THE INTERPLAY BETWEEN ACTIVE HAIR BUNDLE MECHANICS AND ELECTROMOTILITY IN THE COCHLEA

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We present a physical description of cochlear mechanics by examining the interaction between active hair bundle motion and electromotility of the outer hair cell. We use a model for hair bundle mechanics which has been shown to account quantitatively for spontaneous oscillations and non-linear amplification observed in bullfrog hair cells. In the mammalian cochlea outer hair cell electromotility provides an additional mechanical feedback to the hair bundle which couples stereocilia and cochlear mechanics. We show that this combined system can exhibit spontaneous oscillations and can provide active amplification and cochlear nonlinearity.

1. Introduction

At present the mechanism by which the cochlea amplifies sound is unknown. However, several features of the "cochlear amplifier" have been identified. The discovery of otoacoustic emissions and in particular spontaneous otoacoustic emissions provides the most direct support for the proposition that the "cochlear amplifier" is active [1, 2], a hypothesis which is based on the observation that an active process is necessary in order to overcome the effects of viscous damping in the inner ear [3]. Moreover, amplification is frequency selective and nonlinear, the latter allows the ear to function over 120 dB of sound pressure levels [4, 5, 6].

The hair bundle has been proposed to be the key component for active amplification in non-mammalian vertebrates and recent observations indicate that active hair bundle motility may play a role as part of the "cochlear amplifier" in mammals [7, 8]. Indeed, individual hair bundles exhibit many of the features of the cochlea as a whole. Spontaneous oscillations have been observed and have been shown to be active [9, 10, 11, 12, 13, 14, 15]. The hair bundle can amplify mechanical stimulation in a frequency dependent manner[13, 16]. Finally, the response of the hair bundle to external stimulus is nonlinear and compressive [17]. However, it is possible that the hair bundle alone is not sufficient for amplification once it is embedded within the cochlea.

Since the first observations of outer hair cell electromotility, [18, 19], there has been much investigation into how the inner ear can utilise such motility. While the electromotile response is in phase and undiminished for frequencies up to at least 79 kHz with the electric potential difference across the basolateral membrane of the outer hair cell, there is very significant attenuation of the receptor potential created by deflecting the hair bundle [20]. In other words, the outer hair cell membrane capacitance acts to low pass filter the voltage changes across the membrane due to the current through the hair bundle, with a corner frequency which is several octaves below the place frequency of each outer hair cell [21]. This problem would
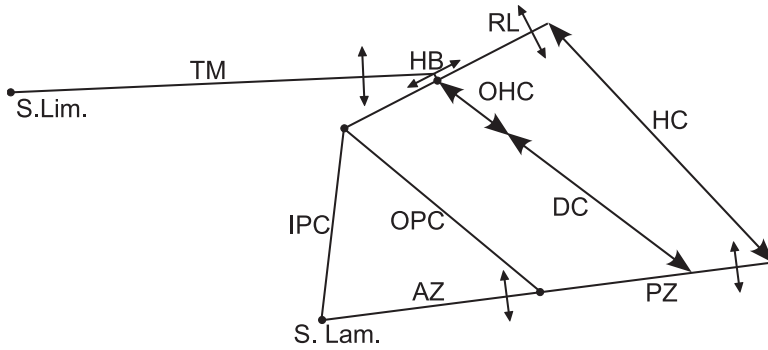
Fig. 1.   Organ of Corti slice. Filled circles – pivot points, arrows – displacements or length changes. S. Lam. – basilar membrane meets spiral lamina, S. Lig. – tectorial membrane meets spiral limbus, IPC – inner pillar cell, OPC – outer pillar cell. Beams: TM – tectorial membrane, HB – hair bundle, RL – reticular lamina, AZ – basilar membrane arcuate zone, PZ – basilar membrane pectinate zone. Springs: OHC – outer hair cell, DC – Deiter cell, HC – Hensen cells

appear to prohibit the electromotile response from amplifying the motion of the organ of Corti on a cycle by cycle basis as is required[22, 23]. However, a targeted deletion in prestin, the membrane protein responsible for electromotility, produces a 40-60 dB loss in cochlear sensitivity *in vivo*[24, 25]. Thus, electromotility would appear to be an essential element of the "cochlear amplifier".

2. Methods

We study the interaction between outer hair cell electromotility and the active hair bundle by considering the interaction of a single effective electromotile outer hair cell with a cross section of the cochlea. The mechanics of the organ of the Corti is described as a system of springs attached to rigid beams (Fig. 1), which pivot about one end. This system is linear for small deflections of the beams about their pivot points. This is expected to be the range over which the organ of Corti operates *in vivo* as, for example, the deflection of a 4 μm outer hair cell hair bundle by only three degrees constitutes its operating range [26].

The hair bundle is described by a model for active hair bundle mechanics which has been shown to quantitatively describe isolated hair bundles from the sacculus of the bullfrog and to be capable of producing the same behaviours which are observed for the hair bundles of the turtle and the rat[27, 28]. The model consists of two coupled differential equations for the position of the hair bundle and the average position of motors, which apply forces on the transduction channels of the hair bundle as they walk along the actin filaments inside the stereocilia of the bundle. Here we employ a version of this model without noise, although a consideration of noise is required for a quantitative understanding of isolated hair bundles[27].

Electromotility is nonlinear over a range of about 200 mV [29]. However, the receptor potential changes by at most 5 mV around the resting potential which allows us to linearise about this point [21]. The electromotile outer hair cell is described as
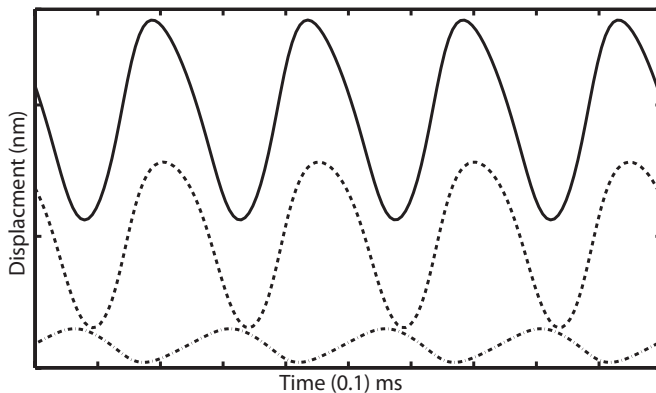
Fig. 2.   Oscillations. From top: hair bundle displacment, pectinate zone displacment, arcuate zone displacement.

a linear piezoelectric material. Indeed, the outer hair cell satisfies the same reciprocal relations which characterise a piezoelectric material within the linear response regime [30].

Finally, we introduce a single effective ion species as an idealisation for the many ion species which are found within the cochlea. We assume that the stria vascularis maintains a constant ion concentration within the endolymph and perilymph which bathe the apical and basal portions of the outer hair cell, respectively. We describe the rate of change in the displacement of charge in the outer hair cell from a reference state as being a linear function of both the open probability of the mechanoelectrical channels of the hair bundle and the electric potential relative to the constant potentials of the scala media and scale tympani.

We find that the dynamics of the entire system may be described by three coupled equations for the deflection of the hair bundle the average motor displacement and the change in the change in the effective charge inside the outer hair cell, in the limit where the other system variables' (Fig. 1) intrinsic relaxation times are small in comparison to these three slower variables. We defer a detailed description of the model to a future publication and simply note that the elastic coupling of the organ of Corti (Fig. 1) introduces a feedback from the electromotile basolateral wall of the outer hair cell to its hair bundle. This feedback may be described, to linear order, as an additional effective stiffness and damping for the hair bundle. The signs of these effective terms depends on the elastic properties of the surrounding organ of Corti.

3. Results

We consider the case where the electromotility of the outer hair cell provides effective negative damping to the hair bundle. Using parameters corresponding to the 4 kHz region of the cochlea we find that this system may oscillate spontaneously at about 4 kHz (Fig. 2). The spontaneous oscillation frequency is not limited by
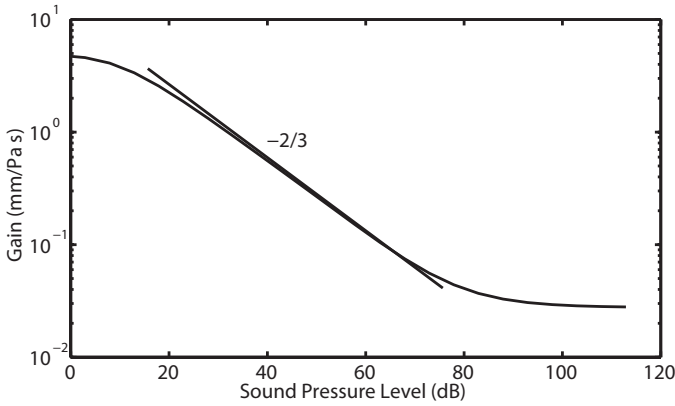
Fig. 3.   Basilar membrane gain.

the membrane capacitance of the basolateral wall of the outer hair cell due to the presence of the feedback.

Small changes in the parameters result in a quiescent system which resides near a critical instability known as a Hopf bifurcation [31, 32]. The response magnitude of the system to a periodic pressure difference across the basilar membrane at a frequency of about 4 kHz displays a region with a power law dependence on stimulus magnitude characteristic of a system near such a critical point (Fig. 3) [31, 32]. This response is very similar to experimental observations of basilar membrane motion [5].

4. Discussion

The gating spring hypothesis is that the open probability of the hair bundle's mechanoelectrical channel is a non-linear function of the displacement of the hair bundle [33, 34, 35]. This is the single essential nonlinearity in our description of the system which in concert with negative feedback from the Ca^{2+} ions, which enter the channel, allows for a region of parameter space for which the system oscillates [27]. The region of nonlinear compression we report (Fig. 3) with a slope of -2/3 is generic to any system which resides near the transition between the region of oscillations and the quiescent region[31, 32]. Such a transition from a quiescent system to an oscillatory one, as a control parameter is varied, is known as a Hopf bifurcation[31, 32].

Our work suggests that amplification in the cochlea may result from a combination of active hair bundle mechanics with electromotility.

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