Supplementary material for the manuscript entitled: A model for auditory sensitivity provided by self-tuned critical oscillations of hair cells

S. Camalet, T. Duke, F. Jülicher and J. Prost

I. GENERIC BEHAVIOR AT A HOPF-BIFURCATION

A. Nonlinear relation between periodic stimulus and displacements

We are interested in the response $x(t)$ of a nonlinear system to a periodic stimulus force $f(t)$. If only one frequency $\nu = \omega/2\pi$ is present we use the Fourier expansions

$$f(t) = \sum_{n=-\infty}^{\infty} f_n e^{in\omega t} \tag{1}$$

$$x(t) = \sum_{n=-\infty}^{\infty} x_n e^{in\omega t} \quad , \tag{2}$$

where the complex coefficients x_n and f_n obey $x_n = x^*_{-n}$ and $f_n = f^*_{-n}$. This representation implies that we focus on the 1:1 limit cycle solution and ignore all transient relaxation phenomena [for a discussion of more complex responses of a forced Hopf bifurcation, see C. Baesens (1987) Ph.D. thesis, Universite Libre de Bruxelles]. We consider the class of systems for which the force at a given time depends in a nonlinear way on the history of the displacements $x(t)$ alone; as we will discuss in section D more complex cases do not change the basic properties. In this situation, the relation between x and f can be expressed as a systematic expansion of the force amplitudes f_n in the amplitudes x_n:

$$f_k = F^{(1)}_{kl} x_l + F^{(2)}_{klm} x_l x_m + F^{(3)}_{klmn} x_l x_m x_n + O(x^4) \quad , \tag{3}$$

where the expansion coefficients $F^{(n)}_{k,k_1,..,k_n}$ are symmetric with respect to permutations of the indices $k_1..k_n$. The limit cycle solutions are invariant with respect to translations in time $t \rightarrow t + \Delta t$. Under these transformations the amplitudes change as $x_n \rightarrow x_n e^{in\omega\Delta t}$ and $f_n \rightarrow f_n e^{in\omega\Delta t}$. Inspection of Eq. (3) shows that the time translation symmetry allows only for those terms $F^{(n)}_{k,k_1,..,k_n} x_{k_1}..x_{k_n}$ for which $k = k_1 + ... + k_n$. For all other cases $F^{(n)}_{k,k_1,..,k_n}$ must vanish which significantly restricts the number of terms.

B. Hopf bifurcation

The nonlinear system exhibits spontaneous oscillations and a Hopf-bifurcation if non-trivial solutions to Eq. (3) with $x_n \neq 0$ exist in the case where all $f_k = 0$, i.e. if no stimulus force is applied. Without loss of generality, we consider here an instability of the mode x_1. In this case, the dominant terms allowed by symmetry read ($f_k = 0$)

$$0 \simeq F^{(1)}_{11} x_1 + 2F^{(2)}_{1,2,-1} x_{-1} x_2 + 6F^{(3)}_{1,1,1,-1} x_1^2 x_{-1} + 6F^{(3)}_{1,1,2,-2} x_2 x_{-2} x_1 \tag{4}$$

$$0 \simeq F^{(2)}_{22} x_2 + 2F^{(2)}_{211} x_1^2 \quad . \tag{5}$$

Eq. (5) determines $x_2 \simeq -2(F^{(2)}_{211}/F^{(2)}_{22})x_1^2$. Inserting this relation in Eq. (4), we obtain to lowest order

$$0 \simeq \mathcal{A} x_1 + \mathcal{B}|x_1|^2 x_1 \quad , \tag{6}$$

where $\mathcal{A} \equiv F^{(1)}_{11}$ and $\mathcal{B} \equiv 3F^{(3)}_{1,1,1,-1} - 4F^{(2)}_{211}F^{(2)}_{1,2,-1}/F^{(2)}_{22}$.

The coefficients $\mathcal{A}(\omega, C)$ and $\mathcal{B}(\omega, C)$ are complex and in general depend on frequency ω and a control parameter which we denote by C. A Hopf bifurcation occurs at a critical point $C = C_c$ at which $\mathcal{A}$ vanishes for a frequency ω_c, i.e. $\mathcal{A}(\omega_c, C_c) = 0$. This can be demonstrated as follows: A spontaneously oscillating solution satisfies

$$|x_1|^2 = -\frac{\mathcal{A}}{\mathcal{B}} \tag{7}$$

Note, that such a solution can only exist if $\mathcal{A}/\mathcal{B}$ is real and negative. At the bifurcation point, $\mathcal{A} = 0$ and $\mathcal{A}/\mathcal{B}$ is therefore real for $\omega = \omega_c$, however the corresponding amplitude $|x_1|^2$ vanishes. In the vicinity of this point we expect to find solutions with finite amplitude. We use the expansion

$$\mathcal{A}(\omega, C) \simeq (\omega - \omega_c)A_1 + (C - C_c)A_2 \tag{8}$$

where A_1 and A_2 are complex coefficients and we neglect higher order terms. Spontaneous oscillating solutions exist only if $\mathcal{A}/\mathcal{B}$ is real. This condition is satisfied for a particular frequency $\omega = \omega_s$ with

$$\omega_s = \omega_c + \frac{Im(A_2/\mathcal{B})}{Im(A_1/\mathcal{B})}(C_c - C) \quad . \tag{9}$$

The ratio $-\mathcal{A}/\mathcal{B}$ at this frequency ω_s changes sign for $C = C_c$; here we assume without loss of generality that it is positive for $C < C_c$. In this case, the system oscillates spontaneously with an amplitude which according to Eq. (7) behaves as $|x_1|^2 = \Delta^2(C_c - C)/C_c$, where

$$\Delta^2 = C_c \left(Re(A_2/\mathcal{B}) - Re(A_1/\mathcal{B}) \frac{Im(A_2/\mathcal{B})}{Im(A_1/\mathcal{B})} \right) \tag{10}$$

is a typical amplitude. We have thus demonstrated that Eq. (6) characterizes a Hopf-bifurcation if the complex coefficient $\mathcal{A}$ vanishes at a critical point C_c for a critical frequency ω_c.

C. Amplified response to sinusoidal stimuli

If a sinusoidal stimulus $f(t) = f_1 e^{i\omega t} + f_{-1} e^{-i\omega t}$, for which all f_n with $n \neq \pm 1$ vanish, Eq. (6) becomes

$$f_1 \simeq \mathcal{A} x_1 + \mathcal{B} |x_1|^2 x_1 \quad . \tag{11}$$

We consider a system that is tuned exactly to the bifurcation, $C = C_c$. In this situation spontaneous oscillations do not occur and $\mathcal{A} = (\omega - \omega_c) A_1$. If the imposed frequency is equal to the critical frequency $\omega = \omega_c$, the coefficient $\mathcal{A}$ vanishes and we can solve Eq. (11) for $|x_1|$ to find the nonlinear response

$$|x_1| \simeq |\mathcal{B}|^{-1/3} |f_1|^{1/3} \quad , \tag{12}$$

as a function of the force amplitude $|f_1|$. This behavior represents an amplified response with a gain

$$r = \frac{|x_1|}{|f_1|} \sim |f_1|^{-2/3} \tag{13}$$

that becomes arbitrarily large for small forces. If the frequency ω is different from ω_c, this nonlinear response still holds as long as the linear term in Eq. (11) is small compared to the cubic term and can be neglected. This is the case if $|x_1|^2 \gg |\mathcal{A}/\mathcal{B}| = |\omega - \omega_c||A_1/\mathcal{B}|$. Therefore, the nonlinear regime characterized by Eq. (12) holds for sufficiently large force amplitudes, $|f_1| \gg |(\omega - \omega_c)A_1|^{3/2}/|\mathcal{B}|^{1/2}$, or if the frequency is sufficiently close to the critical frequency, $|\omega - \omega_c| \ll |f_1|^{2/3}|\mathcal{B}|^{1/3}/|A_1|$.

If the frequency mismatch $|\omega - \omega_c|$ becomes large, or if forces $|f_1|$ are small, a new regime occurs for which the linear term in (11) dominates. In this regime, the response is linear,

$$|x_1| \simeq \frac{|f_1|}{|(\omega - \omega_c) A_1|} \quad , \tag{14}$$

and the gain is constant. This is a passive response if the stimulus frequency is too far from the critical frequency.

D. Additional remarks

The above derivation is based on an expansion (3) in the displacements x_n. This excludes some nonlinearities in the force which can lead to additional nonlinear terms in Eq. (11). The most general form of Eq. (11) is

$$f_1 \simeq \mathcal{A} x_1 + \mathcal{B}|x_1|^2 x_1 + \mathcal{C} x_1 |f_1|^2 + \mathcal{D} x_{-1} f_1^2 + \mathcal{E}|x_1|^2 f_1 + \mathcal{F} x_1^2 f_{-1} + \mathcal{G}|f_1|^2 f_1 \quad . \tag{15}$$

However, for small forces f_1 and small amplitudes x_1, the results derived above are not affected. The regime of nonlinear response $|f_1| \sim |x_1|^3$, as well as the linear response regime $|f_1| \sim |x_1|$ still exist. If $|f_1| \sim |x_1|$, the nonlinear terms in f_1 renormalize the third order term, which in this regime is negligible. If $|f_1| \sim |x_1|^3$, the nonlinear terms in f_1 are of even higher order and can be neglected.

II. OSCILLATIONS GENERATED BY MOLECULAR MOTORS

A. Two state model

The two state model describes force-generation as a result of transitions between two states, a bound state and a detached state of a motor and its track filament. The interaction between a motor at position z along the filament in states 1 and 2 is characterized by two periodic potentials $W_1(z) = W_1(z+l)$ and $W_2(z) = W_2(z+l)$ where l is the period. We introduce the relative position $\xi = z \bmod l$ with respect to the potential period. Detachment and attachment rates are denoted $\omega_1(\xi)$ and $\omega_2(\xi)$, respectively. Oscillations can occur in this model if a large number N of motors move collectively against an external elastic element of modulus K.

We introduce the probability $P_1(\xi)$ and $P_2(\xi)$ of finding a motor bound at position ξ in state 1 or 2, which satisfy the normalization condition

$$\int_0^l d\xi (P_1 + P_2) = 1 \tag{16}$$

For a large number of motors collectively moving with the same velocity v the dynamic equations read

$$\partial_t P_1 + v\partial_\xi P_1 = -\omega_1 P_1 + \omega_2 P_2 \tag{17}$$

$$\partial_t P_2 + v\partial_\xi P_2 = \omega_1 P_1 - \omega_2 P_2 \tag{18}$$

The velocity v is determined by the force-balance condition

$$f = \lambda v + Kz + N \int_0^l d\xi (P_1 \partial_\xi W_1 + P_2 \partial_\xi W_2) \tag{19}$$

where λ is a friction coefficient describing the total friction and z is the displacement of the motors, $\partial_t z = v$. For an incommensurate arrangement of motors with respect to the track filament and a large number N of motors, $P_1(\xi) + P_2(\xi) = 1/l$ and the equations of motions simplify:

$$\partial_t P_1 + v\partial_\xi P_1 = -(\omega_1 + \omega_2) P_1 + \omega_2 / l \quad . \tag{20}$$

We discuss a simple choice for the potentials and transition rates for which the Hopf bifurcation is easy to determine analytically. We consider the potential

$$W_1(\xi) = U \cos(2\pi\xi/l) \tag{21}$$

with amplitude U, and the potential W_2 to be constant. The transition rates are chosen to be periodic functions

$$\omega_1(\xi) = \beta - \beta\cos(2\pi\xi/l) \tag{22}$$

$$\omega_2(\xi) = \alpha - \beta + \beta\cos(2\pi\xi/l) \tag{23}$$

parameterized by two coefficients α and β. With this choice,

$$\omega_1(\xi) + \omega_2(\xi) = \alpha \tag{24}$$

is constant and the fact that ω_1 and ω_2 are positive restricts β to the interval $0 \leq \beta \leq \alpha/2$.

B. Linear response function

In order to determine the linear coefficient $\mathcal{A}$ which determines the stability of the system, we look for small amplitude oscillations close to the resting state with $v = 0$. We write

$$P \simeq p_0 + p_1 e^{i\omega t} \tag{25}$$
$$f \simeq f_1 e^{i\omega t} \tag{26}$$
$$z \simeq z_1 e^{i\omega t} \tag{27}$$

where $p_0 = \omega_2/\alpha l$. To linear order in z_1, we find from Eq. (20)

$$p_1 = -\frac{i\omega z_1}{i\omega + \alpha}\partial_x p_0 \tag{28}$$

The corresponding force is given by

$$f_1 \simeq \mathcal{A} z_1 \tag{29}$$

with

$$\mathcal{A} = i\omega\lambda + K + \chi \quad , \tag{30}$$

where the active response χ of the motors is given by

$$\chi = -N \int_0^l d\xi \frac{i\omega}{i\omega + \alpha}\partial_\xi p_0 \partial_\xi W_1 \tag{31}$$

For the choice of Eq. (21) and (23) the integral can be calculated and we obtain

$$\mathcal{A}(C, \omega) = i\omega\lambda + K - Nk_0 C \frac{i\omega/\alpha + (\omega/\alpha)^2}{1 + (\omega/\alpha)^2} \quad . \tag{32}$$

Here, we have introduced the dimensionless control parameter $C \equiv 2\pi^2\beta/\alpha$ with $0 < C < \pi^2$ and the cross-bridge elasticity $k_0 \equiv U/l^2$ of the motors.

C. Hopf bifurcation

A Hopf bifurcation occurs if there is a pair of values (C, ω) for which $\mathcal{A}$ as given by Eq. (32) vanishes. Such a point indeed exists. For the critical value

$$C_c = \frac{\lambda\alpha + K}{Nk_0} \tag{33}$$

the bifurcation occurs for the critical frequency

$$\omega_c = \left(\frac{K\alpha}{\lambda}\right)^{1/2} \tag{34}$$

The critical frequency is bounded by the fact that $C_c < \pi^2$. The maximal frequency occurs for the maximal possible value of K

$$K_{\max} = N k_0 \pi^2 - \lambda\alpha \tag{35}$$

for which $C_c = \pi^2$. This frequency is given by

$$\omega_{\max} = \alpha \left(N\pi^2 \frac{k_0}{\lambda\alpha} - 1 \right)^{1/2} \tag{36}$$

Note, that the maximal frequency can be significantly higher than the typical rate α of the chemical cycle.