CHIN. PHYS. LETT. Vol. 34, No. 4 (2017) 048702

Auditory Hopf Amplification Revealed by an Energy Method *

Lin Tian(田霖), Zhang-Cai Long(龙长才)**
Colleague of Physics, Huazhong University of Science and Technology, Wuhan 430074

(Received 11 December 2016)

We report on the auditory Hopf amplification contributed by the electrical energy of the hair cell during its bundle deflecting. An energy method to calculate the active force is adopted according to the electrical energy consumption of the hair cell. After some experimental data was analyzed and simulated, we find that the electrical energy determines the value of the active force and enlarges the mechanical response of the hair bundle. This amplification is controlled by the cell voltage and makes the sensor a Hopf vibrator with hearing nonlinear characteristics. A velocity-dependent active force derived previously from the force-gating channel operation strongly reinforces our conclusion.

PACS: 87.15.A−, 87.16.A−, 87.19.lt DOI: 10.1088/0256-307X/34/4/048702

The sense of mammalian hearing exhibits distinguishing characteristics such as high sensitivity to weak sound, nonlinear compression of dynamic range, sharp frequency selectivity, two-tone suppression and combination-tone production.[1] These characteristics endow hearing systems with marvelous signal processing function to extract information from complex acoustic circumstances.[1−3] Active force in the cochlea is suggested to be the origin of these characteristics.[4−12] However, research work is still in the dark about such critical mechanism that it is even impossible to distinguish where this amplification originates from.[13] Recently, we derived an active force from the force-gating channel operation in the hair cell bundle, which amplifies the response of hearing sensor to sound stimulus and makes the sensor a Hopf vibrator with hearing nonlinear characteristics.[13]

In this work, we adopt an energy method to identify the active force within the cochlea according to its electrical energy consumption in carrying out mechanical work. The electrical energy determines the value of the active force and enlarges the mechanical response of the hair bundle. This general physical process reveals an active force similar to that derived from the force-gating channel operation in the hair cell bundle,[14] which is controlled by the cell voltage and provides the Hopf amplification. The Hopf vibrator exhibits the nonlinear phenomena of hearing, which are theoretically demonstrated[2,3,6−11] and are further supported experimentally.[16]

In a moving cause of the hair bundle, the mechanical work ($W_{\rm active}$) carried out by the active force ($F_{\rm active}$) is

$$W_{\rm active} = \int F_{\rm active} dx. \tag{1}$$

This mechanical work corresponds to the consumption of other forms of energy, which is converted to mechanical energy of the hair bundle movement. In deflection of a hair bundle, force-gating channels of the hair bundle open, the ion current enters the hair bundle through the channels, and there is electrical energy consumption $W_{\rm e}$ accompanying the movement of a hair bundle. This electrical energy is the energy source of mechanical amplification. Part of this electrical energy consumption is transformed into mechanical energy of the hair bundle movement,

$$W_{\rm active} = rW_{\rm e}, \tag{2}$$

where r is the ratio of the conversion. Thus the active force in a hair bundle can be obtained from the electrical energy consumption,

$$F_{\rm active} = r\frac{dW_{\rm e}}{dx}, \tag{3}$$

instead of laborious direct measurement by flexible fiber,[15,17] which is prone to error due to complex factors involved in measurement, especially in a moving state, such as frictional force and inertial force. We use this energy method to identify an active force in a moving hair bundle.

To simplify the problem, we consider a voltage-clamped mammalian hair cell, with a constant cell voltage U and not somatic movement driven by electromotility (Fig. 1). When the hair bundle stays in a steady state with deflection x, there is a steady current $I_{\rm met}(x, \dot{x} = 0) = I_0$ through force-gating channels in the hair bundle, and the electrical energy is consumed (Fig. 1(a)). This energy consumption in the steady state is not converted to mechanical energy of the hair bundle because there is no movement and no mechanical work is carried out by the active force in the steady state. Instead, in a moving state of the hair bundle with velocity $\dot{x}$, the active force does carry out mechanical work, and what contributes to the mechanical work is the additional electrical energy consumption in the moving process (in Fig. 1(b)). There is an extra component $I_{\rm extra}$ in the dynamic force-gating channel current $I_{\rm met}(x, \dot{x} \neq 0) = I_0 + I_{\rm extra}$. The dynamic force-gating channel current $I_{\rm met}(x, \dot{x} \neq 0)$ in a moving hair bundle is larger than the steady current $I_{\rm met}(x, \dot{x} = 0)$ with the same deflection x due to the

*Supported by the National Natural Science Foundation of China under Grant Nos 11374118 and 90820001, and the Science Foundation of Hubei Province under Grant No 2013CFB289.
**Corresponding author. Email: longzc01@mails.tsinghua.edu.cn
© 2017 Chinese Physical Society and IOP Publishing Ltd

adaptation of gating channel operation.[18,19] The additional electrical energy consumption, $W_{\mathrm{e(extra)}}$, in a moving process compared with the steady state is

$$W_{\mathrm{e(extra)}} = \int U \cdot [I_{\mathrm{met}}(x, \dot{x} \neq 0) - I_{\mathrm{met}}(x, \dot{x} = 0)]dt. \quad (4)$$

Substituted $W_{\mathrm{e(extra)}}$ in Eqs. (3) and (4), the active force in a moving hair bundle is expressed as

$$F_{\mathrm{active}} = rU \frac{[I_{\mathrm{met}}(x, \dot{x} \neq 0) - I_{\mathrm{met}}(x, \dot{x} = 0)]}{\dot{x}}. \quad (5)$$

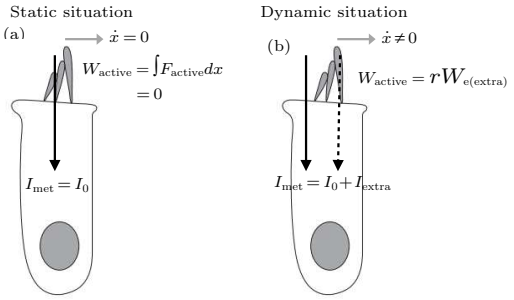

Fig. 1. The static force-gating current (a) and the dynamic force-gating channel current (b). There is an extra electrical energy consumption corresponding to the active force carrying out the mechanical work.

According to Eq. (5), the active force in a moving hair bundle can be obtained by the measurement of the difference between the steady current $I_{\mathrm{met}}(x, \dot{x} = 0)$ and the dynamic current $I_{\mathrm{met}}(x, \dot{x} \neq 0)$ through force-gating channels in the hair bundle.

Steady current through gating channels of a static hair bundle observed in experiments has been described in Refs. [16,18–20] by a Boltzmann function of hair bundle deflection x,

$$I_{\mathrm{met}}(x, \dot{x} = 0) = \frac{I_{\max}}{1 + e^{-(x - x_0)/x_{\mathrm{e}}}} = I_{\max} B(x), \quad (6)$$

where $I_{\max}$, x_0, x_{e} are constants given by experiment, and $B(x) = 1/(1 + e^{-(x-x_0)/x_{\mathrm{e}}})$.

Dynamic gating channel current $I_{\mathrm{met}}(x, \dot{x} \neq 0)$ in a moving hair bundle has not been described in the formula in literature. Without losing generality, it can be described by a polynomial function of the hair bundle deflecting velocity $\dot{x}$

$$I_{\mathrm{met}}(x, \dot{x}) = \varepsilon_0(x) + \varepsilon_1(x)\dot{x} + \varepsilon_2(x)\dot{x}^2 + \ldots, \quad (7)$$

where $\varepsilon_i(x)$ are functions to be determined according to experimental measurements. Among them, $\varepsilon_0(x)$ is the steady current $I_{\mathrm{met}}(x, \dot{x} = 0)$ described in Eq. (6). To reflect the fact that the peak current through gating channels in a hair bundle driven by step stimulus of different amplitudes is a Boltzmann function of deflection x (see Fig. 2 and its caption in Ref. [16]), other $\varepsilon_i(x)$ can be described in the polynomial function of Boltzmann function of deflection x,

$$\varepsilon_i(x) = \sum_{n>0} a_{i,n} B^n(x). \quad (8)$$

Due to the fact that the deflection velocity $\dot{x}$ is small, the dynamic current in Eq. (7) can be approximated to

$$I_{\mathrm{met}}(x, \dot{x}) \approx I_{\max} B(x) + \Big[\sum_n a_{1,n} B^n(x)\Big] \cdot \dot{x} + \Big[\sum_n a_{2,n} B^n(x)\Big] \cdot \dot{x}^2. \quad (9)$$

The first two terms of Eq. (9), $I_{\max} B(x) + a_{1,1} B(x) \cdot \dot{x}$ can reflect the main feature of the gating current in the hair bundle. Between the measured peak current-deflection relation (solid line in Fig. 2(a)) in different step stimuli in literature and the fitted line (dashed line in Fig. 2(a)) by the first two terms of Eq. (9), there is a small difference. This difference is a non-monotonous function of deflection x with a single peak (solid line in Fig. 2(b)). To reflect this difference, the simplest form of the rest terms in Eq. (9) is the quadratic function of $B(x)$, $[a_{2,1} B(x) + a_{2,2} B^2(x)] \cdot x^2$. The dashed line in Fig. 2(b) is the fit line of the difference by the quadratic term of Eq. (9), which has a slight horizontal shift δ compared with the difference to be fitted. Thus the dynamic current can be described by

$$I_{\mathrm{met}}(x, \dot{x}) \approx I_{\max} B(x) + a_{1,1} B(x) \cdot \dot{x} + [a_{2,1} B(x + \delta) + a_{2,2} B^2(x + \delta)] \cdot \dot{x}^2. \quad (10)$$

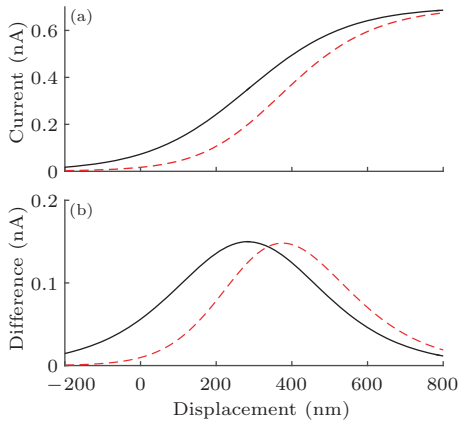

Fig. 2. (a) Measured peak force-gating current (solid line)[16] and the fitting results of $I_{\max} B(x) + a_{1,1} B(x) \cdot \dot{x}$ (dashed line). (b) Difference in (a) (black line) and the fitting results of Eq. (9) (dashed line). The parameters $I_{\max} = 0.67\,\mathrm{nA}$, $x_0 = 284\,\mathrm{nm}$, $x_{\mathrm{e}} = 132\,\mathrm{nm}$ obtained from Ref. [16] provided the measurement. Fitting parameters $a_{1,1} = 150\,\mathrm{nA(m/s)}^{-1}$, $a_{2,1} = 1.5\,\mathrm{mA(m/s)}^{-2}$, $a_{2,2} = -1.5\,\mathrm{mA(m/s)}^{-2}$ and $\delta = 65\,\mathrm{nm}$.

Equation (10) is valid as a general expression in describing the gating current in the hair bundle. This can be demonstrated by its ability to describe the temporal variance of the gating current in the whole stimulus process. Figure 3 illustrates an example of this. It is demonstrated that the time variance of the gating current produced by Eq. (10) (Fig. 3(d)) is highly consistent with the measured one (Fig. 3(b)).

Equation (10) demonstrates that there is an additional velocity-dependent component in the dynamic gating current compared with the steady force-gating

current $I_{\max}B(x)$. According to Eq. (5), the active force in a moving hair bundle identified by the energy method is velocity-dependent,

$$F_{\text{active}} = rU_m a_{1,1}B(x) + rU_m[a_{2,1}B(x+\delta) + a_{2,2}B^2(x+\delta)]\cdot\dot{x}. \quad (11)$$

The efficacy of the active force in Eq. (11) can be directly tested by experimental results. Figure 4(a) is the measured temporal variance of the active force in the hair bundle driven by the step stimulus (Fig. 3(a)), and Fig. 4(b) is the corresponding active force obtained by Eq. (11). It is illustrated that the active force given by Eq. (11) is quite consistent with the measurement.

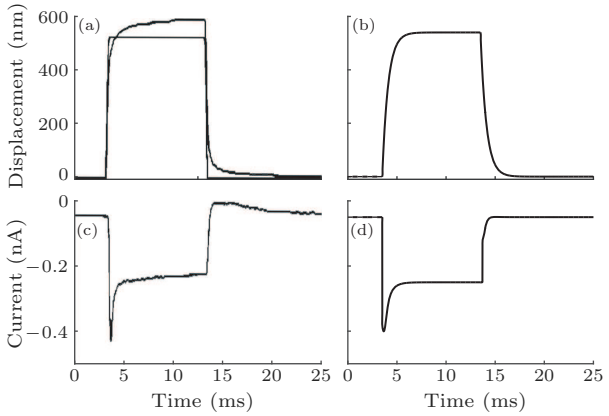

Fig. 3. (a, c) The hair bundle motion and the channel current after a step Piezo stimulus.[16] (b, d) The simulated by the exponential process with a time constant 0.6 ms. The parameters are the same as those in Fig. 2.

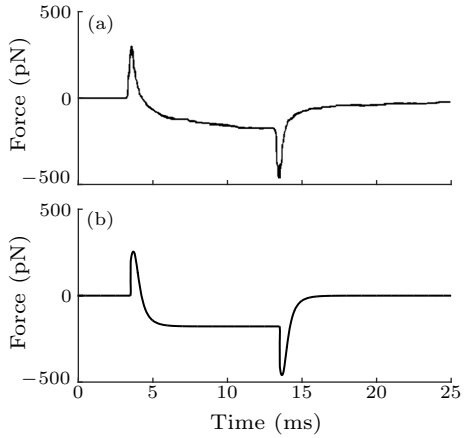

Fig. 4. (a) Glass fiber measured extra force produced by the step-stimulus driven moving hair bundle.[16] (b) The active force calculated by the energy method. The parameters are the same as those in Fig. 2. The rate r of the energy transduction is adopted as a constant $r = 2\%$.

The efficacy of the active force in Eq. (11) can be further tested by measuring the compound force in the hair bundle. Experimentally measured force F in the hair bundle[16] is the compound of the spring force and the active force in the hair bundle

$$F = k_s x - F_{\text{active}}, \quad (12)$$

where k_s is the linear spring coefficient of the hair bundle. Using Eq. (11), the compound force in a hair bundle is

$$F = k_s x - rU\cdot a_{1,1}B(x) - rU\cdot[a_{2,1}B(x+\delta) + a_{2,2}B^2(x+\delta)]\cdot\dot{x}. \quad (13)$$

Figure 5(a) is the measured force in a hair bundle driven by step stimuli with different amplitudes,[16] and Fig. 5(b) is the corresponding force obtained by Eq. (13). It is clear that the result is highly consistent with the direct measurements.

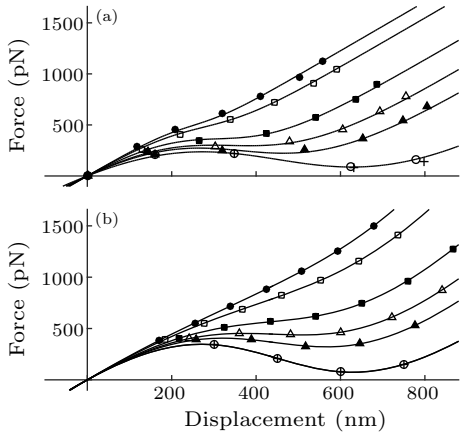

Fig. 5. (a) The force-displacement relations measured at successive times after the transduction current reaches its peak in response to step stimuli: $t = 0$, 0.07, 0.27, 0.47, 0.67, 3.9 and 8 ms.[16] (b) The corresponding force versus the displacement. The successive times ($t = 0$, 0.07, 0.27, 0.47, 0.67, 3.9 and 8 ms) and the parameters ($x_0 = 300$ nm, $x_e = 100$ nm, $U = 84$ mV, $k_s = 3$ mN/m and $\tau = 0.6$ ms) are the same as the experimental measurement. The fitting parameters are $r = 2\%$, $a_{1,1} = 100\,\text{nA}\cdot(\text{m/s})^{-1}$, $a_{2,1} = 2\,\text{mA}\cdot(\text{m/s})^{-2}$, $a_{2,2} = -1\,\text{mA}\cdot(\text{m/s})^{-2}$ and $\delta = 65$ nm.

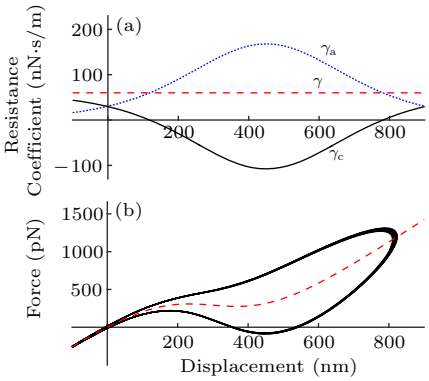

Fig. 6. (a) The linear friction resistance coefficient γ (horizontal dashed line), the negative resistance coefficient $\gamma_a(x)$ (dotted line) and the compound resistance γ_C (solid line). (b) The force-displacement trajectory of spontaneous hair bundle oscillation, with velocity-dependent force (solid line). The parameters are $x_0 = 300$ nm, $x_e = 100$ nm, $U = 84$ mV, $k_s = 3$ mN/m, $\tau = 0.6$ ms, $a_{1,1} = 80\,\text{nA}\cdot(\text{m/s})^{-1}$, $a_{2,1} = 0.4\,\text{mA}\cdot(\text{m/s})^{-2}$, $a_{2,2} = -0.4\,\text{mA}\cdot(\text{m/s})^{-2}$, $\delta = 68$ nm, $m = 3$ ng and $\gamma = 60\,\text{nm}\cdot(\text{m/s})^{-1}$.

Equation (13) shows that the active force in the hair bundle consists of two parts: the velocity-independent part and the velocity-dependent part. The velocity-independent part $rU_m a_{1,1}B(x)$ makes force in a hair bundle, $k_s x - rU_m a_{1,1}B(x)$ is smaller

than its linear spring force $k_s x$ and produces the negative stiffness effect. However, due to its velocity-independent character, this part will make the trajectory of periodic motion of a hair bundle a single line in a force-displace plot (dashed line in Fig. 6(b)), which does not enclose a zone with area. Thus the velocity-independent active force does not carry out any mechanical work in hair bundle's periodic motion, and makes no contribution to mechanical amplification of hair bundle movement. The velocity-dependent part will make the trajectory of periodic motion of a hair bundle in force-displace plot a close curve (solid curve in Fig. 6(b)), which encloses a zone with an area corresponding to its mechanic work in a period movement. Thus it is the velocity-dependent active force, instead of the negative stiffness effect, which makes a contribution to the mechanical amplification of hair bundle movement.

Movement of a hair bundle driven by the active force is controlled by

$$m\ddot{x} = -k_s x + F_{\text{active}} - \gamma\dot{x}, \tag{14}$$

where m is the mass of a hair bundle, and γ is the frictional resistance coefficient of the hair bundle motion. Using Eq. (13), the equation is written as

$$m\ddot{x} + \gamma\dot{x} - rU \cdot [a_{2,1}B(x+\delta) + a_{2,2}B^2(x+\delta)] \cdot \dot{x} + k_s x - rU \cdot a_{1,1}B(x) = 0. \tag{15}$$

In Eq. (15), the velocity-dependent active force is a negative resistance with coefficient $\gamma_a(x) = rU_m[a_{2,1}B(x+\delta) + a_{2,2}B^2(x+\delta)]$, which provides the mechanical energy for hair bundle movement, the velocity-independent active force and the spring force of the hair bundle compose compound spring force of the hair bundle with negative stiffness.

Equation (15) shows that the hair bundle driven by the velocity-dependent active force is a Hopf vibrator controlled by the compound resistance coefficient $\gamma_C = \gamma - \gamma_a$. When the minimum of γ_C is below zero axis, the hair bundle is destabilized and oscillates spontaneously with limit cycle as shown in Fig. 6(b). Remarkable theoretic research has demonstrated that this kind of self-tuned Hopf vibrator behaves with a series of nonlinear characteristics of hearing.[4,7]

The essentials of the velocity-dependent active force in the hair bundle can be interpreted from the adaptation of gating channel operation, and the corresponding physiological structure changes powered by electricity.[14] In this adaptation process, the open probability of the force-gating channels in the hair bundle[14] is

$$P(x) \approx B(x) + \frac{\tau}{x_e}[B(x+x_a) - B^2(x+x_a)] \cdot \dot{x}. \tag{16}$$

This channel gate open in the hair bundle will elongate the tip link of the hair bundle and will release the link spring force as the active force

$$\begin{aligned} F &= k_g DNP(x) \\ &= k_g DNB(x) + k_g DN\frac{\tau}{x_e}[B(x+x_a) \\ &\quad - B^2(x+x_a)] \cdot \dot{x}, \end{aligned} \tag{17}$$

where k_g is the spring coefficient of the gating spring, D is the length released by one opened channel, and N is the number of gating channels in a hair bundle.

Equation (17) is consistent in form with Eq. (11). According to the derivation of Eq. (17), the velocity-independent active force is produced by the steady force-gating channel open in the hair bundle, and the velocity-dependent active force is produced by the adaptation of force-gating channel operation in the hair bundle. Compelling evidence has shown that the adaptation of the hair bundle gating operation is produced by Ca^{2+} ion binding with adaptation motors in the hair bundle, which allows adaptation motor in the hair bundle slipping along the actin core of stereocilia to reclose opened force-gating channels.[21–23] It can be suggested that it is the Ca^{2+} ion binding process that releases the electrical energy carried by Ca^{2+} ions and converts it into mechanical energy for mechanical amplification of hair bundle movement. The final source of electrical energy for the active mechanical amplification is the bioenergy, by which ion pumps maintain the cell voltage and provide Ca^{2+} ions with the electrical energy to be consumed for mechanical amplification.

The physics method adopted in this work reveals that the velocity-dependent force for hearing amplification is powered by electricity. This has not been recognized previously from the scope of biology and mathematics. This electricity-powered amplifying force is tuned by cell voltage. The tuning mechanism will affect, or can be utilized to adjust hearing performance, such as selective hearing attention.

References

[1] Moore B C J 2003 *An Introduction to the Psychology of Hearing* (London: Academic Press)
[2] Martignoli S and Stoop R 2010 *Phys. Rev. Lett.* **105** 048101
[3] Camalet S et al 2000 *Proc. Natl. Acad. Sci. USA* **97** 3183
[4] Hudspeth A J 2008 *Neuron* **59** 530
[5] Hudspeth A J et al 2010 *J. Neurosci.* **104** 1219
[6] Eguíluz V M et al 2000 *Phys. Rev. Lett.* **84** 5232
[7] Jülicher F et al 2001 *Proc. Natl. Acad. Sci. USA* **98** 9080
[8] Kern A and Stoop R 2003 *Phys. Rev. Lett.* **91** 128101
[9] Stoop R and Kern A 2004 *Phys. Rev. Lett.* **93** 268103
[10] Magnasco M O 2003 *Phys. Rev. Lett.* **90** 058101
[11] Barral J and Martin P 2012 *Proc. Natl. Acad. Sci. USA* **109** E1344
[12] Zhao X H and Long Z C 2007 *Chin. Phys. Lett.* **24** 3183
[13] Ashmore J et al 2010 *Hear. Res.* **266** 1
[14] Tian L et al 2016 *Chin. Phys. Lett.* **33** 128701
[15] Martin P et al 2000 *Proc. Natl. Acad. Sci. USA* **97** 12026
[16] Kennedy H J et al 2005 *Nature* **433** 880
[17] Bormutha V et al 2014 *Proc. Natl. Acad. Sci. USA* **111** 7185
[18] Eatock R A 2000 *Annu. Rev. Neurosci.* **23** 285
[19] Fettiplace R and Ricci A J 2003 *Curr. Opin. Neurobiol.* **13** 446
[20] Fettiplace R 2006 *J. Physiol.* **576** 29
[21] LeMasurier M and Gillespie P G 2005 *Neuron* **48** 403
[22] Stauffer E A et al 2005 *Neuron* **47** 541
[23] Holt J R et al 2002 *Cell* **108** 371