels open in response to the deflection of a hair bundle, a predominantly K^+ current flows into the cell. As a consequence of this transduction current, the hair cell depolarizes, activating voltage dependent calcium channels. The increased Ca^{2+} concentration promotes the release of neurotransmitter resulting in action potentials of the afferent nerve fibers. In addition, in some lower vertebrate hair cells, the higher Ca^{2+} concentration leads to opening of calcium dependent potassium channels [23], resulting in a hyperpolarization of the membrane potential. Depending on the temporal properties of these channels and the stimulus frequency applied, this may give rise to an electrical tuning phenomenon [23,24].

The basic ionic currents of hair cells resulting from a deflection of a hair bundle are quite well known. The first step, initiating the transduction current in response to this deflection, is less well understood. The present level of understanding is mostly based on studies on hair bundle mechanics.

3.2. Hair bundle mechanics and gating springs

The first detailed mechanophysiological studies were also performed on lower vertebrate hair cells [25,26]. These studies consisted of determining the force-displacement relationship, $F(X)$, i.e., the force needed to displace a hair bundle over a certain distance X, either under static or dynamic conditions. Using this relationship, components of the mechanical impedance of a hair bundle were derived.

The most dominant property of a hair bundle appears to be its stiffness. Obviously, stiffness is essential in restoring the hair bundle's position after mechanical stimulation. It was found that a considerable part of the stiffness originates from the pivoting region where the bundle inserts into the apical plate [25]. Another part is related to the transduction apparatus located in the bundle's tip [27]. This part of the stiffness is dependent on the fraction of transduction channels open and manifests itself as a reduction in stiffness (gating compliance). Maximum reduction was found at bundle deflections at which roughly half the channels are open and the hair cell's electrical sensitivity to bundle deflection is maximal [27]. These observations currently form the basis of the most widely accepted mechanical model of the first step of mechano–electrical transduction in hair cells.

In this model, termed gating spring model, it is assumed that the deflection of a hair bundle is transferred into a direct force on the transduction channel's gate via an elastic element, the gating spring [28,27]. The related free energy difference between the open- and closed states favours opening of the gate of the transduction channel when the hair bundle is deflected. Structures that have been postulated to be associated with the gating springs are the tip links [29] (see also Fig. 1).

By applying this mechanism to a two state model of the channel, a statistical mechanical formulation has been derived relating the transduction channel's open probability, $p_0(X)$, and the (total) force $F(X)$, to bundle deflection X [27] (see Fig. 4).

The predicted sigmoidal current-deflection rela-

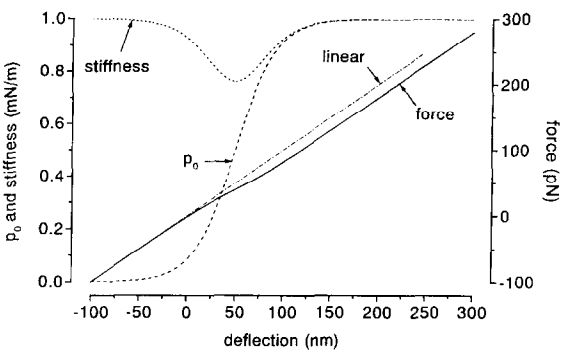

Fig. 4. Open probability of a two state transduction channel, $p_0 = [1 + \exp - Z(X - X_0)/kT]^{-1}$ and force $F = S_{piv.}X + N_{gs}\gamma K_{gs}X - N_{gs}Z[1 + \exp - Z(x - x_0)/kT]^{-1}$ needed for a deflection of a hair bundle, X, as described by the gating spring theory [27]. The last term in F corresponds to the relief in tension of the gating springs when transduction channels open. Here, k is the Boltzmann constant, T denotes de absolute temperature, X_0 is the deflection at which half the channels are open and N_{gs}. is the number of channels per bundle. The gating force, $Z = \gamma d K_{gs}$, when applied to the bundle's tip, may extend one gating spring with stiffness K_{gs} over the swing (d) of the transduction channel. The geometrical factor, γ, relates the deflection of the tip of the hair bundle X, to the extension of a gating spring, x, according to $x = \gamma X$. The related stiffness, dF/dX, exhibiting the gating compliance (stiffness dip) has also been added. For comparison, the force-displacement curve, in the case of no gating (linear) is also shown. Parameters used: $N_{gs} = 100$; $Z = 200$ fN; $X_0 = 50$ nm; $S_{piv.} + N_{gs}\gamma K_{gs} = 1$ mN·m^{-1}.

tionship (Fig. 4) has been found in hair cells of several types of organs. The associated reduction of the stiffness, however, has only been observed directly in saccular hair cells [27,30]. It is not yet clear whether cochlear hair cell bundles exhibit similar gating compliance. Some studies seem to confirm, to some extent, the results found in saccular hair cells [31], while others report a linear $F(X)$ relationship, implying a deflection independent stiffness [32]. As will be discussed, lateral line hair cells show deflection dependent reductions in stiffness, similar to saccular hair cells.

3.3. Adaptation

Hair cells adapt their electrical responses to prolonged static deflections of their hair bundle [33]. This adaptation, at least in saccular hair cells, is mediated by a mechanical relief on the transduction channels [34], as can be accounted for by assuming an additional resistive component in the mechanical impedance, in addition to compliant components (see Fig. 8). In cochlear hair cells of turtles [35] and neonatal mice [32] electrical adaptation has also been demonstrated but no mechanical counterpart as in saccular hair cells has been found.

In terms of the gating spring model, adaptation can be interpreted as the sliding of one end of the gating spring, which decreases the tension and thereby the channel's open probability [34]. In addition, the involvement of a molecular adaptation motor has been postulated [36]. The motor may retentive the gating spring counteracting the passive slipping of one end of the gating spring, as to keep a certain fraction of the channels open. Tip links connecting shorter to taller stereocilia are in a suitable position to facilitate these mechanisms [29]. Explanation of adaptation in terms of reconformation of mechanical elements in the contact region [6] is less straightforward, but cannot be excluded.

4. Mechanics of the lateral line cupula

4.1. Measurements and model

The implications of hair cell bundle mechanics on the overall performance of a hair cell organ have extensively been studied in supraorbital canal neuromasts of the ruffe (*Acerina cernua* L.) and clown knifefish (*Notopterus chitala*).

The submicrometer dynamic behaviour of the cupula of such neuromasts has been measured in response to fluid flow artificially generated in the canal [37]. It was shown by applying pharmacological agents, that the frequency response of the cupula is strongly dependent on the condition of hair cells underlying the cupula [38,39]. On basis of such studies, it was possible to develop a mathematical formulation integrating the interaction between hydrodynamics and hair cell mechanics [40].

In its most simple form, the cupula is treated as a fluid driven (hemi)sphere to which hair bundles impart an elastic coupling with respect to the frame of reference. The hydrodynamics can be shown to be adequately described by unsteady (periodic) Stokes streaming theory (where it is assumed that the nonlinear Reynolds number is small (< 1), but where the linear Reynolds number (Re_{ac}) may vary from small (< 1) values to large (> 1) values). Therefore, the model accounts for the frequency dependence of a fluid boundary layer driving the cupula.

The model predicts the functional significance of the four most important physical parameters of the system. These parameters include collective hair bundle stiffness of the underlying hair cells, S, the radius of the cupula, r, and the fluid's density ρ and dynamic viscosity μ. It was shown that the model's response to fluid flow at a certain frequency, f, is dependent on only two dimensionless numbers which can be expressed in the four physical parameters. One is the well known linear Reynolds number for unsteady flow, $Re_{ac} = f/f_t = f(2\pi\rho r^2/\mu)$, which is the stimulus frequency scaled with respect to the transition frequency, f_t, at which inertial and viscous fluid forces are equally important. The remaining parameter, termed $P_c(= Sr\rho/6\pi\mu^2)$, completely determines the shape of the frequency response and thus can be used as a measure to characterize the mechanical tuning properties.

Responses do not resemble the behaviour of a simple second order oscillator. The reason for this is that the fluid is distributed in a boundary layer around the cupula, which cannot be modeled using a simple lumped parameter model.

Model responses adequately describe the mea-

sured data. From the values of f_t (ca. 10 Hz) and P_c (ca. 80) resulting from fits of the supraorbital neuromasts of ruff, and from a measured cupular diameter of 300 μm and an estimation of about 1000 hair cells underlying this cupula, the mechanical stiffness of a hair bundle under in vivo conditions can be inferred. The result is about 2.7×10^{-14} N · m · rad^{-1} for the pivotal stiffness of a 15 μm long lateral line hair bundle in vivo [37]. This value is comparable to results from in vitro studies on hair cells of other organs [25,26,41]. Comparison of measured and model responses also yields a value for the viscosity of the canal fluid which was found to be close to 6 times that of water. However, due to effect of the canal wall on the boundary layer around the cupula [42], this is likely to be an overestimation [43].

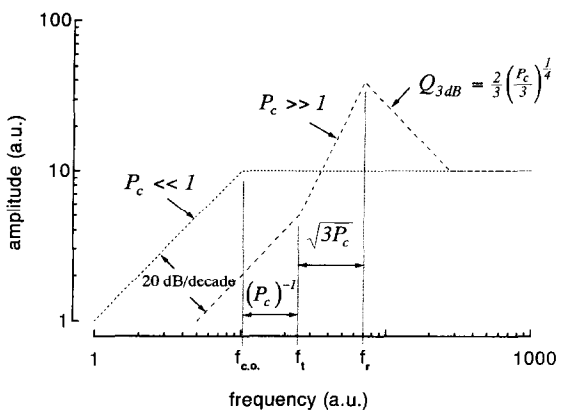

Fig. 5. Amplitude response of an elastically coupled tectorial structure, represented schematically by linearized sections to illustrate the resulting detecting characteristics. The linearized sections are based on the (complete) complex displacement X_0 which is given by [40]: $X_0 = D_0(iRe + \frac{1}{2}\sqrt{2}(i-1)\,\mathrm{Re}^{\frac{3}{2}} - \frac{1}{3}Re^2)/(P_c + iRe + \frac{1}{2}\sqrt{2}(i-1)\,\mathrm{Re}^{\frac{3}{2}} - \frac{1}{3}Re^2)$, with D_0 the fluid displacement, $Re = Re_{ac} = f/f_t = f(2\pi\rho r^2/\mu)$, the (linear) ac Reynolds number, $P_c = Sr\rho/6\pi\mu^2$ and $i = \sqrt{-1}$. Here, S denotes stiffness, r characteristic (linear) dimension of the tectorial structure and ρ and μ are fluid density and dynamic viscosity respectively. Tuning characteristics depend on P_c. Two extreme situations are shown: (a) $P_c \ll 1$, short dashes: The tectorial structure detects velocity (20 dB decade^{-1}) up to the cutoff frequency $f_{co} = f_t P_c$. No resonance occurs. (b) $P_c \gg 1$, long dashes: The tectorial structure detects velocity up to the characteristic transition frequency f_t. Resonance occurs at approximately $f_r = f_t\sqrt{3P_c}$ with quality factor $Q_{3\,dB} = \frac{2}{3}[P_c/3]^{1/4}$. For intermediate values of P_c, a gradual change of the frequency response takes place as described by the expression for X_0.

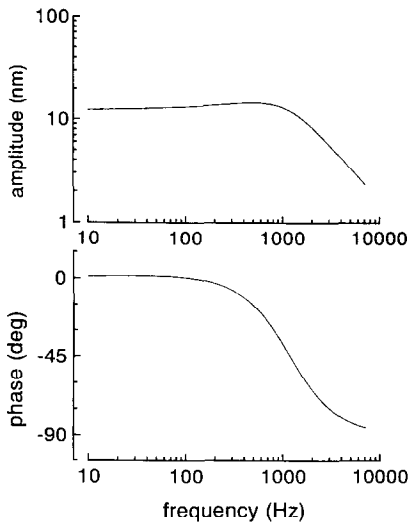

Fig. 6. Calculated frequency response (amplitude and phase) of an inner hair cell bundle based on the expression for X_0 (see legend Fig. 5) as a function of the frequency of a driving fluid flow with a velocity of 100 μm·s^{-1}. Parameters used are typical for an inner hair cell located about 14 mm from the stapes [41]: hair bundle stiffness 0.82×10^{-3} N·m^{-1}, hair bundle length = 5.2 μm; the viscosity was taken equal to that of water (10^{-3} kg (m s)$^{-1}$) resulting in $f_t \approx 5.9$ kHz and $P_c \approx 0.23 < 1$. Therefore, low pass characteristics with cutoff frequency $f_t P_c \approx 1.3$ kHz are to be expected.

4.2. Extension of the model to other hair cell systems and single hair bundle

In auditory and other mechanosensory organs the mechanical tuning characteristics are of prime importance. The use of the dimensionless number P_c may be extended to estimate the mechanical frequency characteristics of fluid driven, elastically coupled tectorial structures, having shapes other than (hemi) spherical. This is in parallel to the general significance of Reynolds numbers, for the calculation of which a characteristic dimension is required rather than a precise geometrical shape.

The calculated amplitude characteristics of fluid driven tectorial structures are schematically shown in Fig. 5, for low and high values of P_c. It has been shown [40] that if $P_c \ll 1$, there is no resonance and the system's response to fluid velocity has low-pass

characteristics with a cutoff frequency given by $f_{co} = f_t P_c$. If, however, $P_c \gg 1$, the system is tuned at a frequency approximately equal to $f_r = f_t\sqrt{3P_c}$ with quality factor equal to $Q_{3\,dB} = \frac{2}{3}[P_c/3]^{1/4}$. Since P_c is proportional to both hair bundle stiffness and (linear) characteristic dimension, tuning will be enhanced if more hair bundles are coupled to a larger tectorial structure. Absolute sensitivity at frequencies below f_r, however, will then decrease, since it is inversely proportional to P_c.

The model may also be applied to a single hair bundle driven by a fluid flow. Using estimated stiffness and length for inner hair cell bundles [41], which are presumably fluid driven, this yields the frequency response to constant velocity depicted in Fig. 6. It shows that solely on the basis of their micro- and hydromechanical properties, single hair bundles cannot be expected to be tuned. In addition, responses are attenuated with 20 dB decade^{-1} at frequencies exceeding approximately 1 kHz.

4.3. Effect of nonlinear (gating) stiffness on the mechanics of the cupula

The nonlinearity of hair bundle stiffness (gating compliance) may also be expected to effect the dynamics of tectorial structures. The mechanics of the lateral line cupula has indeed been found to be nonlinear [44]. Nonlinearity disappeared when the underlying hair cells and their bundles were damaged, suggesting that the hair cells, via their (nonlinear) gating compliance, cause the cupular mechanical nonlinearity. Further support for the notion that the transduction channels are the source of cupular nonlinearity comes from the close match between the measured responses and results from a model of

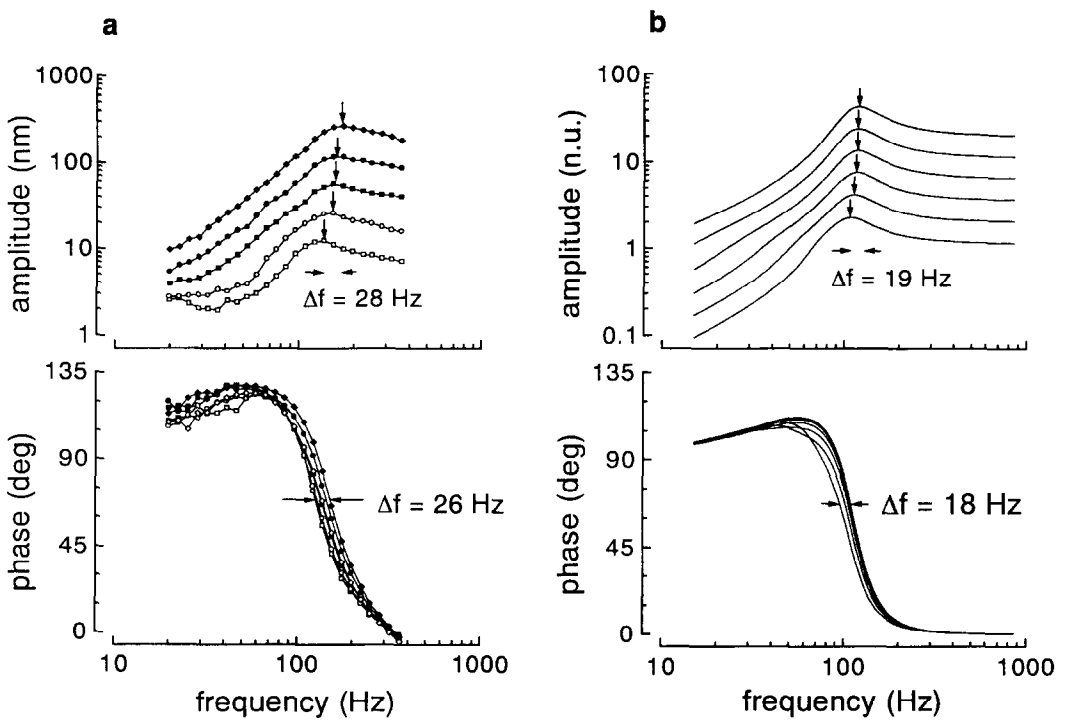

Fig. 7. Shift of cupular resonance frequency in ruffe as a function of level of stimulation. (a) Measured frequency responses of the cupula (no. III, following Jakubowski's numbering [46]) in the supraorbital canal in ruffe. Levels of stimulation are approximately 7 dB apart. (b) A comparable shift in resonance frequency was calculated over the same dynamic range of stimulus levels using parameters from previous studies [44]. Calculations in the time domain were made using a 4th order Runge–Kutta algorithm to combine nonlinear gating compliance with cupular hydrodynamics [45]. Amplitudes are normalized with respect to X_0.

cupular mechanics that includes the gating compliance [45].

Comparing the simulated responses with measured cupular nonlinearity, parameters of transduction were estimated under in vivo conditions [44]. The elementary gating force Z was of the order of 100 fN, in close approximation to in vitro studies [27,30]. The number of transduction channels per hair bundle was estimated to be of the order of 300.

A related consequence of the hair bundle stiffness not being constant is that the resonance frequency of a tectorial structure, which is dependent on the ratio of total stiffness to mass, is level dependent. This level dependence has been observed in the lateral line organ, as can be seen in Fig. 7. Resonance frequencies were found to shift tens of Hertz when the stimulus level of fluid flow in the canal was increased with a factor of approximately 25 (Fig. 7a). Similar shifts can be accounted for by the model of cupular mechanics incorporating the gating spring mechanics [45] (Fig. 7b).

A more detailed study of mechanical harmonic distortion caused by the gating spring dynamics gives predictions that may readily be verified in experimental studies on the mechanics of the lateral line organ and other hair cell systems [47].

4.4. Effects of transduction channel blockers on the mechanics of the cupula

Hair cell transduction channels have been shown to be reversibly blocked by aminoglycoside antibiotics [48], as well as by the diuretic amiloride and derivatives [49]. The half-blocking concentrations of both types of blockers are comparable (of the order of tens of μM).

The influence of these blockers on the mechanical properties of hair bundles has not extensively been investigated. Following application of aminoglycosides, an increase of hair bundle stiffness [27,50] and a possibly enhanced action of the molecular adaptation motor [36] has been reported. No information is available on the mechanical effects on hair cells in vitro induced by amiloride.

We recently compared the effects of these specific channel blockers on the mechanics of the cupula. When applied to the lateral line organ, it was found that the aminoglycoside dihydrostreptomycin and amiloride have an almost identical reversible effect on the mechanical frequency response of the cupula [38,51]. In both cases, the most prominent change in the frequency response is not a shift in frequency, as would result from stiffness changes, but rather a change in the damping characteristics. This change can be accounted for when hair bundle mechanics is extended with a resistive element R (see Fig. 8). The value of the element R per hair bundle decreases from about 2 to 0.5 $\mu N \cdot s \cdot m^{-1}$ as a result of application of the blockers at half-blocking concentrations.

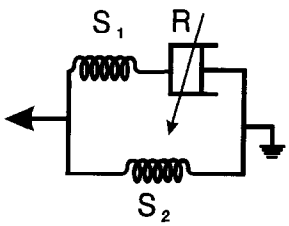

Fig. 8. Possible model of hair bundle mechanics. The horizontal arrow indicates the motion of the hair bundle. A change in the strength of resistive element (R) in series with a spring (S_1), both in parallel to another spring (S_2) accounts for the mechanical changes induced by dihydrostreptomycin and amiloride. Both channel blockers, when applied in concentrations of about tens of μM, reduce the value of R about fourfold.

A similar model for hair bundle impedance has been proposed earlier to explain the mechanically induced electrical adaptation [34] (see also subsection Adaptation). In that model, S_1 represents the gating spring and S_2 is associated with the pivoting stiffness of a hair bundle. A comparable value of R (6 $\mu N \cdot s \cdot m^{-1}$) was needed to explain the time constant of adaptation. No direct evidence exists for adaptation in lateral line hair cells, but extracellular potentials from the lateral line organ decrease at low frequencies as would be expected if the hair cells electrically adapt [12].

There is experimental evidence that a molecular motor is involved in adaptation, which is influenced by aminoglycosides [36]. The model considered here does not include such a motor. Alternative models, possibly including a molecular motor, may therefore also account for the observed phenomena.

From electrophysiological experiments it was previously found that the voltage dependence of the blocks caused by dihydrostreptomycin and amiloride

have different characteristics [48,49]. The identical mechanical effects of the two drugs described here, suggest more similarity in their mode of action on the transduction channel. From this similarity, however, no firm conclusions can be reached regarding the coincidence of their site of binding. In this respect, it is interesting that recent immunocytochemical experiments indicate that the two types of drugs block a common binding site at the stereociliar tips, which is presumably related to the transduction channel and possibly located in the contact region [52].

Evidently, more research is needed to establish the effects of the conformational changes of the transduction channel induced by these blockers and to investigate to what extent the existing models of hair bundle mechanics can account for it.

5. Concluding remarks

It has been demonstrated that the study of the mechanics of a tectorial structure gives information on the transduction process of the underlying hair cells under in vivo conditions. In this respect hair cells provide, via their hair bundle, a mechanical handle on the molecular forces involved in the gating of ion channels.

From the various experiments described, it appears that conformational changes of as few as 10^5 mechanoreceptor molecules, the estimated number related to a single neuromast, can change the dynamics of gross mechanical structures such as the cupula in the lateral line organ. This reflects the delicate construction of a mechanosensitive system that successfully performs its task to funnel the information encoded in a fluid flow efficiently into the mechanorecepting hair cells.

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