The hair-cell bundle:
sensor and amplifier for hearing.

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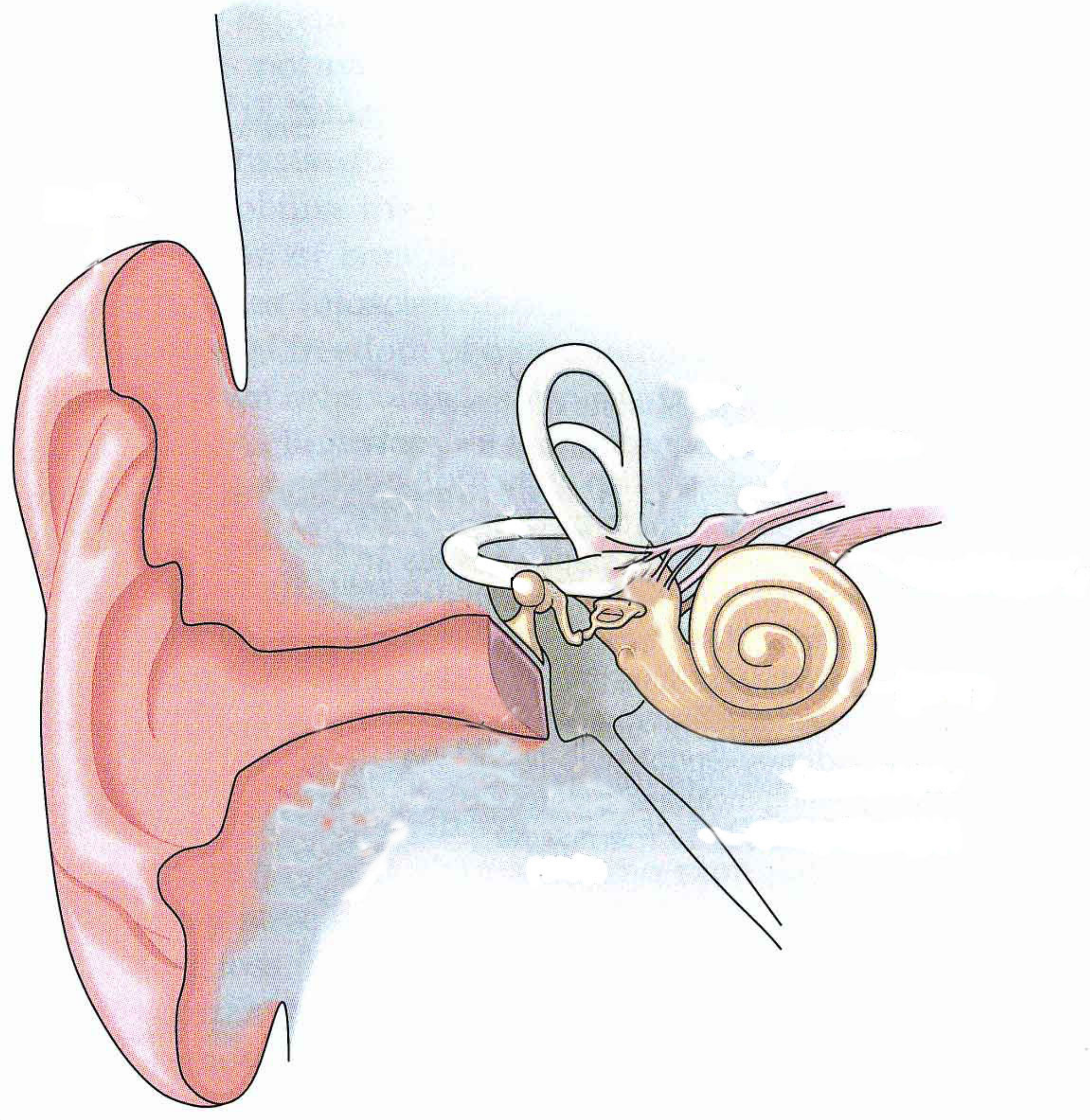


Hearing specifications

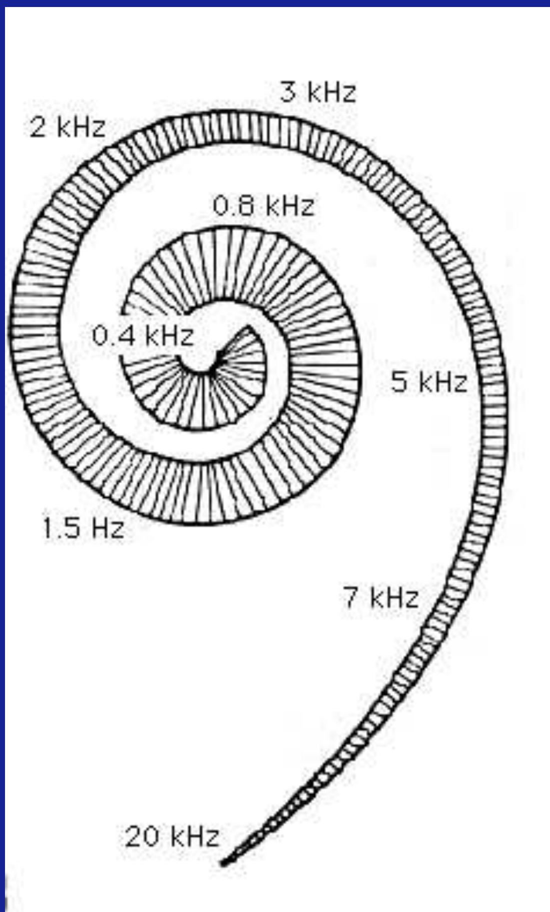
- frequency range (20 Hz - 20 KHz; up to 100 kHz in whale and bats)
- sensitivity (limited by thermal noise)
- frequency selectivity $(\Delta f / f \cong 0.25\%)$
- dynamical range (1 – 1,000,000 ; sound pressure: 20 μPa → 20 Pa)

The resonance hypothesis

→ energy accumulation from cycle to cycle of stimulation

« Sympathetic vibration »

Hermann von Helmholtz (1821-1894)



« (…) the radial fibers of the basilar membrane may be approximately regarded as forming a system of stretched strings (…). In that case the laws of their motion would be the same as if every individual string moved independently from the others, and obeyed the influence of the periodically alternating pressure of the fluid (…). Consequently any exciting tone would set that part of the membrane into sympathetic vibration (…). »

(from "On the sensation of tones", 1877)

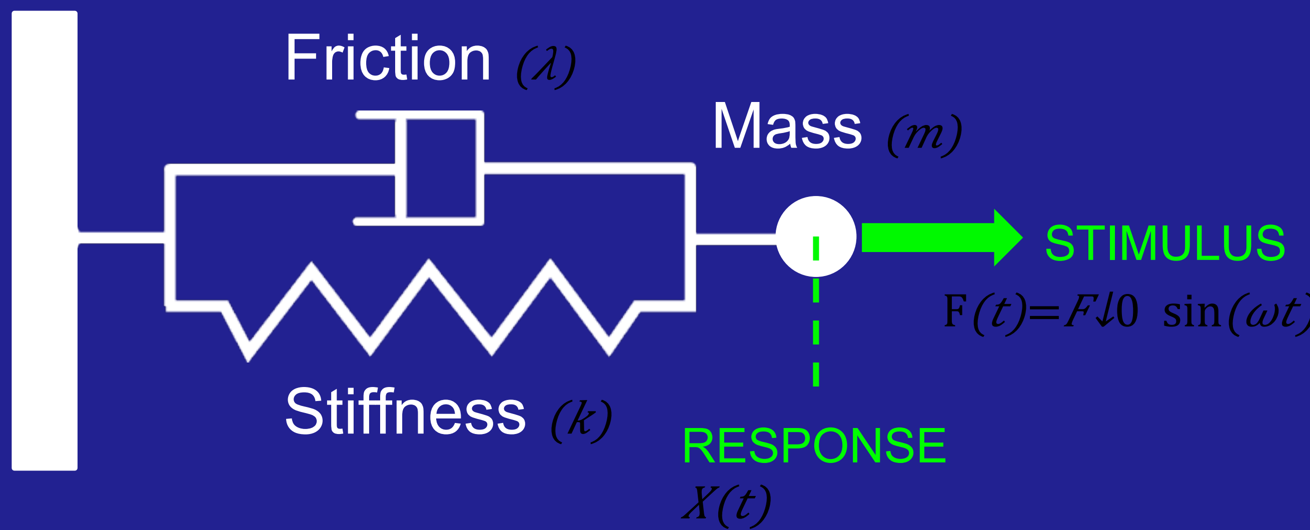
Place of Section	Breadth of Membrane or Length of Transverse Fibres	
	Millimetres	Inches
0·2625 mm. [=0·010335 in.] from root . . .	0·04125	·00162
0·8626 mm. [=0·033961 in.] from root . . .	0·0825	·00325
Middle of the first spire	0·169	·00665
End of first spire	0·3	·01181
Middle of second spire	0·4125	·01624
End of second spire	0·45	·01772
At the hamulus	0·495	·01949

¶

The breadth therefore increases more than twelvefold from the beginning to the end.

Harmonic oscillator

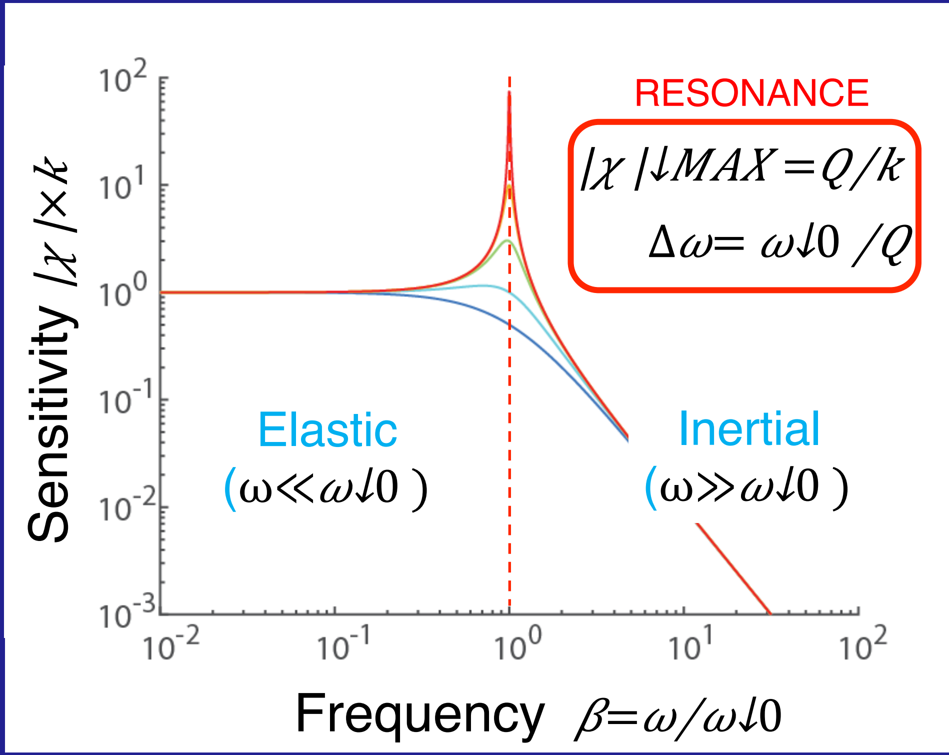
→ passive mechanical properties



Equation of motion:

$$m X + \lambda X + k X = F(t)$$

Mechanical resonance



RESPONSE FUNCTION

$$\chi = \frac{1/k}{[1-\beta^2 + i\beta/Q]}$$

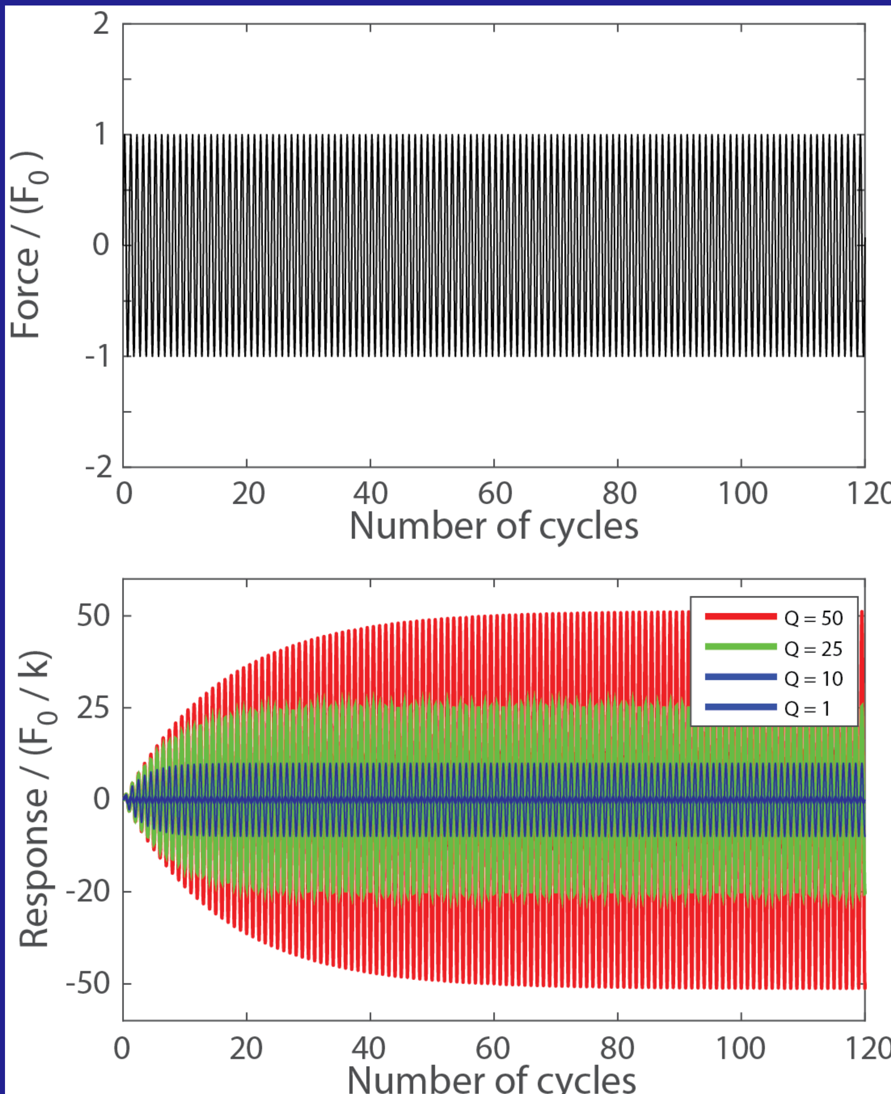
with $\chi = X/F$

$(F(t) = F e^{i\omega t}; X(t) = X e^{i\omega t})$

Characteristic frequency: $\omega_0 = \sqrt{k/m}$

Quality factor: $Q = \sqrt{k m}/\lambda = \omega_0/\Delta\omega$

high sensitivity ↔ slow response growth



STIMULUS

$$F(t)=F_0 \sin\omega_0 t$$

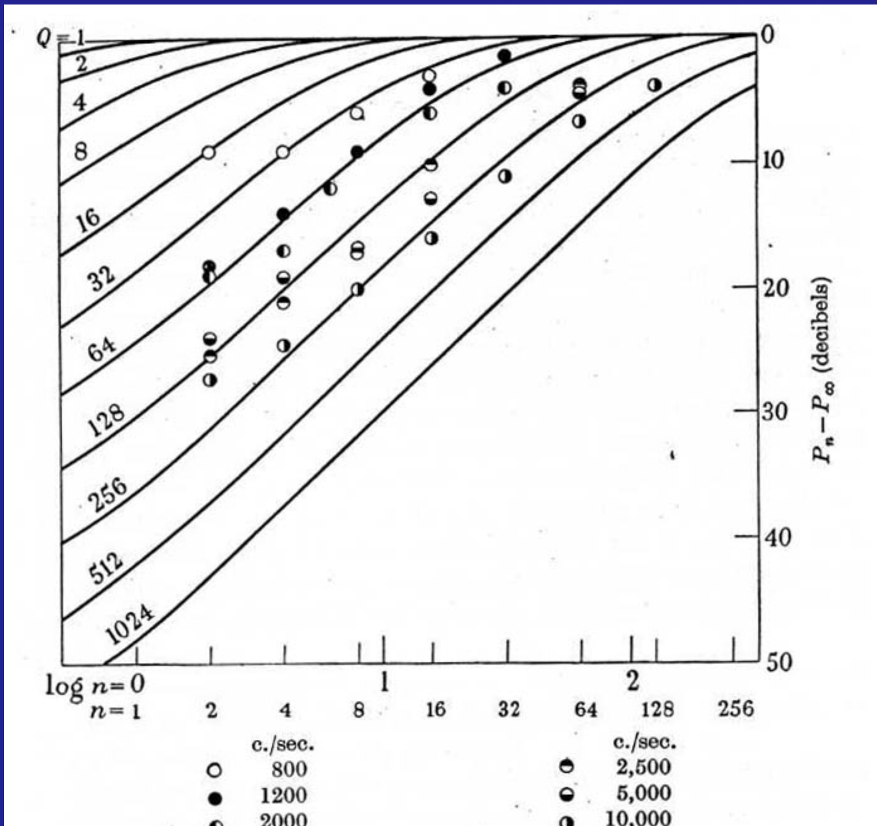
RESPONSE

$$X(t)\cong -Q F_0/k\,[1-\exp(-t/\tau)]\times\cos\omega_0 t$$

response max: $Q F_0/k$

response time: $\tau=2Q/\omega_0$

Sound-pressure level $P_n = 20\log(F_n)$ to get a threshold vibration X_0 after *n* cycles of oscillations.



Quality factors infered:

frequency (c./sec.)	Q	time constant $= Q/\pi f_0$ (msec.)
10,000	300	10
5,000	150	10
2,500	150	19
2,000	80	12
1,200	60	16
800	32	13

(Gold and Pumphrey, Proc Roy Soc Lond (1948))

➡ highly tuned resonator

$$X_0 \cong QF_n/k\,[1-\exp(-\pi n/Q)] = QF_\infty/k$$

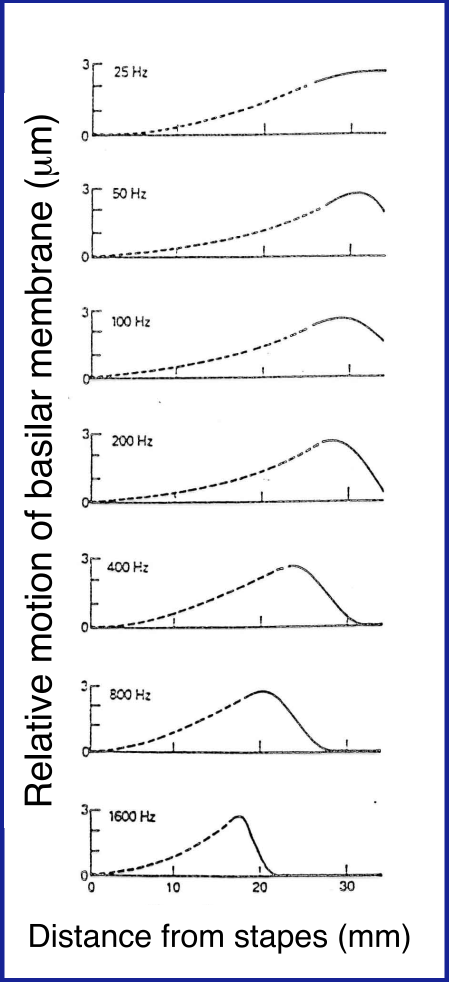
→ $$P_n - P_\infty \cong -20\log[1-\exp(-\pi n/Q)]$$

« We would then regard the cochlea no longer as a passive instrument where nerve endings merely record the displacement due to an applied force, but as an active mechanism where an applied signal releases a chain of events involving an additional source of energy. »

Thomas Gold, 1948

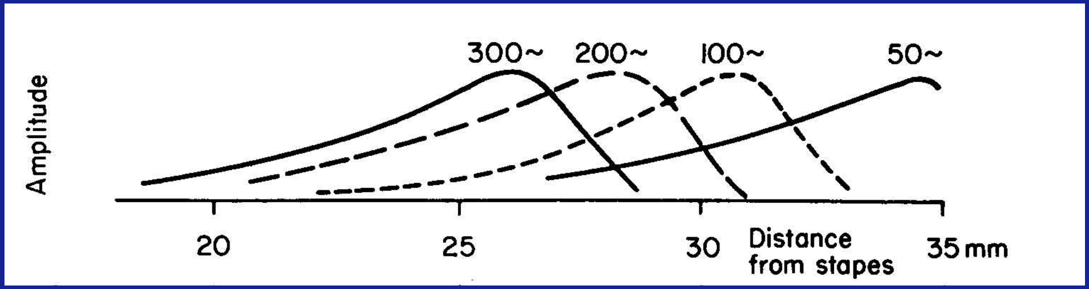
Passive (and broad) resonance

Georg von Békésy (1899-1972)



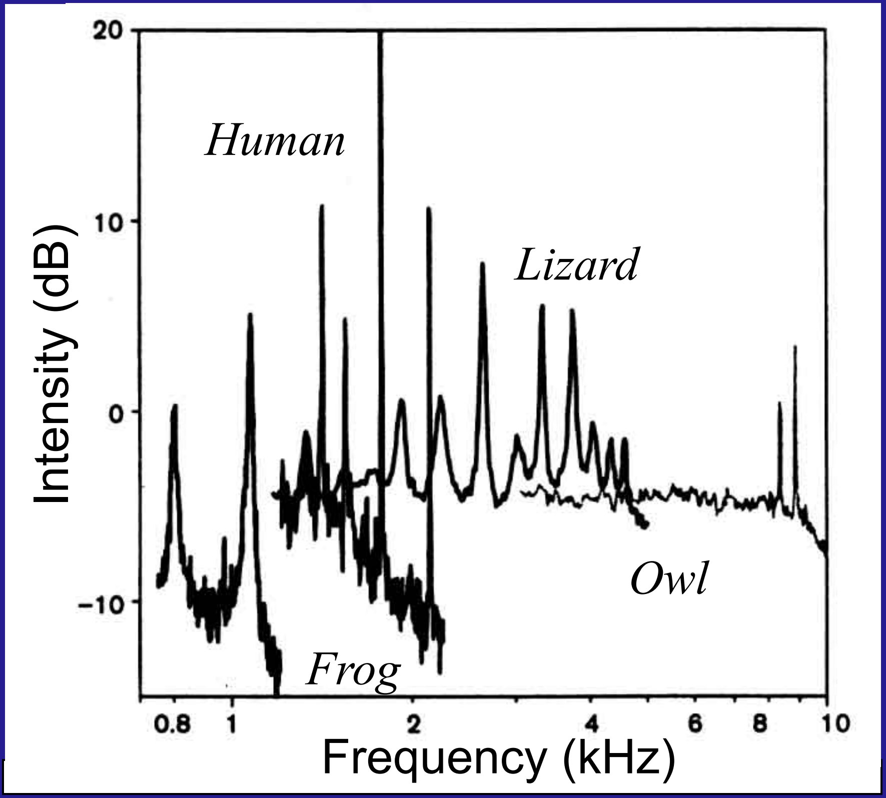
Envelope of basilar-membrane vibration

(in human cadavers...)



The ear can sing!

Spontaneous oto-acoustic emissions (S.O.A.Es)



(G.A. Manley and C. Köppl, 1998)

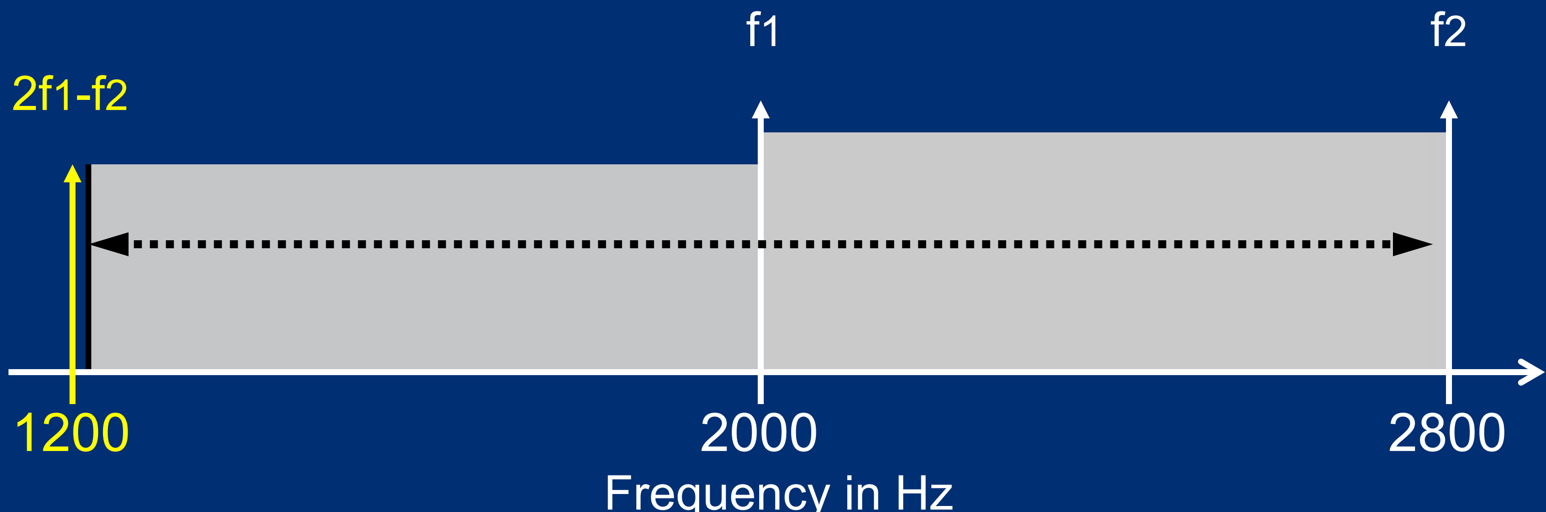
Not a high-fidelity sound receiver!

Tartini
(1692-1770)

« Phantom tones »

→ two-tone stimulus:

$$F(t) = \overline{F}\,\sin\left(2\pi f_1 t\right) + \overline{F}\,\sin\left(2\pi f_2 t\right) \qquad (f_1 < f_2)$$



- primary tone f_1
- primary chirp f_2
- f_1 and f_2

(Source: Daniel Pressnitzer, ENS, Paris)

« Phantom tones »

$$F(t) = \bar{F}\sin(2\pi f_1 t) + \bar{F}\sin(2\pi f_2 t) \qquad (f_1 < f_2)$$

- f_2-f_1 must be small (f_2/f_1 = 1.1-1.3)
- perceived even at low levels (threshold ≅ 20 dB)
- distortion at $2f_1$-f_2 dominates
- relative level at $2f_1$-f_2 nearly independant of stimulus level (15-20%)

⇨ Auditory nonlinearity

(J.L. Goldstein, JASA (1967))

Static nonlinearity

Stimulus: $F(t) = F\sin(2\pi f_1 t) + F\sin(2\pi f_2 t)$

Response: $X(t) \cong \chi F + \alpha F$

Primaries:
f_1 and f_2

Quadratic distortions:
$2f_1$, $2f_2$, $f_2 - f_1$ and $f_1 + f_2$

Cubic distortions:
$3f_1$, $3f_2$, $2f_2 - f_1$, $2f_1 - f$
$2f_1 + f_2$ and $2f_2 + f_1$

$X_{f_1} \propto F$; $X_{f_2} \propto F$
$X_{2f_1 - f_2} \propto F^3$

Does NOT explain
the auditory nonlinearity!

Relative level of cubic distortion: $X_{2f_1 - f_2} / X_{f_1} \propto F^2$

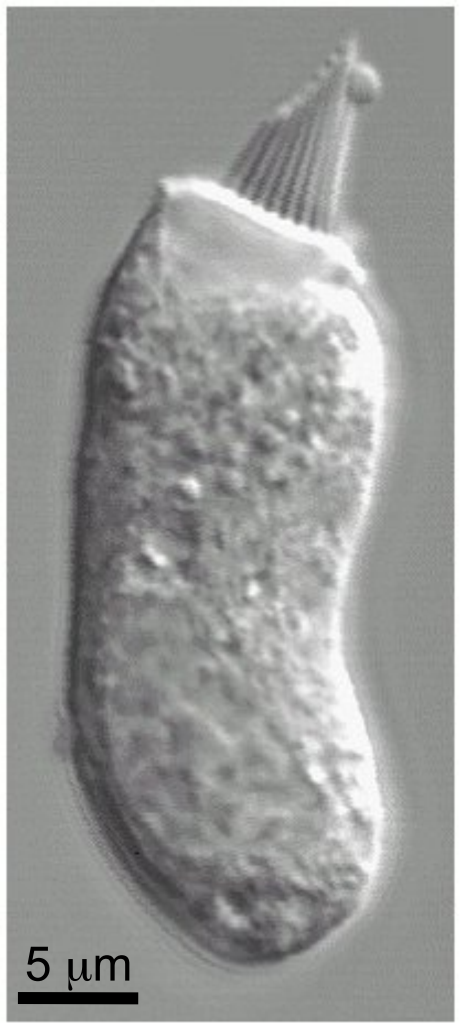
Non-linear interference in hearing

→ two-tone stimulus:

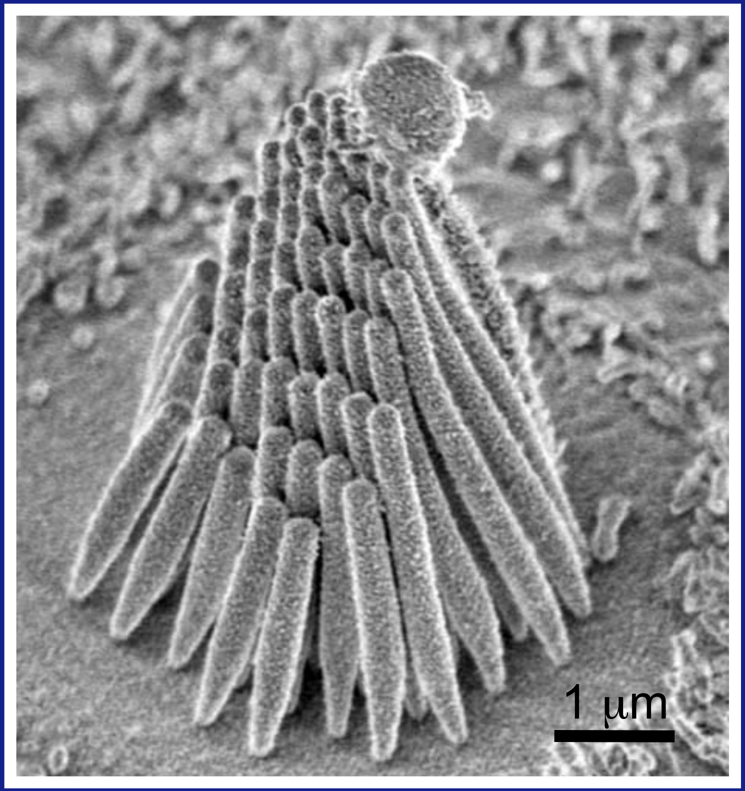
$$F(t) = F_1 \sin(2\pi f_1 t) + F_2 \sin(2\pi f_2 t)$$

- DISTORTIONS: tones that are not present in the sound stimulus are perceived.
- MASKING: the perceived loudness of a (test) tone diminishes in the presence of a second (masker) tone at a nearby frequency.

The hair cell

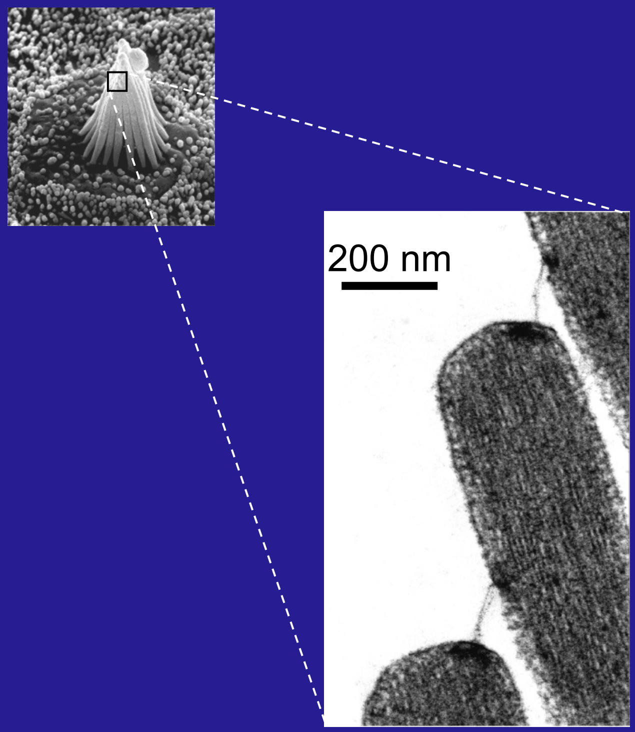


(A.J. Hudspeth)

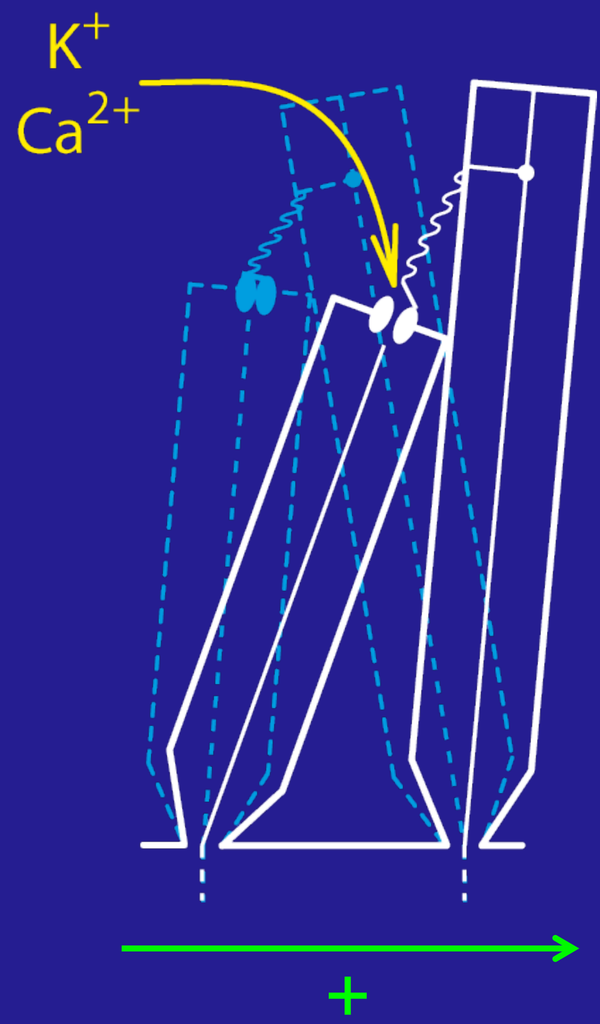


(P. Gillespie)

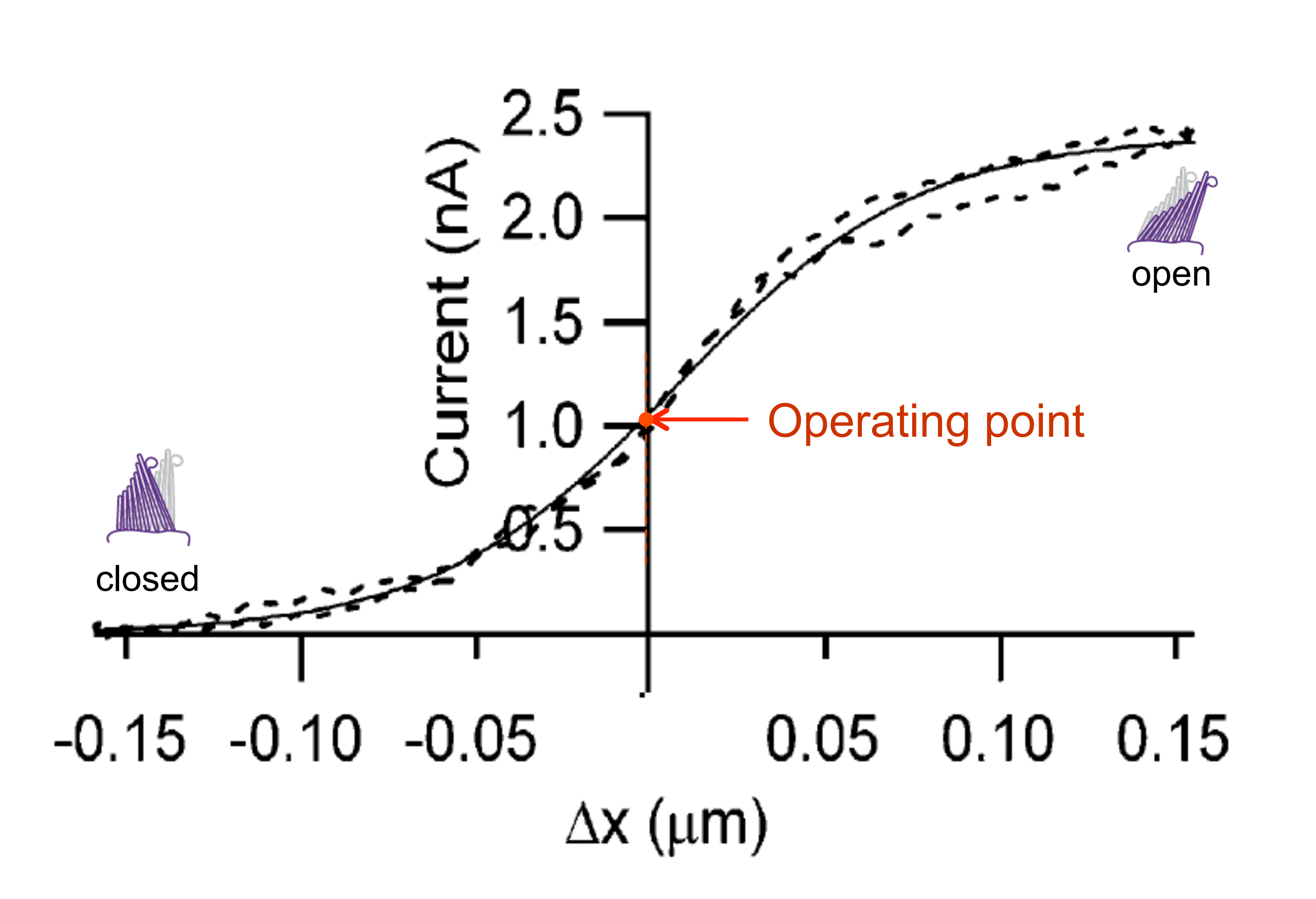
The hair-cell bundle: mechanical antenna



(A.J. Hudspeth)



Transduction current



(Johnson et al, Neuron (2011))

Passive mechanical properties

Mass: $m = 60 \times 10^{-15}$ kg

Stiffness: $k = 1$ mN/m

Viscous drag: $\lambda = 80$ nN·s/m

$f_0 = \frac{1}{2\pi}\sqrt{k/m} = 25$ kHz

$Q = \sqrt{km}/\lambda = 0.1$

OVERDAMPED!

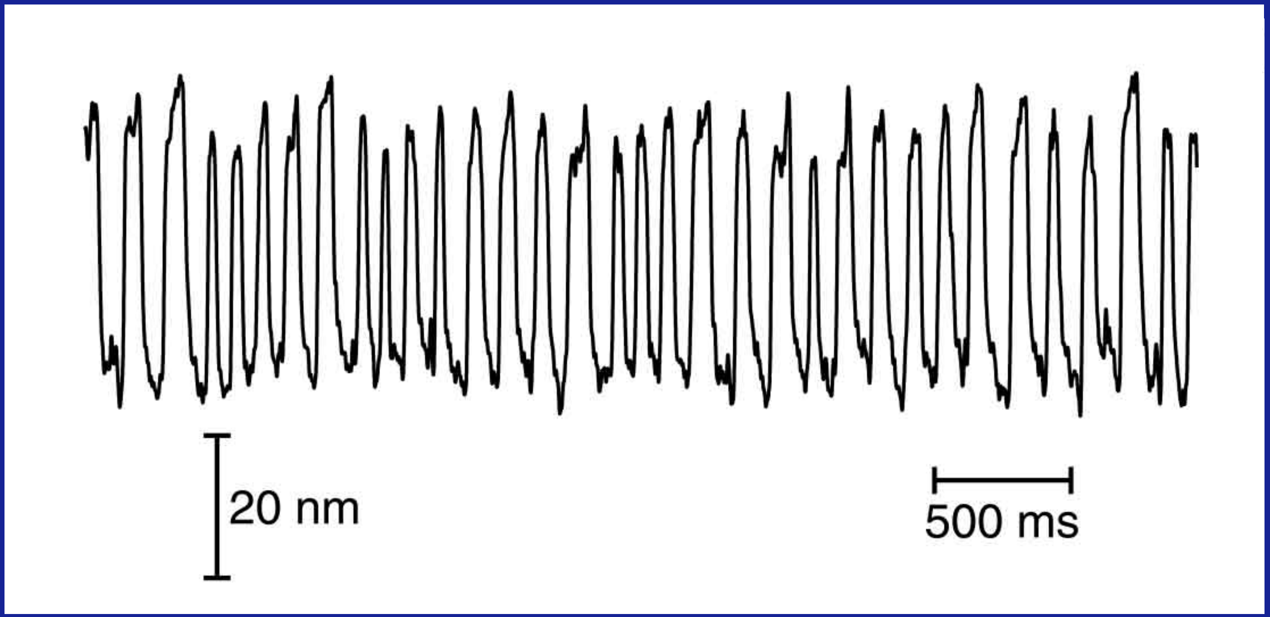
(bullfrog)

The hair-cell bundle

→ sensory and motile

1 μm

SPONTANEOUS OSCILLATIONS

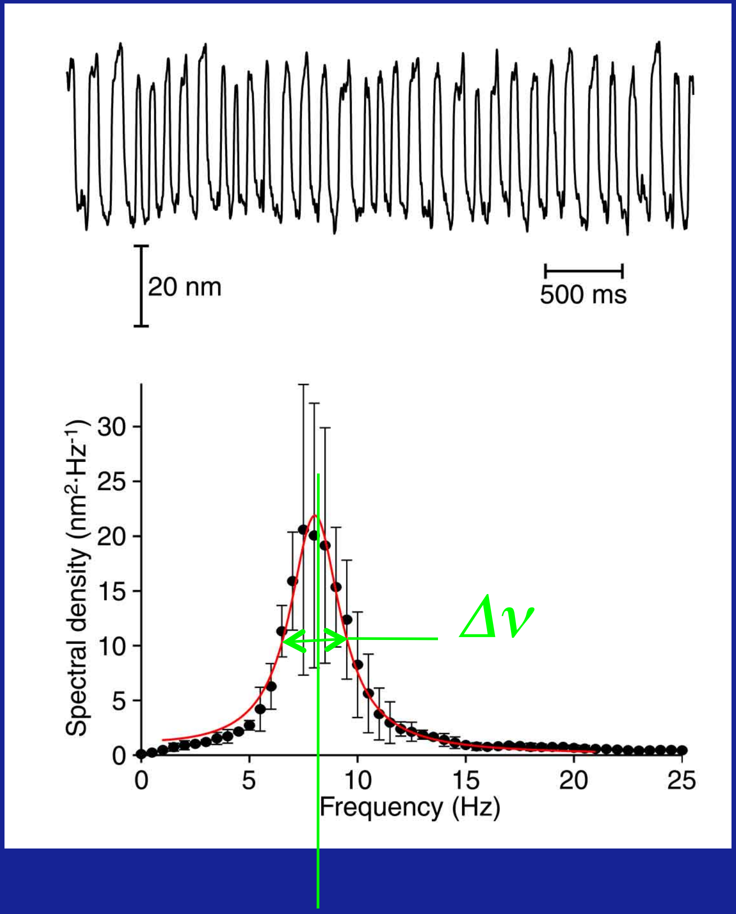


(Martin and Hudspeth, PNAS (1999))

Characteristic frequency

Hair-bunde position

Spectral density



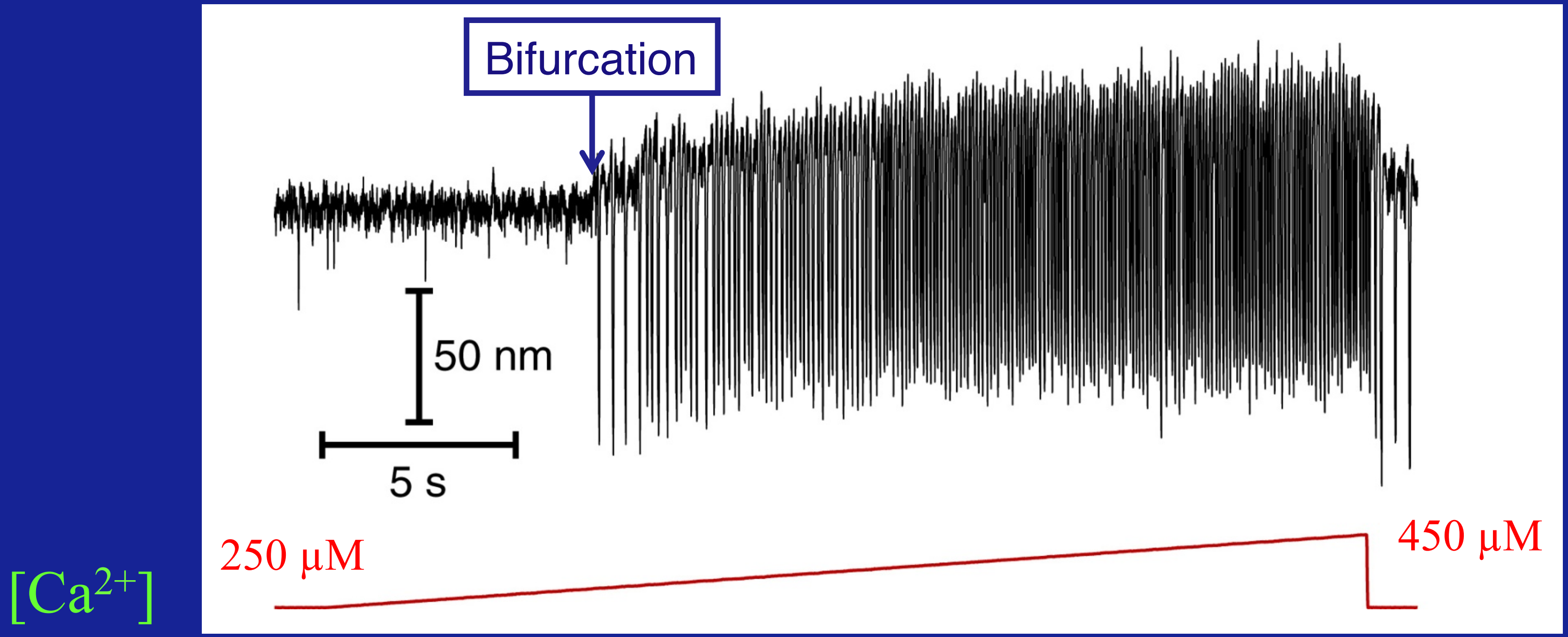
Noisy!

Low quality factor
(Q = $\nu_C/\Delta\nu \cong 2$)

characteristic frequency: ν_C (range: 5-50 Hz)

Oscillatory instability

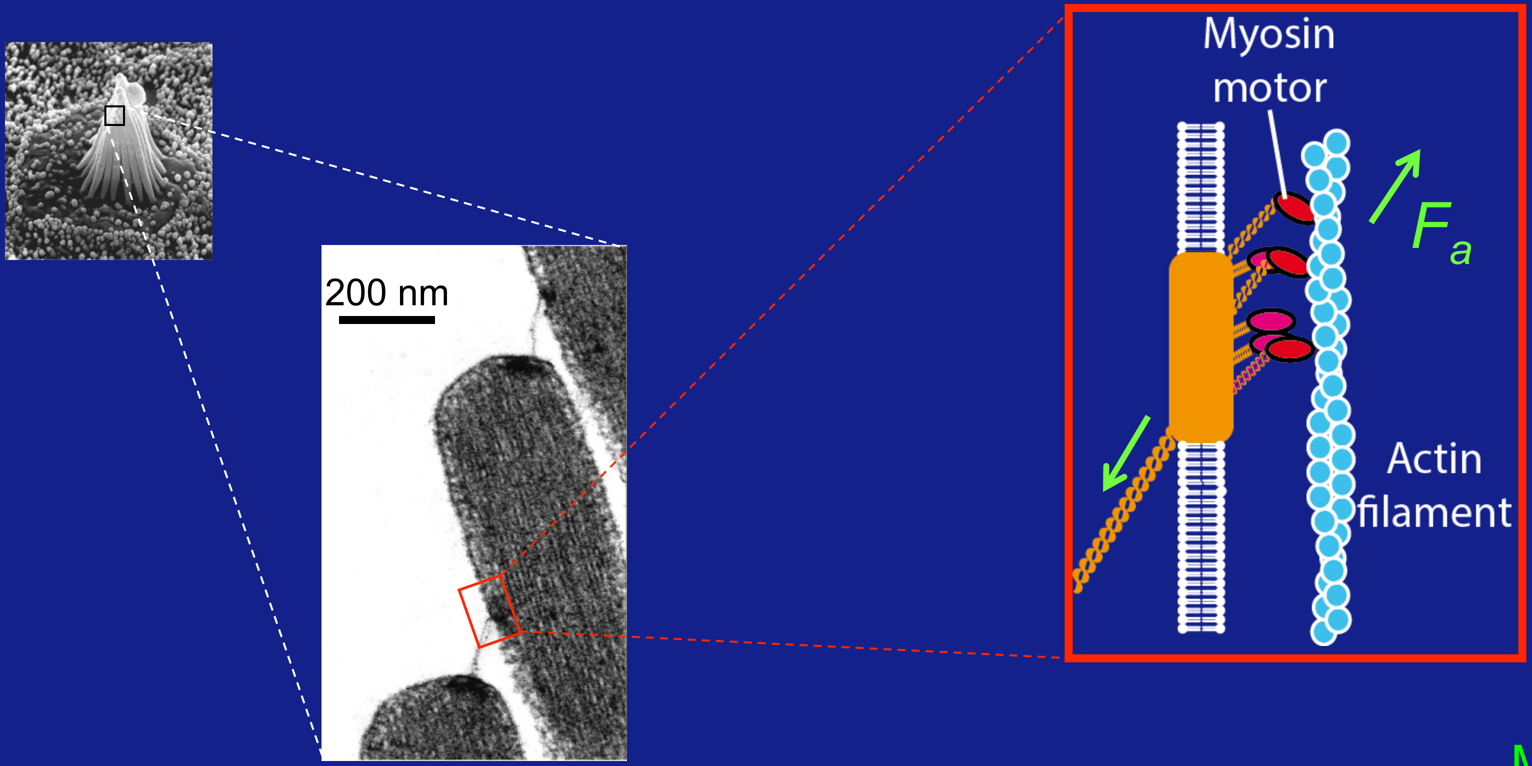
→ calcium = control parameter



(Tinevez, Jülicher and Martin, Biophys J (2007))

Adaptation motors:

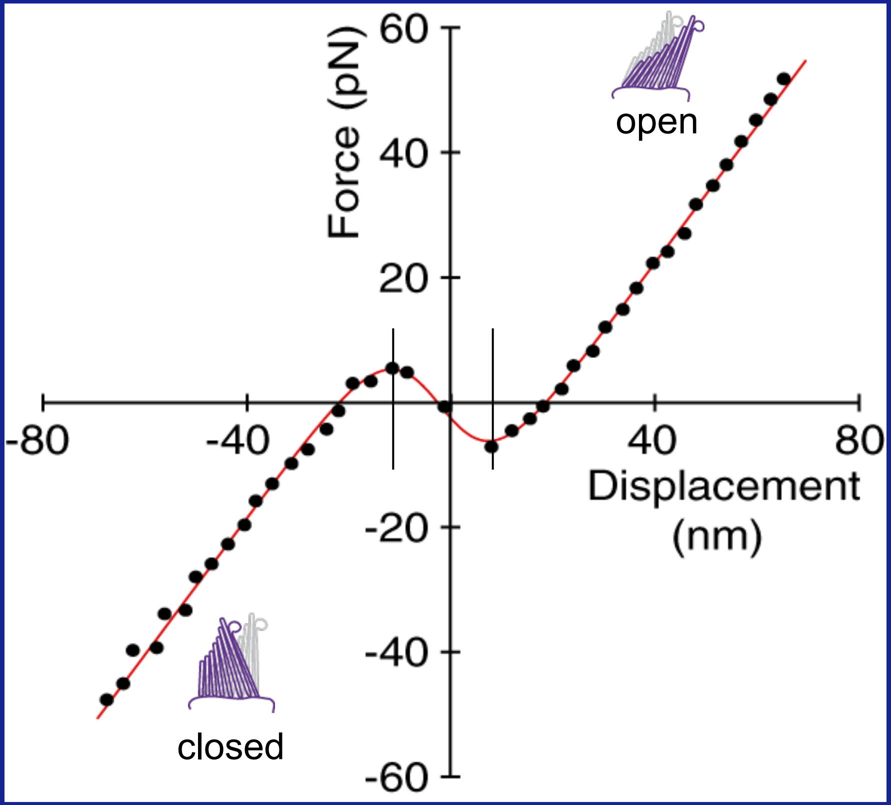
→ set the tip links under tension

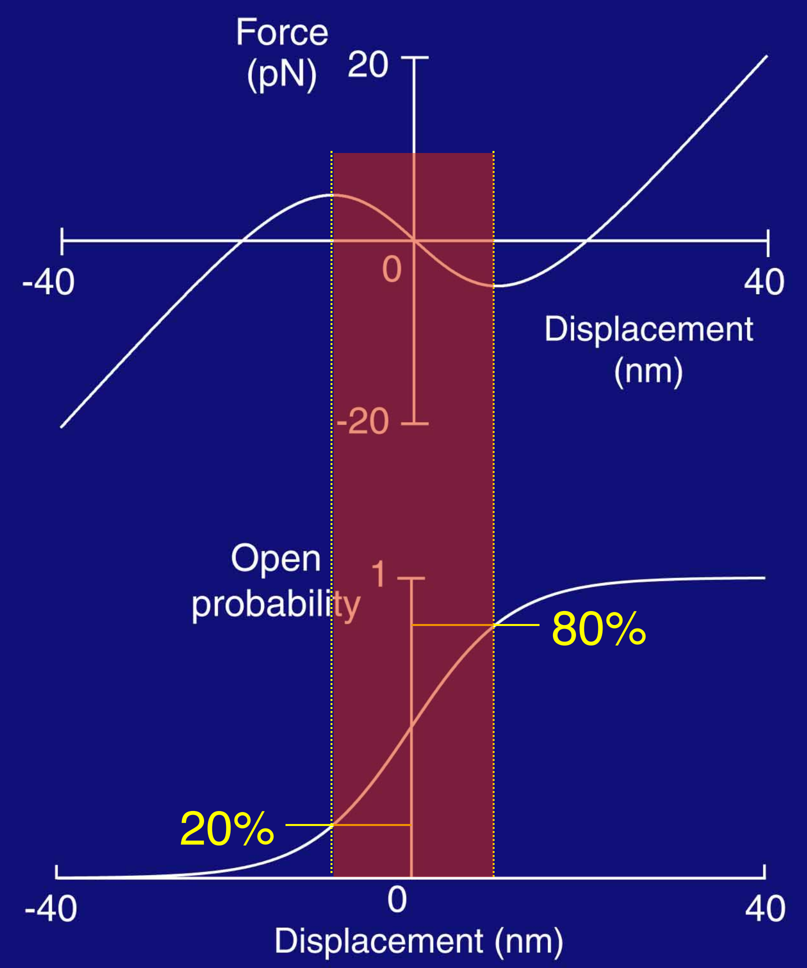


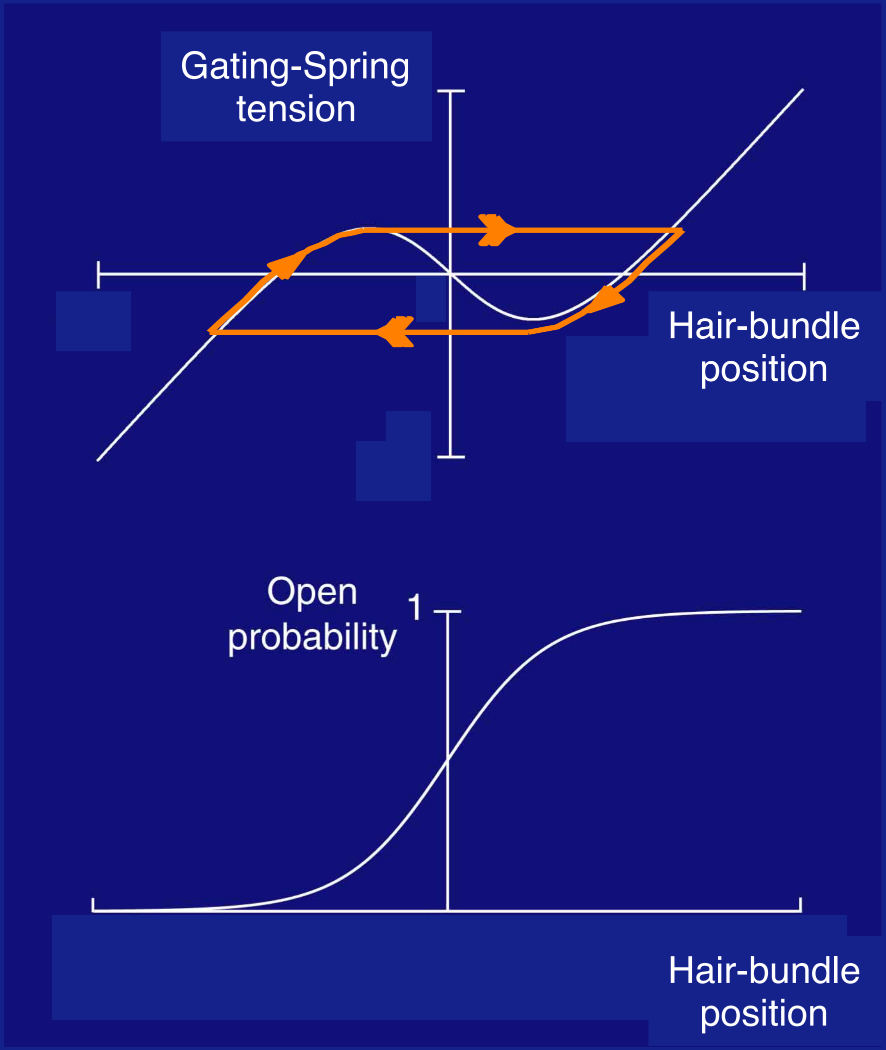
Myosin 1c
(Myosin 7a)

Negative stiffness

→ (passive) mechanical instability




Force
(pN)
20
0
-20
-40
40
Displacement
(nm)
Open
probability
1
80%
20%
-40
0
40
Displacement (nm)



Gating-Spring tension
Hair-bundle position
Open probability
1
Hair-bundle position

Active dynamical system

Hair bundle: $$\lambda \frac{dX}{dt} = -K_{GS}\left(X - X_a - D\,P_o\right) - K_{SP}X + F_{EXT}$$

Motor: $$\lambda_a \frac{dX_a}{dt} = K_{GS}\left(X - X_a - D\,P_o\right) - F_a$$

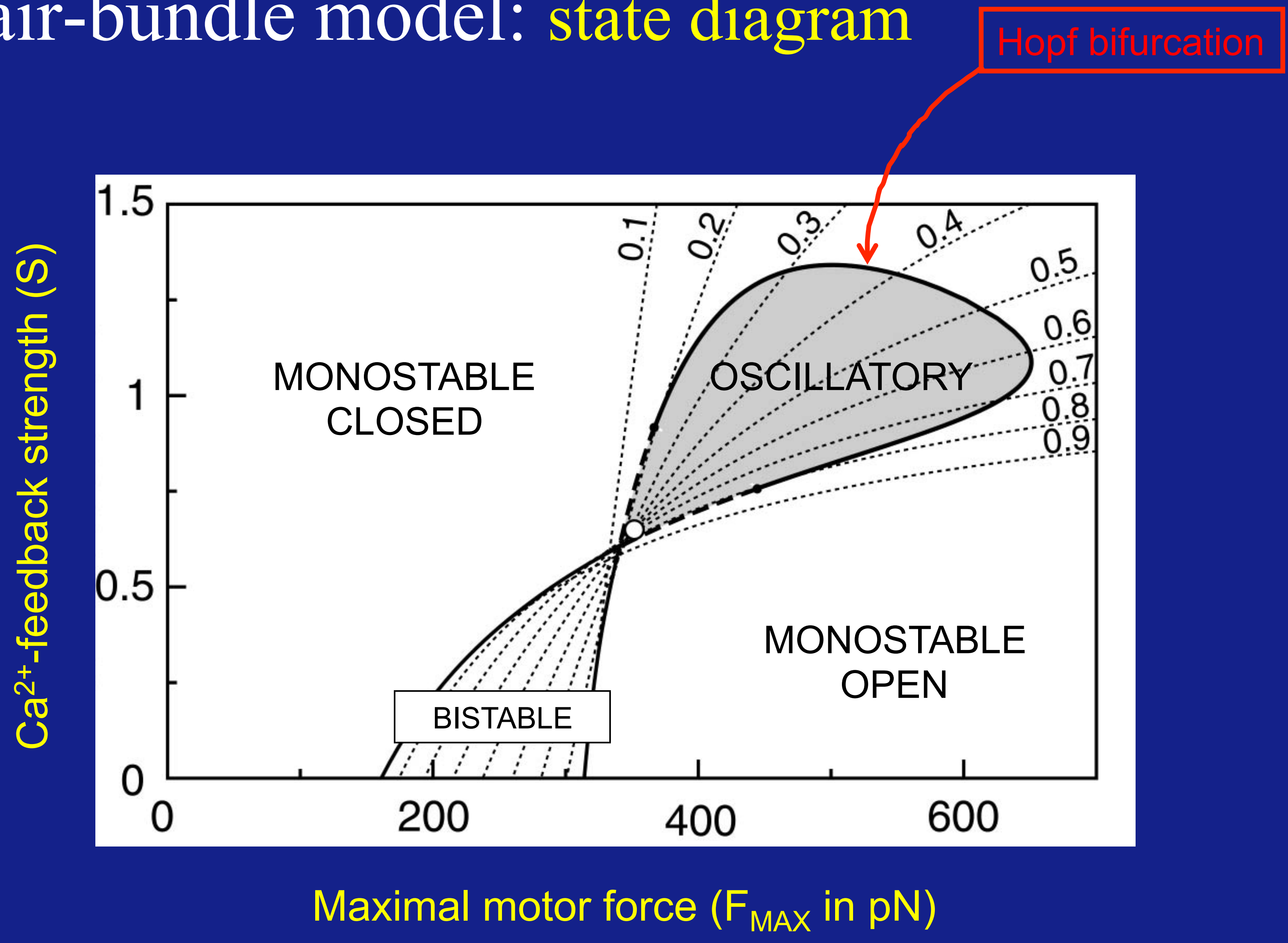
Tip-link tension

Motor force: $$F_a = F_{\max}\left(1 - S\,P_o\right)$$

Open probability: $$P_o = 1/\left(1 + A\exp\left(-\left(X - X_a\right)/\delta\right)\right)$$

(Nadrowski, Martin and Jülicher, PNAS (2004))

Hair-bundle model: state diagram



A simpler linear model

$k = K_{GS}(1 - D P'_{o})$

$k = k + K_{SP}$

$F_a = k \; X_a$

$\tau_a = \lambda_a / (k + S F_{MAX} P'_{o})$

Bundle position: $\lambda X = -kX + F_a$

Active force: $\tau_a \; F_a = k X - F_a$

$$(\lambda \; \tau_a) X = -(\lambda + k \; \tau_a) X - (k - k) X$$

m_{EFF} λ_{EFF} k_{EFF}

Linear stability analysis

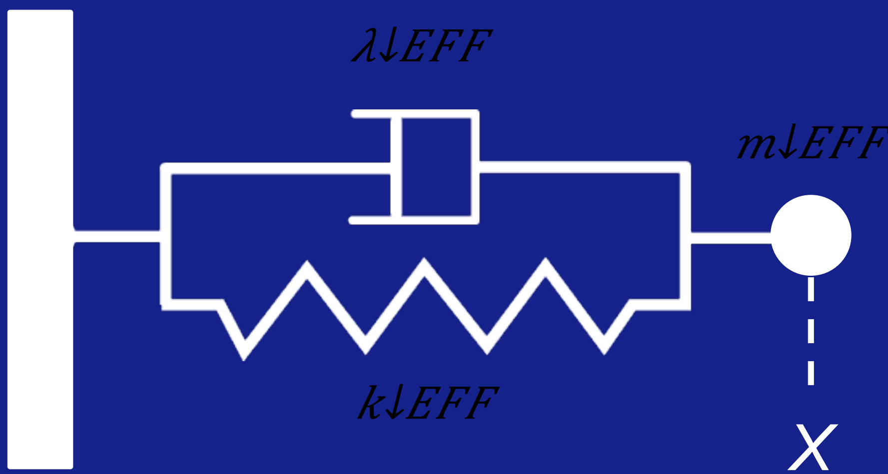
Bundle position: $\lambda X = -kX + F_a$

Adaptation force: $\tau_a F_a = kX - F_a$

$$(\lambda \tau_a) X = -(\lambda + k \tau_a) X - (k - k) X$$

m_{EFF} λ_{EFF} k_{EFF}

An effective (active) spring-mass system



stiffness: $k_{EFF} = k - k$

« mass »: $m_{EFF} = \lambda \tau_a$

friction: $\lambda_{EFF} = \lambda + k \tau_a$

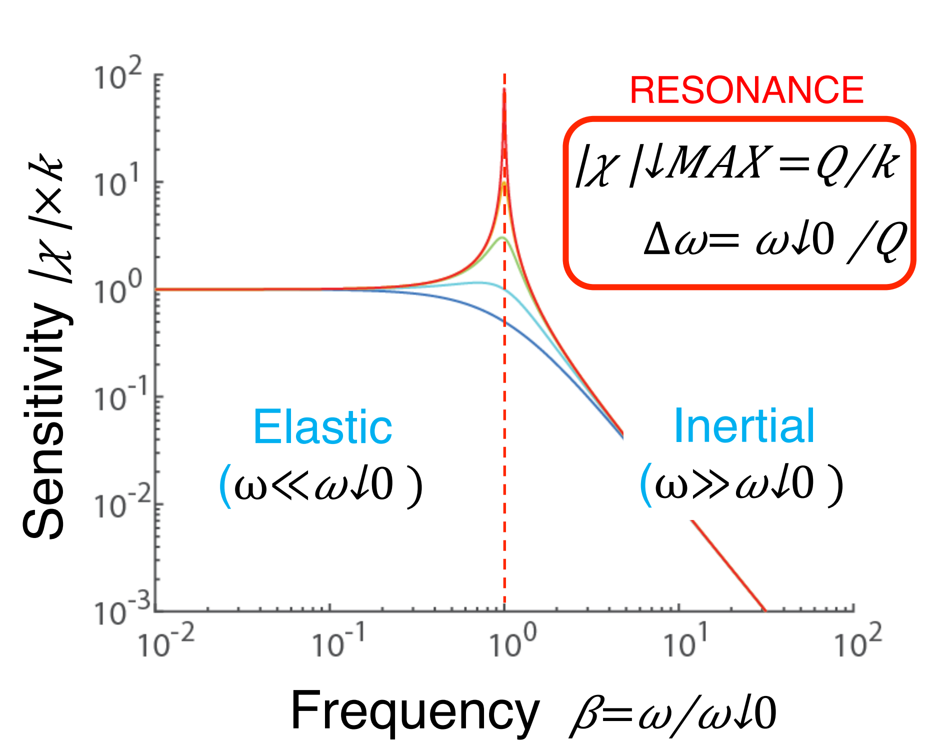
if $k > 0$, $\lambda_{EFF} > \lambda$: increased damping

if $k < 0$, $\lambda_{EFF} < \lambda$: reduced damping

Resonant behavior if $Q = \sqrt{k_{EFF} m_{EFF}} / \lambda_{EFF} > 1$

Hopf bifurcation at $\lambda_{EFF} = 0$ with frequency $\sqrt{k_{EFF} / m_{EFF}}$

Mechanical resonance



RESPONSE FUNCTION

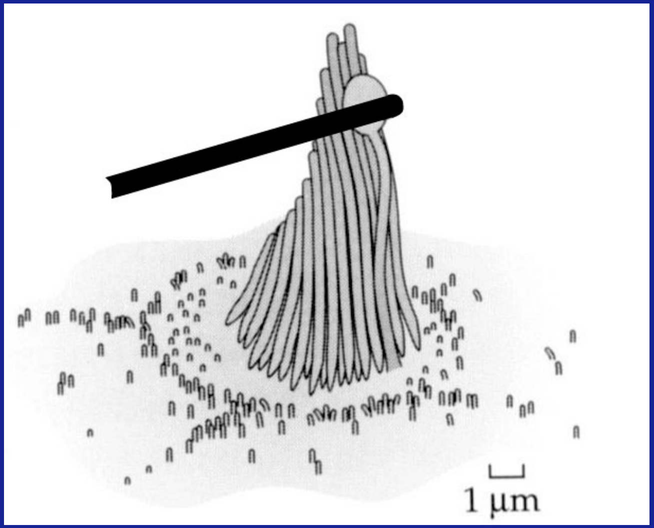
$$\chi = \frac{1/k}{[1-\beta^2 + i\beta/Q]}$$

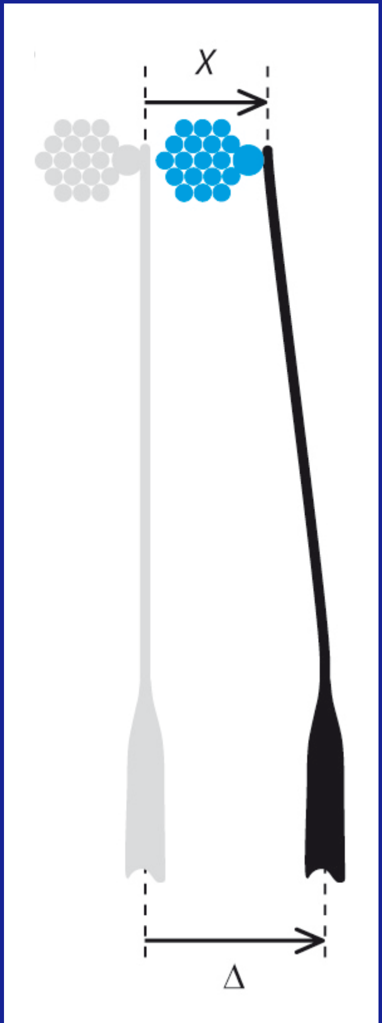
with $\chi = X/F$

$(F(t) = F\, e^{i\omega t}; X(t) = X\, e^{i\omega t})$

Characteristic frequency: $\omega_0 = \sqrt{k/m}$

Quality factor: $Q = \sqrt{k\,m}/\lambda = \omega_0/\Delta\omega$

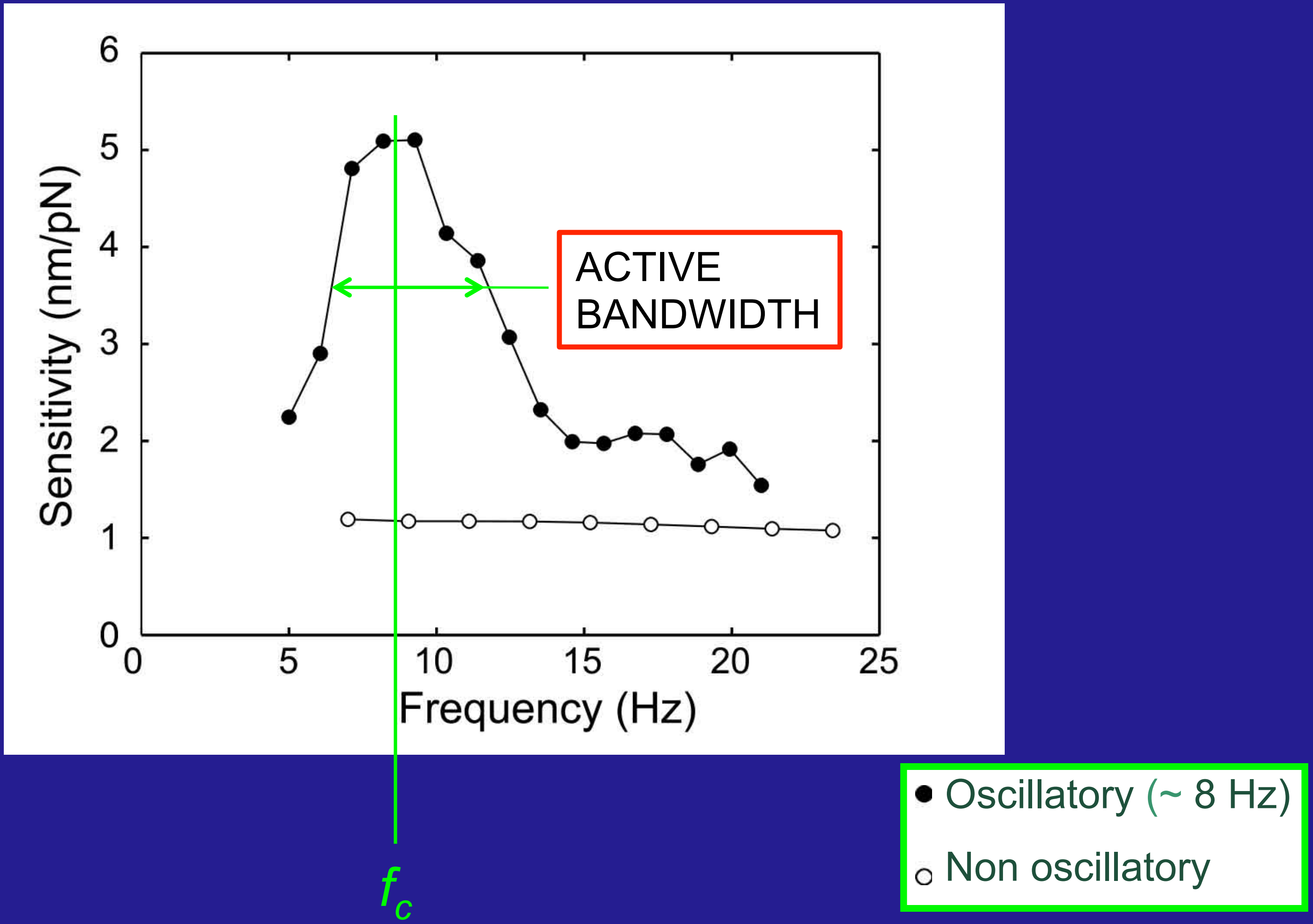

1 µm


X
Δ

Active resonance

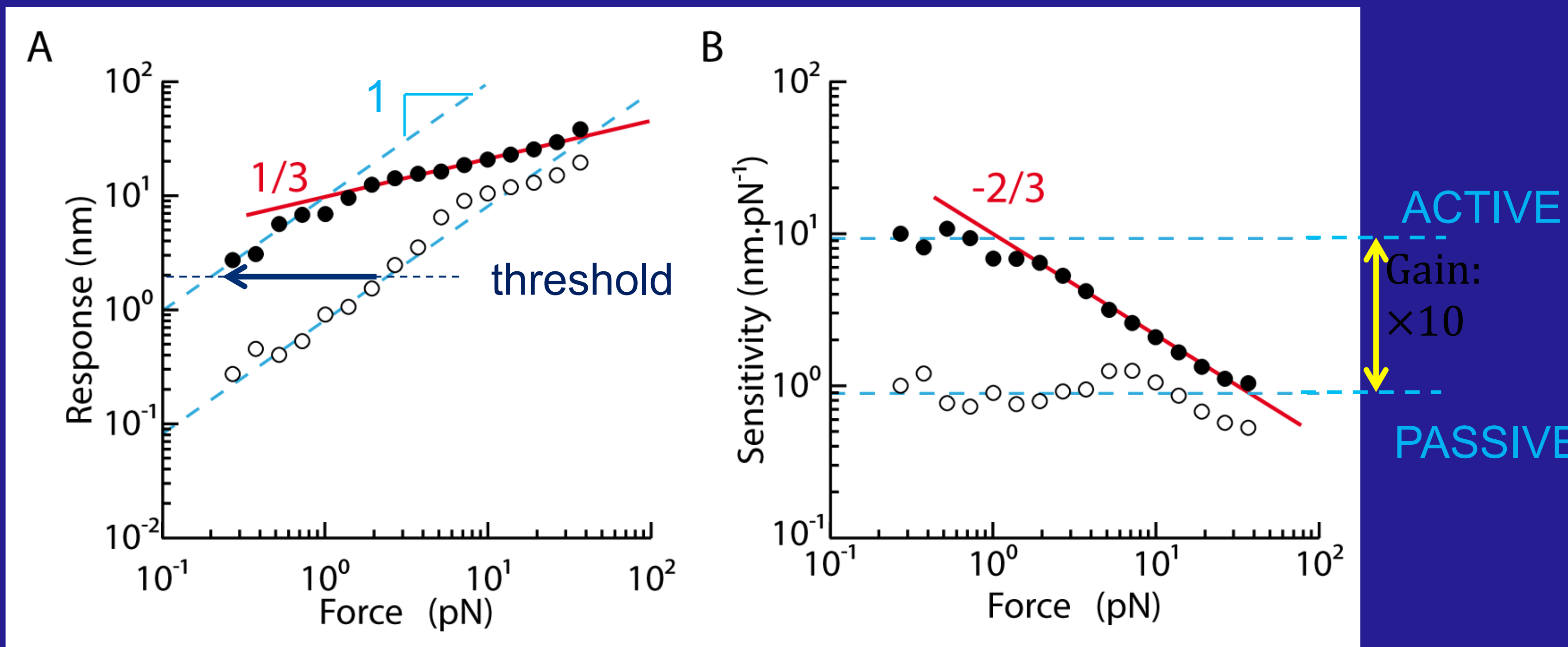
($F_1 \cong 5$ pN)

STIMULUS: $F(t)=F_1 \sin(2\pi f_1 t)$



Dynamic non-linearity

STIMULUS: $F(t)=F_1 \sin(2\pi f_1 t)$



● at resonance (f_1 = 9 Hz)
○ off resonance (f_1 = 180 Hz)

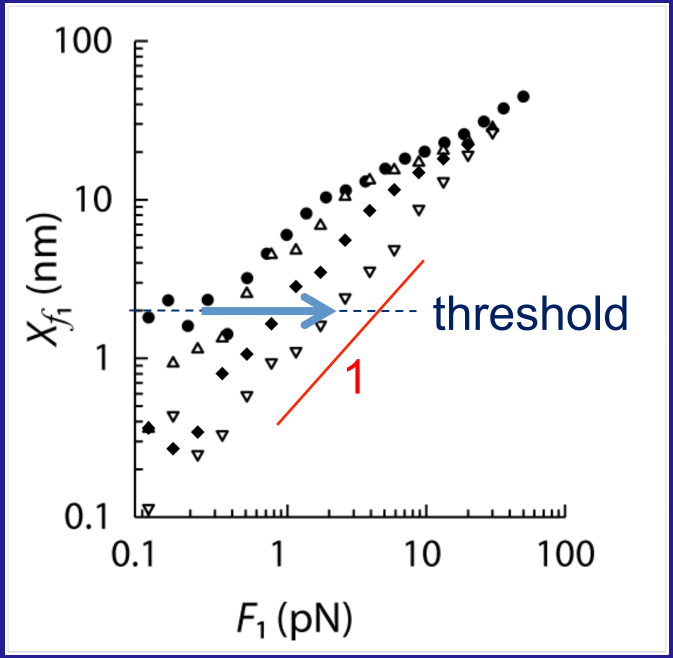
(Martin and Hudspeth, PNAS (2001))

Two-tone response

$$F(t) = \underbrace{F_1 \sin(2\pi f_1 t)}_{\text{test tone}} + \underbrace{F_2 \sin(2\pi f_2 t)}_{\text{masker tone}}$$

($f_2 / f_1 = 1.1$)

At resonance
(f_1 , $f_2 \approx f_c$)



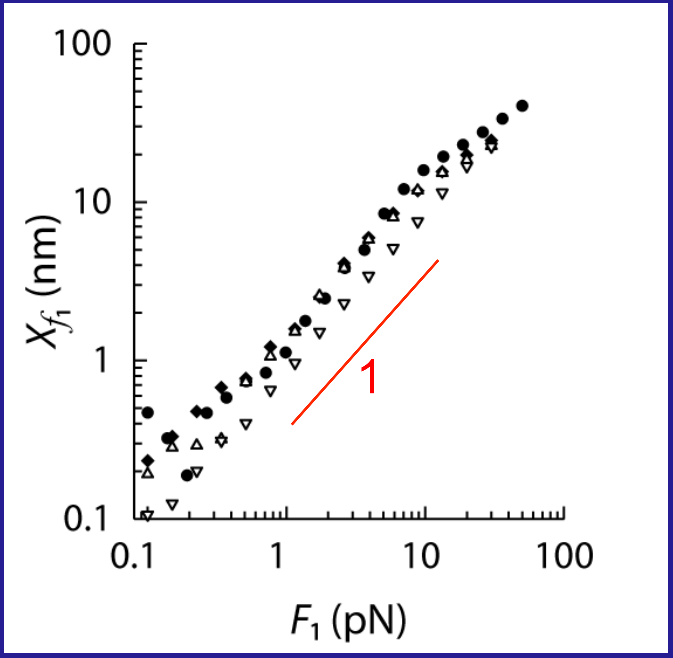
● F_2 = 0 pN

△ F_2 = 2 pN

◆ F_2 = 5 pN

▽ F_2 = 20 pN

Off resonance
(f_1 , $f_2 >> f_c$)



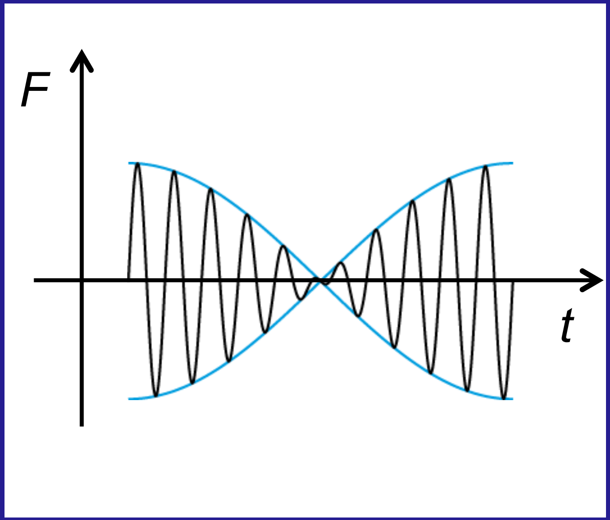
➡ Frequency-specific masking

Two-tone stimulus

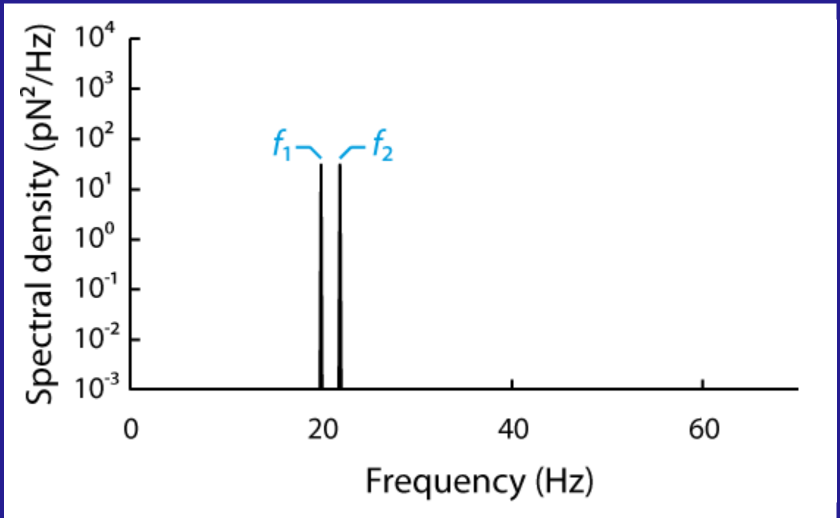
$$F(t) = \bar{F}\sin(2\pi f_1 t) + \bar{F}\sin(2\pi f_2 t)$$

$(f_2/f_1 = 1.1)$

Beating pattern



Power spectrum



High-fidelity amplifier?

$$F(t) = \bar{F}\sin(2\pi f_1 t) + \bar{F}\sin(2\pi f_2 t) \qquad (\bar{F} = 2\ \text{pN})$$

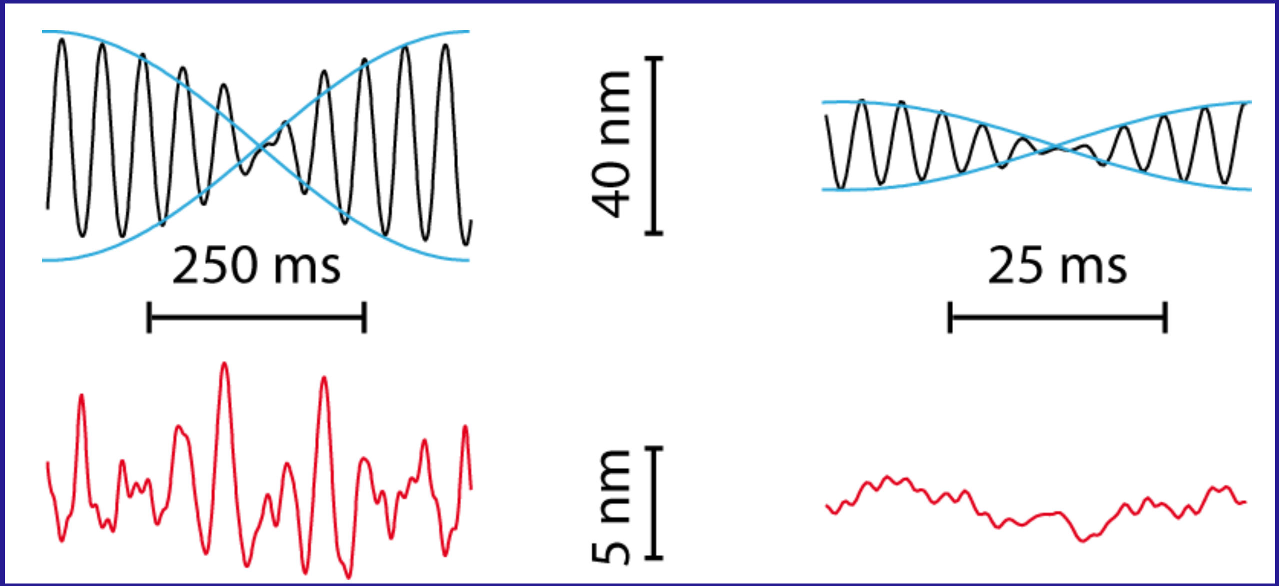
At resonance (f_1 , $f_2 \approx f_c$)

Off resonance (f_1 , $f_2 >> f_c$)

HB motion

Distortions

(primaries filtered out)



f_1 = 20 Hz
f_2 = 22 Hz

f_1 = 200 Hz
f_2 = 220 Hz

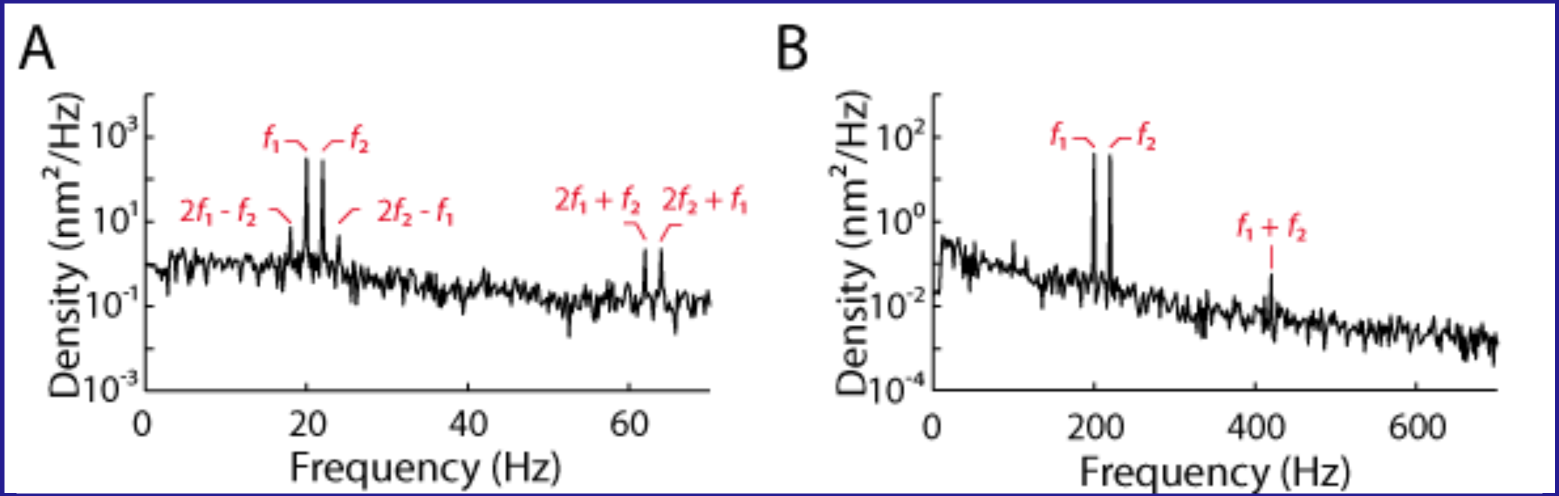
Distortion products

$$F(t) = \bar{F}\sin(2\pi f_1 t) + \bar{F}\sin(2\pi f_2 t)$$

($\bar{F}$ = 2 pN)

At resonance (f_1 , $f_2 \approx f_c$)

Off resonance (f_1 , $f_2 >> f_c$)

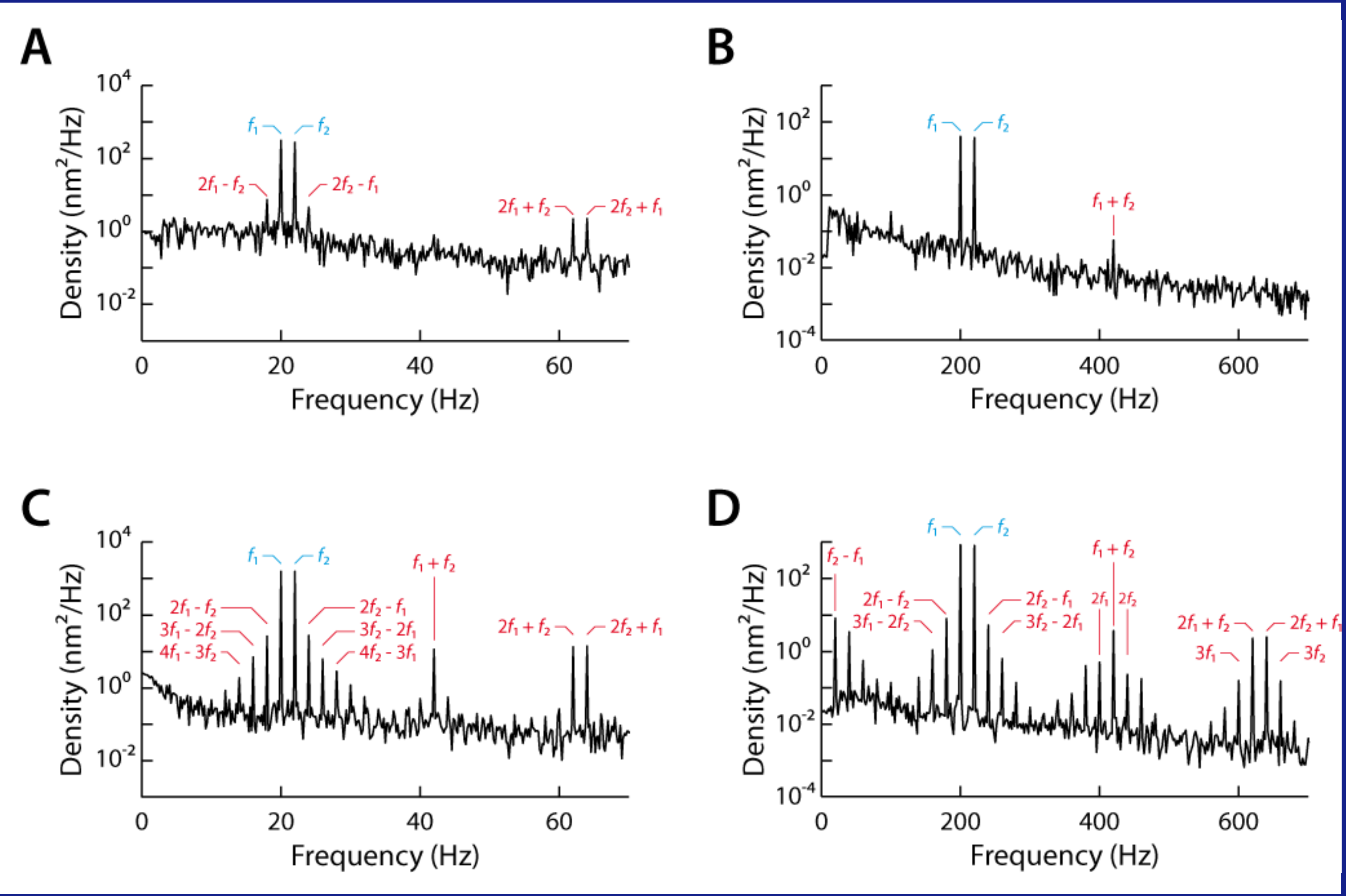


At resonance
(f_1 , $f_2 \approx f_c$)

Off resonance
(f_1 , $f_2 >> f_c$)

2 pN

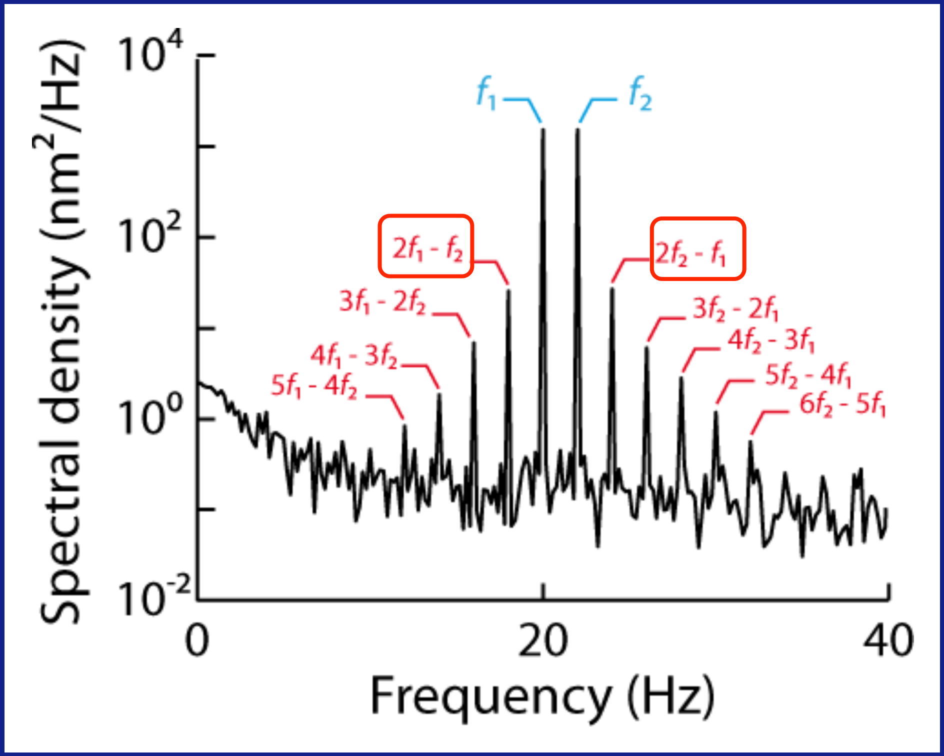
10.1 pN



“Colored” response

$$F(t) = \bar{F}\sin(2\pi f_1 t) + \bar{F}\sin(2\pi f_2 t)$$

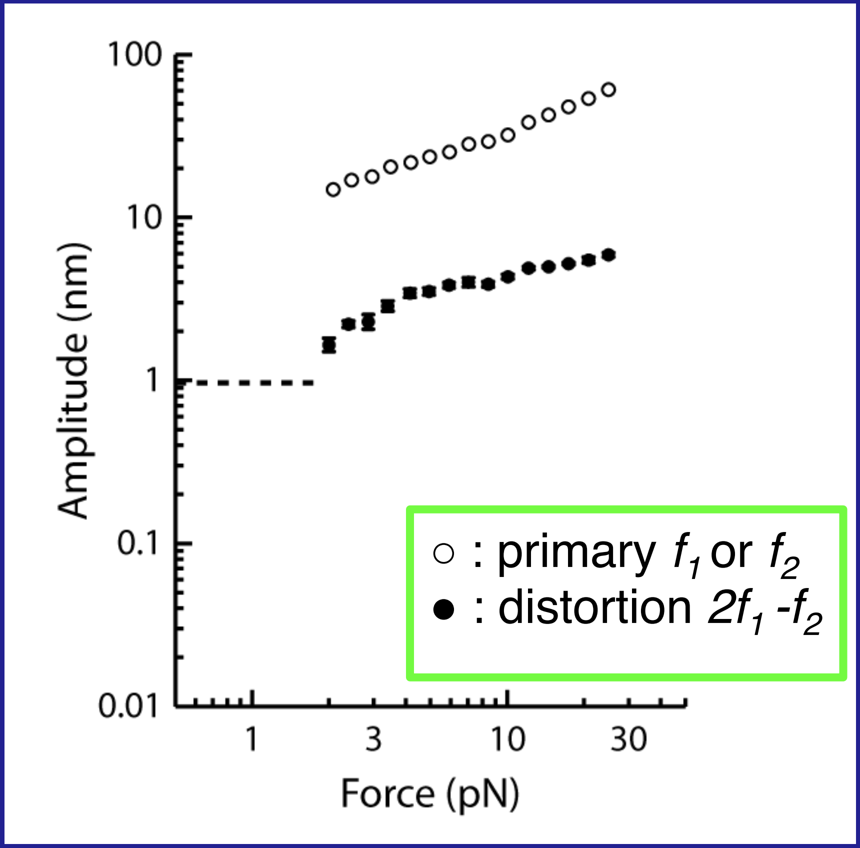
($\bar{F}$ = 10.8 pN)



CUBIC DISTORTIONS

Distortion $2f_1$-f_2 at resonance

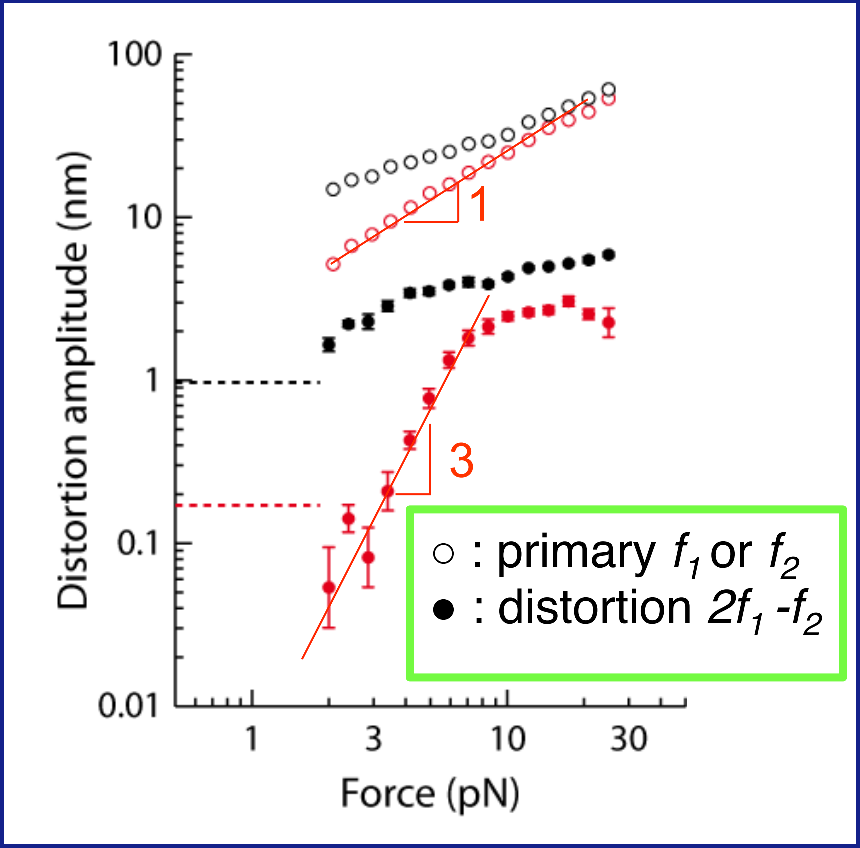
$(f_1\ ,\ f_2 \approx f_c)$



CONSTANT RELATIVE LEVEL (~15%)!

Distortion $2f_1$-f_2

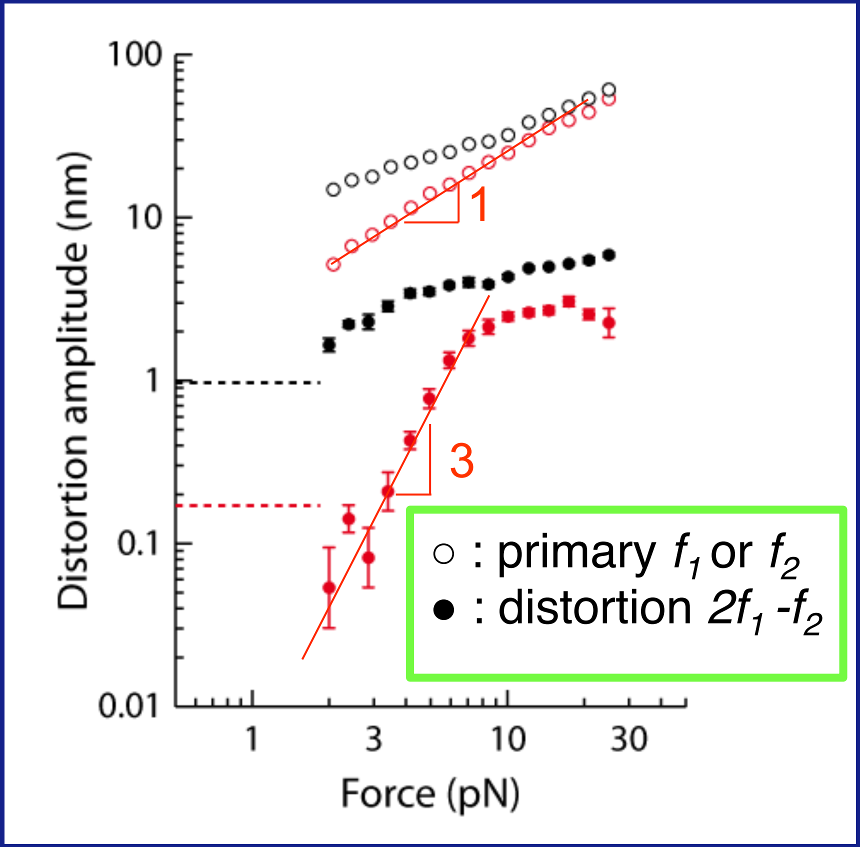
At resonance – Off resonance

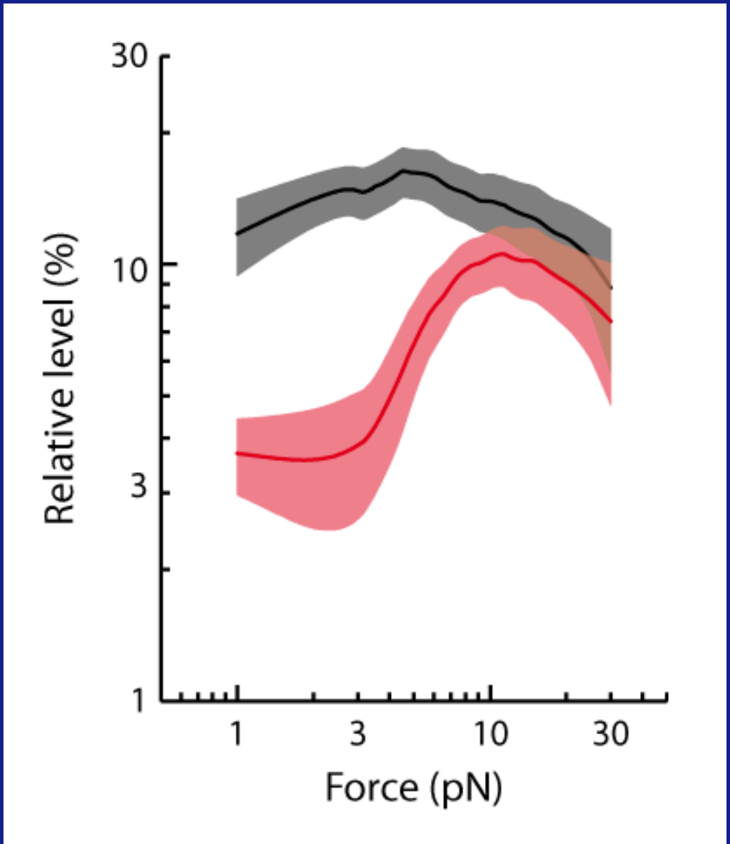


ACTIVE MECHANICS ↔ PASSIVE MECHANICS
(black) (red)

Distortion $2f_1$-f_2

At resonance – Off resonance





ACTIVE MECHANICS ↔ PASSIVE MECHANICS
(black) (red)

« Phantom tones » from a single oscillatory hair bundle

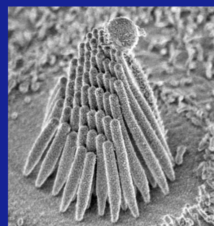
$$F(t) = \overline{F}\cos(2\pi f_1 t) + \overline{F}\cos(2\pi f_2 t)$$

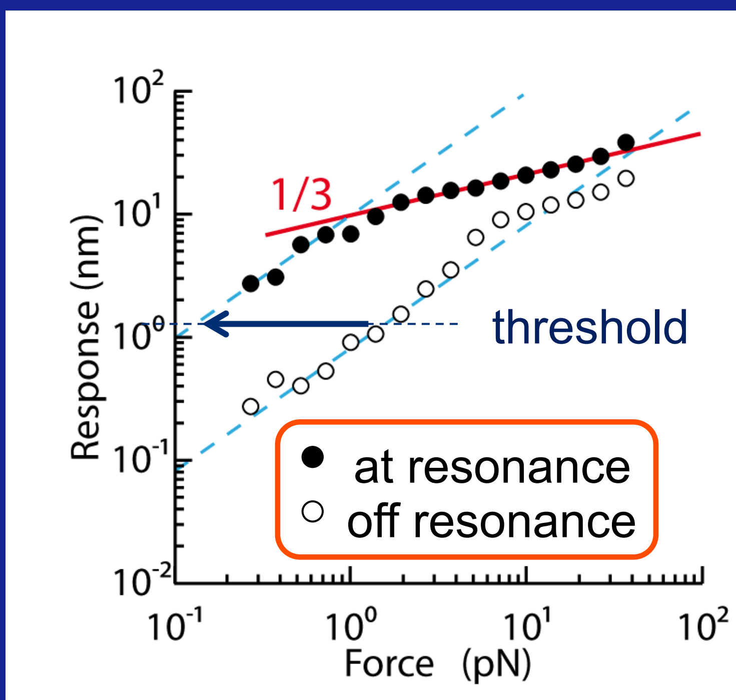
- cubic distortion dominates ($2f_1$-f_2, $2f_2$-f_1)
- appear at low stimulation levels ($\overline{F} \geq 1$ pN)
- relative level at $2f_1$-f_2 nearly independant of stimulus level (15-20%)
- inherent frequency specificity (f_1 and f_2 must be near f_C)

→ because of nonlinear amplification from active oscillation!

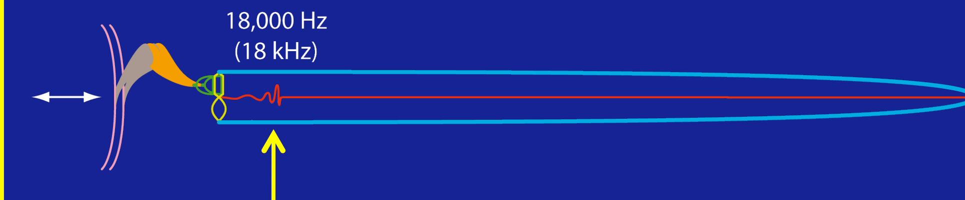
(Barral and Martin, PNAS (2012)

SINGLE HAIR-BUNDLE

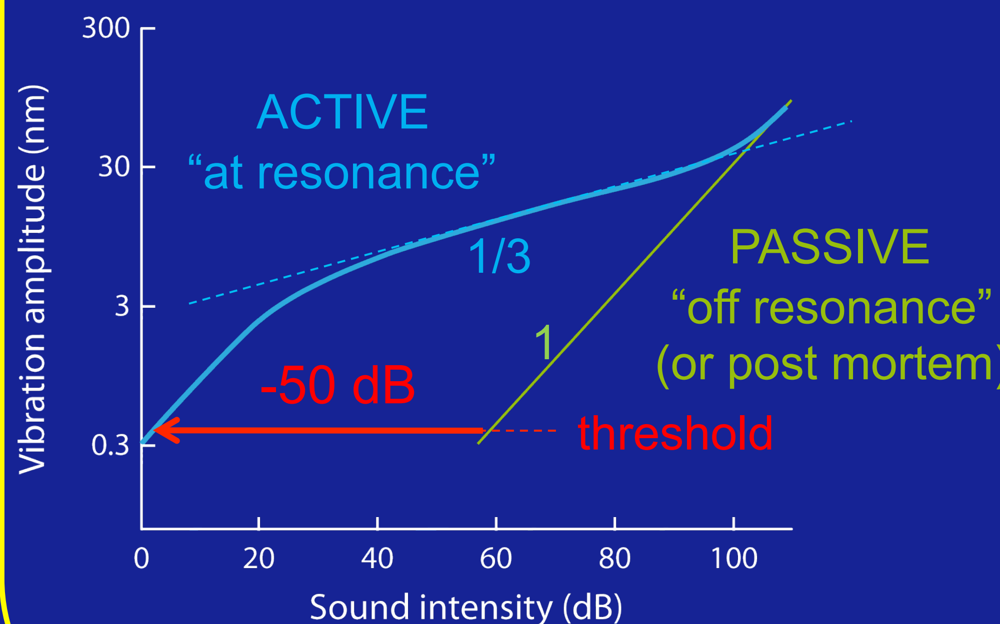




COCHLEA IN VIVO



⇒ Same physics!



(inspired by: Ruggero et al., JASA (1997))

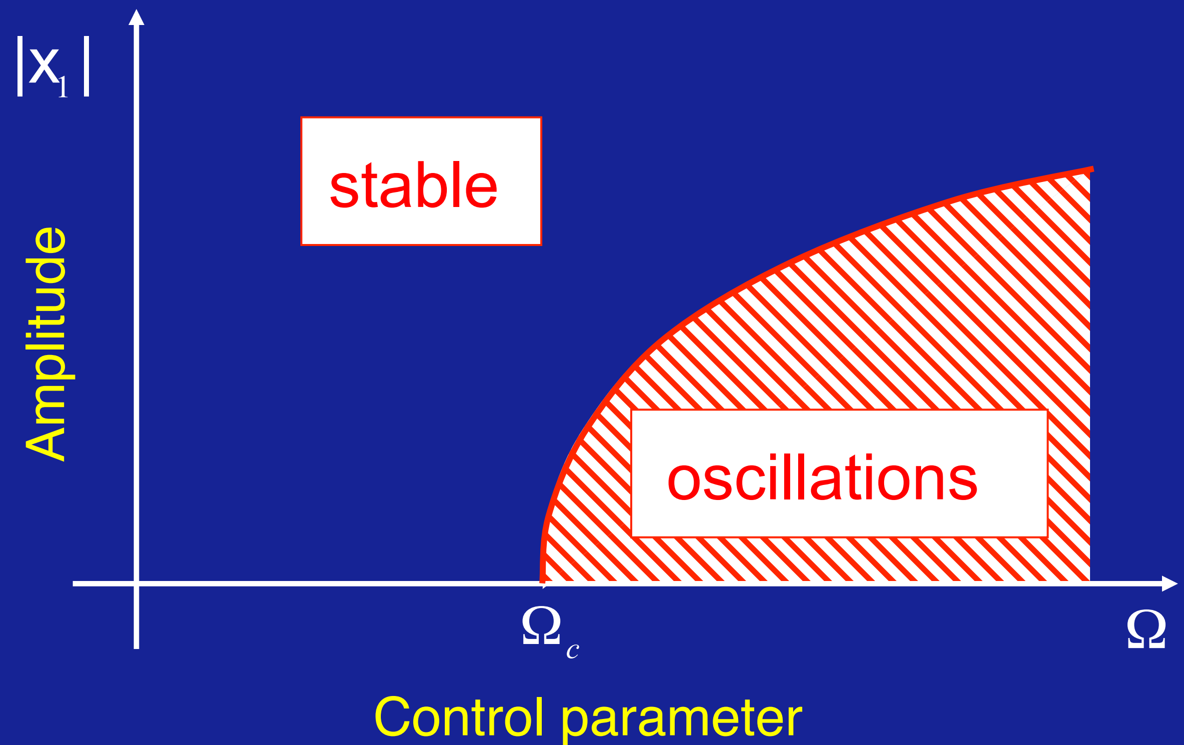
A useful concept:
the « critical » oscillator

(Choe, Magnasco, Hudspeth, PNAS (1998); Camalet, Duke, Jülicher, Prost, PNAS (2000)
Eguíluz, Ospeck, Choe, Hudspeth, Magnasco, Phys. Rev. Lett. (2000);
Jülicher, Andor and Duke, PNAS (2001))

Hopf bifurcation

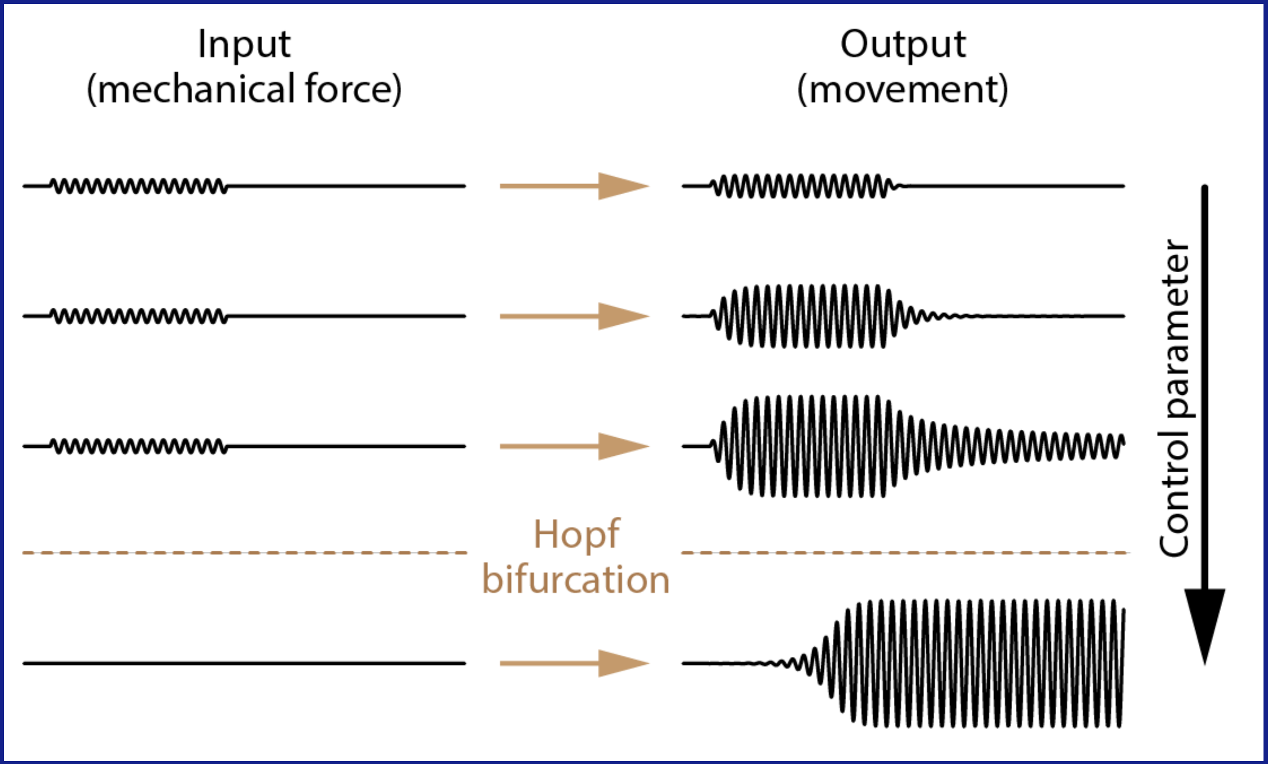
→ « Normal form »

$$dZ/dt \cong -(\Omega_c - \Omega - i\ 2\pi f_c)\ Z - B|Z|^2\ Z + F/\Lambda$$



with X=Re(Z)

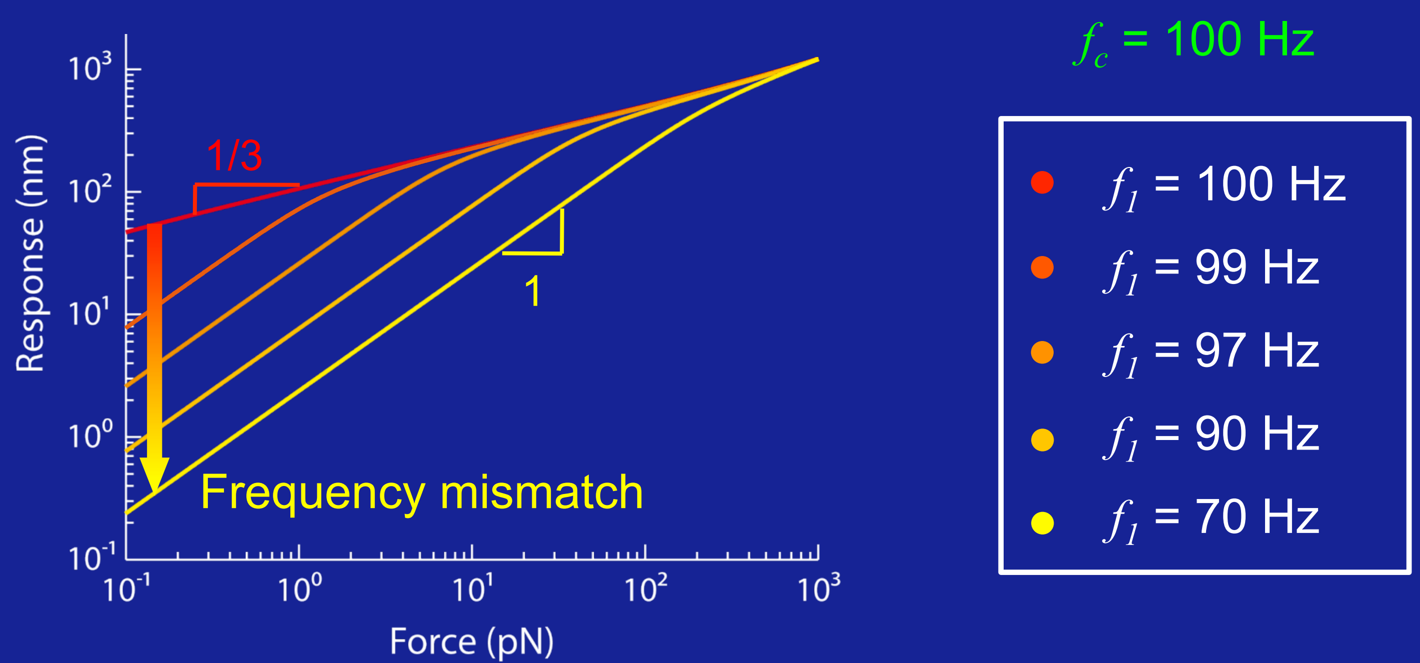
Critical point: $\Omega = \Omega_C$



(Hudspeth, Nat Neurosci (2014))

« Critical » oscillator: generic properties

$$F(t)=F_1 \sin(2\pi f_1 t) \rightarrow X(t)=\sum_n X_n e^{i n\omega t}$$



$$F_1 \cong A(f_1)\, X_1 + B\, |X_1|^2 X_1$$

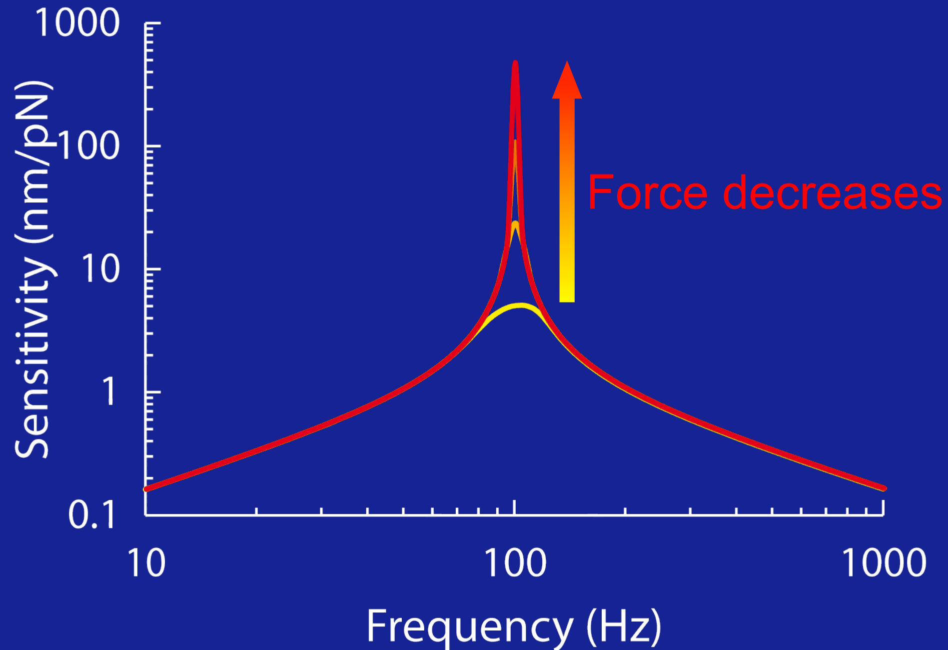
with: $A(f_1 = f_c) = 0$!

(Choe, Magnasco, Hudspeth, PNAS (1998); Camalet, Duke, Jülicher, Prost, PNAS (2000)
Eguíluz, Ospeck, Choe, Hudspeth, Magnasco, Phys. Rev. Lett. (2000))

« Critical » oscillator: generic properties

$$F(t)=F_1 \sin(2\pi f t) \rightarrow X(t)=\sum_n X_n e^{i n 2\pi f t}$$

(f_c = 100 Hz)



F_1 = 100 pN

F_1 = 10 pN

F_1 = 1 pN

F_1 = 0.1 pN

$$F_1 \cong A(f)\, X_1 + B\, |X_1|^2 X_1$$

with: $A(f = f_c) = 0$!

(Choe, Magnasco, Hudspeth, PNAS (1998); Camalet, Duke, Jülicher, Prost, PNAS (2000) Eguíluz, Ospeck, Choe, Hudspeth, Magnasco, Phys. Rev. Lett. (2000))

Two-tone distortions

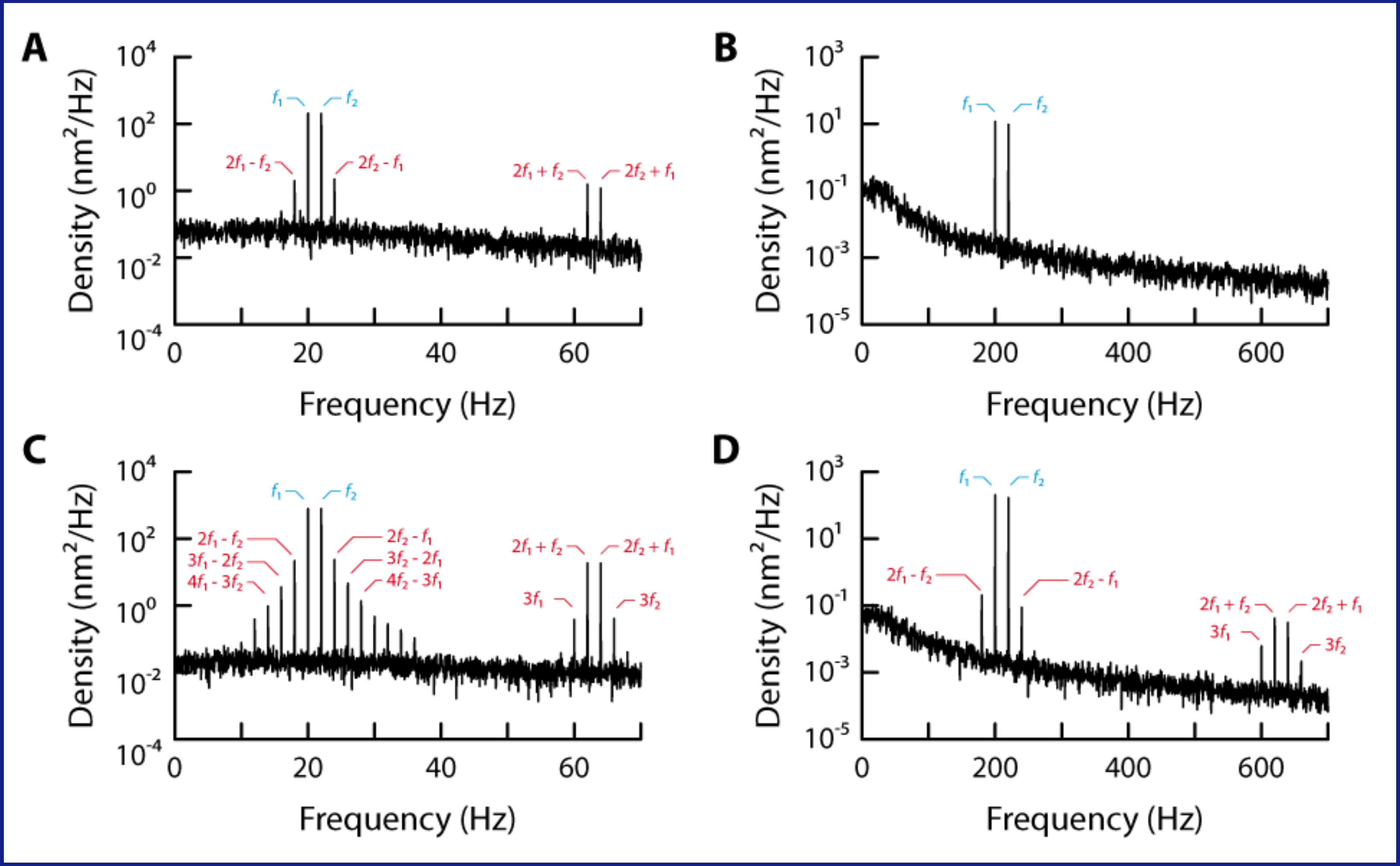
(simulations)

At resonance (f_1 , $f_2 \approx f_c$)

Off resonance (f_1 , $f_2 >> f_c$)

0.9 pN

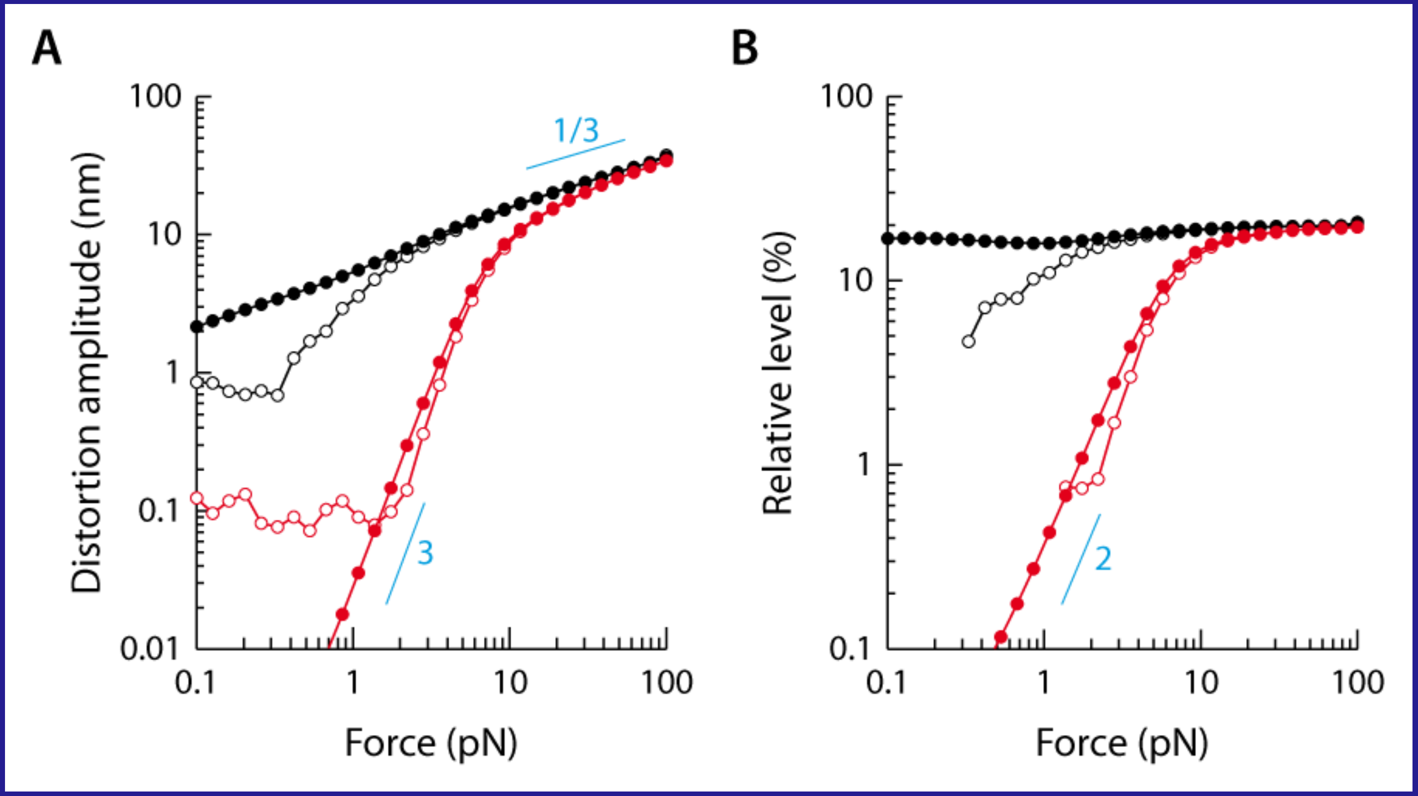
3.6 pN



Distortion $2f_1$-f_2: level functions

$$F(t) = \bar{F}\sin(2\pi f_1 t) + \bar{F}\sin(2\pi f_2 t)$$

(simulations)



No noise

● : at resonance
● : off resonance

With noise

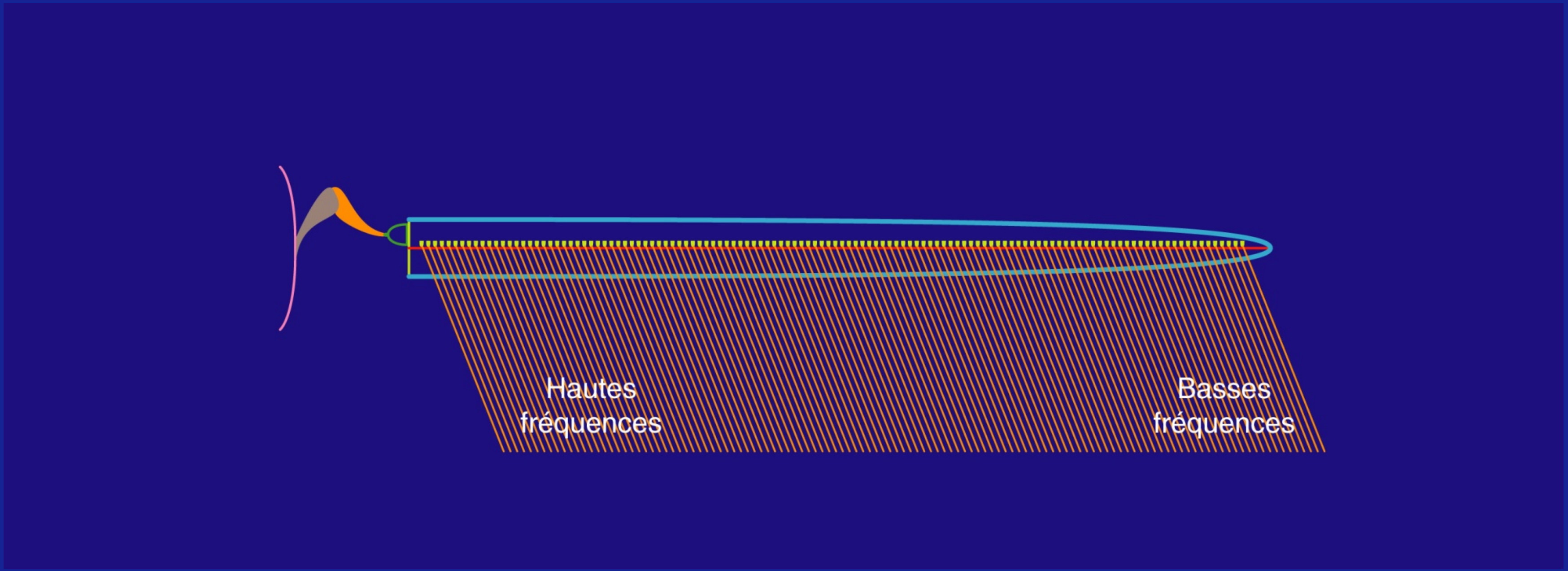
○ : at resonance
○ : off resonance

Critical oscillators: nonlinear amplifiers for hearing

1. Amplified movements for small stimuli
2. Extended dynamic range of responsiveness
3. Increased frequency selectivity
4. « Essential » compressive nonlinearity: prominent masking and cubic distortions within the active bandwidth.

Outlook:

tonotopic organisation of critical oscillators



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cnrs dépasser les frontières
institut Curie
UPMC PARIS UNIVERSITAS

Coming next:

1. The physical limit to mechanosensitivity of a single hair cell: noise and friction
2. Teaming-up to boost mechanosensitivity: the effects of mechanical coupling.
3. Mechanical gradients to tune the characteristic frequency of a hair cell