Amplitude death state for hearing

Kang-Hun Ahn
Department of Physics, Chungnam National University, Daejeon, 305-764, Republic of Korea
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We propose amplitude death phenomenon as an underlying mechanism of auditory transduction. When non-identical auditory hair bundles are elastically coupled, their spontaneous oscillations can be quenched to form an amplitude death state. We show, in this state, the hair cells are quiet and ready to detect oscillatory stimulus with coupling-strength dependent amplification. Numerical demonstration of the mechanism suggests that the non-uniformity of coupled hair cells can contribute to noise-robust auditory transduction.

One of the surprising aspects of hearing is that the sound we hear may cause similar or smaller displacement of hearing organ than we expect from thermal fluctuation in equilibrium[1]. In ear, hair cells transform mechanical stimuli into neuronal signal with great sensitivity. Gold[2] has pointed out the ear has high damping due to the fluid in it and argued that the ear must contain active amplifier to achieve the high sensitivity and frequency selectivity. The hair cells indeed amplify their inputs relying on active feedback process[3, 4]. Gold's regenerative mechanism for hearing naturally lead to predict emitting sound of the ear due to the positive feedback oscillations. The ear indeed emits sound which is known as spontaneous otoacoustic emission[5] and individual hair cells also show spontaneous motion of hair bundles[6, 7]. The signal amplification might rely on the entrainment of the external signal to its spontaneous motion as usual radio engineering. However, direct application of the entrainment mechanism to hearing is problematic, because, if the hair bundles move spontaneously, the auditory neuron must receive strong noisy signal even in the absence of the external sound.

The hair cell must be able to amplify weak stimuli and must be quiet in the absence of sound signal, which is coined here as *quiet amplifier*. The hair cells described by a generic mathematical model[8] and a biophysical model[9] can be quiet amplifiers. In these models, the hair cells are assumed to operate at the critical point of Hopf bifurcation[10], so the active amplification of weak stimuli is possible without relying on the entrainment mechanism. In reality, however, there exists noise in the process of gene expression thus it is more natural to assume a distribution of physical parameters of hair bundles rather than assuming all hair bundles are equivalent and located at the critical point. Furthermore, the ability to amplify weak signal is limited by temporal fluctuations which hides criticality.

In this Letter, we provide a mechanism how the hair cells can be quiet amplifiers in spite of the noise and non-uniformity. We will show coupled hair bundles can enhance amplification and suppress mechanical fluctuations through *amplitude death* phenomenon which means quenching of the oscillation due to the coupling of the oscillator. This intriguing phenomenon was noted in the 19th century by Rayleigh[11], who found that adjacent organ pipes can suppress each other's sound. Amplitude death is universal behavior that appears when any two or many different oscillators are mutually coupled[12–14]. The phenomenon can help auditory transduction as we will demonstrate in this work using numerical simulation of coupled hair bundles. While noisy fluctuations and unwanted spontaneous oscillation is strongly suppressed, the oscillators in the amplitude death state react sensitively to weak oscillatory stimulus. In this viewpoint, the disorder in hair bundles' size can contribute to hearing.

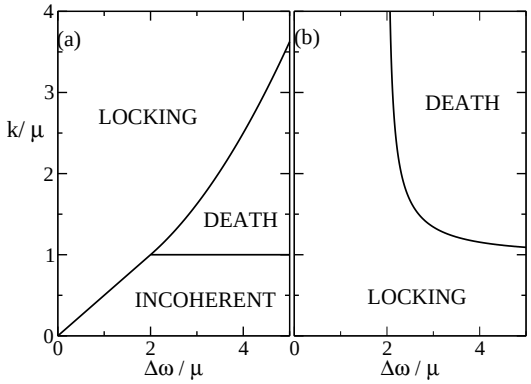

FIG. 1: The approximate phase diagram of two coupled oscillators when (a) $\mu_1 = \mu_2 = \mu > 0$ and (b) $\mu_1 = -\mu_2 = \mu > 0$. In the regime of LOCKING, the natural frequencies of the two oscillators are locked with arbitrary relative phase, while the oscillation frequencies are different in the INCOHERENT regime. The amplitude of oscillation is zero in the amplitude DEATH regime.

A simple generic mathematical equations describing amplitude death is

$$\begin{aligned} \dot{z}_1 &= (\mu_1 + i\omega_1 - |z_1|^2)z_1 + k(z_2 - z_1) \\ \dot{z}_2 &= (\mu_2 + i\omega_2 - |z_2|^2)z_2 + k(z_1 - z_2), \end{aligned} \tag{1}$$

where z is a complex variable of time, ω_i is natural frequency of individual oscillator, and k represents the coupling strength. In the absence of the coupling ($k = 0$), the model describes weakly nonlinear system near a supercritical Hopf bifurcation [8, 11]. For a single oscillator, the oscillatory solution $z_i = \sqrt{\mu_i}e^{i\omega_i t}$ becomes stable and the fixed point $z = 0$ becomes unstable when $\mu_i > 0$.

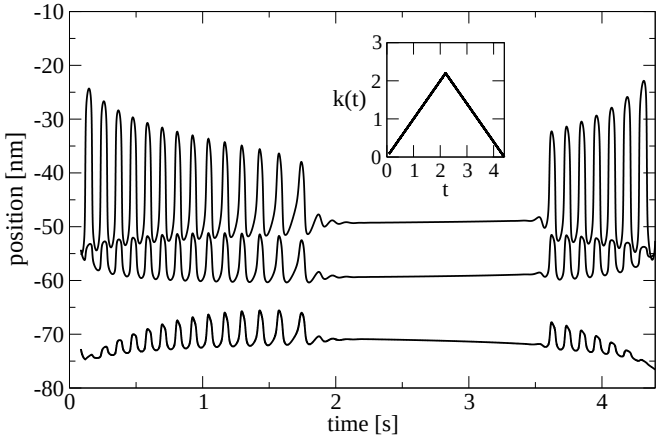

FIG. 2: The positions of three coupled hair bundles as a function of time. To investigate the effect of various coupling strength, the coupling constant $k(t)$ changes as a function of time as shown in the inset (in units of pN/nm). We choosed ($f_{\max}$[pN],$k_{\rm sp}$[pN/nm])= (337,0.58),(329,0.69),(357,0.58). Offset values for the displacement are added for clearance.

When two oscillators have stable oscillatory solutions with different frequencies, coupling between the oscillators can induce instability of the oscillatory motion. For instance, when $\mu = \mu_1 = \mu_2 > 0$, the amplitude death appears[12] if

$$|\Delta\omega| > 2\mu, \quad \text{and} \quad \frac{1}{2}(1+(\frac{\Delta\omega}{2\mu})^2) > \frac{k}{\mu} > 1, \qquad (2)$$

where $\Delta\omega = \omega_1 - \omega_2$ is the frequency mismatch (Fig. 1 (a)). Also if one of the oscillators has stable oscillatory solution, while the other is at its stable fixed point, the oscillatory motion can be quenched by the coupling. For instance, when $\mu = \mu_1 = -\mu_2 > 0$ (Fig. 1(b)), the stability of the fixed point $z_1 = z_2 = 0$ is determined by the sign of real part of the Lyapunov exponent λ satisfying the eigenvalue equation; $((\mu+k+\lambda)^2+\omega_1^2)((\mu-k-\lambda)^2+\omega_2^2)+2k^2(\mu+k+\lambda)(\mu-k-\lambda)+2k^2\omega_1\omega_2+k^4 = 0$. The amplitude death regime arises when both of the two eigenvalues have negative sign. This condition is met when

$$|\Delta\omega| > 2\mu, \quad \text{and} \quad k > \frac{|\Delta\omega|\mu}{\sqrt{|\Delta\omega|^2-4\mu^2}}. \qquad (3)$$

Note that in any cases the amplitude death requires certain finite frequency mismatch $\Delta\omega$ which was not usually assumed in previous hearing research.

To investigate the response of the amplitude death state to oscillatory stimulus, let us consider the coupled oscillators subjected to periodic forcing as $\dot{z}_i = (\mu_i + i\omega_i - |z_i|^2)z_i + k(z_j - z_i) + Fe^{i\omega t}$. The external periodic force $Fe^{i\omega t}$ excites the oscillators in the amplitude death state, and the oscillation frequencies are locked to the driving frequency ω. Analytic expression for the oscillation amplitude and phase can be obtained when we consider a special case $\mu = \mu_1 = \mu_2$ and the locking frequency ω matches with the mean oscillator frequency $\bar{\omega} = (\omega_1+\omega_2)/2$. Due to the symmetry, we can write $z_1(t) = z_0\exp(i\omega t)$ and $z_2(t) = z_0^*\exp(i\omega t)$. The complex amplitude z_0 satisfies a simple equation

$$(\mu + i\frac{\Delta\omega}{2} - |z_0|^2)z_0 + k(z_0^* - z_0) + F = 0. \qquad (4)$$

The phase difference between the oscillators depends only on the amplitude of the oscillation and the coupling strength;

$$R^2 - \mu + 2k = \frac{\Delta\omega}{2}\cot\phi, \qquad (5)$$

where $z_0 = R\exp(i\phi)$. It is interesting to note that there is intrinsic phase difference between the oscillators even for very weak stimulus limit.

For weak stimulus, the phase difference is given by $\cos\phi \approx \frac{-\mu+2k}{\sqrt{(-\mu+2k)^2+(\Delta\omega/2)^2}}$ and the amplitude is approximated as a linear response $R \approx F\cos\phi/(k(1-\cos 2\phi)-\mu)$. Nonlinearity becomes significant for $R > 1$, where the amplitude R approximately satisfies $R^3 - \mu R \approx F$ and the oscillators move in same phase $\cos\phi \approx 0$. In this case, the 1/3 law appears as in the critical oscillator model[8]. So, the mechanical response at the average frequency $\omega = \bar{\omega}$ in the amplitude death state is approximated as

$$R \approx \frac{1}{\mu}F\frac{\sqrt{(1-2\frac{k}{\mu})^2+(\frac{\Delta\omega}{2\mu})^2}}{1-2\frac{k}{\mu}+(\frac{\Delta\omega}{2\mu})^2} \quad (R<1) \qquad (6)$$

$$R \approx F^{1/3} \quad (R>1). \qquad (7)$$

The oscillation amplitude R is linear in F for weak stimulus limit in contrast to the essential nonlinearity of a single oscillator of $\mu = 0$[8]. As can be seen in Eq.(6) and Eq.(2), the sensitivity defined by R/F can be enhanced strongly as the coupling strength k increases, and even diverges at the verge of the amplitude death regime $k = \frac{\mu}{2}(1+(\frac{\Delta\omega}{2\mu})^2$. Thus, the essential nonlinearity appears again at this special coupling.

Now we investigate the possibility of the amplitude death phenomenon in a concrete biological system. For this purpose, we choose hair bundles of a bullfrog's hair cell, which has been concretely modeled in Ref.[7, 9]. Active hair-bundle movements results from Ca^{2+}-dependent activity of the molecular motors which are connected to transduction ion channels through gate springs. We assume elastic coupling between hair bundles then the equations of motion for the position of i-th hair-bundle X_i and its molecular motor $X_{a,i}$ are written as

$$\lambda\frac{dX_i}{dt} = F_{\rm gs,i} - k_{\rm sp,i}X_i + k(X_{i-1}+X_{i+1}-2X_i)$$

$$\lambda_a\frac{dX_{a,i}}{dt} = -F_{\rm gs,i} + F_{a,i}, \quad (i=1,2,\cdots,N) \qquad (8)$$

where λ and λ_a are parameters relating the force and velocity. We used closed boundary condition $X_0 = X_{N+1} = 0$, $X_{a,0} = X_{a,N+1} = 0$, $F_{\rm gs,i} = -k_{\rm gs}(X_i - X_{a,i} - DP_{o,i})$ is the force generated by the gating spring, $F_{a,i} = 0.14 f_{\rm max,i}(1-0.65P_{o,i})$ is the active force from the molecular motor, and $P_{o,i} = 1/(1+\exp(\frac{X_i - X_{a,i} + 16.7{\rm nm}}{4.53{\rm nm}}))$ is the open probability of the i-th ion channel[9].

The non-uniformity of the hair bundles has been simulated by introducing a distribution of the maximal gating spring force $f_{\rm max}$ and the bundles' pivot stiffness $k_{\rm sp}$. Fig. 2 shows the positions of three hair bundles which are coupled with slowly time-varying constant $k(t)$ as shown in the inset. One can see that the oscillation of three hair bundles becomes quenched simultaneously. Since the coupling constant for the quenching depends on degree of mismatch between hair bundles, we can not say in this work universal value of k for the bifurcation, but the appearance of the amplitude death is clear. The difference between the k values for the quenching and revival of the oscillation indicates that the bifurcation is subcritical.

We will show the amplitude death mechanism survives in a more realistic model including effects of inertia, noise, and large number of hair bundles. Hair bundles of human's outer hair cells are coupled through tectorial membrane which has finite mass and stiffness. To mimic the inertia of the membrane, we introduce the coordinate of the elastically coupled massive elements $S_{\rm i}$ which are also coupled to hair bundles (See Fig. 3 (a)). The governing equations of motions for the N coupled hair bundles are

$$
\begin{aligned}
m\ddot{\rm S_i} &= -\gamma_m \dot{\rm S_i} + k({\rm S_{i+1}} - 2{\rm S_i} + {\rm S_{i-1}}) + \sum_{\rm j=1}^{N} f_{\rm HB,j}\delta_{\rm i,2j-1}, \\
\lambda \dot{X_{\rm j}} &= -f_{\rm HB,j} - k_{\rm gs}(X_{\rm j} - X_{\rm a,j} - DP_{\rm o,j}) - k_{\rm sp,j}X_{\rm j} \qquad (9)
\end{aligned}
$$

where $i = 1, 2, ..., 2N$ is index for the mass, $j = 1, 2, ..., N$ is the index for hair bundles, γ_m is the frictional constant of the mass. The j-th hair bundles is assumed to be tight to the 2j-1 th mass, ${\rm S_{2j-1}} = X_{\rm j}$, and $f_{\rm HB,j}$ is the force exerted on the mass exerted by j-th hair bundle.

The inclusion of inertia, spatial dimensionality, or detail shape of the coupling is not a important factor to formation of the amplitude death state. The key to the death state is the non-uniformity of the hair bundles. Using Gaussian random number generators, we simulate random distribution of parameters around $f_{\rm max} = 342$ pN and $k_{\rm sp} = 0.65$ pN/nm with the variance about 50pN and 0.3 pN/nm, respectively. Fig. 3 shows numerical results from a particular set of the parameters which contains 10 self-oscillating hair bundles and 40 static bundles in the absence of coupling (Fig. 3(b)). As the coupling strength increases, the mutual coherence of the bundles' oscillation is developed. We find that at a coupling strength which is not unreasonable value $k \approx 8$ pN/nm, the oscillation become quenched and a stable amplitude death state appears (Fig. 3 (c)).

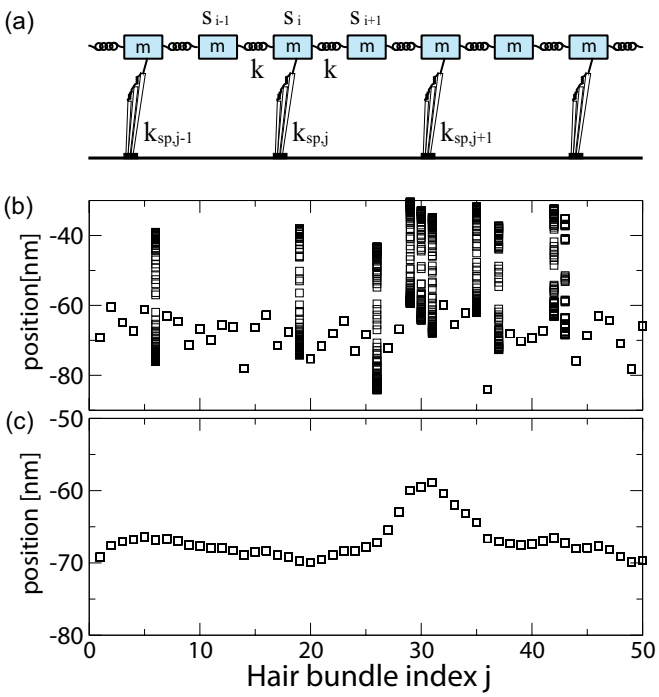

FIG. 3: (a) Schematic for the elastically coupled hair bundles with massive membrane. (b) The stroboscopic view (snap shots at every 10 ms for 1 second.) of 50 uncoupled hair bundles. (c) The same view of amplitude death state ($k = 10$ nN/μm). We used m=2 μg.

The neural response of the hair cells to stimulus is not directly proportional to the mechanical displacement of the hair bundles, so the sum of displacement of all the bundles does not have direct significant meaning in auditory transduction. The influx of Ca^{2+} triggers the release of the neural transmitter, and also affects the conductance of K^+ channel thereby changes the membrane voltage of the hair cell. Therefore, the open probability of the transduction ion channel P_o is more relevant to the neural information. Note that multiple of hair cells are involved in auditory transduction for a single tone. (The human cochlear has $\sim$ 3,500 inner hair cells and $\sim$ 11,000 outer hair cells. Inner hair cells are innervated by auditory nerve.) In this respect, the averaged value of the open probability

$$P_o^* = \frac{1}{N}\sum_{j=1}^{N} P_o(X_j, X_{a,j}),$$

is encoded in auditory nerve potential. The sound stimulus is delivered to hair bundles through fluid velocity of the limp liquid in cochlea and also through movement of basilar membrane. The effect is modeled by adding external force $F(t)$ to the exerted on the hair bundle. For the noisy environment, we include also noise force $F_{\rm N}(t)$

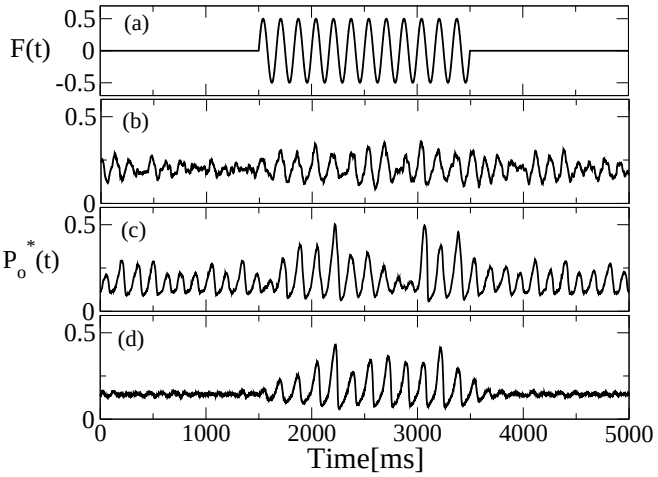

FIG. 4: (a) The signal force applied on hair bundles as a function of time in units of pN. The ion-channel open probability averaged over 50 hair bundles for (b) incoherent ($k = 0$), (c) locking ($k = 2$pN/nm), and (d) amplitude death dominant state ($k = 10$ nN/μm) of 50 hair bundles. The noise strength was chosen $D_N = 2.8\ 10^{-27}$ N s.

i.e., we add $F(t)+F_{N,j}(t)$, in the right hand side of Eq.(9) where $< F_{N,j}(t)F_{N,j'}(s) >= 2D_N\delta(t-s)\delta_{j,j'}$ (D_N is the noise strength).

Fig. 4 shows, in the absence of signal (when $F(t) = 0$ in Fig. 4 (a)), the hair bundles movement have three classes. *Incoherent regime* exists where the averaged open probability has random fluctuations due to the distribution of different hair bundles (Fig. 4 (b)). *Locking dominant:* The incoherent regime evolves to coherent locking regime where the hair bundles develop mutual coherence as the coupling increases[15] (Fig. 4 (c)). In this regime, due to its strong spontaneous oscillation in P_o^*, it is difficult to detect when the signal arrives. This problem can be overcome when the hair bundles are in *amplitude death* state (Fig. 4 (d)). In this state, fluctuations are strongly suppressed because other hair bundles' spontaneous motions are quenched. One can see the noisy fluctuation in the absence of coupling (Fig. 4 (b)) is suppressed in the amplitude death regime (Fig. 4 (d)). The sound signal is amplified and properly encoded in P_0 so that it is clearly visible when the signal is arrived in Fig. 4 (d).

In summary, we have proposed a mechanism for auditory transduction which operates robust non-uniformity and noise. When coupled non-identical oscillators form amplitude death state, oscillatory stimulus can be detected with active amplification and precise time-arrival information. The oscillation amplitude driven by oscillatory stimulus is linear, but its sensitivity can be controlled by the coupling strength which can even diverge at the boundary of the amplitude death regime. Beyond the linear regime of the stimulus strength F, conventional nonlinear regime $R \sim F^{1/3}$ appears showing compressive nonlinearity. We demonstrate the amplitude death mechanism through realistic biophysical models for elastically coupled bullfrog's hair bundles, which indicates the non-uniformity of the hair bundles can contribute to auditory transduction through amplitude death mechanism. The mechanism proposed here is not sensitive to spatial dimension or number of oscillators and it is worth investigating the auditory transduction in non-vertebrates, for instance, insects of which neuron spikes are coupled to active antennal motion[16].

Dierkes et.al.[15] have studied coupled hair bundles where the coupling caused synchronization but didn't show amplitude death. It seems that the bundles went directly from incoherent to locking regime. We think the reason is probably due to their non-uniformity (frequency gradient) was not sufficient to cause the amplitude death (See Fig. 2 (a) and Ref.[14]).

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