Enhanced signal-to-noise ratios in frog hearing can be achieved through amplitude death

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In the ear, hair cells transform mechanical stimuli into neuronal signals with great sensitivity, relying on certain active processes. Individual hair cell bundles of non-mammals such as frogs and turtles are known to show spontaneous oscillation. However, hair bundles in vivo must be quiet in the absence of stimuli, otherwise the signal is drowned in intrinsic noise. Thus, a certain mechanism is required in order to suppress intrinsic noise. Here, through a model study of elastically coupled hair bundles of bullfrog sacculi, we show that a low stimulus threshold and a high signal-to-noise ratio (SNR) can be achieved through the amplitude death phenomenon (the cessation of spontaneous oscillations by coupling). This phenomenon occurs only when the coupled hair bundles have inhomogeneous distribution, which is likely to be the case in biological systems. We show that the SNR has non-monotonic dependence on the mass of the overlying membrane, and find out that the SNR has maximum value in the region of amplitude death. The low threshold of stimulus through amplitude death may account for the experimentally observed high sensitivity of frog sacculi in detecting vibration. The hair bundles’ amplitude death mechanism provides a smart engineering design for low-noise amplification.

1. Introduction

The ear can actively amplify weak signals to achieve great sensitivity and a wide dynamic range of hearing. Hair cells of the vertebrate inner ear are the mechano-transducers which have been proposed to amplify weak signals by generating active forces [1,2]. While amplification in the mammalian cochlea is widely believed to originate from the membrane dynamics involving outer hair cell motility [3], non-mammalian vertebrates lack outer hair cells. Nevertheless, the ear of lower vertebrates achieves acute hearing [4–6]. The exact mechanism is not yet clearly known. Hair bundle motility probably underlies the amplification process. Unlike mammalian hair cells, spontaneous oscillations have been observed in individual hair cells of turtles [1] and frogs [2,7]. The spontaneous oscillations are believed to result from adaptation dynamics driven by molecular motors in hair bundles [1,2,8]. The oscillation may provide an amplification mechanism through a synchronization process [9,10], where the oscillation frequency is locked to the frequency of the external stimulus. However, in recent experiments under more natural conditions than previously studied, frog hair bundles with an overlying membrane are found not to spontaneously oscillate, but are, in fact, quiescent [11,12]. Furthermore, one can imagine that the auditory neuron would receive strong noisy signals from spontaneous oscillations [2,7,8], as their magnitudes are about 20–50 nm, which can cause significant changes in the open probability of the mechanotransducer channel [7,8].

If the spontaneous activity of the bundles is suppressed by their overlying membrane, then how does this activity contribute to frogs’ auditory transduction? Here, we try to answer this question by providing a low-noise amplification mechanism for the bullfrog sacculus. Using numerical simulations of models of bullfrog sacculi, we investigate the mechanotransduction properties of inhomogeneous hair bundles with elastic coupling and mechanical loading. We show that a low-noise...
amplification arises as a result of inter-bundle interactions and hair bundle motility. A phenomenon that provides for this low-noise amplification mechanism is amplitude death—the cessation of oscillation owing to the coupling of oscillators [13]. This intriguing phenomenon was first noted in the nineteenth century by Rayleigh [14], who found that adjacent organ pipes can suppress each other’s sound.

Because amplitude death is a universal phenomenon appearing when any two or more different oscillators are coupled [10,15], it has gained a great deal of attention in the physics community. The required conditions for amplitude death of the oscillators are the coupling between them and their inhomogeneity. The frog saccules may satisfy these requirements. First, the hair bundles of a frog’s sacculus in vivo are coupled through the otoconial membrane [16]. As for the inhomogeneity, the hair bundles may have different dynamical properties. Experiments report that some of the hair bundles show spontaneous oscillation, whereas the others remain quiescent [2,11]. The frequencies of spontaneous oscillations in the saccules are randomly distributed in a sacculus with a range of $5–50$ Hz [17].

Noise is the natural constraint that limits the sensitivity of sensory systems. To investigate the noise effect carefully, we develop a numerical calculation method for thermal noise force. In the absence of any active process, according to the equipartition theorem, the average kinetic energy of a passive mechanical sensor in thermal equilibrium is given by the thermal energy. This theorem is satisfied by the thermal noise force. Equipped with the noise force, we simulate the dynamics of hair bundles with an overlying membrane, and find that the amplitude death phenomenon suppresses noise and enhances the signal transmission. We find that there exists an optimal value of the mass of the overlying membrane which gives the maximum signal-to-noise ratio (SNR). The hair bundles in this optimal condition turn out to be in the region where amplitude death is seen, which indicates that the hair bundles are likely to exploit amplitude death for signal transmission.

2. Physical model for elastically coupled hair bundles through a massive membrane

We consider the dynamical properties of bullfrog hair cell bundles coupled by an overlying membrane with finite mass. We model the membrane by an overlying membrane with finite mass. We consider the dynamical properties of bullfrog hair cell bundles coupled by an overlying membrane, which are elastically coupled to each other and also attached to hair bundles (figure 1). We model the membrane by a massive membrane tied to the mass at $(i,j) = (l(l),l(l))$, so that $S_{i,j}(t) = X_{i,j} f_{HB,j}$ is determined through equation (2.2), which is the force on the membrane of the $l$-th hair bundle. $f_{i,j}$ is the thermal noise force exerted on the $l$-th hair bundle. $y$ is the friction constant per mass of the membrane, $k$ is the inter-bundle elastic coupling strength and $\lambda$ is the friction constant of a free-standing hair bundle. $\delta_{i,j}$ is the Kronecker delta, which is $1$ if $i=j$, otherwise $0$. The acoustic stimulus delivered to the hair bundles is $f(t)$. The individual hair bundles are based on the rigorous model for bullfrog saccules hair cells [8,18]. In this model, active hair bundle movement results from the Ca$^{2+}$-dependent activity of the molecular motors, which are connected to transduction ion channels through gate springs. $k_{sp}$ is the intrinsic stiffness of the pivot spring of the $l$-th hair bundle. While the bundle’s position $X_{i,j}$ is set to zero when the pivot spring force vanishes, its actual equilibrium position can be about $-70$ nm owing to the gating spring. Equation (2.3) describes the molecular motor position $X_{i,j}$ of the $l$-th hair bundle where $\lambda_{i,j}$ is the parameter relating a force to the velocity of the molecular motor. $F_{o,j} = 0.14 f_{\max} (a_1 - 0.65 P_{o,j})$ is the active force from the molecular motor. $D$ is the gating spring elongation and $P_{o,j} = 1/(1 + \exp(X_{i,j} - X_{o,j} + 16.7 \text{ nm}/4.53 \text{ nm}))$ is the open probability of the $l$-th ion channel. To simulate the inhomogeneity of hair bundles, we used the non-uniform distribution of pivot spring stiffness $k_{sp}$ and the maximal force of the motor molecules $f_{\max}$, where these parameters are influenced by the minute difference in the size of the hair bundles. Using Gaussian random number generators (gsdev function in numerical recipes in FORTRAN [21]), we generated random distributions of parameters around $\langle f_{\max} \rangle = 342$ pN and $\langle k_{sp} \rangle = 0.65$ pN nm$^{-1}$ with a variance of approximately $7$ pN and $0.05$ pN nm$^{-1}$, respectively. Figure 1a,c shows an example of the set of parameters and their spatial distribution. The experimental error of the parameters in Martin et al. [8] can be considered as the upper bound of the actual variance of the parameters, so we have chosen smaller values than the experimental errors. This is not harmful to proving the existence of amplitude death as the phenomenon arises more easily for larger variance.

For most active biological systems, accurate treatment of the thermal noise force is important, because the coherence of spontaneous motion is often vulnerable to thermal noise. The autocorrelation function of the thermal noise force is usually expressed using the white noise approximation, $\langle f_{i,j}(t) f_{i,j}(t + \tau) \rangle \propto \delta(\tau)$ ($\delta(\tau)$ is the Dirac delta function, which is defined to be zero except at $\tau = 0$, and $\int \delta(\tau) \, d\tau = 1$). The noise force strength is determined to satisfy the equipartition theorem, so the proportionality constant is approximated by $2k_{B}T$ times the frictional constant. In reality, however, the correlation time is not exactly zero, so it is not possible to have the exact Dirac delta function. For the system with a finite correlation time, we have to re-determine the strength of the noise force; otherwise, the thermal noise does not satisfy the equipartition theorem, (velocity$^2$) = $k_{B}T/m$, where $T$ is the temperature. Thus, we derive and use a relation between the noise force strength and its correlation time, satisfying the equipartition theorem. The autocorrelation function of the thermal noise force$^2$ then reads

$$
\langle f_{i,j}(t) f_{i,j}(t + \tau) \rangle = \frac{2k_{B}T \lambda_{i,j} \delta(\tau)}{\exp[2/\lambda_{i,j} \lambda_{s}/m] \epsilon r f(\pi/2(\lambda_{s}/m)) \sqrt{\pi} \tau} e^{-\tau/\tau_c},
$$

(2.4)
where \( \lambda_S = \lambda + m g \) is the net friction constant for an individual hair bundle. One can note that the magnitude of the noise force has roughly \( \approx 1/\sqrt{\tau_c} \) dependence on the correlation time for \( \tau = 0 \). Using equation (2.4), we determine the correct amplitude of the noise force which satisfies the equipartition theorem (see electronic supplementary material for the derivation of the formula).

Some further remarks on our model are due. The coupling in equation (2.1) describes the elastic coupling for small amplitude oscillation, and the motion of hair bundles is assumed to be unidirectional to mimic the fact that the bundles’ deflection is mainly in the directions towards the tallest or the shortest bundle. While we find the amplitude death phenomenon also in a purely one-dimensional array, we choose the particular two-dimensional array shown in figure 1a to describe the structure of the hair bundle array in a saccus (see fig. 3 of [11]). To describe the internal dynamics of the membrane, we consider an additional mass element between two hair bundles. So, we use 100(N = 10) mass elements for the overlying membrane, whereas 50 hair cells are beneath the membrane. We simulate 50 hair cells for computational efficiency, even though the number of hair cells in a frog’s saccus is about 10 times larger [11]. Because we do not find any significant difference from 10 hair cells concerning amplitude death, we do not think the size of the array is an important factor in amplitude death. We used a closed boundary condition, as in biological systems. The effective mass \( m \) includes a fluid compartment and an otolithic mass that are assumed to move in unison with the hair bundles. Unfortunately, there is no experimentally known value for the effective mass owing to the difficulty of its measurement. In our simulations, we

Figure 1. (a) Schematic figure for the elastically coupled hair bundles with mechanical loading and a schematic figure for a free-standing hair bundle. (b) An example of the parameter distribution. The symbols in red denote the parameters for the hair bundles which have spontaneous oscillating motion in their free-standing states. (c) Spatial distribution of the spontaneously moving hair bundles (red) and quiescent bundles (grey). (d) The stroboscopic view (snap shots at every 0.5 s for 100 s) of 50 uncoupled hair bundles (\( k = 0 \)). Each hair cell is numbered using the hair cell index \( i \). The position of the oscillating hair bundles is spread out as the centre frequency of their motion is about 5 Hz. (e) The stroboscopic view of the amplitude death state (\( k = 2 \text{ pN nm}^{-1} \)), which shows the cessation of the spontaneous oscillation shown in (d). Parameters used are listed in table 1. (Online version in colour.)
Table 1. List of the parameters for the simulations. When other values for the parameters are used, they are listed in the figures or in the figure captions.

<table>
<thead>
<tr>
<th>parameter</th>
<th>definition</th>
<th>value</th>
<th>references</th>
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<tbody>
<tr>
<td>m</td>
<td>the mass of one unit of cross-cut membrane</td>
<td>2 μg</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>thermal noise correlation time</td>
<td>1.4 ms</td>
<td></td>
</tr>
<tr>
<td>k</td>
<td>inter-bundle elastic coupling stiffness</td>
<td>0–2 pN nm⁻¹</td>
<td></td>
</tr>
<tr>
<td>γ</td>
<td>friction constant per mass of the membrane</td>
<td>0.5 kHz</td>
<td></td>
</tr>
<tr>
<td>kgs</td>
<td>gating–spring stiffness</td>
<td>0.75 pN nm⁻¹</td>
<td>[8]</td>
</tr>
<tr>
<td>D</td>
<td>gating spring elongation</td>
<td>60.9 nm</td>
<td>[8]</td>
</tr>
<tr>
<td>(kbp)</td>
<td>mean value of hair bundle pivot stiffness</td>
<td>0.65 pN nm⁻¹</td>
<td>[8]</td>
</tr>
<tr>
<td>δkbp</td>
<td>variance of hair bundle pivot stiffness</td>
<td>0.05 pN nm⁻¹</td>
<td></td>
</tr>
<tr>
<td>(f0max)</td>
<td>mean value of maximal motor force</td>
<td>342 pN</td>
<td>[18]</td>
</tr>
<tr>
<td>δf0max</td>
<td>variance of maximal motor force</td>
<td>7 pN</td>
<td></td>
</tr>
<tr>
<td>λ</td>
<td>friction of a hair bundle</td>
<td>2.8 μN s m⁻¹</td>
<td>[18]</td>
</tr>
<tr>
<td>λa</td>
<td>friction of adaptation motors</td>
<td>10 μN s m⁻¹</td>
<td>[19]</td>
</tr>
<tr>
<td>T</td>
<td>temperature</td>
<td>300 K</td>
<td></td>
</tr>
<tr>
<td>Pω</td>
<td>open probability of the ω-th ion channel</td>
<td>1/(1 + \exp(X2 - X0 + 16.7 nm/4.53 nm))</td>
<td>[18,20]</td>
</tr>
<tr>
<td>N</td>
<td>linear size of the two-dimensional mass array</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Nc</td>
<td>number of hair cells</td>
<td>50</td>
<td></td>
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use 2 μg for m, which will be shown here to be close to an optimal value for high SNR. Because a frog sacculus is a detector for low-frequency vibration and sound of wavelengths larger than the size of the sacculus, we assume that the acoustic stimulus is uniform across all units.

3. Results and discussion

3.1. Amplitude death of coupled hair bundles

When the non-identical hair bundles are coupled elastically with sufficient strength, we find their spontaneous oscillations become quenched at a certain strength in the absence of thermal noise (figure 1a,b). While the value for the coupling strength varies depending on the distribution of the hair cell parameters, we find that amplitude death arises at around $k \approx 1$ pN nm⁻¹. The origin of amplitude death lies in the stabilization of the fixed point (quiescent bundle state) as a consequence of interaction. It can occur in coupled oscillators with parameter mismatch [13], time-delayed coupling [22] and nonlinear coupling [23]. The amplitude death phenomenon of coupled hair bundles in our simulation arises as a result of parameter mismatches. The existence of this phenomenon is evidenced by the recent experimental observation of the cessation of spontaneous oscillations of hair bundles in bullfrog sacculi when they are coupled by an overlying membrane [11].

The amplitude death region in the presence of thermal noise shows, instead of perfect quenching, suppressed fluctuations of mechanical motions (figure 2a). We performed numerical simulations using 17 sets of the parameters with the same mean values and variances. Even though we show only four of them in figure 2f for better visibility of the figure, we found amplitude death in all cases (see electronic supplementary material, figure S8). To examine the occurrence of amplitude death, it proves useful to plot the positional variance $\delta X$ instead of its Fourier component, because the spontaneous motion is not very sinusoidal. As inter-bundle coupling strength increases, the positional variance $\delta X$ increases rapidly owing to synchronized spontaneous movement. It decreases later owing to amplitude death. Amplitude death arises at around $k = 1$ pN nm⁻¹ (see also electronic supplementary material, figure S8). This cross-over value for amplitude death is not universal, but it depends on the distribution of the parameters, the membrane mass or the noise correlation time. We find that the cross-over to the amplitude death region arises at weaker coupling strength for shorter thermal correlation time $\tau_c$ (see electronic supplementary material, figure S5a).

3.2. Response of open channel probability to external stimulus

Let us consider the neural response of the hair bundles in the amplitude death state. The influx of cations through the transduction channels depolarizes the cell membrane, which opens voltage-gated channels at the base of the hair cell and generates a synaptic current [24]. The information on the auditory stimulus is passed along the auditory nerve in the form of a spike train. Simplifying the process, we assume that the neuron spike rate is proportional to the transduction current [25]. Then, concerning the spike rates of a bundle of neurons, rather than the averaged displacement of hair bundles, it is more appropriate to consider an averaged open probability,

$$P_o' = \frac{1}{N_c} \sum_{i=1}^{N_i} P_{o; i},$$

(3.1)

where $N_i$ is the number of hair cells.

In figure 2h–d, we plot $P_o'(t)$ when a pure tone stimulus at a frequency of 6 Hz is applied when time is more than 40 s and less than 60 s. Compared with the case of uncoupled
3.3. Signal-to-noise ratio

The sources of noise can be divided into those which arise from (i) fluctuation associated with an active force generated by hair bundles, (ii) thermal fluctuation associated with the Brownian motion of hair bundles, and (iii) fluctuation associated with the stochastic nature of channel opening. Source (i) appears to dominate at weak couplings where the bundles are free-standing or showing collective spontaneous motion. Source (ii) is the main source of noise in the amplitude death region where the hair bundles’ spontaneous movements are suppressed.

The hair bundles’ active forces magnify the mechanical response of the oscillatory stimulus, but this amplification also enhances the background noise. To investigate the competition between the signal amplification and the noise reduction, we calculate the power spectra of mechanical displacement,

$$\tilde{S}_X(\omega) = \frac{1}{N} \sum_{j=1}^{N} |\hat{S}_j(\omega)|^2, X_j(\omega) = \frac{1}{T_o} \int_{t}^{t+T} X_j(t) e^{i\omega t} dt,$$

(3.2)

where $T_o$ is the time period for the Fourier transformation and $\omega = 2\pi f$ is the angular frequency. We plot $\tilde{S}_X(\omega)$ for an $f = 6$ Hz pure tone signal of amplitudes 0.05 pN (figure 3a–c) and 0.5 pN (figure 3d–f). When a weak acoustic signal is applied to uncoupled hair bundles, the signal can be drowned in the power spectrum as shown in figure 3a. While one can see an amplified signal by weakly coupled hair bundles in figure 3b, the intrinsic noise is also strong and the single tone signal at 6 Hz is vaguely seen (see arrow in figure 3b). In contrast to these cases, the input acoustic signal can be clearly seen in the amplitude death region (figure 3c) where the background noise level is severely reduced by about two orders of magnitude.

For the signal with sufficient strength (figure 3d–f), the amplification of the oscillatory stimulus is more prominent than the background noise reduction. For the signal with an amplitude of $F = 0.5$ pN, the power spectra of coupled hair bundles in figure 3c,f show the second harmonic at $2f = 12$ Hz owing to the nonlinearity. This is in contrast to the case of uncoupled hair bundles (figure 3d), which does not show the harmonics. When a weak signal is applied to the system in the amplitude death region, noise reduction (rather than signal amplification) more significantly contributes to the enhancement of the signal transmission (figure 3a–c). Provided the neuronal threshold is low enough, the amplitude death phenomenon allows the auditory systems to have a low threshold of acoustic stimulus.

SNR is a measure that compares the level of a desired signal with the level of background noise. It is defined by

$$\text{SNR} = \lim_{\Delta \omega \rightarrow 0} \frac{\tilde{S}_X(\Omega)}{\Delta \omega \int_{\Omega - \Delta \omega/2}^{\Omega + \Delta \omega/2} \tilde{S}_X(\omega) d\omega},$$

(3.3)

where $\Omega$ is the angular frequency of the oscillatory stimulus; $F(\Omega) = F \sin \Omega t$ in equation (2.1). In figure 3g–i, we plot the SNR for various parameters. We find that the SNR increases steadily as we decrease the noise correlation time (figure 3g). Because the noise strength and the bandwidth of the thermal noise is inversely proportional to the correlation time, our finding indicates a positive role of noise in the sense that the SNR increases with the noise strength. However, the physical origin of this phenomenon must be different from the orthodox theory of stochastic resonance [26], because

Figure 2. (a) The positional variance $\delta X = \sqrt{\langle X^2 \rangle - \langle X \rangle^2}$ of the averaged displacement $X = 1/N \sum X_i$ over hair cells where $\langle \rangle$ means time average, which shows suppression of the mechanical fluctuation of hair bundles as the inter-bundle coupling strength increases. The initial $\delta X$ increase is due to the synchronization of the hair bundle movement. Each colour denotes the result for each set of parameters, which is shown in the inset. The response of the averaged open probability $P^o(t)$ to a 6 Hz stimulus $F(t) = \sin(6 \times 2\pi$ (time $^{-1})$) pN for 40 s < time < 60 s (otherwise, $F(t) = 0$) is shown (b) when the hair bundles are uncoupled ($k = 0$), (c) when the hair bundles show a coherent spontaneous motion ($k = 0.5$ pN mm$^{-1}$) and (d) when the hair bundles are in the amplitude death region ($k = 2$ pN mm$^{-1}$). In the amplitude death state (d), the spontaneous fluctuation in (c) is strongly suppressed but the response is still significantly stronger than the uncoupled case in (b). Parameters used are listed in table 1. (Online version in colour.)
we observed that SNR is simply decreased by a fictitious increase of the noise strength at a fixed correlation time.

3.4. Optimal loading for signal-to-noise ratio and amplitude death

Our simulation of the system shows that the SNR has approximately monotonic dependence on the elastic coupling strength $k$ (figure 3h). Meanwhile, we find that the SNR has non-monotonic dependence on the mass of the overlying membrane (figure 3i). We find that there exists an optimal value of the mass which maximizes SNR. This is a result of the competition between active amplification and noise reduction. The force signal to a hair bundle is more amplified (accelerated) for lighter masses, but the hair bundle’s motion also becomes more noisy. This noisy motion is suppressed by the inter-bundle coupling.

Figure 3. The power spectra of mechanical displacement $\tilde{S}_X(\omega)$ as a function of frequency $f = \omega/2\pi$ when a 6 Hz stimulus is applied with amplitudes of $(a–c) F = 0.05$ pN and $(d–f) F = 0.5$ pN. The coupling strengths are $(a,d) k = 0$, $(b,e) k = 0.3$ pN nm$^{-1}$, $(c,f) k = 1.4$ pN nm$^{-1}$. The time period for Fourier transformation $T_a$ is 100 s. Note the remarkable change in the noise floor level in the figures from $(a)$ to $(f)$. A second harmonic at 12 Hz appears in $(e,f)$. $(g)$ SNR as a function of the correlation time $\tau_c$ for $k = 1.2$ pN nm$^{-1}$. $(h)$ SNR as a function of the coupling strength $k$ for the various masses and $\tau_c = 1.4$ ms. $(i)$ SNR and $\Delta X$ as a function of the mass $m$ for $\tau_c = 1.4$ ms and $k = 1.2$ pN nm$^{-1}$, which shows that the SNR has maximum value at $m = 3 \mu g$ in the amplitude death region. The inset shows the power spectra for different mass $m$. For the simulation from $(g)$ to $(i)$, $F = 0.1$ pN. We used the averaged power spectra over 10 different trials of the thermal noise force. Parameters used are listed in table 1. (Online version in colour.)
and we find that the maximal SNR arises when the hair bundles are in the amplitude death region. Figure 3i shows that, when SNR reaches its peak value at \( m = 3 \) μg, the positional variance \( \delta X \) is already minimal. Therefore, we conclude that the active hair bundles of a bullfrog’s sacculus may rely on the amplitude death mechanism to enhance signal transmission.

There has been a long-standing problem with regard to the anomalously low threshold of acoustic stimulus in hair bundles [27]. If the individual hair bundle is described by a mass \( m \) on a spring of stiffness \( \kappa \), its positional fluctuation in thermal equilibrium is \( \delta X = \sqrt{\kappa T/\kappa} \) according to the equipartition theorem. Thus, theoretical \( \delta x \) is larger than 2 nm because in no inner-ear organ has the bundle stiffness been found to exceed \( \kappa \sim 1 \) pN nm\(^{-1} \) [27]. But many experimental data suggest that the displacement of less than 0.1 nm is readily detectable (see Bialek [27] and references therein). We think that amplitude death may provide a key to this problem. In the amplitude death region, the positional fluctuations of coupled hair bundles are strongly suppressed, so that \( \delta x \) can be as small as 0.1 nm in spite of thermal noise. In this region, the hair bundles can detect even \( F \sim 0.05 \) pN where the signal is clearly visible compared with the background noise level (figure 3c). This signal would be completely drowned out if they were uncoupled (figure 3d). Assuming that \( F \sim 0.05 \) pN is the minimum detectable stimulus, we can estimate the mass per hair bundle as \( m \approx 0.05 \) pN/\( a_0 \), where \( a_0 \) is the smallest detectable peak acceleration of vibration. Lewis et al. [6] reported that a frog’s sacculus can detect the acceleration down to \( a_0 \sim 10^{-6} \) g \( \sim 10^{-5} \) m s\(^{-2} \). From this value, we estimate \( m \approx 5 \) μg, which is not significantly different from the mass causing the maximal SNR in figure 3i. This estimation leads us to reason that the anomalously low stimulus threshold \( \delta x \sim 0.1 \) nm might be achieved through the amplitude death mechanism, which is difficult to detect by an individual hair bundle [8].

### 3.5. Frequency selectivity

In figure 4a, b, we plot the mechanical response of the hair bundles \( |X(\omega)| = |1/N_c \sum_\ell \tilde{X}_\ell(\omega)| \) for the stimulus of frequency \( f = \omega/2\pi \). The spontaneous oscillating region (figure 4a) shows slightly better frequency selectivity than the amplitude death region (figure 4b) only for weak enough stimuli (\( F \leq 0.8 \) pN). For the stimuli with \( F > 0.8 \) pN, the broadening of the response spectra in both regions is similar. There is no significant difference in the frequency selectivity between the two regions because of the inhomogeneous distribution of hair bundles. The inhomogeneity in our calculation was sufficient to prevent the hair bundles from locking to a single-frequency mode. The frequency selectivity is quantified in terms of height \( |X_{\text{max}}| \) of the spectral peak at its characteristic angular frequency \( \omega_0 \), and its quality factor \( Q = \omega_0/|\omega_2 - \omega_1| \), where the half width \( |\omega_2 - \omega_1| \) is defined by \( |X_{\text{max}}| = |X_{\text{max}}| = |X_{\text{max}}|/2 \). Our numerical results for coupled hair bundles of a frog’s sacculus show \( Q \sim 1 \) (figure 4c). This is consistent with electrophysiological recordings from frog auditory nerve
fibres which indicate a high sensitivity to small stimuli (approx. 0.1 nm) but poor frequency selectivity ($Q < 1$) [4,5]. A recent experiment [12] even reports the absence of frequency tuning in frog saccule when hair bundles are coupled to an overlying membrane. The complete disappearance of frequency selectivity in Strimbu et al. [12], however, is probably caused by the heavier weight of the artificial membrane in the experiment. In our calculations, as we increase the membrane mass, we observe that the peak frequency is lowered and eventually the frequency selectivity disappears (see the electronic supplementary material, figure S4).

3.6. Comparison with existing models and experiments
Our theory as well as the lower frequency selectivity in experiments [4,5,12] are in contrast to the theoretical prediction in Dierkes et al. [28]. The coupled hair bundle model [28] shows sharp frequency selectivity, but amplitude death did not appear in the model. We think one of the reasons for the discrepancy is that their non-uniformity was not sufficient to cause amplitude death. It might also be useful to note that, when characteristic frequencies are similar, coupling oscillatory and quiescent hair bundles can cause amplitude death more efficiently.

Eguíluz et al. [29] and Camalet et al. [25] proposed a generic model which might underlie the essential nonlinearity [30], where hair cells are assumed to operate at the critical point of Hopf bifurcation [9]. According to the critical oscillator model [25,29], the amplitude response of hair bundles to an oscillatory stimulus with strength $F$ scales as approximately $F^{1/3}$ for arbitrarily weak signals. In our model, the hair cell bundles in the amplitude death region show a linear response at weak stimuli. The response evolves to the region where it shows compressive rates close to a one-third law (figure 4d). The cross-over of the growth from linear to one-third nonlinear rates in figure 4d is consistent with the analytic formula derived from the generic mathematical model of amplitude death (see electronic supplementary material). The hair bundle nonlinearity shown here is similar to what has been consistently observed in experiments on mammalian cochlea after Rhode [30], where the transition between linear and compressive nonlinear growth has been reported [31–33]. Our theory is not incompatible with the theory [18,25] of individual hair bundles. As in Nadorwski et al. [18], our individual hair bundles are assumed to be near the Hopf bifurcation critical point. They were randomly distributed near the critical point with a small distribution width.

Stochastic resonance is a phenomenon where SNR is maximized in the presence of a specific non-zero-level noise. This phenomenon widely occurs in threshold systems, such as a two-state system separated by an energy barrier. It has been speculated that, in the case of free-standing hair bundles (such as inner hair cell bundles), noise plays a role in acoustic signal processing, by enhancing the sensitivity of the system through stochastic resonance [34]. While it has been reported that applying noise to saccule may enhance the SNR [35], it is difficult to judge whether the sensation is indeed improved by stochastic resonance. One of the reasons is that the generic stochastic resonance model is not applicable to a coupled system with active dynamics. Instead, we ask whether noise plays any positive role in signal transmission. We find that a direct increase in the noise strength (e.g. by increasing temperature) at a fixed $\tau$, simply decreases the SNR. In this sense, the orthodox stochastic resonance phenomenon does not occur in the system. Meanwhile, we may say that noise can have a positive role in signal transmission, in the sense that thermal noise enhances the SNR by suppressing the spontaneous activity of hair bundles. To explain the process, we need to mention that there are two different types of apparently similar hair bundles moving in the presence of noise. The first type spontaneously oscillates regardless of noise. The second type is quiescent in the absence of noise, but they are in motion in the presence of noise. As the thermal correlation time becomes shorter, the motion of the second type of hair bundles vanishes, thereby enhancing the SNR (see the electronic supplementary material, figure S3a).

Barral et al. [36] performed experiments on a hair bundle of the bullfrog saccule which was coupled to simulated ‘cyber’ bundles. They argue that the coupling increases the phase coherence between hair bundles, which endows the hair bundles with better characteristics. This is in contrast to our suggestion that the cessation of the oscillation has useful properties. We think the discrepancy between the two is a question of the strength of the coupling and the inhomogeneity of the bundles. Barral et al. [36] went up to around 0.5 pN nm$^{-1}$ stiffness, where we expect they could also observe amplitude death if they increased the coupling stiffness. Regarding the coupling strength, how strong is strong enough for the amplitude death phenomenon depends on the inhomogeneity of hair bundles (see the electronic supplementary material). We believe that, if the two bundles are sufficiently different (e.g. one is quiescent and the other is oscillating), the experiments of the type described by Barral et al. [36] can show amplitude death even for a coupling of 0.5 pN nm$^{-1}$ stiffness.

4. Conclusion
Using numerical simulations, we have demonstrated that a signal amplification and a noise reduction in coupled hair bundles can appear through amplitude death. The SNR can be maximized when the coupled hair bundles are in the amplitude death state. While individual hair bundles in a frog’s saccule show spontaneous oscillation, we think that this oscillation in vivo is suppressed to obtain high SNR. Our finding is consistent with the recent experimental observation [11] showing the absence of spontaneous oscillations when they are coupled with an overlying membrane.

When individual systems are coupled, the net system is often described as coupled individual systems or sometimes is considered as one new system. In which class do our hair bundles in the amplitude death region belong? The minimum inter-bundle coupling strengths for amplitude death in most of our calculations were comparable to the intrinsic stiffness of hair bundles ($k_{Qy} = 0.65$ pN nm$^{-1}$). Because the amplitude death phenomenon can arise even when the inter-bundle coupling is weaker than the intrinsic stiffness, we think that the hair bundles in the amplitude death region can be considered as weakly coupled independent oscillators although more quantitative analysis is necessary to clarify this issue.

The transduction mechanism presented in this study can be used to fabricate low-noise amplification in acoustic sensors. A cantilever-type mechanical sensor can act in a similar way to a hair cell bundle when it has a biomimetic feedback action [37,38]. The amplitude death phenomenon
in a coupled array of these biomimetic sensors will lead to a low-noise amplification with an enhanced SNR.

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Endnotes
1 The coordinates of the l-th hair cell bundles are \( t_l = (2l - 1)\text{mod}N + \text{floor}((2l - 1)/N)\text{mod}(2), t_l = \text{floor}((2l - 1)/N) + 1. \)
2 We simulate the noise force by running random variable \( g_{\beta, l} \) in the form of \( f_{\beta, l}(t) \propto \sum g_{\beta, l} \exp(-\sqrt{2l/\tau_c} - k - (1/2))^2, \) where \( g_{\beta, l} = 0 \) and \( (g_{\beta, l}^2) = 1. \)

References