ENERGETICS OF SENSORY TRANSDUCTION

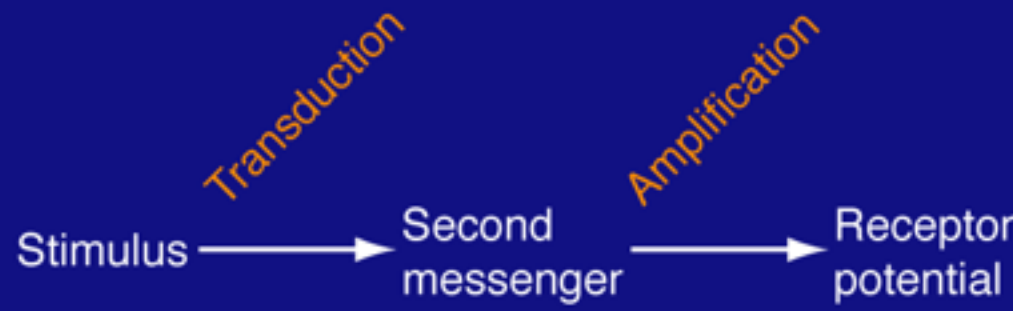
Vision:

500-nm photon

$E \approx 240\ kJ \cdot mol^{-1}$

≈ 400 zJ per molecule

($\sim 100 \cdot kT$)



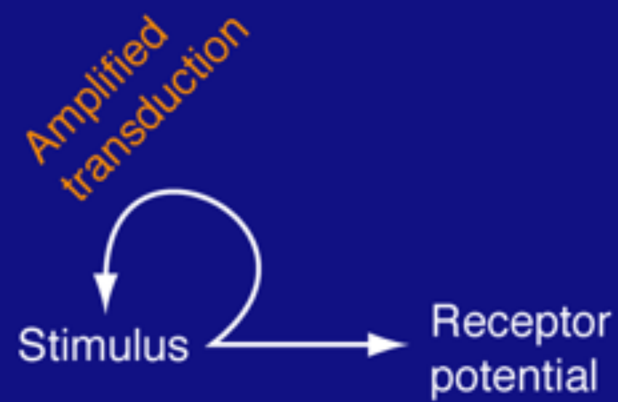
Hearing:

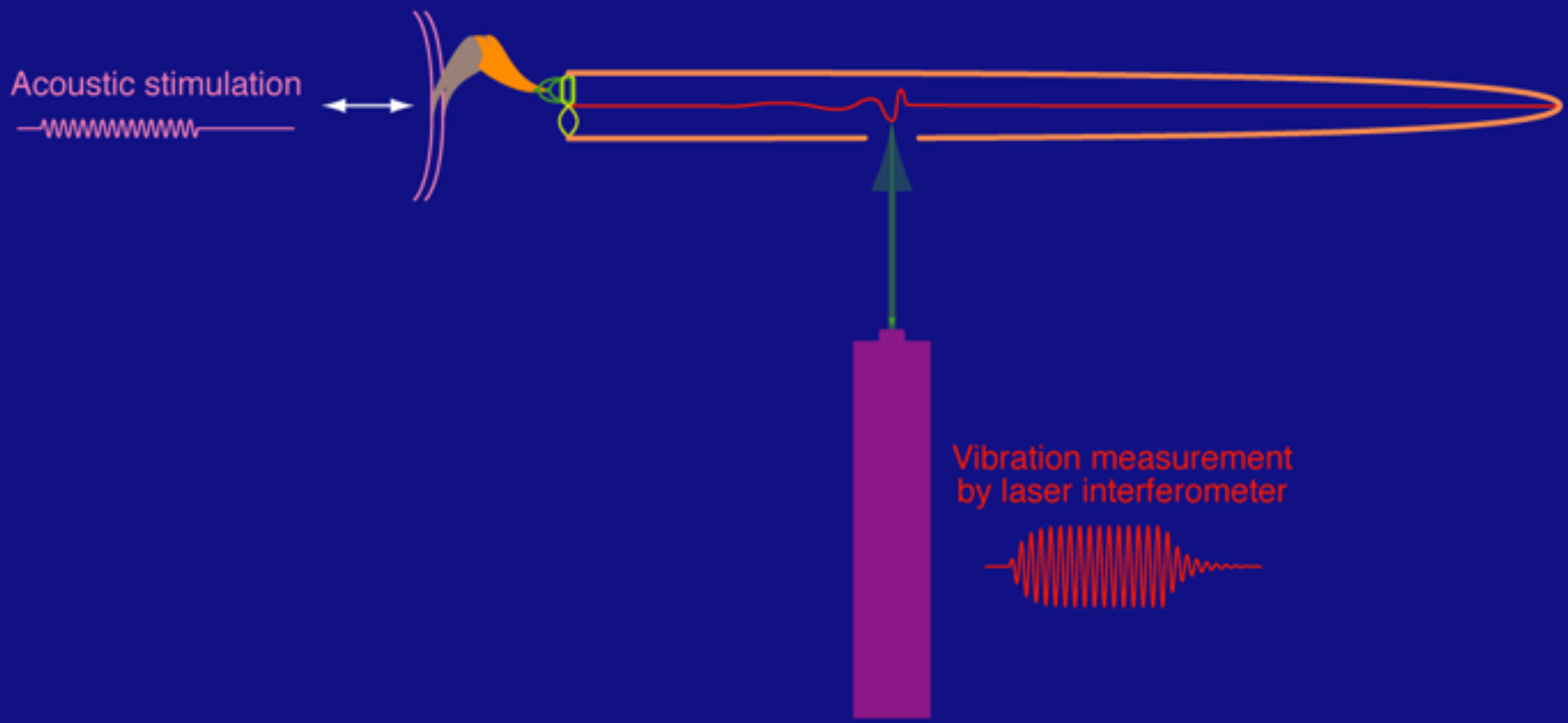
±0.3-nm vibration

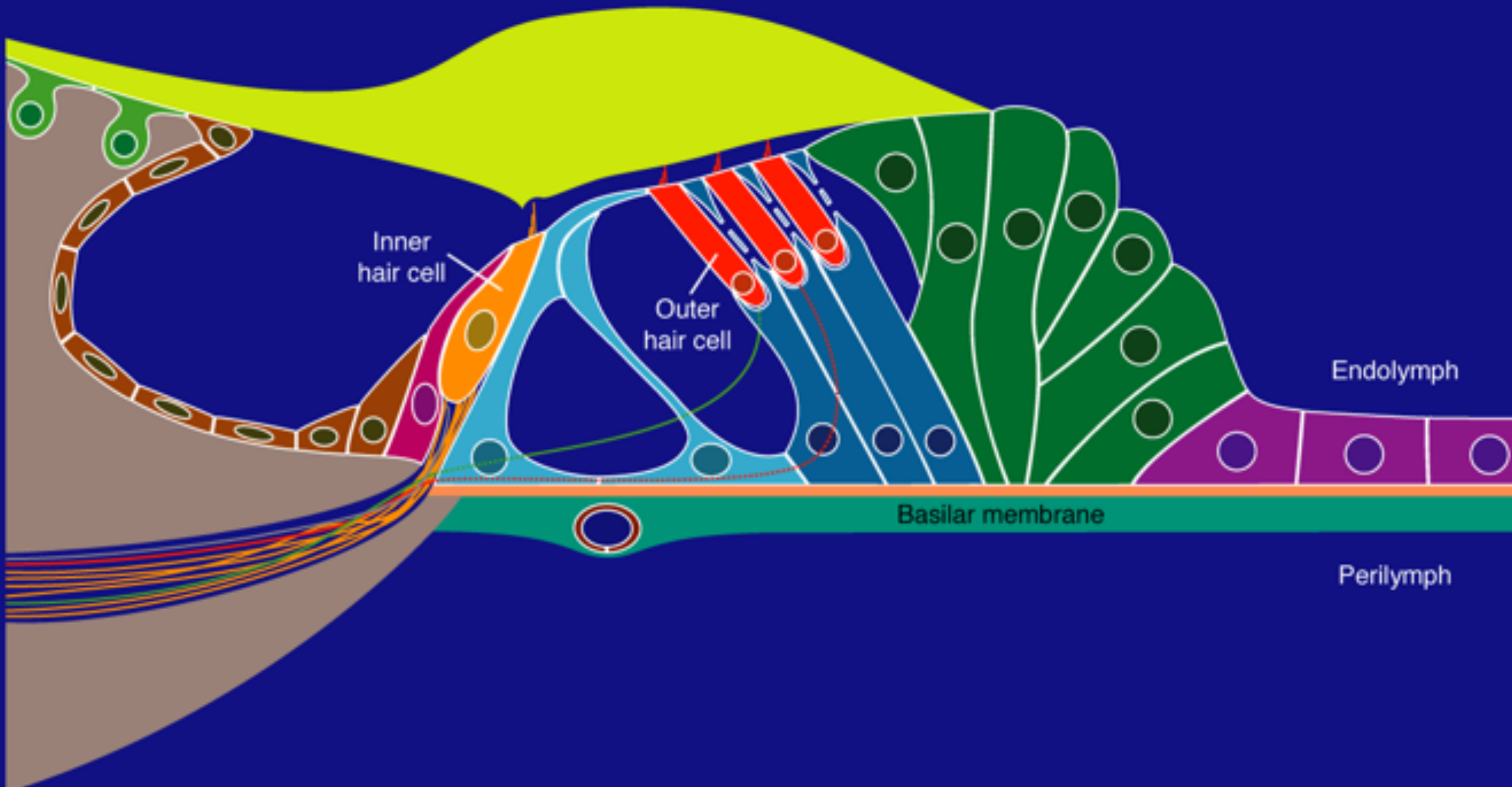
$\Delta G \approx 0.3\ kJ \cdot mol^{-1}$ per cycle

≈ 0.5 zJ per molecule per cycle

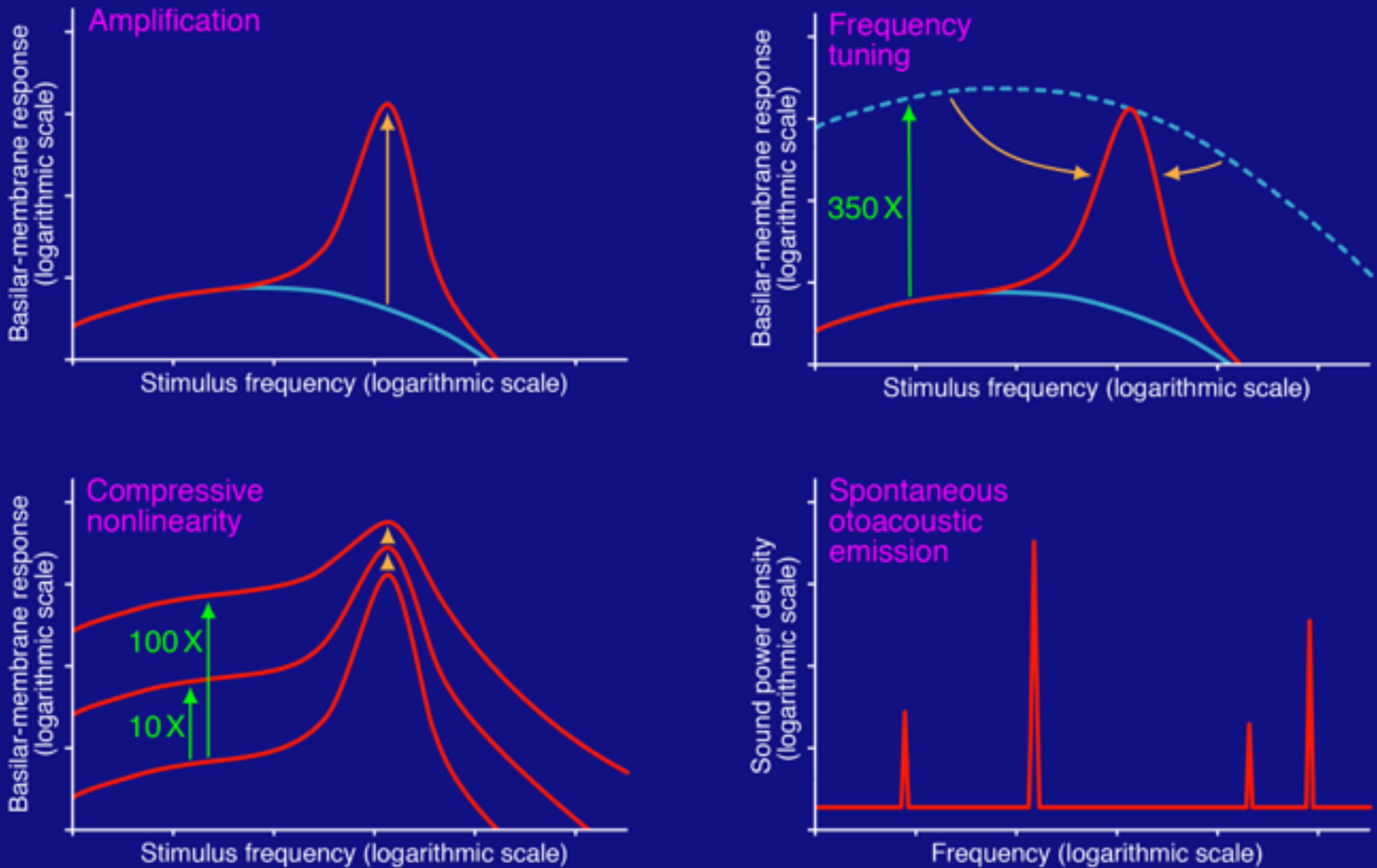
($\sim 0.1 \cdot kT$ per cycle)



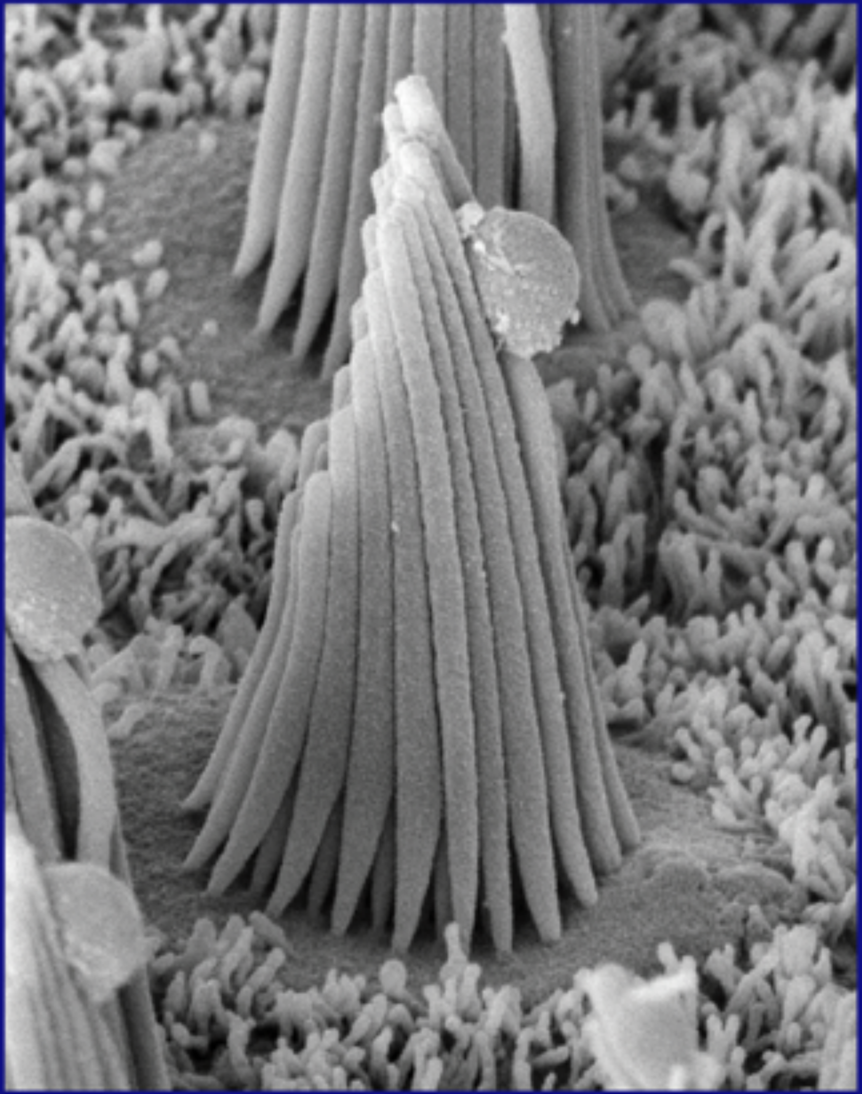

Acoustic stimulation
Vibration measurement
by laser interferometer

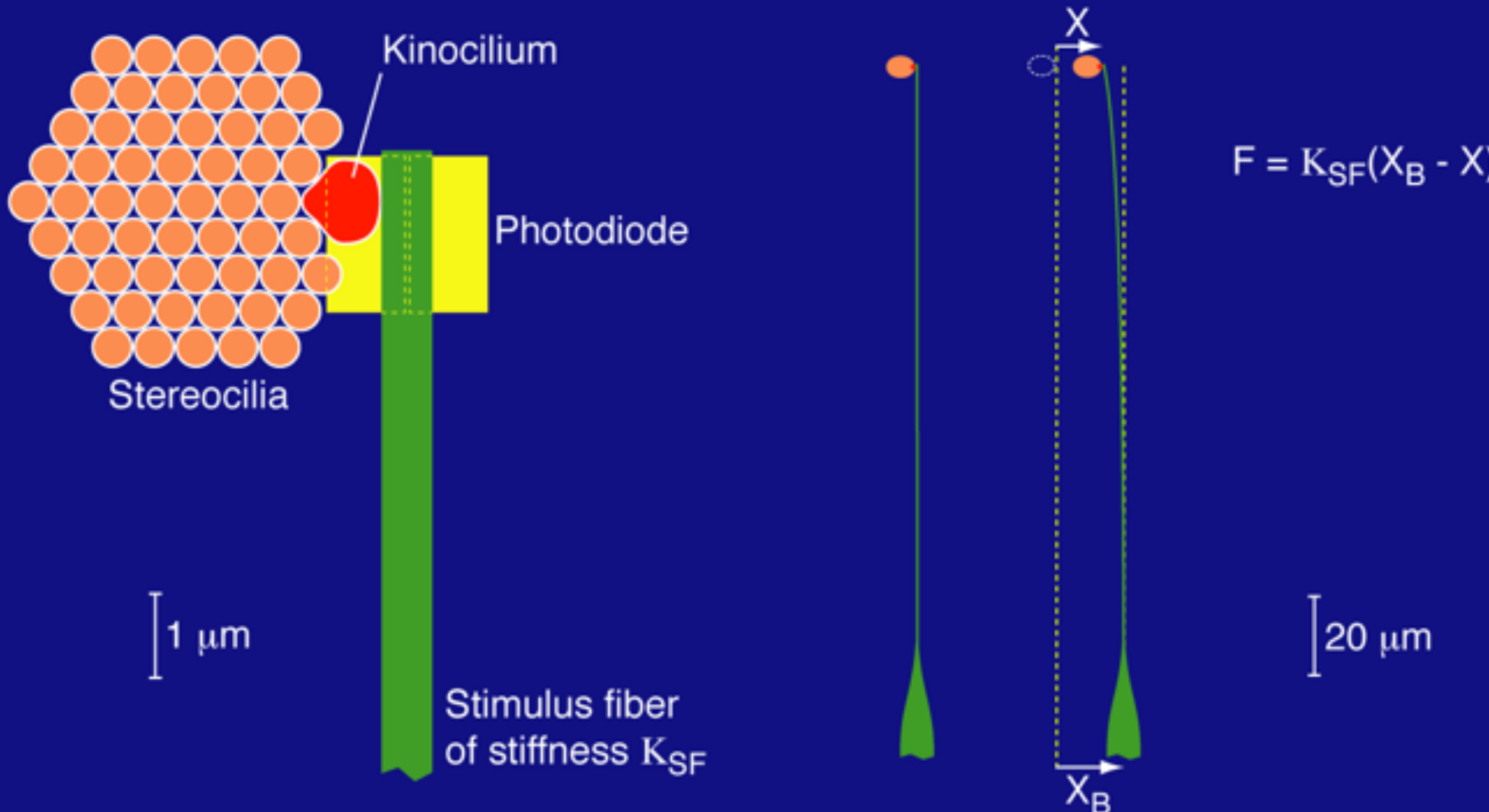

Inner
hair cell
Outer
hair cell
Endolymph
Basilar membrane
Perilymph

THE ACTIVE PROCESS OF HAIR CELLS

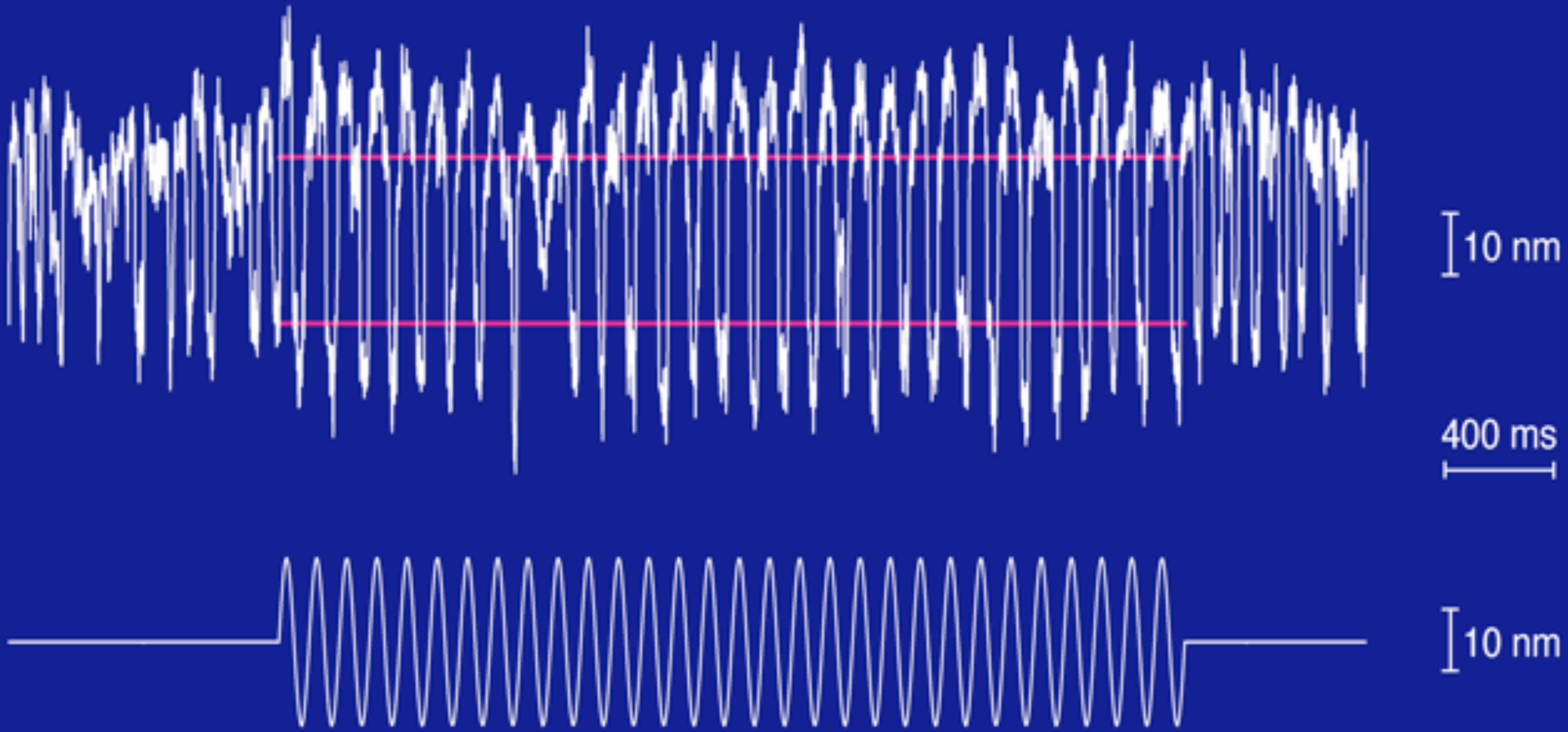


MANIFESTATIONS OF THE EAR'S ACTIVE PROCESS BY INDIVIDUAL HAIR BUNDLES





Kinocilium
Photodiode
Stereocilia
1 μm
Stimulus fiber
of stiffness K_{SF}
X
$F = K_{SF}(X_B - X)$
20 μm
X_B


10 nm
400 ms
10 nm

At any time,

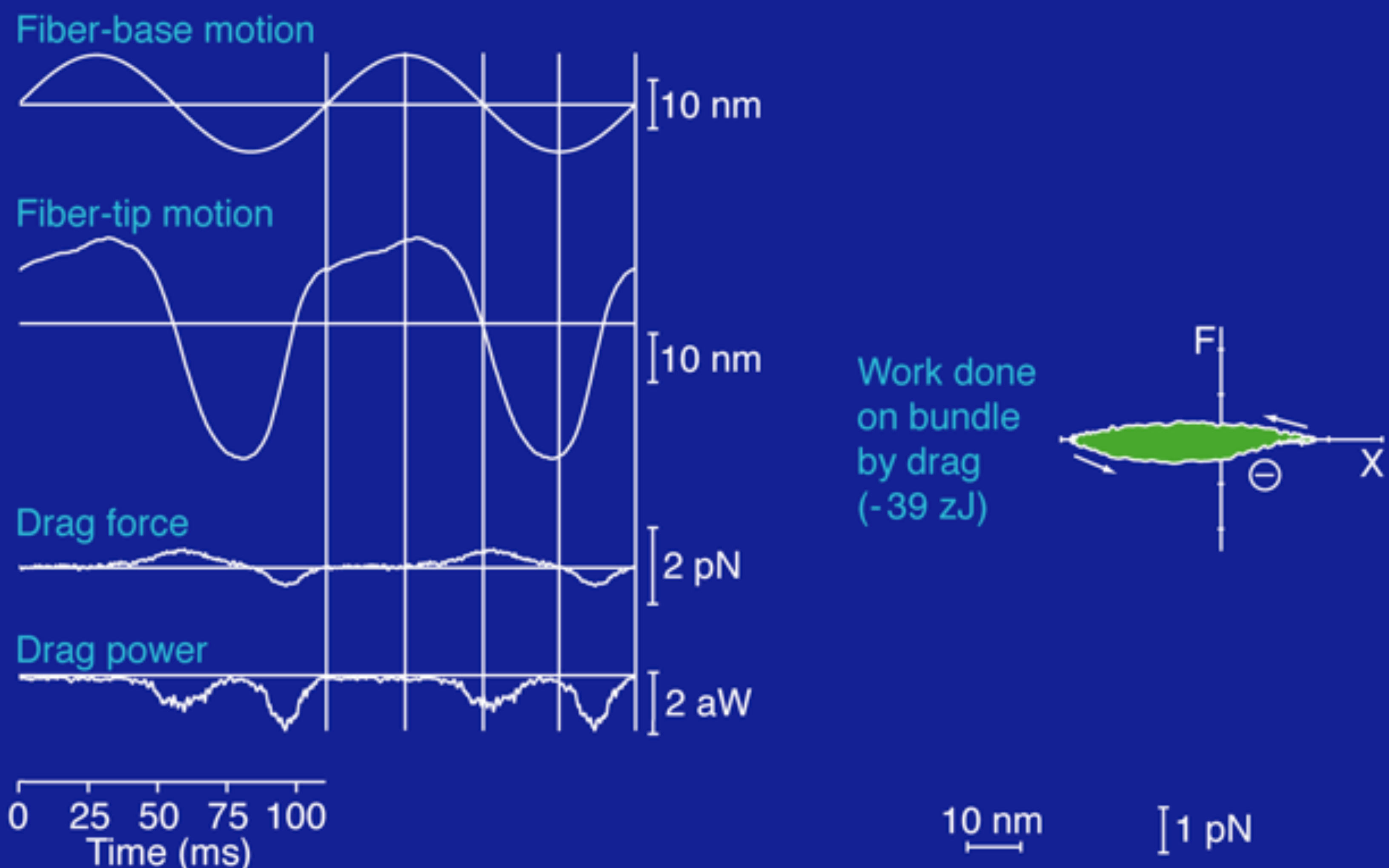
$$F_{EXTERNAL} + F_{INERTIAL} + F_{DRAG} + F_{ELASTIC} + F_{ACTIVE} = 0$$

$$F_{ACTIVE} = - K_{SF}(X_B - X) - (m_{HB} + m_{SF})\cdot\frac{d^2X}{dt^2} - (\xi_{HB} + \xi_{SF})\cdot\frac{dX}{dt} - K_{HB}X$$

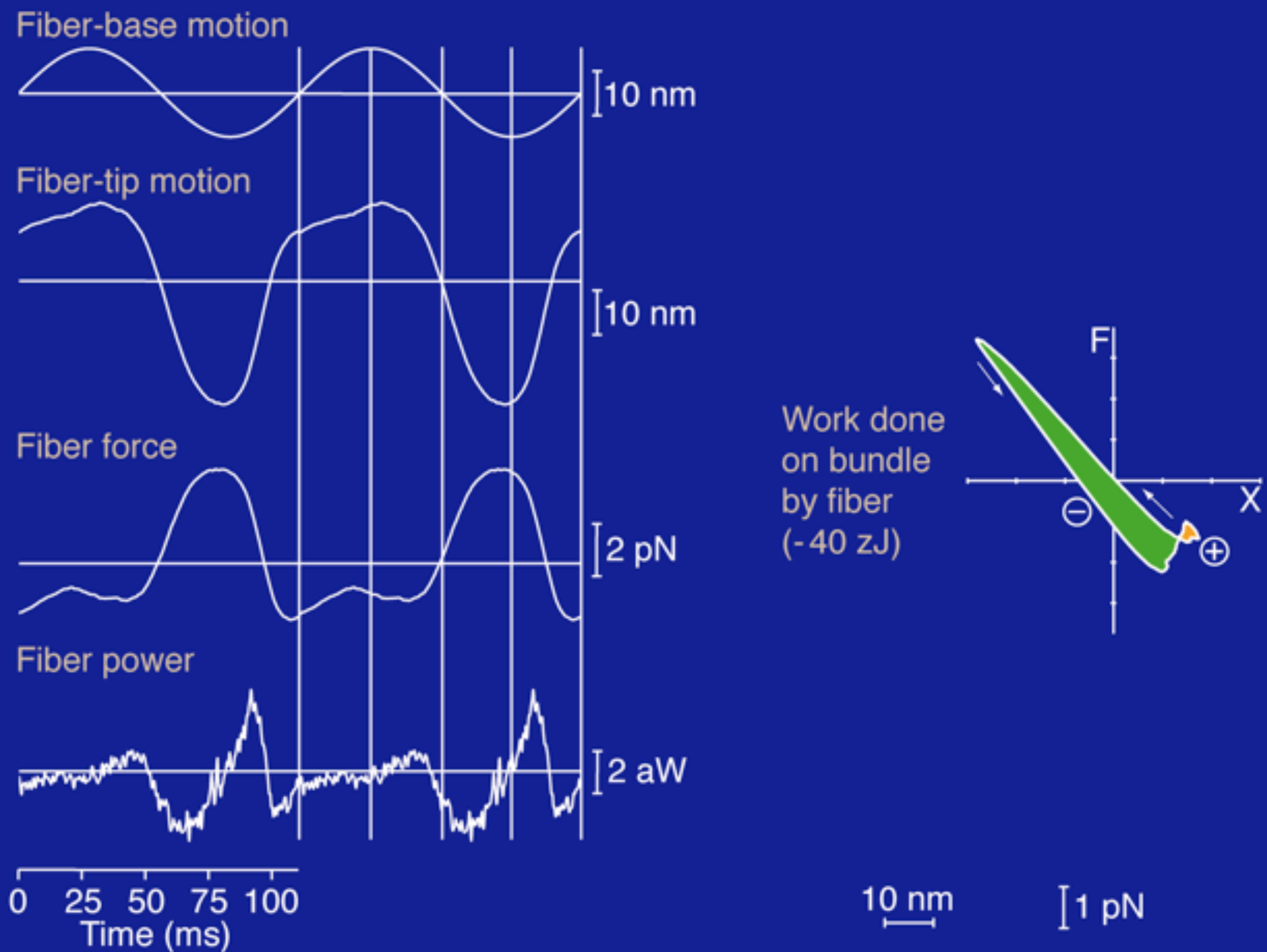
Over an average cycle,

$$\overline{W}_{EXTERNAL} + \xcancel{\overline{W}_{INERTIAL}} + \overline{W}_{DRAG} + \xcancel{\overline{W}_{ELASTIC}} + \overline{W}_{ACTIVE} = 0$$

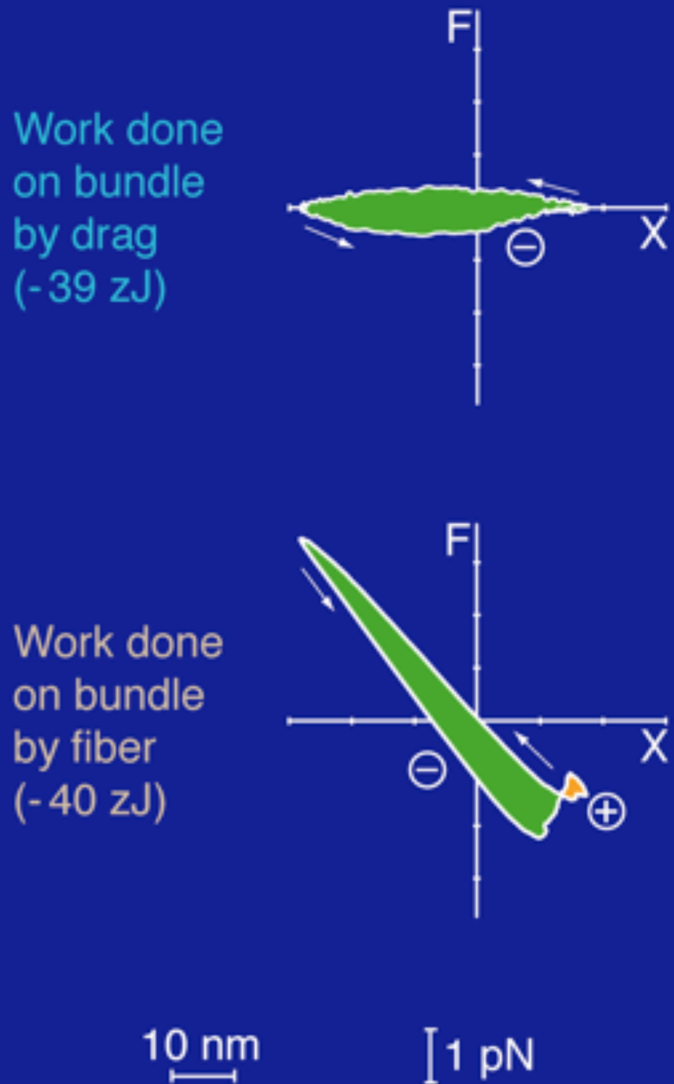
$$\overline{W}_{ACTIVE} = - K_{SF}\oint(X_B - X)\cdot dX - (\xi_{HB} + \xi_{SF})\oint\frac{dX}{dt}\cdot dX$$



Fiber-base motion
10 nm
Fiber-tip motion
10 nm
Drag force
2 pN
Drag power
2 aW
0
25
50
75
100
Time (ms)
Work done
on bundle
by drag
(-39 zJ)
F
X
10 nm
1 pN

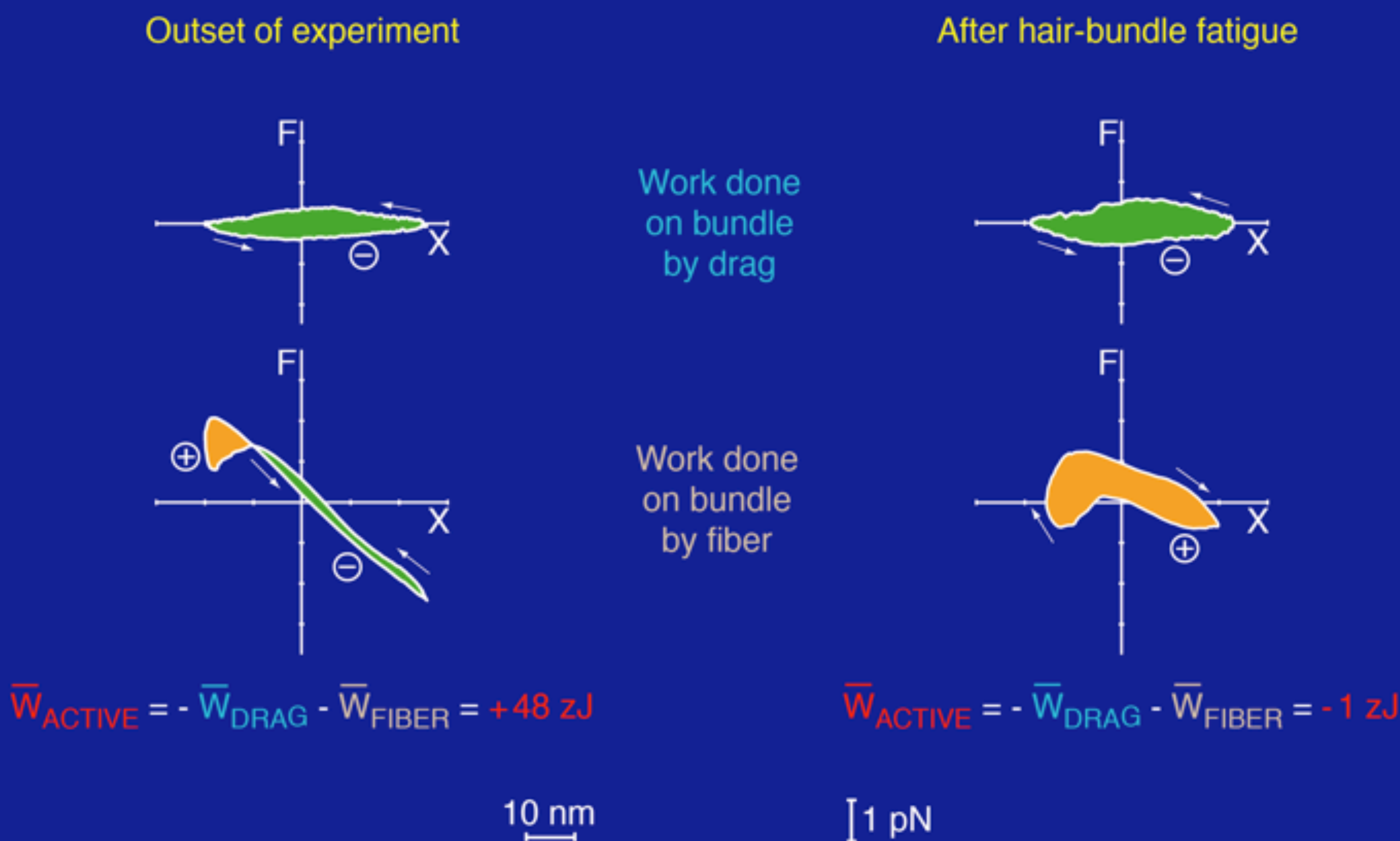


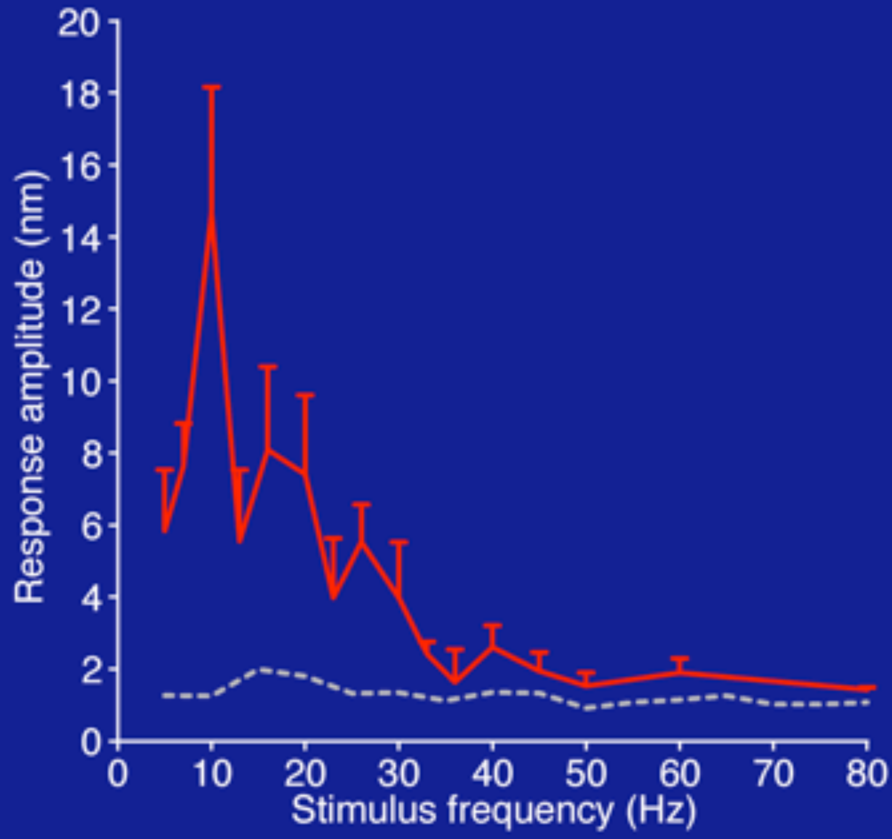
Fiber-base motion
10 nm
Fiber-tip motion
10 nm
Fiber force
2 pN
Fiber power
2 aW
0
25
50
75
100
Time (ms)
Work done
on bundle
by fiber
(-40 zJ)
F
X
⊖
⊕
10 nm
1 pN



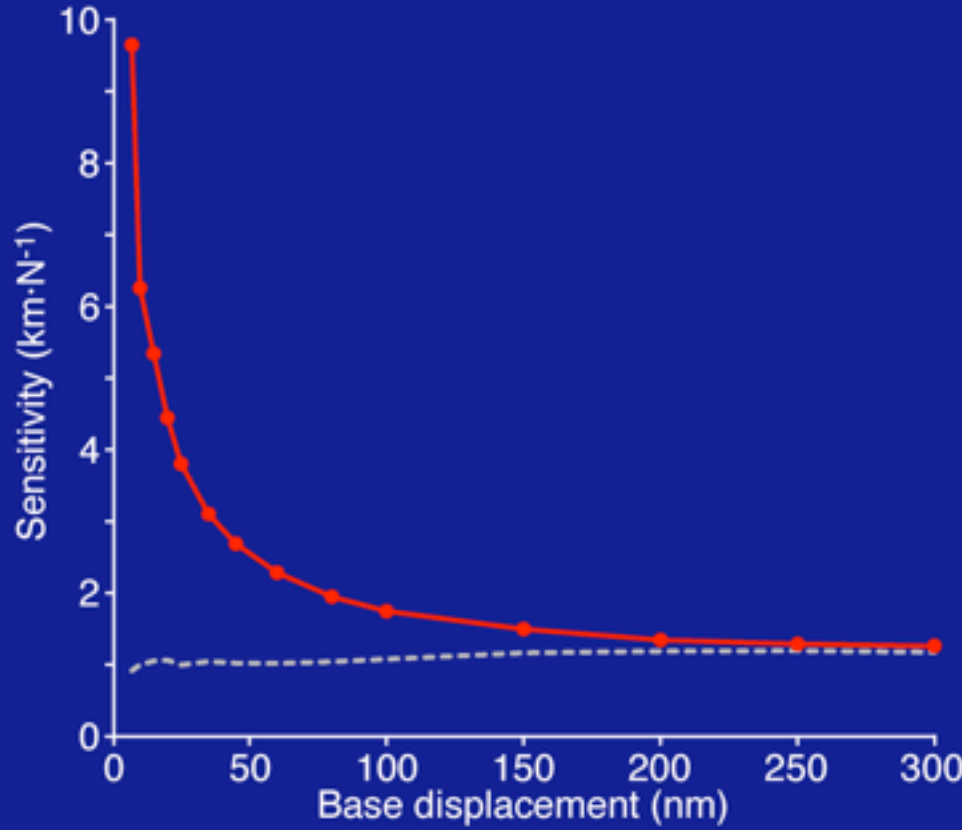
$$\overline{W}_{ACTIVE} = -\,\overline{W}_{DRAG} - \overline{W}_{FIBER}$$

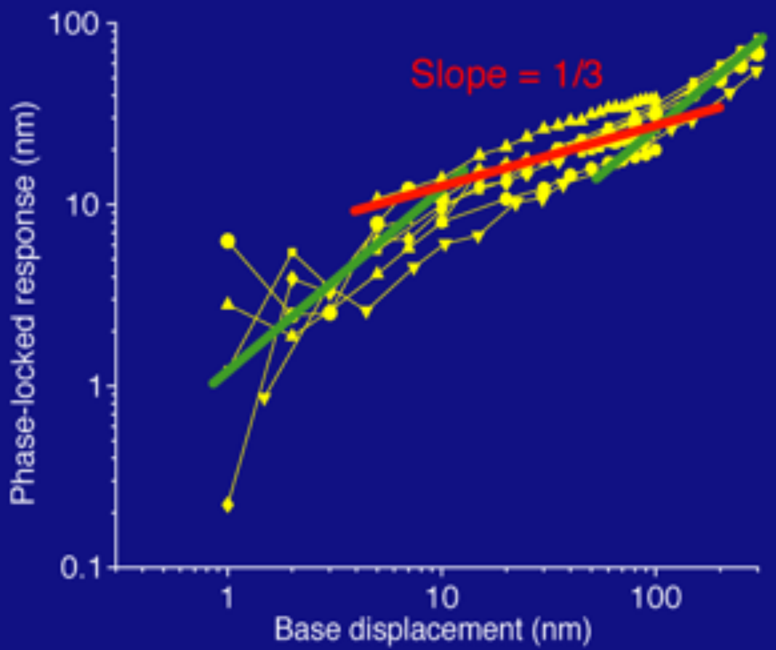
$$\overline{W}_{ACTIVE} = +79\ zJ$$


Outset of experiment
After hair-bundle fatigue
F
X
F
X
Work done on bundle by drag
F
X
F
X
Work done on bundle by fiber
$\overline{W}_{ACTIVE} = - \overline{W}_{DRAG} - \overline{W}_{FIBER} = +48$ zJ
$\overline{W}_{ACTIVE} = - \overline{W}_{DRAG} - \overline{W}_{FIBER} = -1$ zJ
10 nm
1 pN

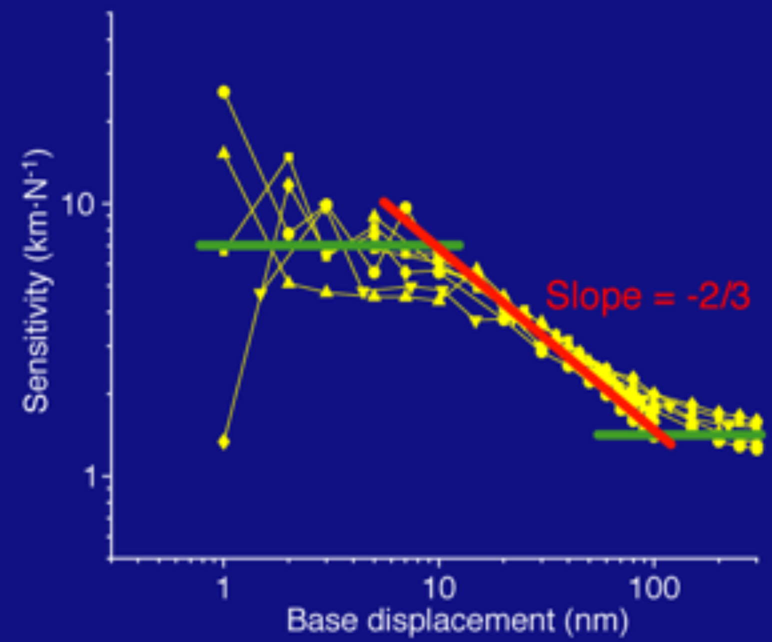


Response amplitude (nm)
20
18
16
14
12
10
8
6
4
2
0
0
10
20
30
40
50
60
70
80
Stimulus frequency (Hz)

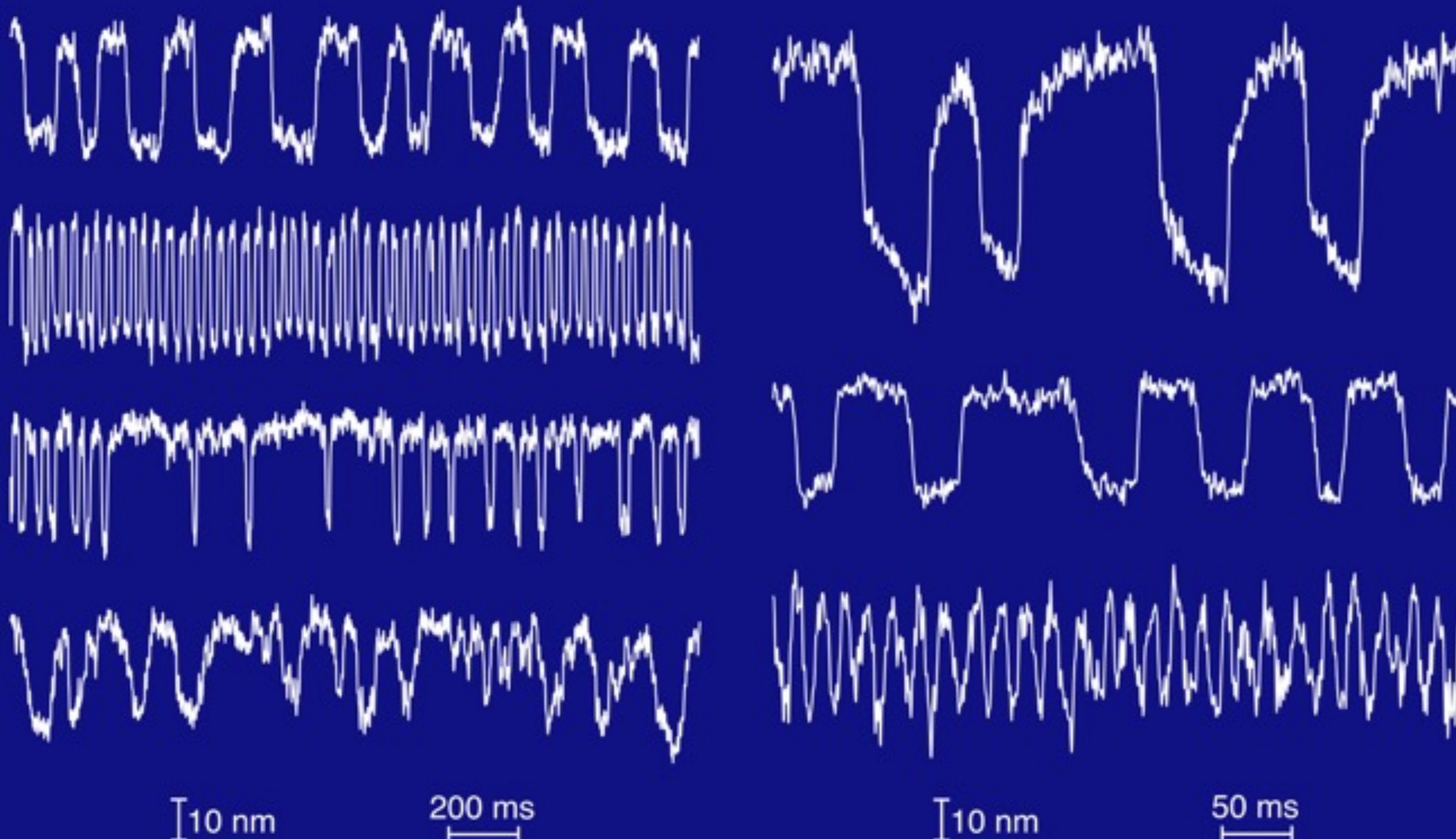

10
8
6
4
2
0
Sensitivity (km·N-1)
0
50
100
150
200
250
300
Base displacement (nm)



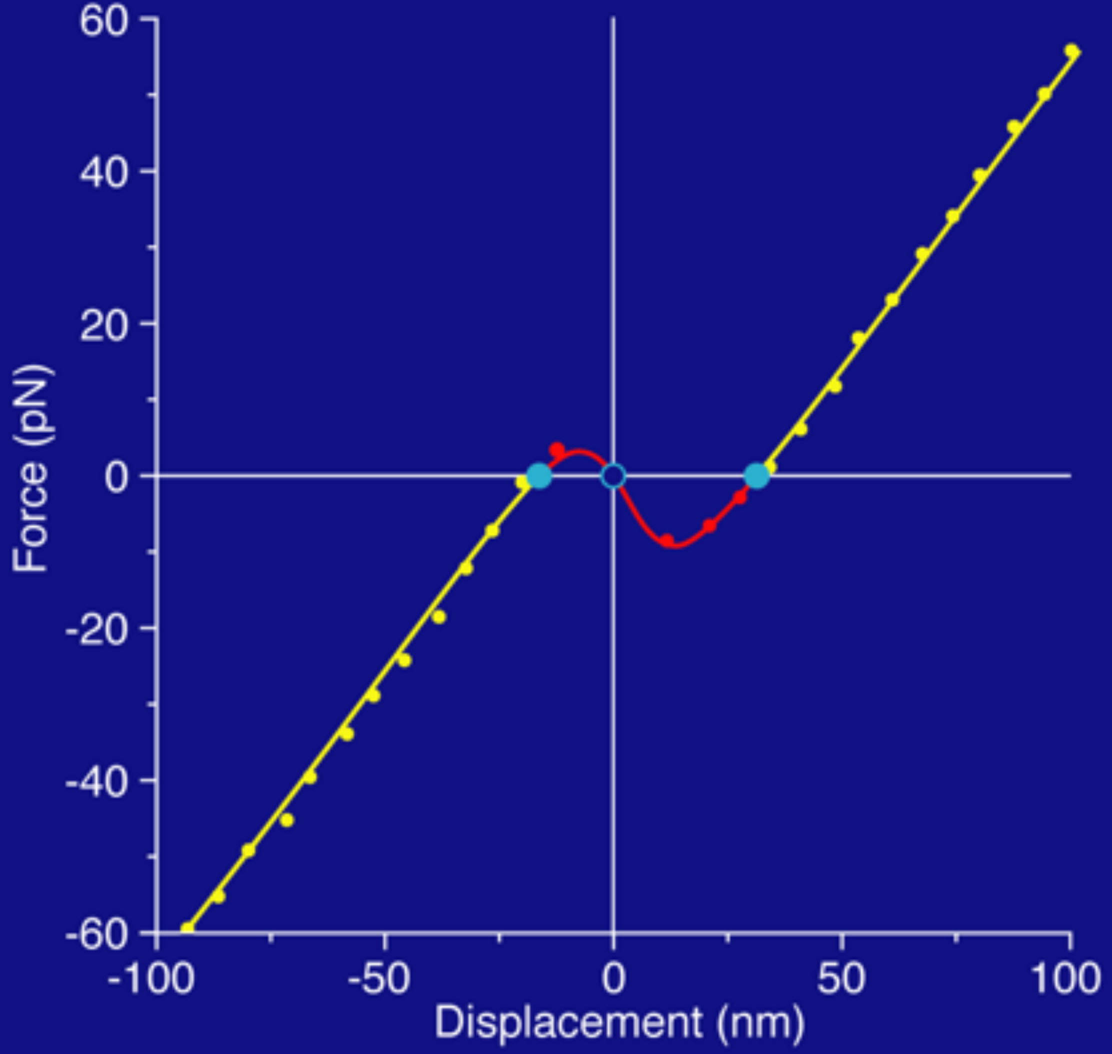
Slope = 1/3
100
10
1
0.1
Phase-locked response (nm)
1
10
100
Base displacement (nm)



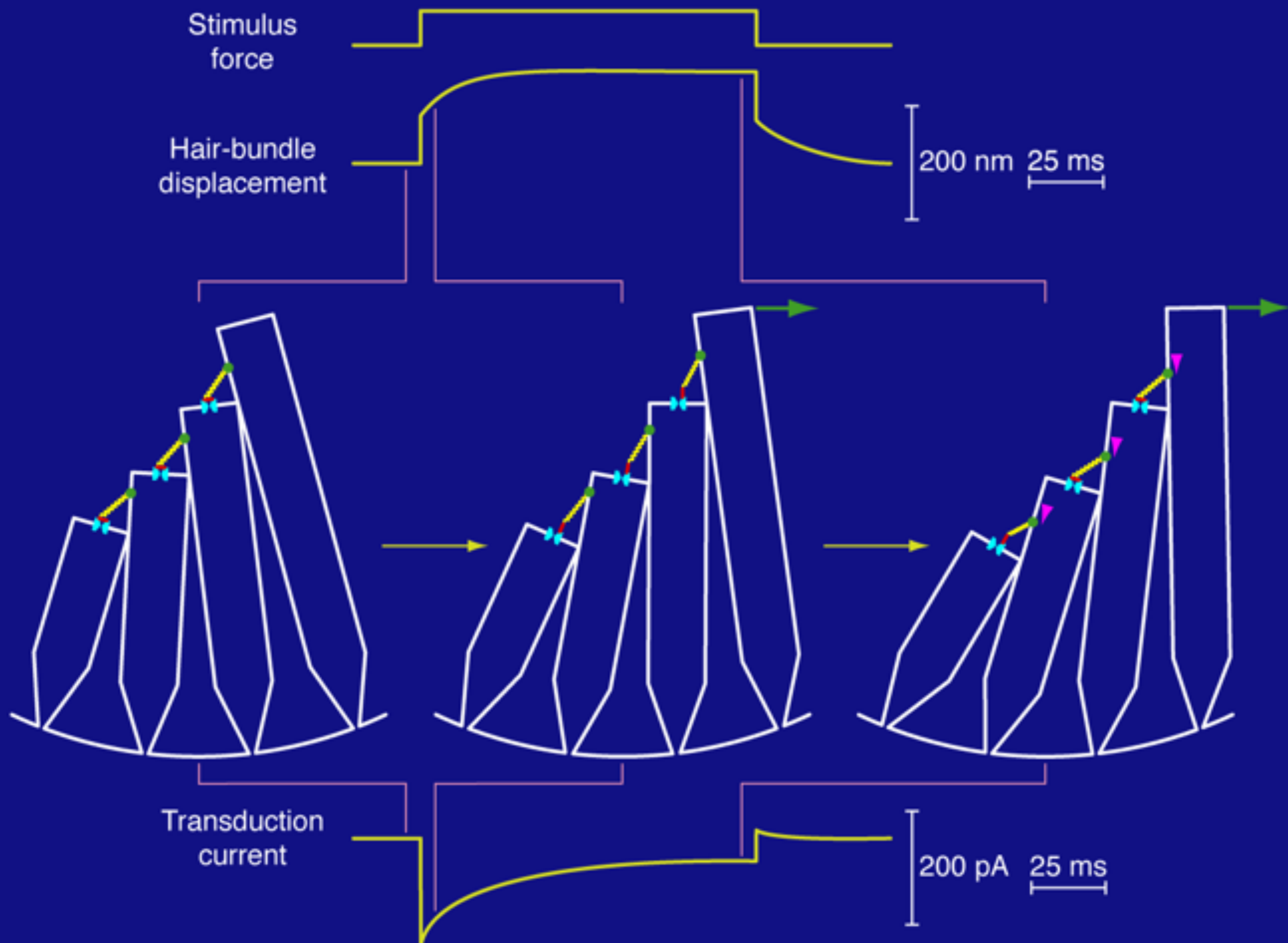
Slope = -2/3
10
1
Sensitivity (km·N⁻¹)
1
10
100
Base displacement (nm)

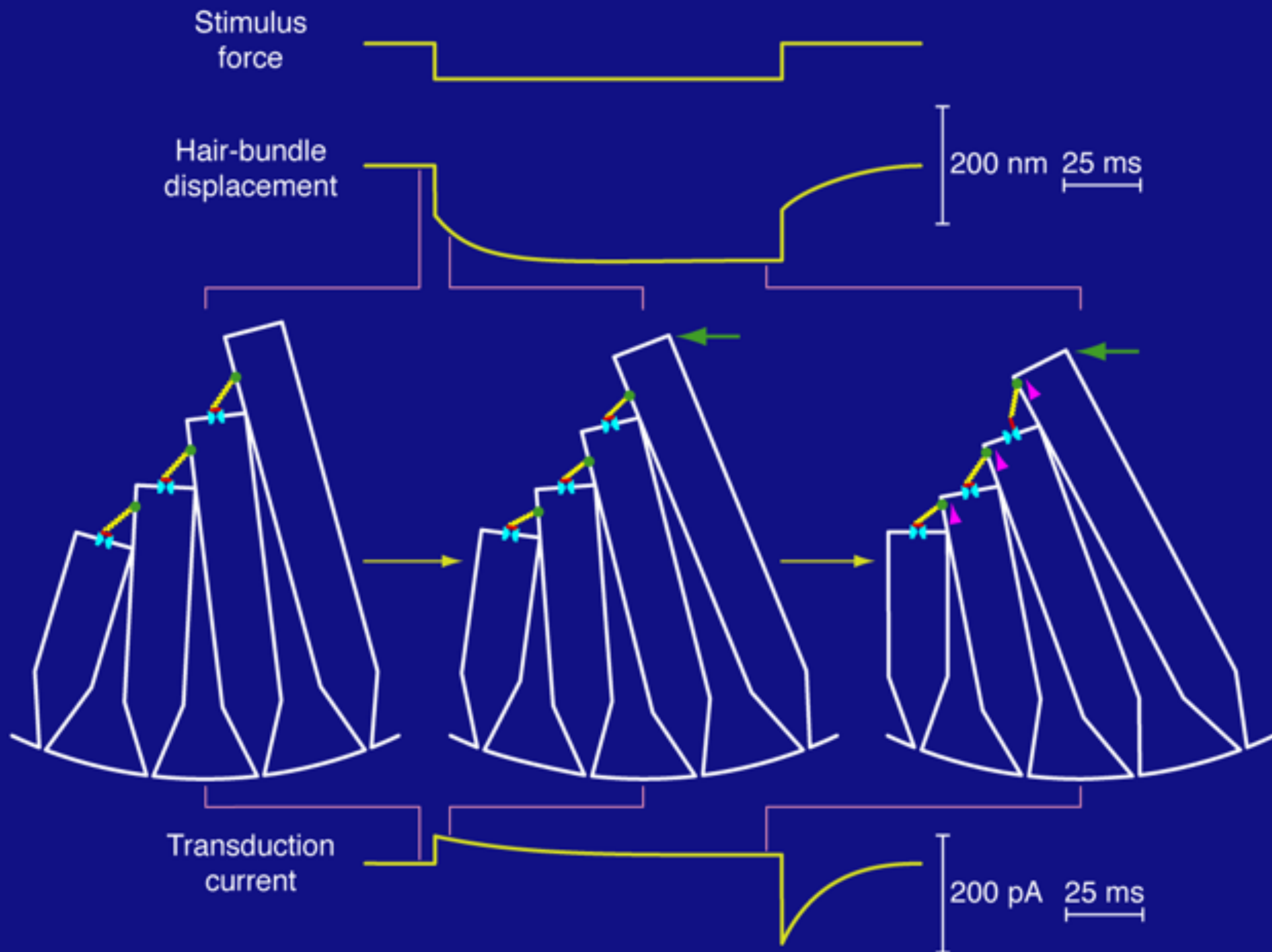


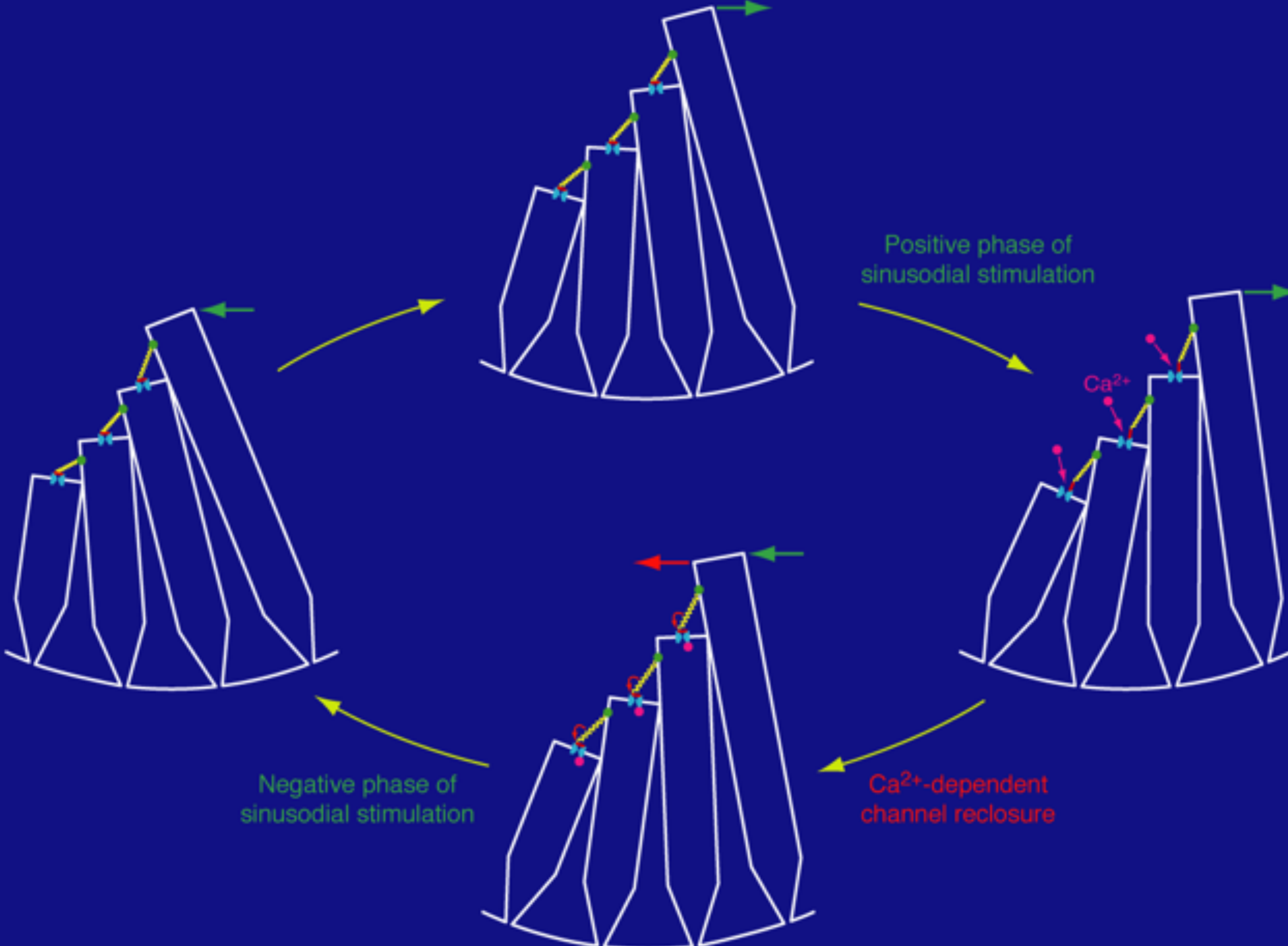
10 nm
200 ms
10 nm
50 ms



60
40
20
0
-20
-40
-60
Force (pN)
-100
-50
0
50
100
Displacement (nm)


Stimulus
force
Hair-bundle
displacement
200 nm
25 ms
Transduction
current
200 pA
25 ms


Stimulus force
Hair-bundle displacement
200 nm
25 ms
Transduction current
200 pA
25 ms



Positive phase of
sinusodial stimulation
Ca2+
Ca2+-dependent
channel reclosure
Negative phase of
sinusodial stimulation

DYNAMICAL DESCRIPTION OF HAIR – BUNDLE MOTION AND ADAPTATION

Drag coefficients — Channel-gating force — Elastic forces — External force

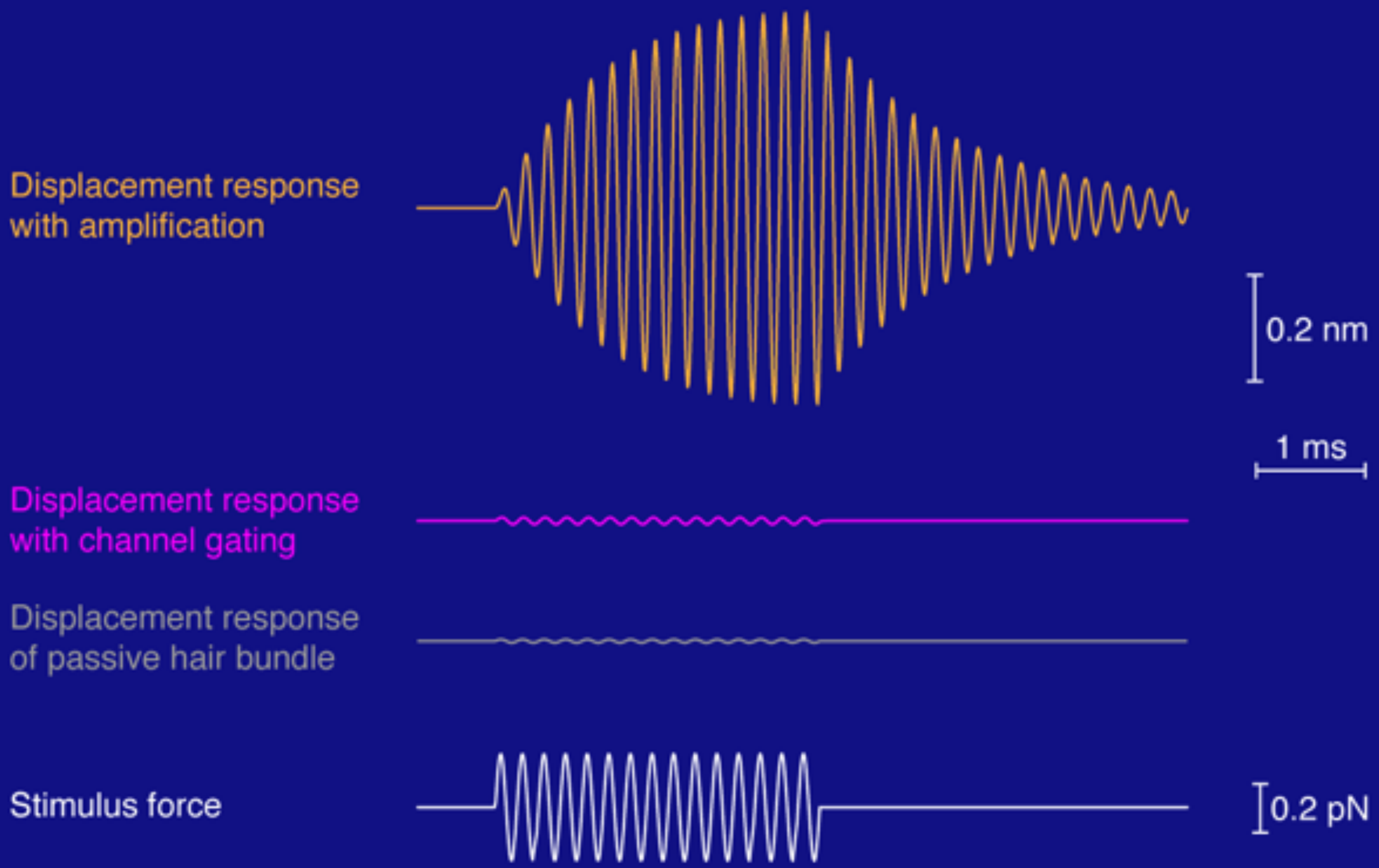
Hair-bundle velocity

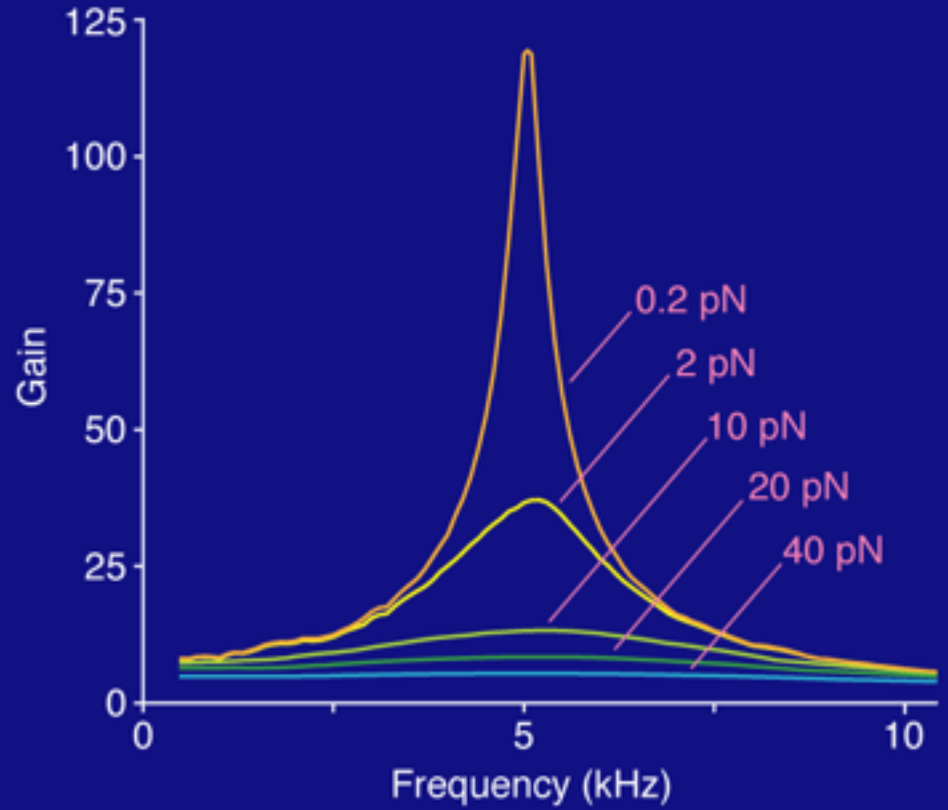
$$\dot{x} = \left(\frac{1}{\xi_{HB} + \xi_{EXT}}\right)\left[A(x-a) - B(x-a)^3 - (\kappa_{SP} + \kappa_{EXT})x + F_{EXT}\right])$$

Adaptation rate

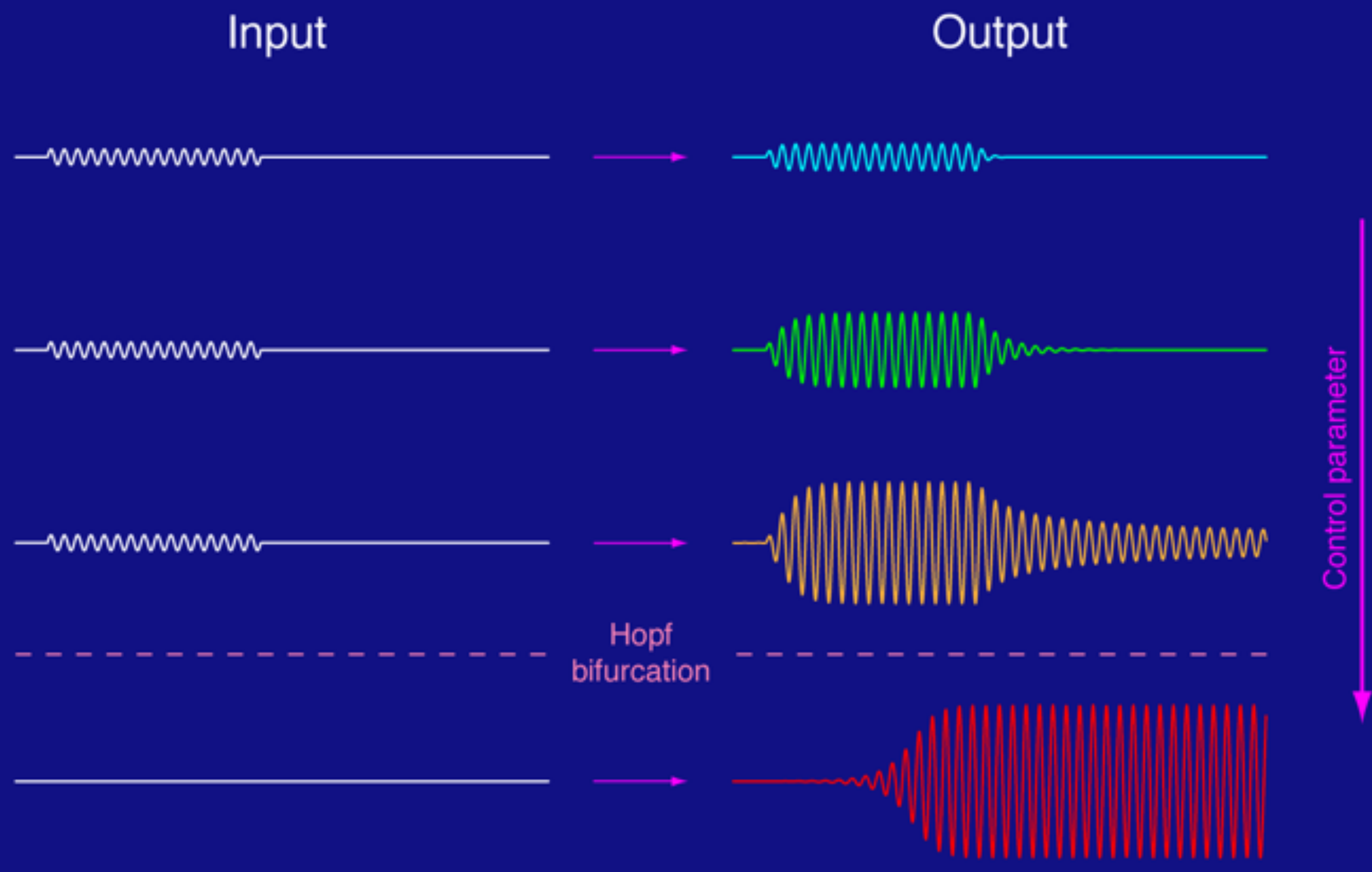
$$\dot{a} = \frac{1}{\tau}(Cx - a)$$

Adaptation time constant


Displacement response
with amplification
0.2 nm
1 ms
Displacement response
with channel gating
Displacement response
of passive hair bundle
Stimulus force
0.2 pN



125
100
75
50
25
0
Gain
0
5
10
Frequency (kHz)
0.2 pN
2 pN
10 pN
20 pN
40 pN


Input
Output
Control parameter
Hopf
bifurcation

Equation for a generic Hopf bifurcation with stimulation by a force $Fe^{i\omega t}$:

$$\frac{dz}{dt} = (\mu + i\omega_0)z - |z|^2 z + Fe^{i\omega t}$$

z, displacement (complex variable: $z = x + iy$)

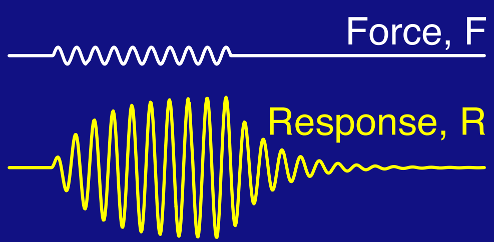
ω_0, natural (characteristic) frequency

μ, control parameter

During stimulation near bifurcation ($\mu \approx 0$) and near resonance ($\omega \approx \omega_0$),

response $R \approx F^{1/3}$, amplification with compressive nonlinearity

sensitivity $S = \frac{R}{F} \approx F^{-2/3}$



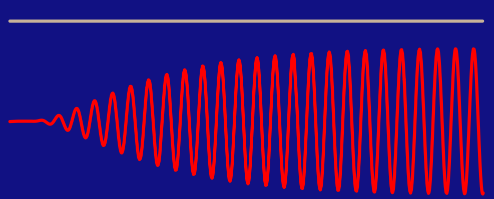
In the absence of stimulation,

$\mu < 0$,

$z = 0$, a quiescent system

$\mu > 0$,

$z = \sqrt{\mu}\, e^{i\omega_0 t} = \sqrt{\mu}\,[\cos(\omega_0 t) + i \cdot \sin(\omega_0 t)]$, a stable limit cycle



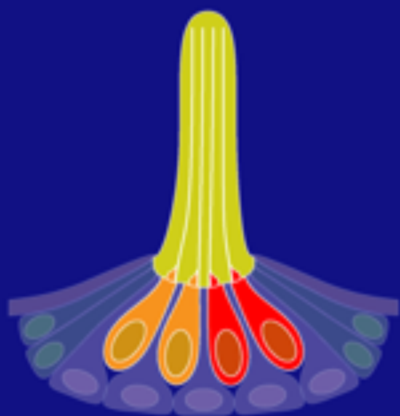
ADVANTAGES OF OPERATION NEAR A HOPF BIFURCATION

Principal virtues	
amplification	100-fold to 1000-fold gain in humans
frequency tuning	0.2 % frequency discrimination in humans
compressive nonlinearity	1,000,000-fold amplitude range in humans
Simplicity	
two-dimensional	minimal requirement for resonant tuning and oscillation
codimension-1	adjustment of only one parameter required to traverse bifurcation
local	bifurcation about a fixed point
Entrainment	easy phase-locking to periodic stimuli
Frequency constancy	frequency of resonant responsiveness near that of spontaneous oscillation
Epiphenomena	
combination tones	generation of responses at nonharmonic frequencies, *e.g.* $2f_1 - f_2$
spontaneous otoacoustic emissions (SOAEs)	unprovoked production of one or more pure tones

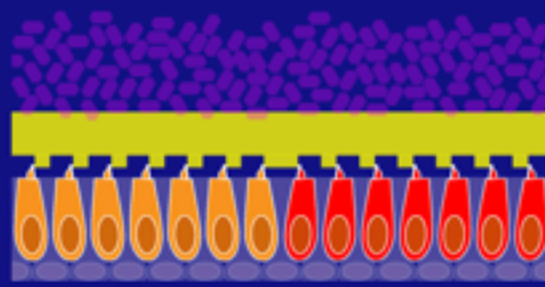
Defining characteristics of the cochlear active process

THE MECHANICAL LOADS OF HAIR BUNDLES

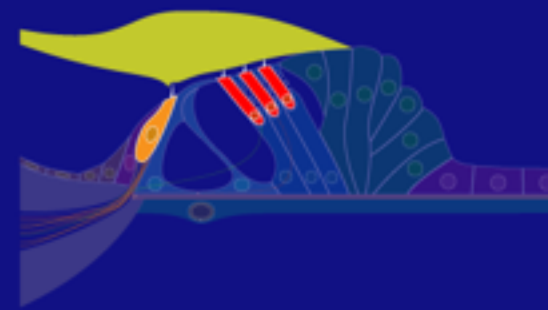
Cupular organs
lateral-line organs and semicircular canals

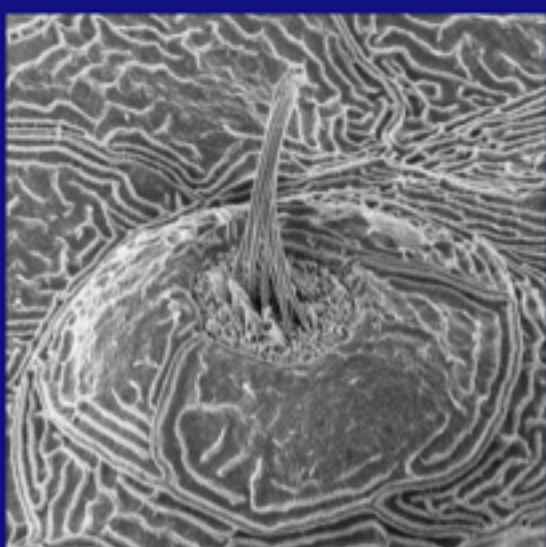


Otolith organs
utricles and saccules

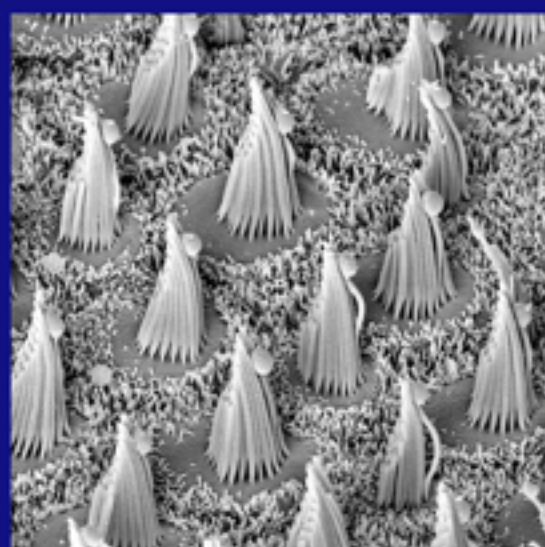


Tectorial organs
cochleas and basilar papillas

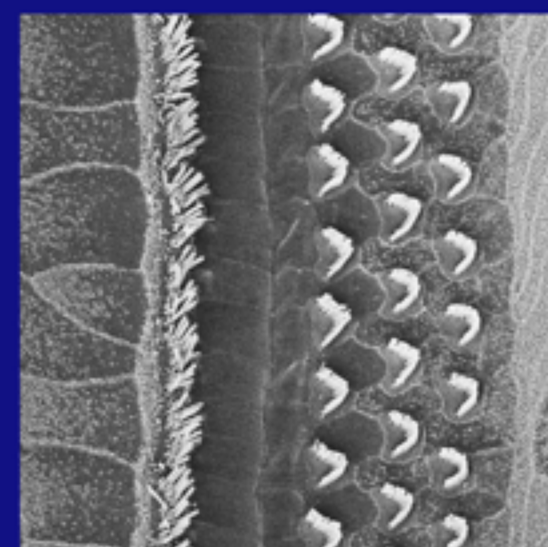




Zebrafish's lateral-line organ



Bullfrog's sacculus



Mouse's cochlea

DYNAMICAL DESCRIPTION OF HAIR – BUNDLE MOTION AND ADAPTATION

Experimentally accessible parameters

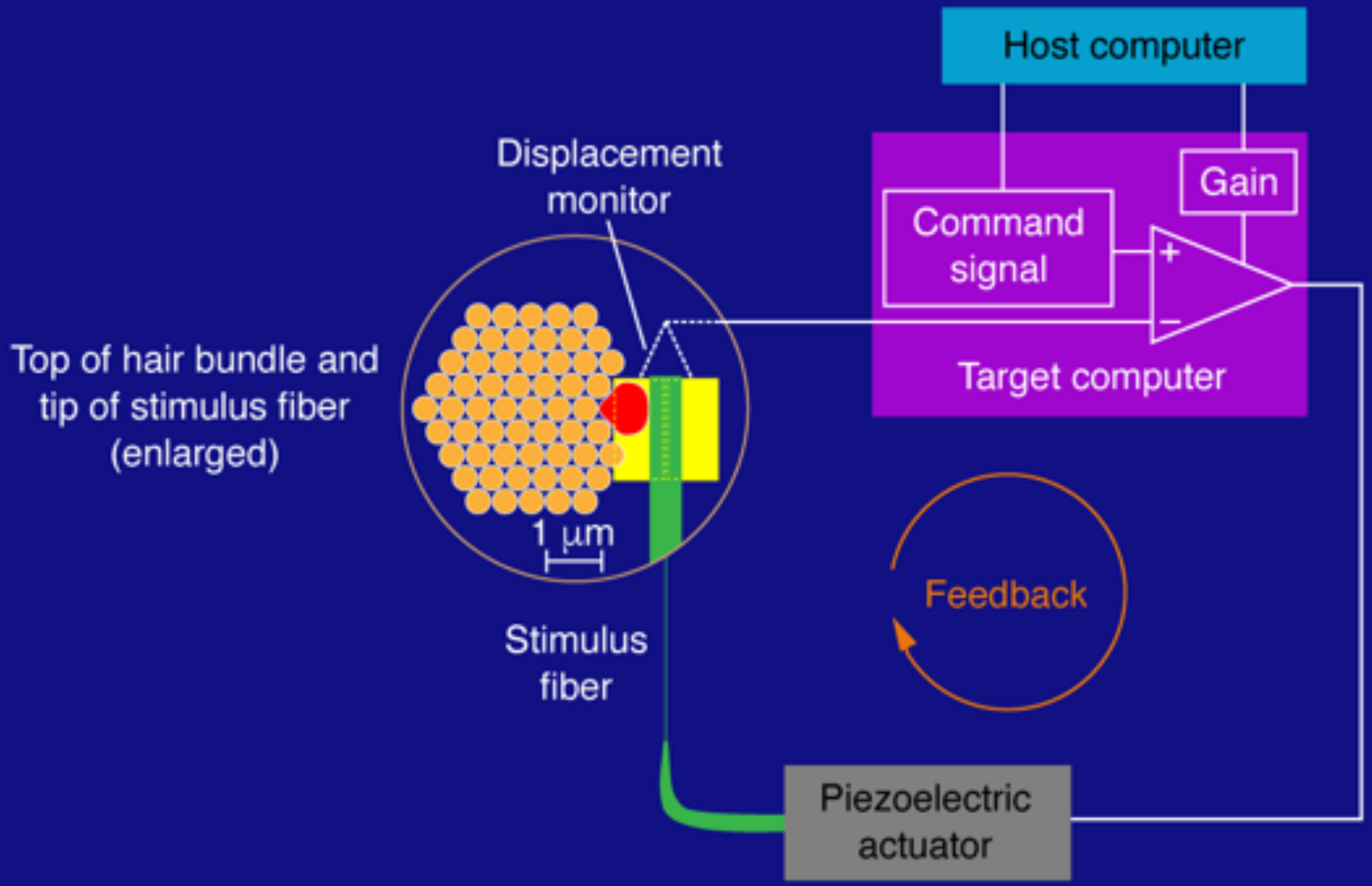
Hair-bundle velocity

$$\dot{x} = \left(\frac{1}{\xi_{HB} + \xi_{EXT}}\right)\left[A(x-a) - B(x-a)^3 - (\kappa_{SP} + \kappa_{EXT})x + F_{EXT}\right]$$

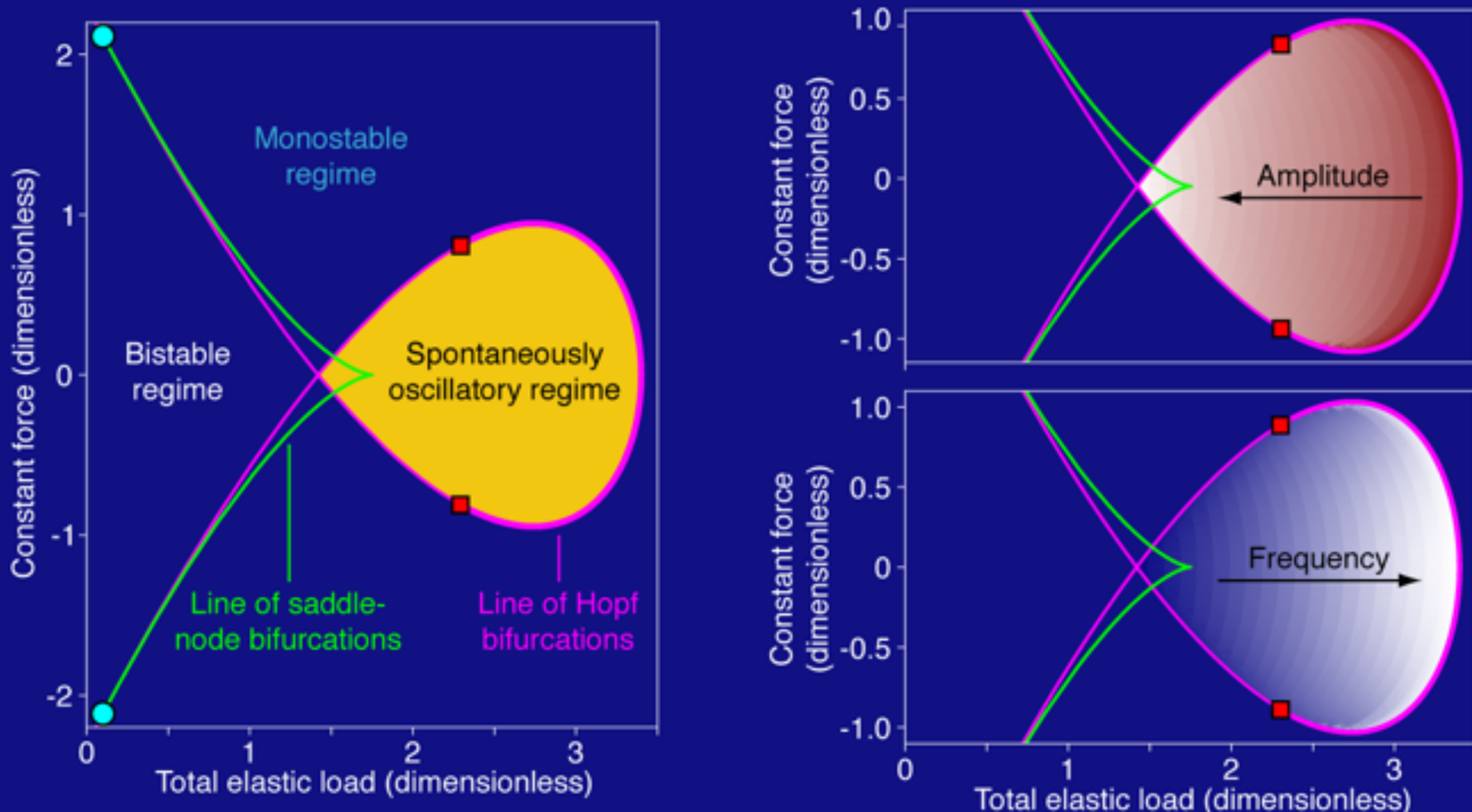
Adaptation rate

$$\dot{a} = \frac{1}{\tau}(Cx - a)$$

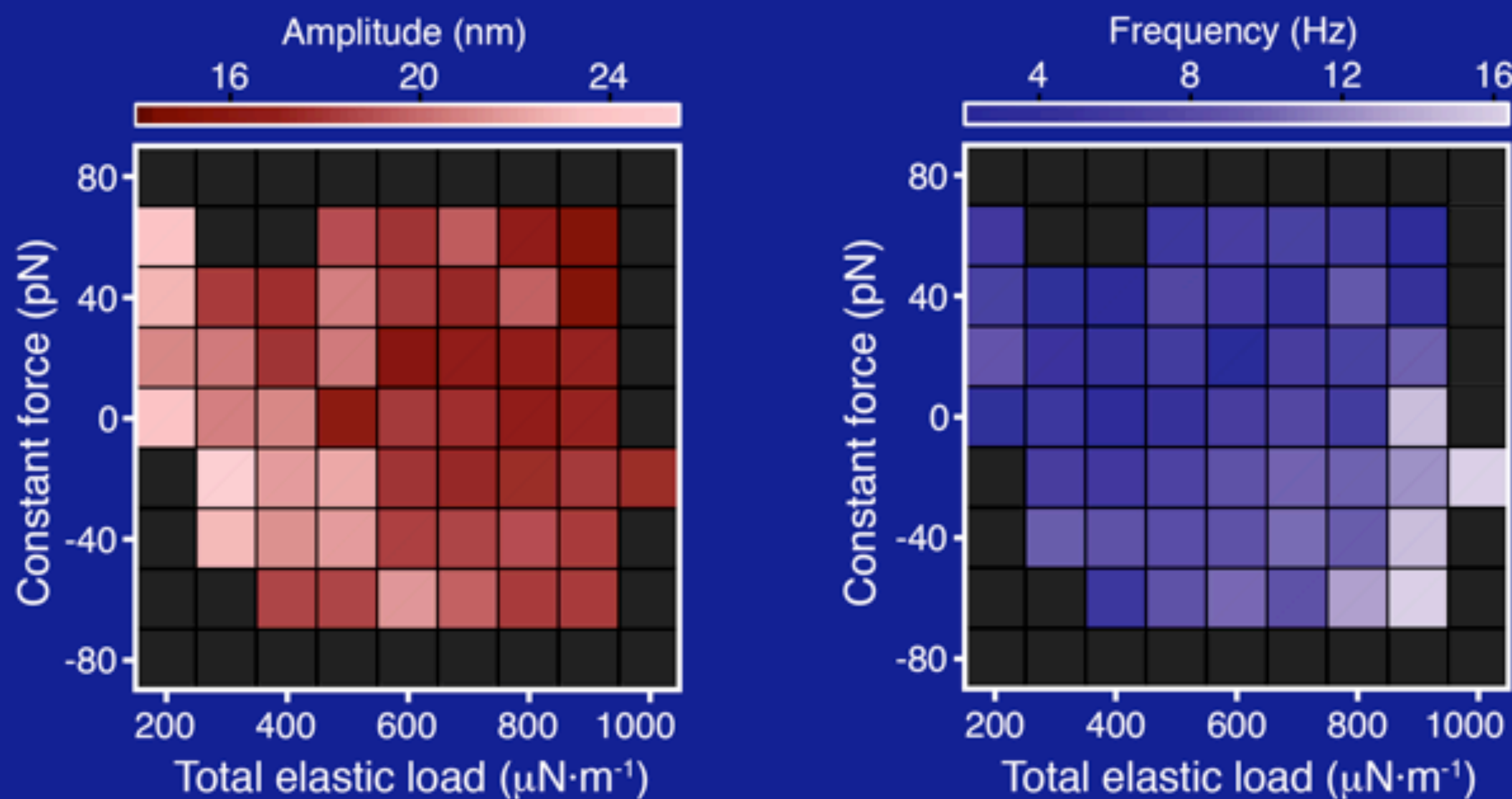
MECHANICAL – LOAD CLAMP



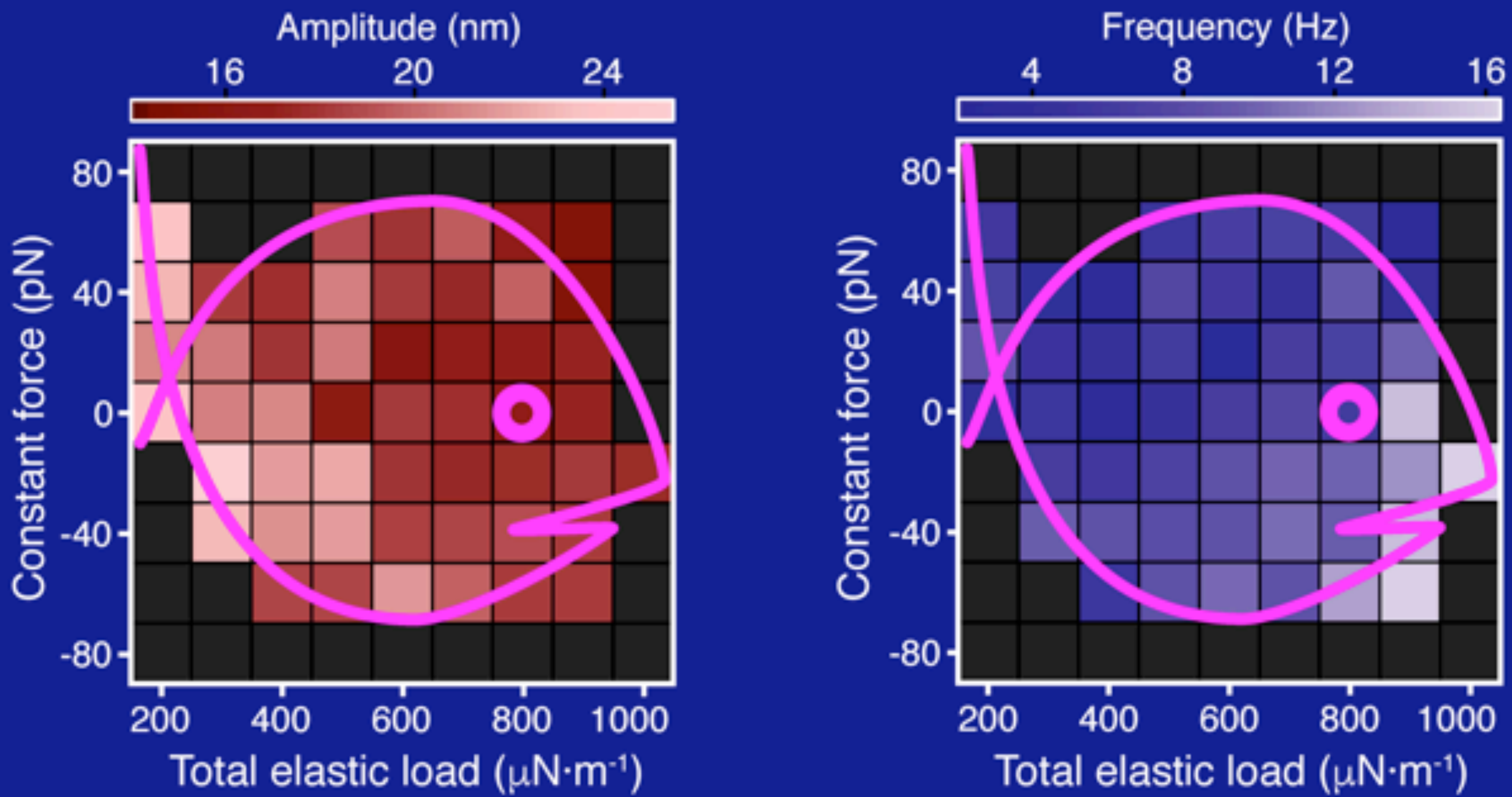
THEORETICAL STATE DIAGRAM



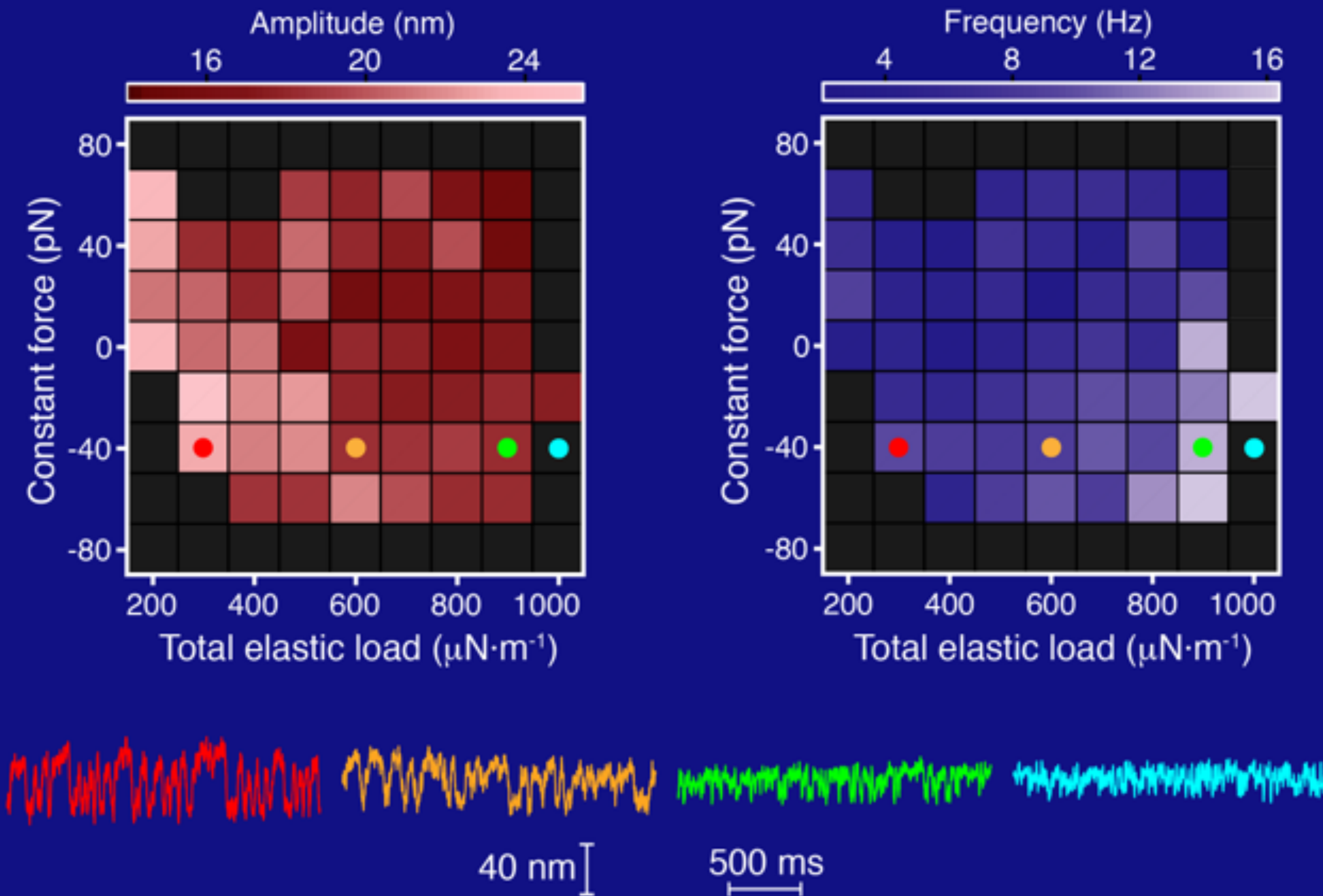
EXPERIMENTAL STATE DIAGRAM

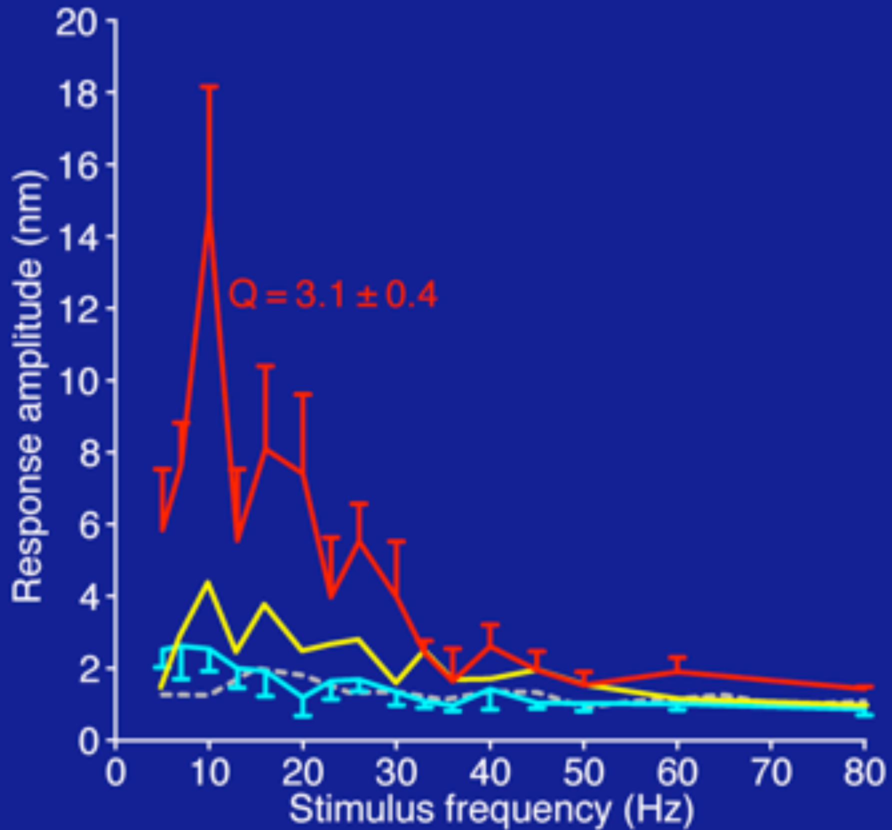


EXPERIMENTAL STATE DIAGRAM



EXPERIMENTAL STATE DIAGRAM



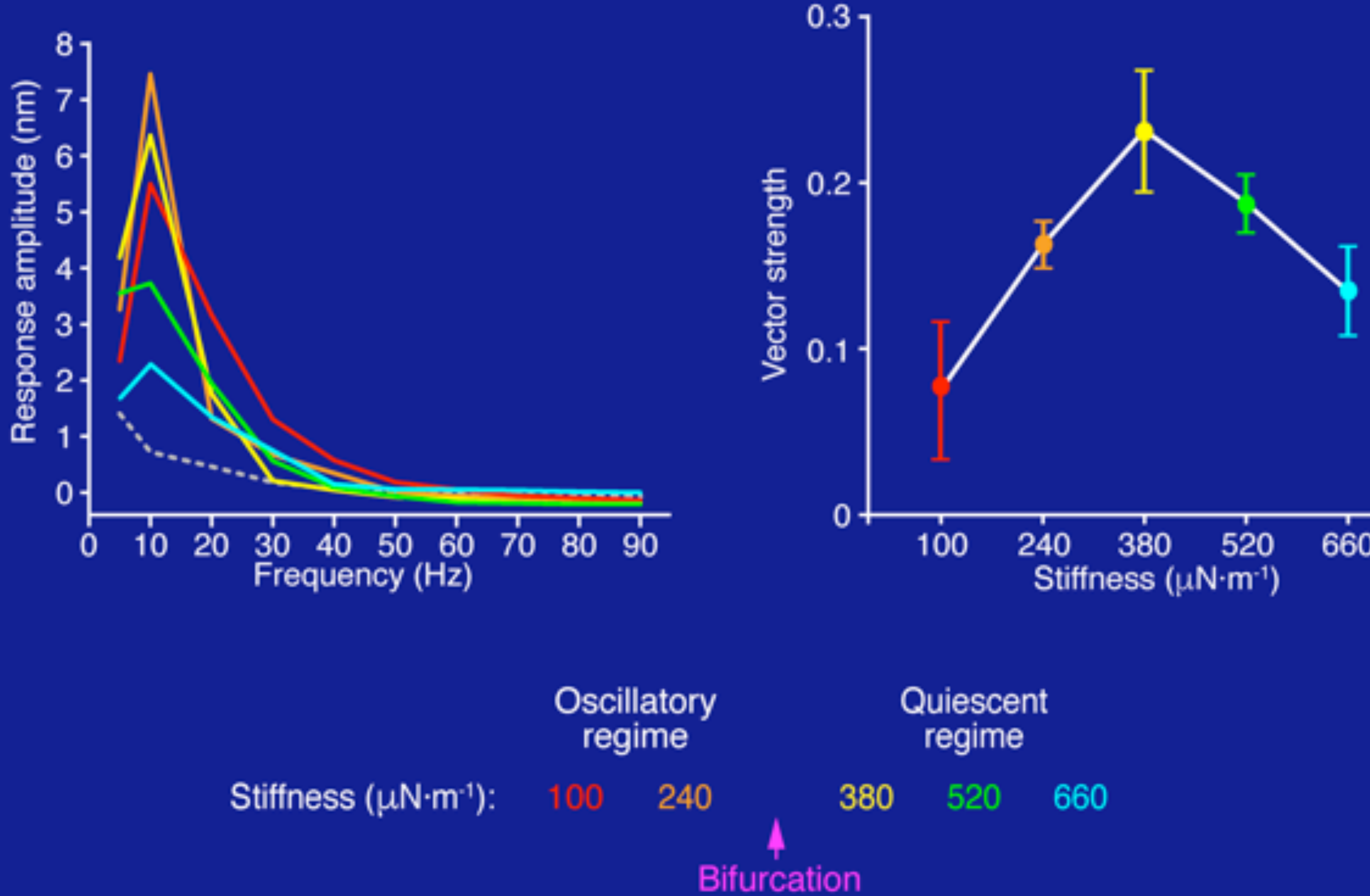


Oscillatory regime

Quiescent regime

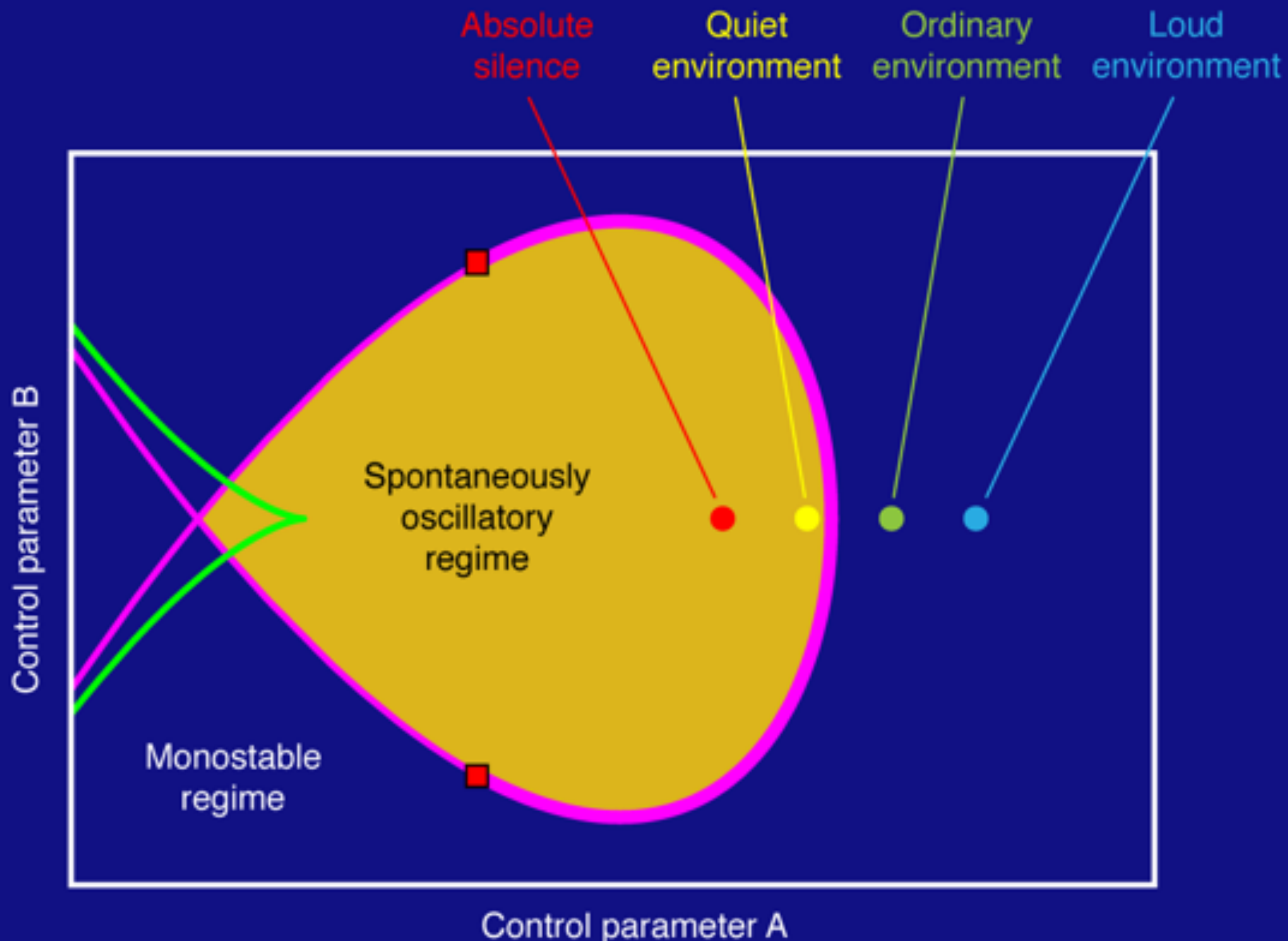
Stiffness (μN·m⁻¹): 300 400 500

Bifurcation

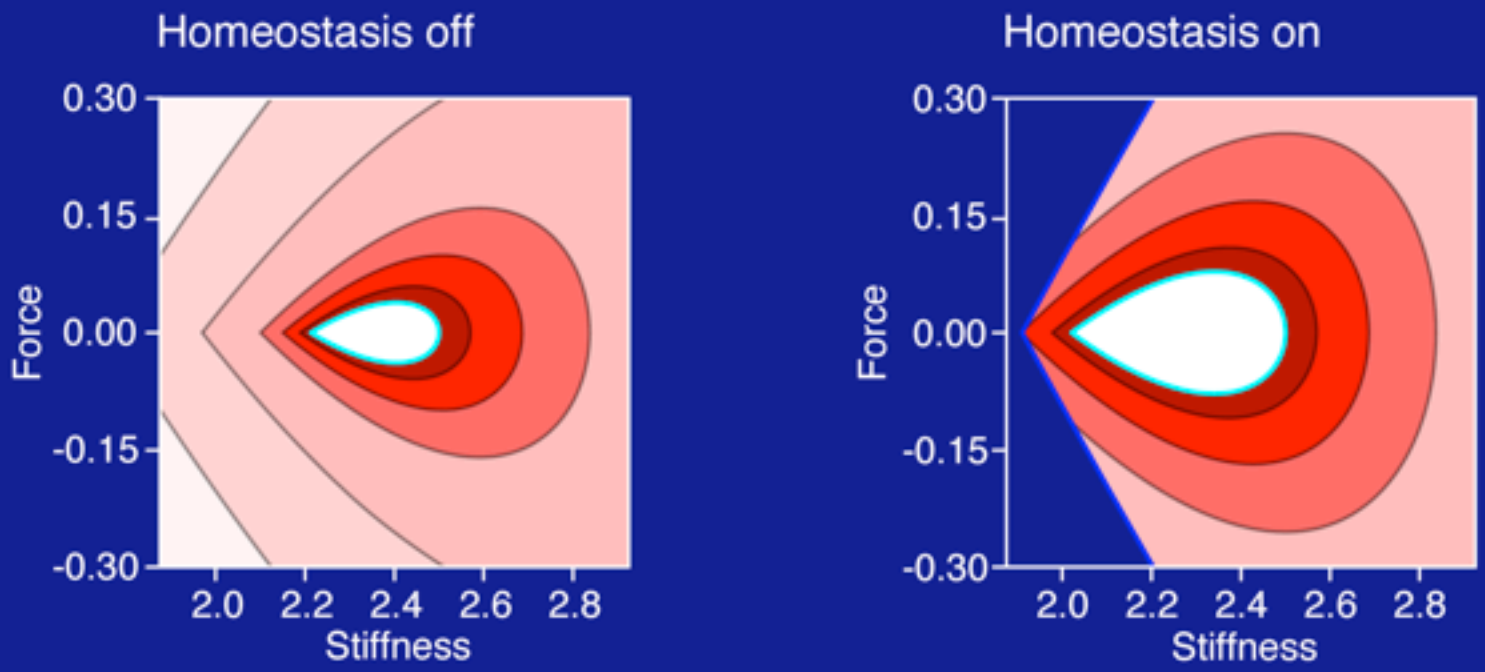


Response amplitude (nm)
0
1
2
3
4
5
6
7
8
0 10 20 30 40 50 60 70 80 90
Frequency (Hz)
Vector strength
0
0.1
0.2
0.3
100 240 380 520 660
Stiffness (µN·m-1)
Oscillatory regime
Quiescent regime
Stiffness (µN·m-1):
100
240
380
520
660
Bifurcation

SELF – TUNED CRITICALITY



HOMEOSTATIC REGULATION OF HAIR – BUNDLE SENSITIVITY



ADVANTAGES OF HAIR CELLS FOR BIOPHYSICAL INVESTIGATION

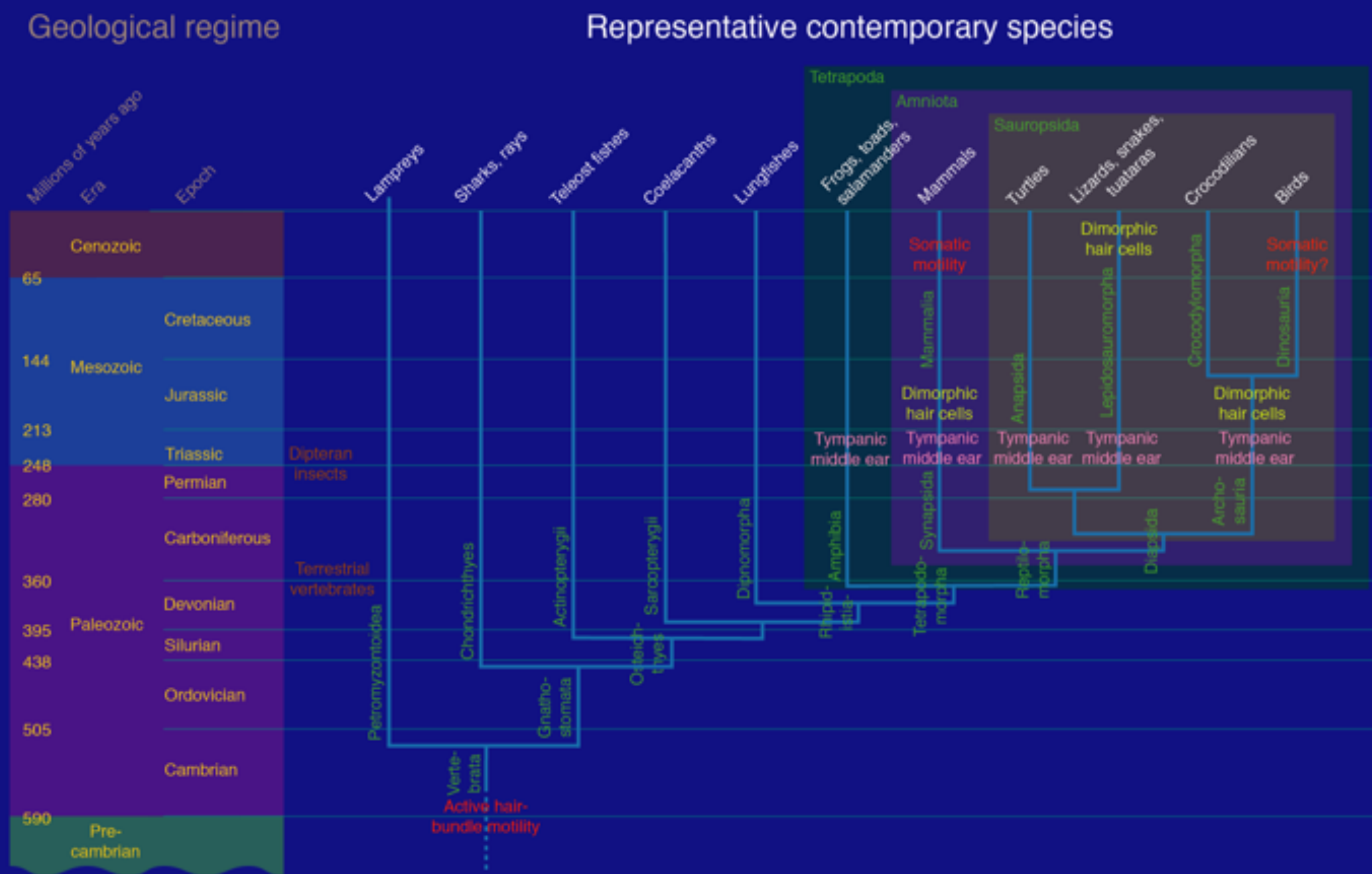
Stereotyped cells with high reproducibility

Experimental accessibility

Ability to measure and control conjugate variables
- displacement and force of hair bundle
- voltage and current across cellular membrane

Few relevant degrees of freedom
- hair-bundle motion along axis of symmetry
- state of adaptation

Evolutionary pressures on system
- threshold near level of thermal noise
- energetic efficiency



Geological regime
Representative contemporary species
Millions of years ago
Era
Epoch
Lampreys
Sharks, rays
Teleost fishes
Coelacanths
Lungfishes
Frogs, toads, salamanders
Mammals
Turtles
Lizards, snakes, tuataras
Crocodilians
Birds
Tetrapoda
Amniota
Sauropsida
Cenozoic
65
Cretaceous
144
Mesozoic
Jurassic
213
Triassic
248
Permian
280
Carboniferous
360
Devonian
395
Paleozoic
Silurian
438
Ordovician
505
Cambrian
590
Pre-cambrian
Dipteran insects
Terrestrial vertebrates
Somatic motility
Dimorphic hair cells
Somatic motility?
Mammalia
Lepidosauromorpha
Crocodylomorpha
Dinosauria
Anapsida
Dimorphic hair cells
Dimorphic hair cells
Tympanic middle ear
Tympanic middle ear
Tympanic middle ear
Tympanic middle ear
Tympanic middle ear
Synapsida
Archo-sauria
Diapsida
Amphibia
Reptilio-morpha
Tetrapodo-morpha
Rhipid-istia
Dipnomorpha
Sarcopterygii
Actinopterygii
Osteich-thyes
Chondrichthyes
Gnatho-stomata
Petromyzontoidea
Verte-brata
Active hair-bundle motility