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

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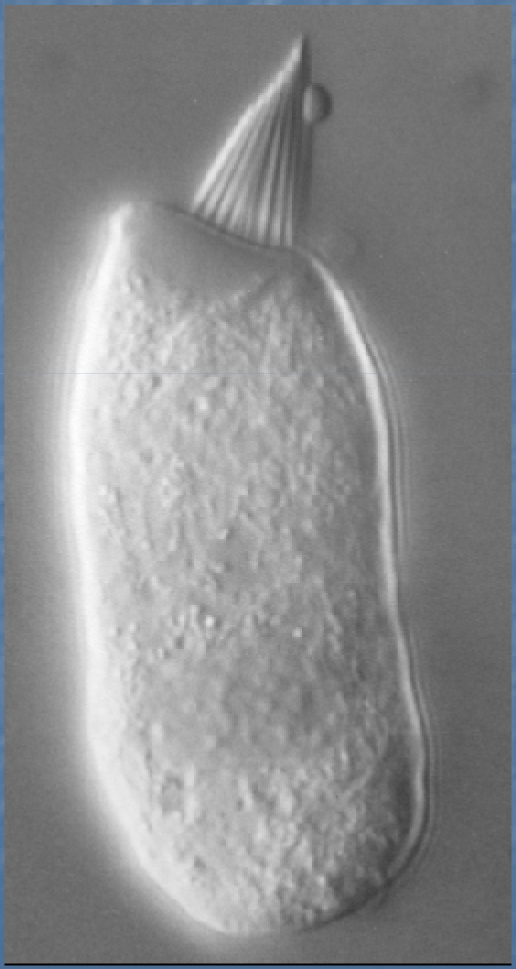
BENG 250B

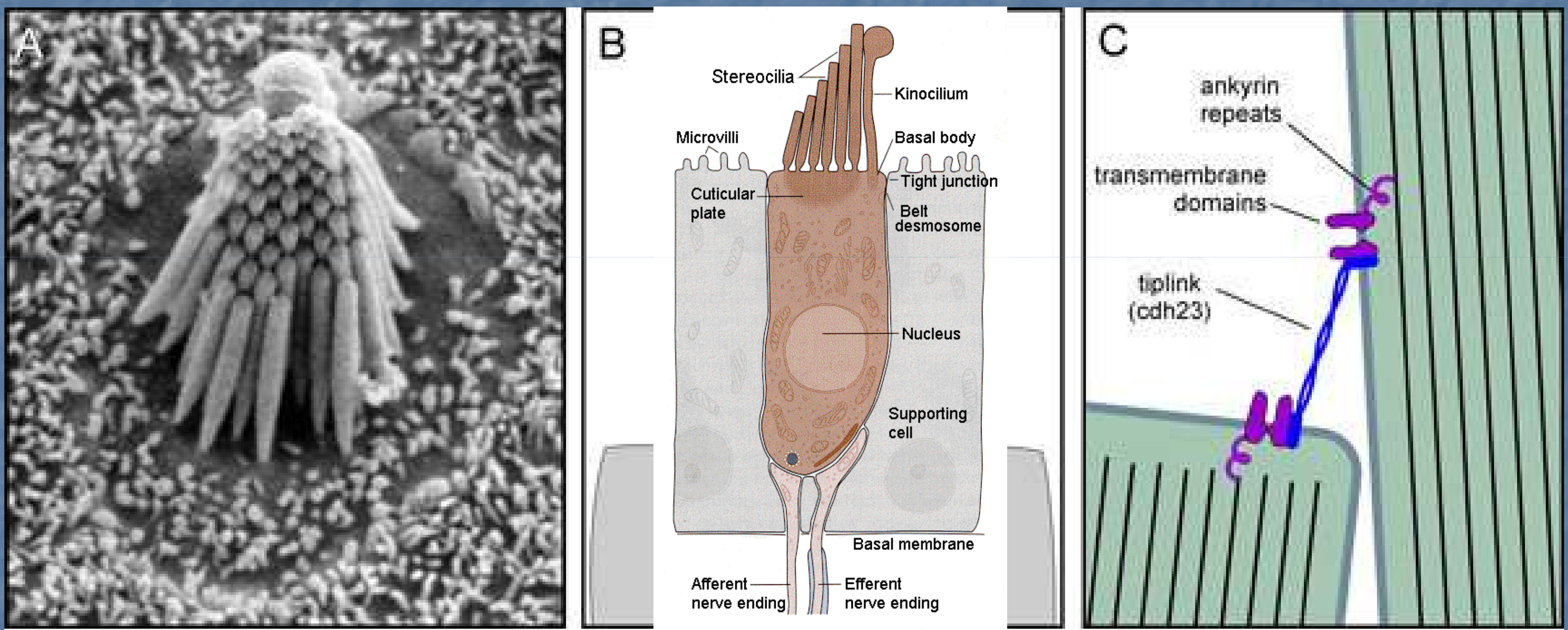
May 15, 2007

Outline

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



Inner Hair Cell Physiology



Theoretical and Computational Biophysics Group
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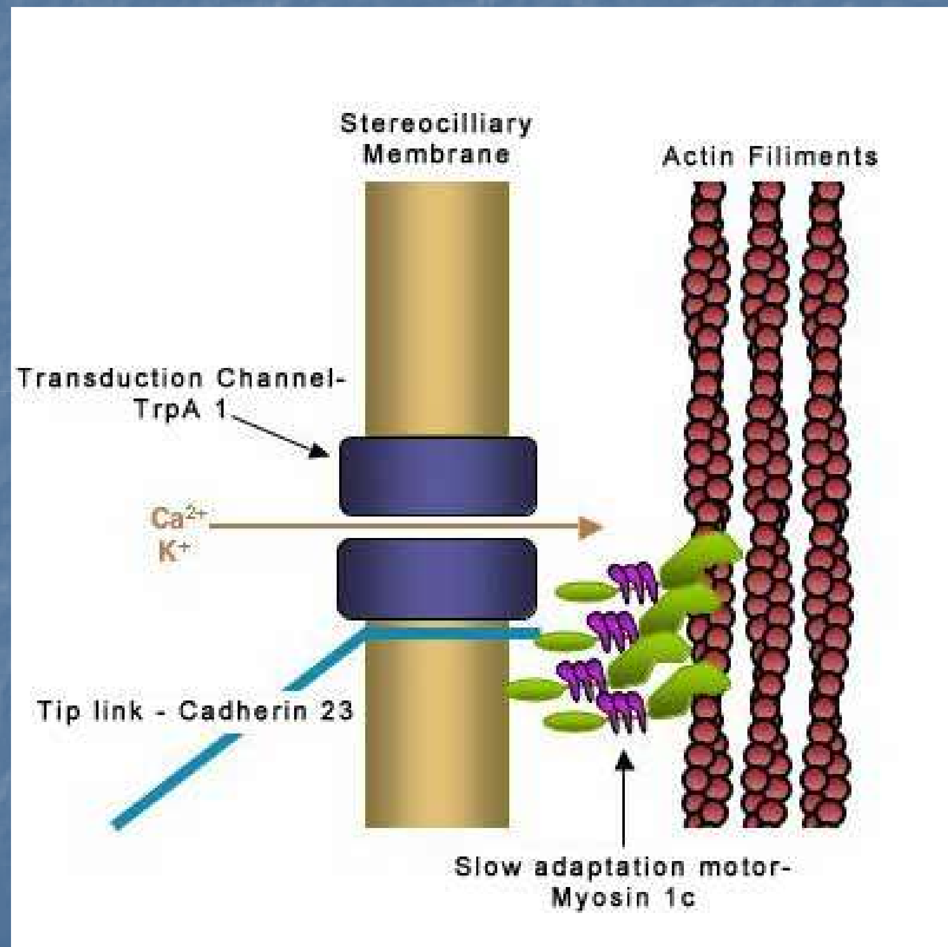
University of Illinois at Urbana-Champaign

Inner Hair Cell Physiology

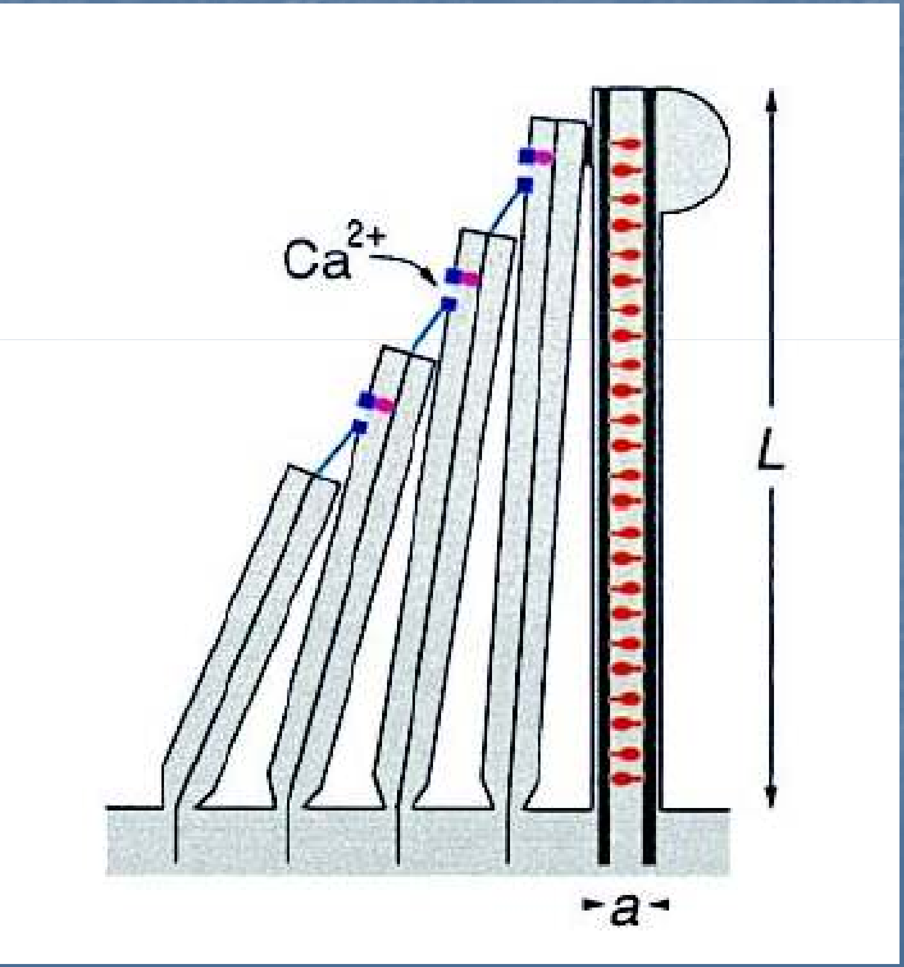
- Myosin tunes the response by moving along the actin filament at ATP hydrolysis rate (α)
- Ion channels completely close if the bundle is deflected for 1/10 sec



West Virginia University Center for Neuroscience

Inner Hair Cell Physiology

- Kinocilium is responsible for Hopf Bifurcation
- Isolated, vibrates at $\Lambda = 4L$
- $\omega_c = (K\alpha/\lambda)^{1/2}$
- $\omega_c = (k_s\alpha/\eta L^3)^{1/2}$
- Kinocilium length defines ω_c



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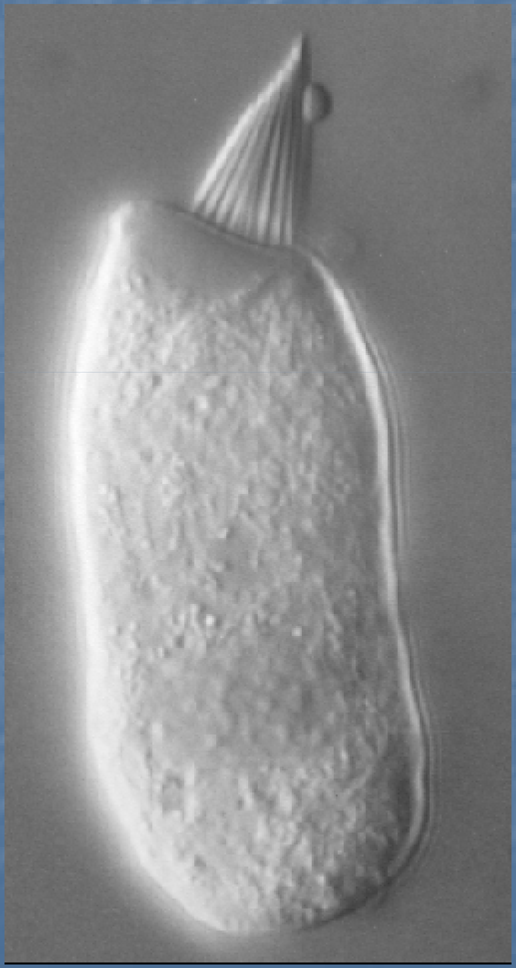


Criteria for Hearing

- 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 ≤ Thermal)
- Non-linear amplification

Criteria for Hearing

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

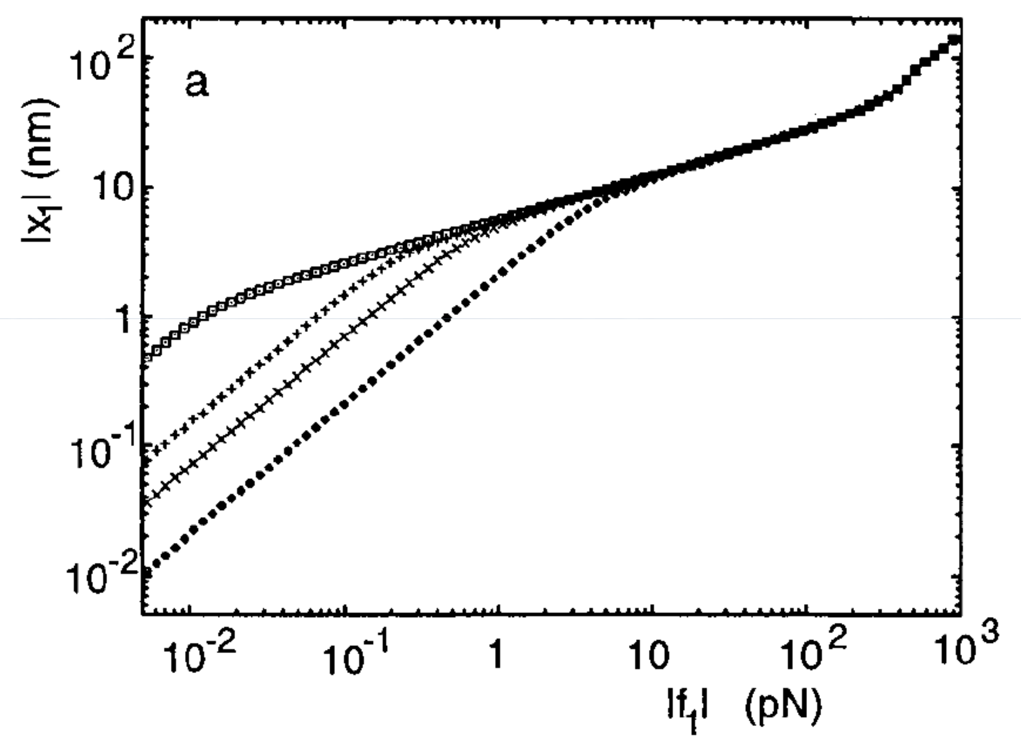
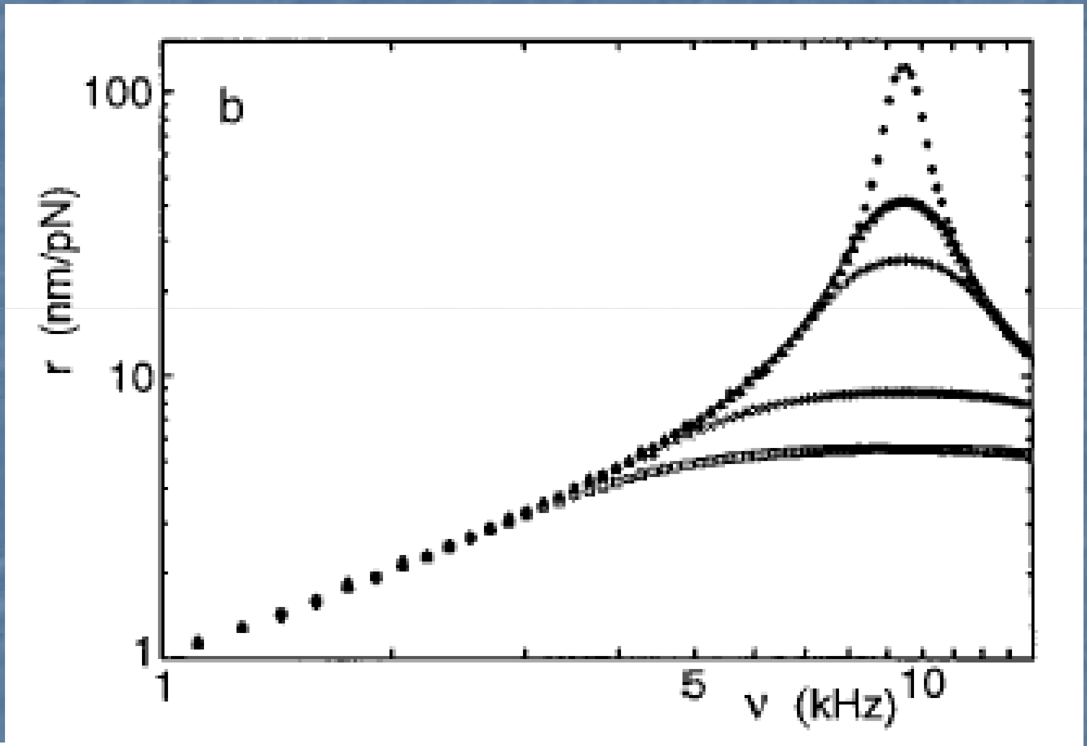


Fig. 1. Response to external forces near a Hopf bifurcation (*a*) Amplitude x_1 as a function of force f_1 at various driving frequencies ν (◇ 2 kHz, × 5 kHz, □ 10 kHz, + 13 kHz). (*b*) Gain r as a function of frequency ν for different amplitudes f_1 (◇

Criteria for Hearing

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



+ 13 kHz). (*b*) Gain *r* as a function of frequency *ν* for different amplitudes f_1 (◇ 0.01 pN, △ 0.05 pN, + 0.1 pN, × 0.5 pN, □ 1 pN). Although the form of these curves

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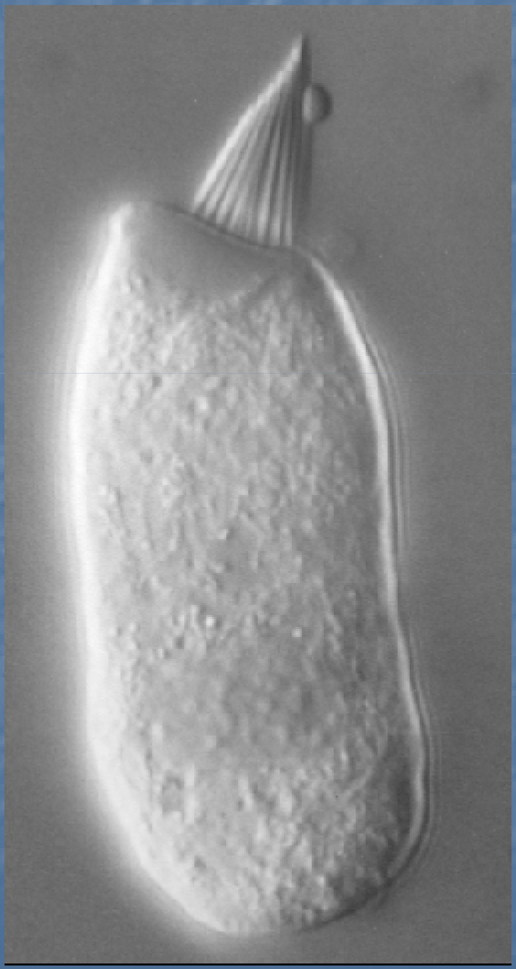
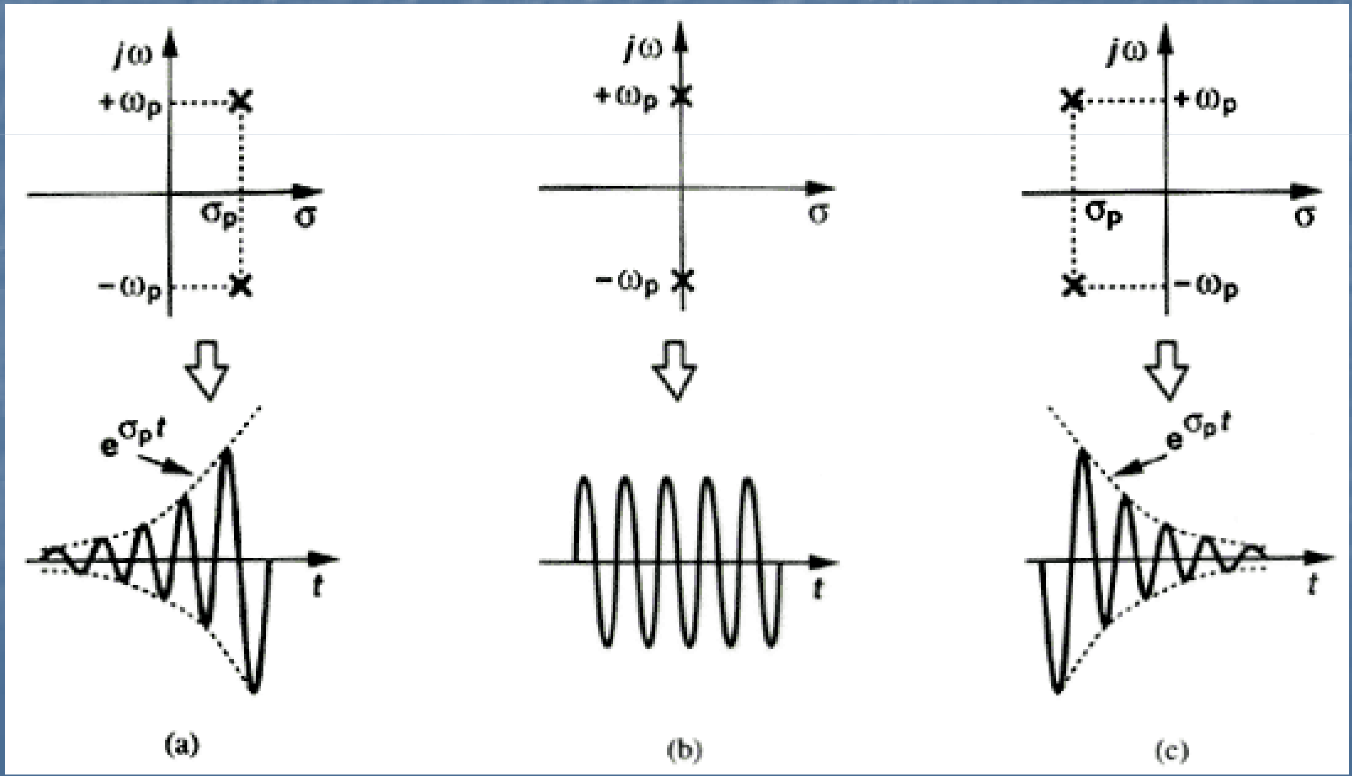


Andronov-Hopf Bifurcation

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



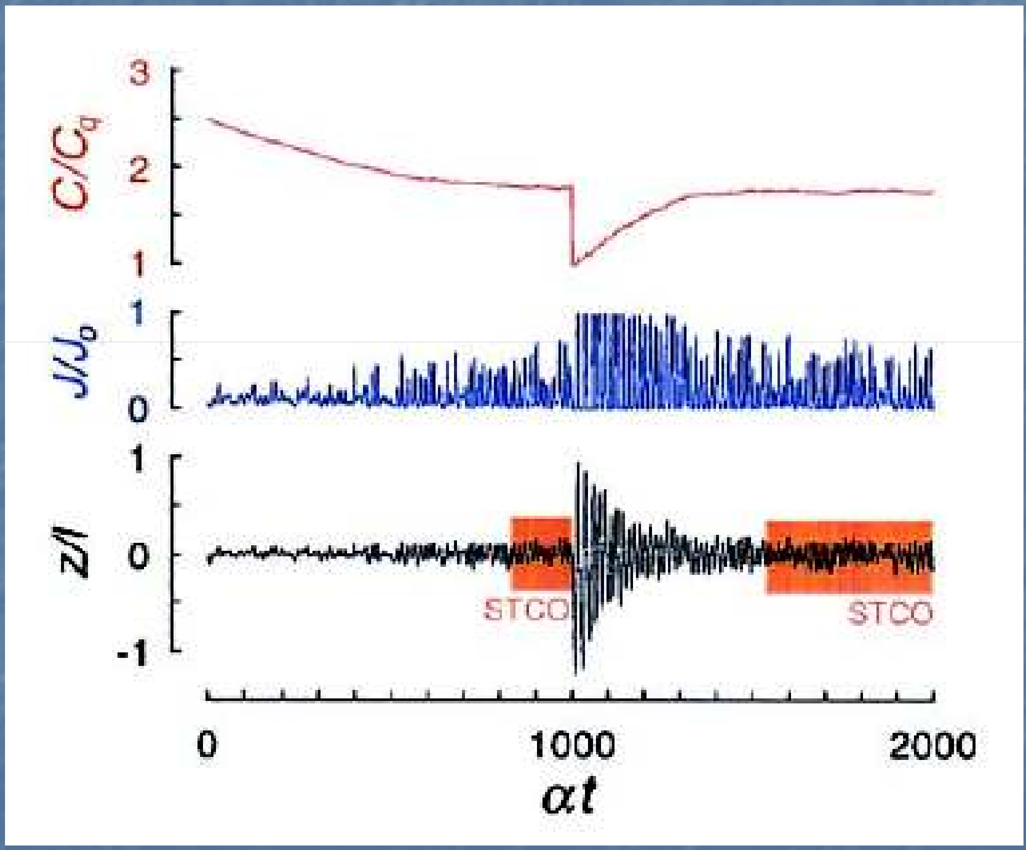
Andronov-Hopf Bifurcation

- Stimulus (force) $f(t) = f_1 e^{i\omega t} + f_{-1} e^{-i\omega y}$
  - $f_1 = Ax_1 + B|x_1|^2 x_1 + \ldots.$
  - $A(C_c,\omega) = 0$

- Response (deflection) $x(t) = \sum x_n e^{in\omega t}$
  - $C = C_c$ $|x(t)|$ 📫 $|B(C,\omega)|^{-1/3}|f_1|^{1/3}$
  - r varies with $|f_1|^{-2/3}$

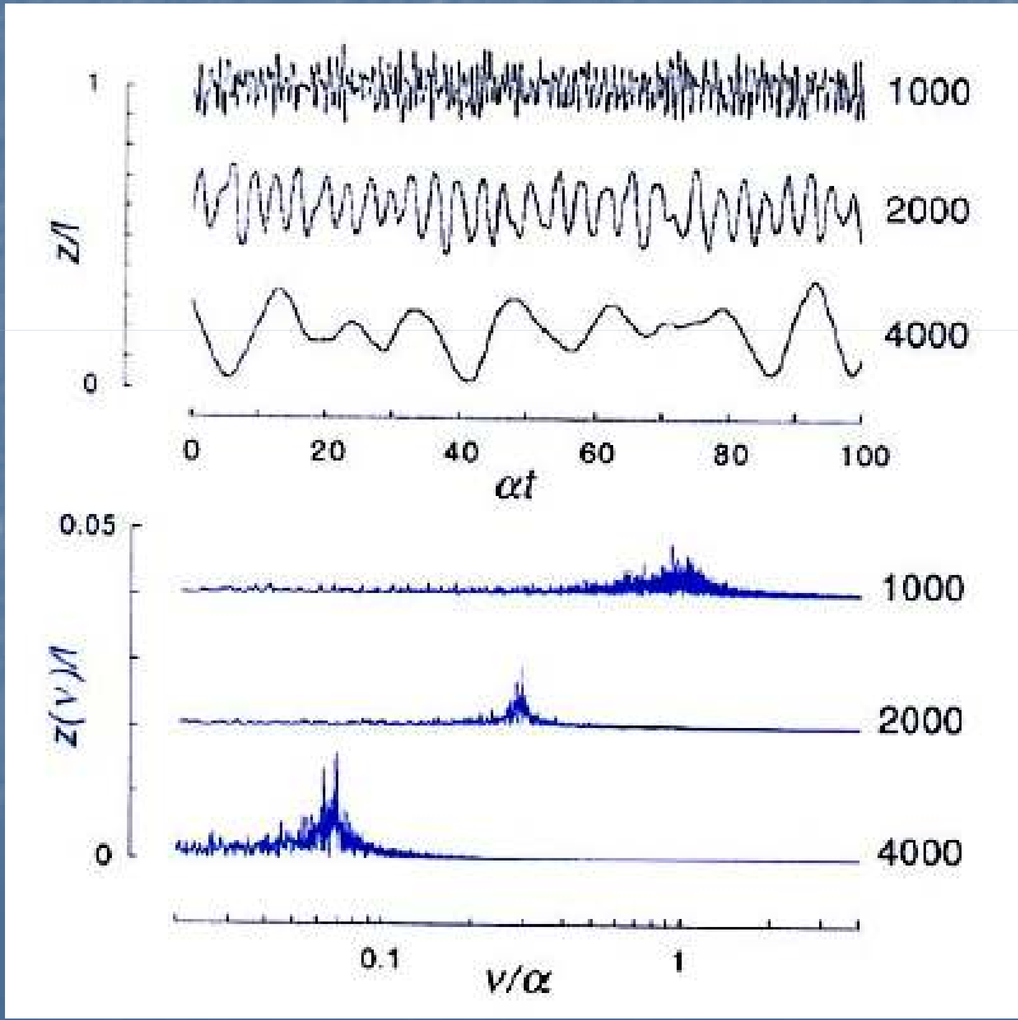
Andronov-Hopf Bifurcation

- C changes with x
  - $x < \delta$, C ↓
  - $x > \delta$, C ↑
  - $(1/C)(\partial C/\partial t) = (1/\tau)(x^2/\delta^2 - 1)$
- Noise added
  - Brownian motion
  - Stochastic
  - Monte Carlo simulation



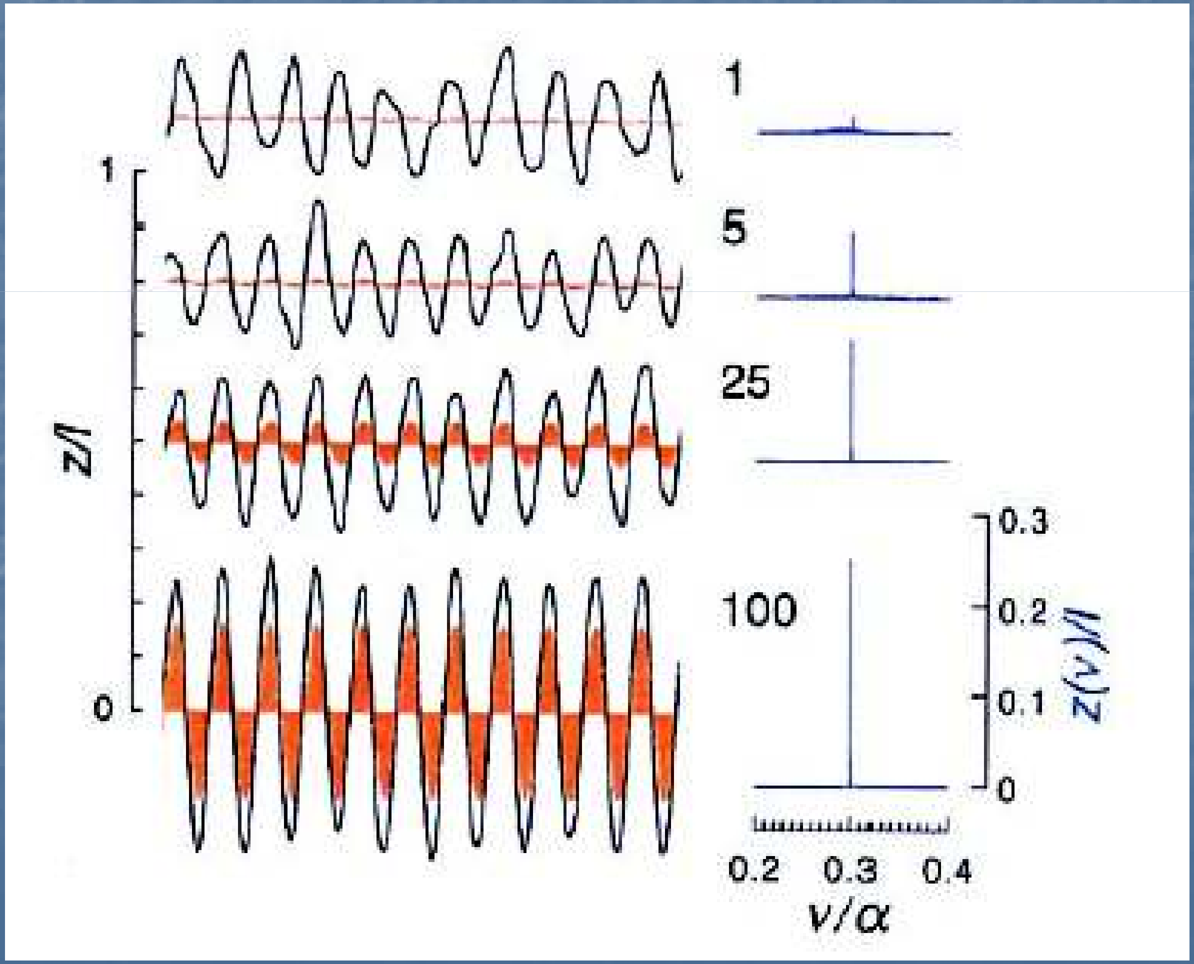
Andronov-Hopf Bifurcation

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



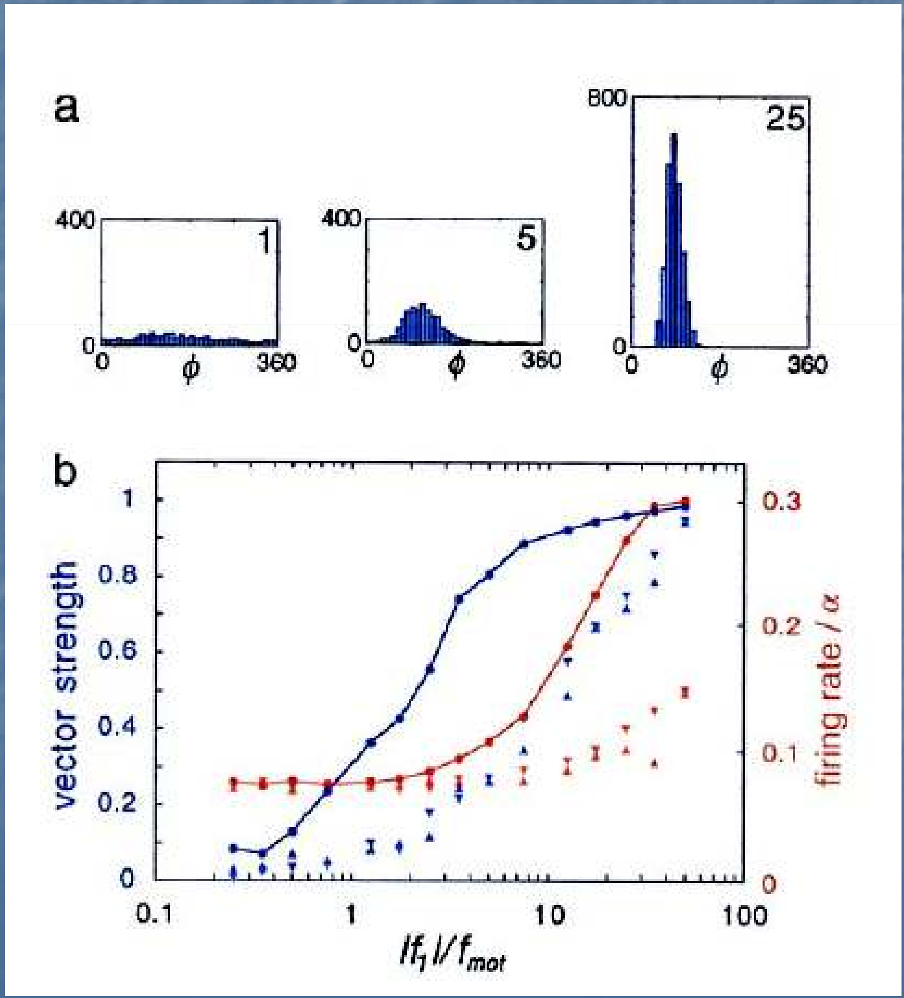
Andronov-Hopf Bifurcation

- Response to sin() input near C_c
- n = 2000
- Low f1
  - 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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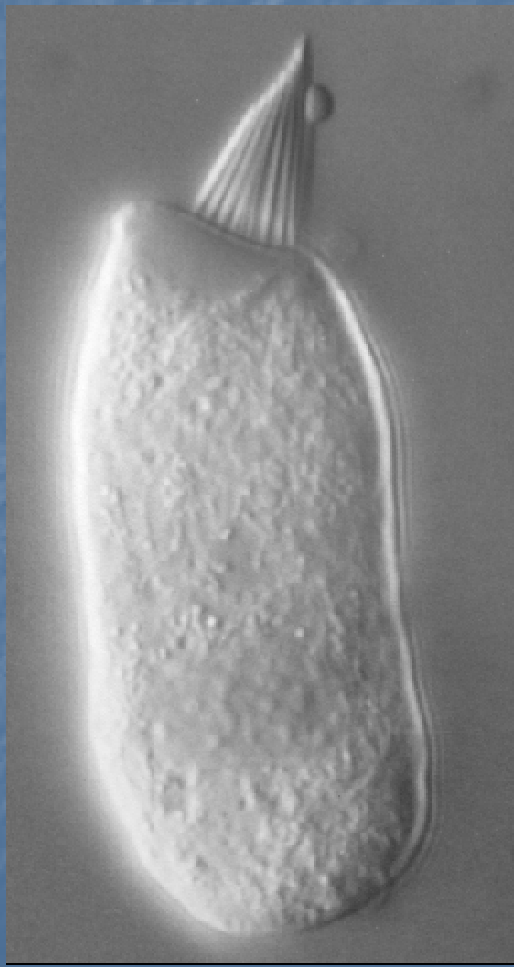

Strengths & Weaknesses

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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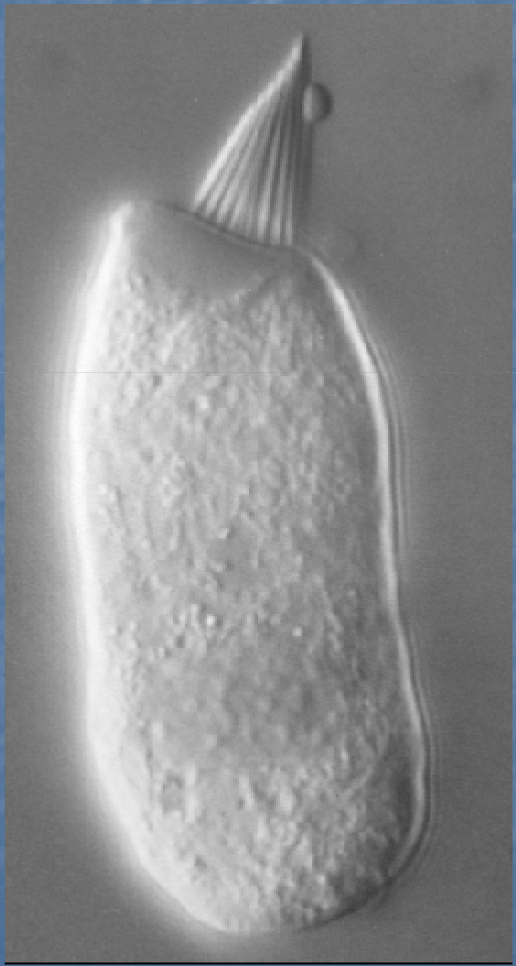

Take-home Message

- 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?

Jonathan Ashmore, UCL Ear Institute