Auditory sensitivity provided by self-tuned critical oscillations of hair cells

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BENG 250B

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Outline

- Inner hair cell physiology
- Criteria for hearing
- Hopf bifurcation model
- Strengths and weaknesses
- Take-home message
Inner Hair Cell Physiology
Inner Hair Cell Physiology

- Myosin tunes the response by moving along the actin filament at ATP hydrolysis rate ($\alpha$)
- Ion channels completely close if the bundle is deflected for 1/10 sec
Inner Hair Cell Physiology

- Kinocilium is responsible for Hopf Bifurcation
- Isolated, vibrates at \( \Lambda = 4L \)
- \( \omega_c = (Ka/\lambda)^{1/2} \)
- \( \omega_c = (k_s a/\eta L^3)^{1/2} \)
- Kinocilium length defines \( \omega_c \)
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Criteria for Hearing

- High range of frequencies (20Hz-20kHz) with high resolution
- > 1kHz signal – must be mechanical transducer
- Each cell must be responsive to particular frequency
  - Must synapse at that frequency
- Sensitivity (Audible Sound \( \leq \) Thermal)
- Non-linear amplification
Criteria for Hearing

- Non-linear response for small stimulus ($f_1 \ssim f_{th}$)
- Low-gain filter for large stimulus

Fig. 1. Response to external forces near a Hopf bifurcation (a) Amplitude $x_1$ as a function of force $f_1$ at various driving frequencies $\nu$ (\( \bigcirc \) 2 kHz, \( \times \) 5 kHz, \( \square \) 10 kHz, + 13 kHz). (b) Gain $r$ as a function of frequency $\nu$ for different amplitudes $f_1$ (\( \bigcirc \)
Criteria for Hearing

- Mechanical Gain shows a peak for a given kinocilium length
- Laser interferometry of basilar membrane shows similar results

\[ r \text{ (nm/pN)} \]

(b) Gain \( r \) as a function of frequency \( v \) for different amplitudes \( f_1 \) (\( \diamond 0.01 \text{ pN}, \triangle 0.05 \text{ pN}, + 0.1 \text{ pN}, \times 0.5 \text{ pN}, \square 1 \text{ pN} \)). Although the form of these curves...
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Andronov-Hopf Bifurcation

- Maintain two poles on imaginary axis
- S-space
- $C < C_c$: unstable
- $C > C_c$: stable
- $C = C_c$: bifurcation
Andronov-Hopf Bifurcation

- **Stimulus (force)** \( f(t) = f_1 e^{i\omega t} + f_{-1} e^{-i\omega t} \)
  - \( f_1 = A x_1 + B |x_1|^2 x_1 + \ldots \)
  - \( A(C_{cr}, \omega) = 0 \)

- **Response (deflection)** \( x(t) = \sum x_n e^{i n \omega t} \)
  - \( C = C_c \ |x(t)| \leq |B(C, \omega)|^{-1/3} |f_1|^{1/3} \)
  - \( r \) varies with \( |f_1|^{-2/3} \)
Andronov-Hopf Bifurcation

- C changes with x
  - $x < \delta$, $C \downarrow$
  - $x > \delta$, $C \uparrow$

- $(1/C)\left(\frac{\partial C}{\partial t}\right) = \frac{1}{\tau}(x^2/\delta^2 - 1)$

- Noise added
  - Brownian motion
  - Stochastic
  - Monte Carlo simulation
Andronov-Hopf Bifurcation

- Simulations with different numbers of molecular motors keeping constant steady-state tension in tip links
- $C_c$ varies with $1/n^2$
- $\alpha$ (ATP hydrolysis rate)
Andronov-Hopf Bifurcation

- Response to \( \sin() \) input near \( C_c \)
- \( n = 2000 \)
- Low \( f_1 \)
  - Phase alignment
- Intermediate \( f_1 \)
  - \( x \sim |f_1|^{1/3} \)
Andronov-Hopf Bifurcation

- **Ion flux**
  - Depolarizes membrane
  - Generates synaptic current (< 1kHz)

- **Weak stimulus**
  - Firing rate constant
  - Phase lock increases
Andronov-Hopf Bifurcation

- Benefits of Noise
  - Self-tuned critical oscillations are incoherent
  - Weak stimuli don’t increase amplitude

- Model accounts for “adaptation”
  - Firing rate decreases with strong stimuli
  - Not with weak stimuli

- Critical oscillations explain otoacoustic emissions
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Strengths & Weaknesses

Strengths
- Numerical analysis
- Thorough modeling

Weaknesses
- Mammals have no kinocilia
- Few corollaries to specific studies in non-mammals
- Cilia and synapse characteristics when freq > 1kHz
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Take-home Message

- Dynein motors control ion channels to tune the hair cell to critical frequency
- Critical oscillations allow for non-linear gain
- A force equal to that of one myosin motor is enough to generate a response using phase-locking
Questions?

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