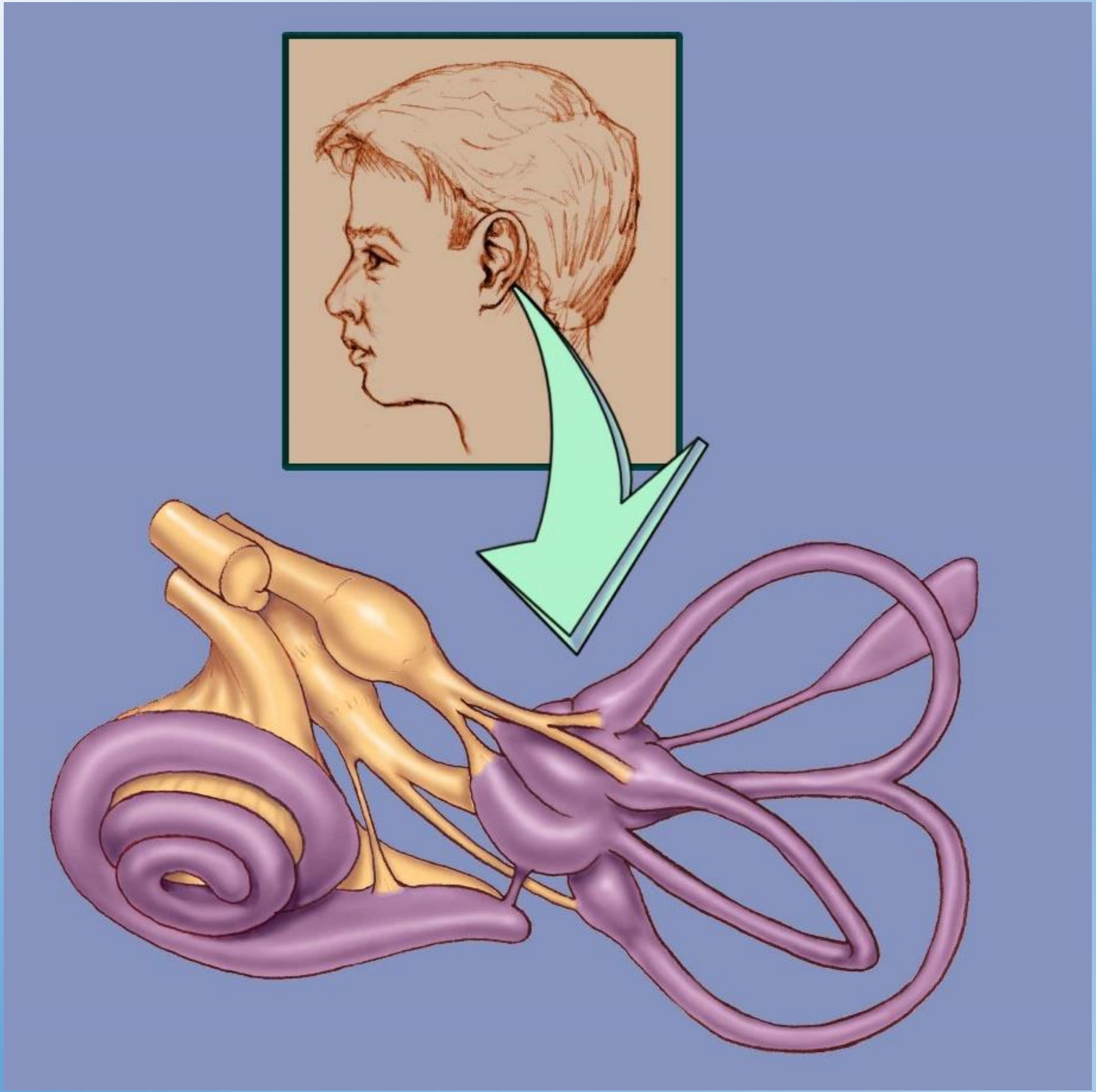


From Sound to Action Potentials - a Tour of the Inner Ear

William E. Brownell

Professor Emeritus, Dpt Oto–H&N Surgery

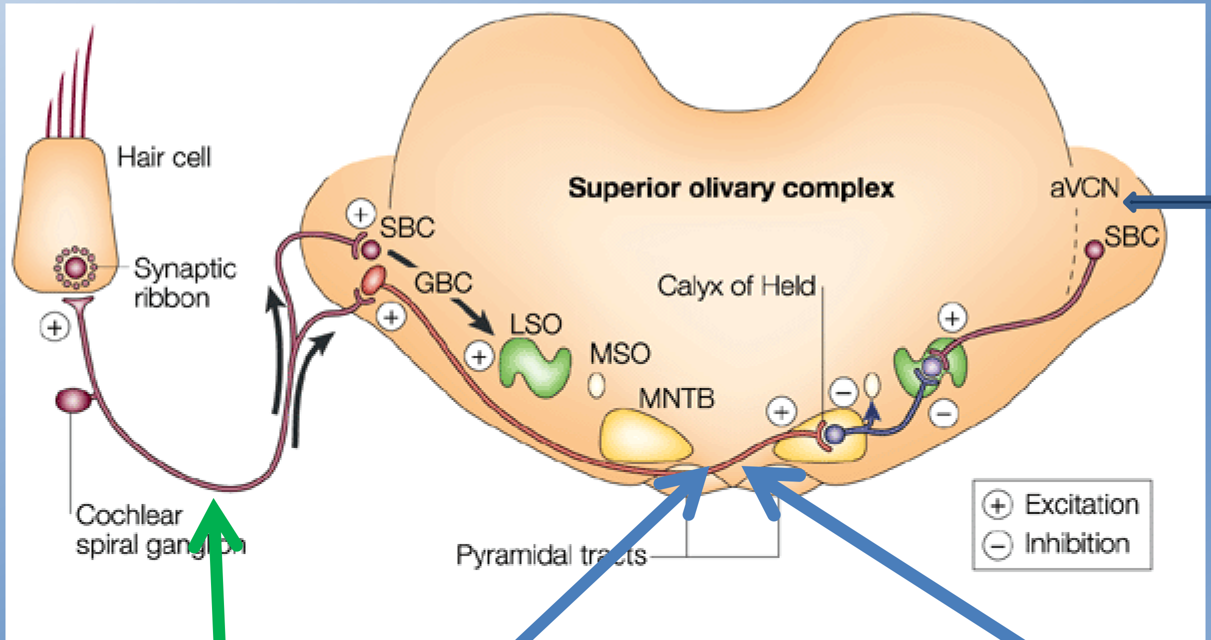
ARO seminar series, September 17, 2020

brownell@bcm.edu

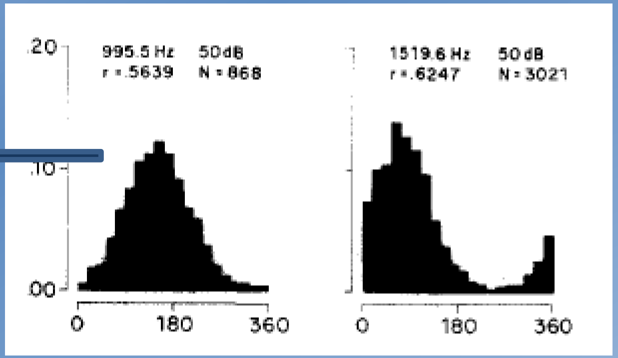
ASSOCIATION FOR RESEARCH IN OTOLARYNGOLOGY FOUNDED IN 1973

Baylor College of Medicine

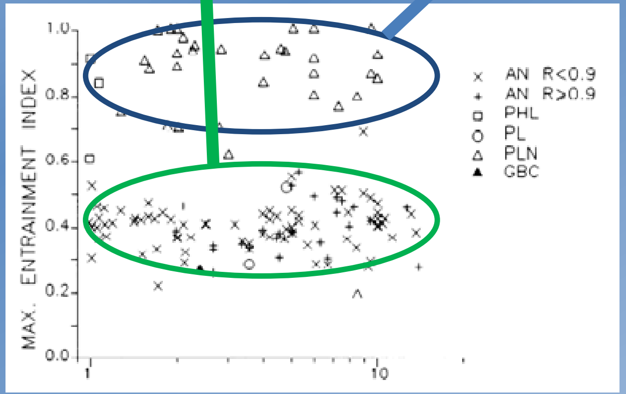
ACTION POTENTIALS in the auditory brainstem



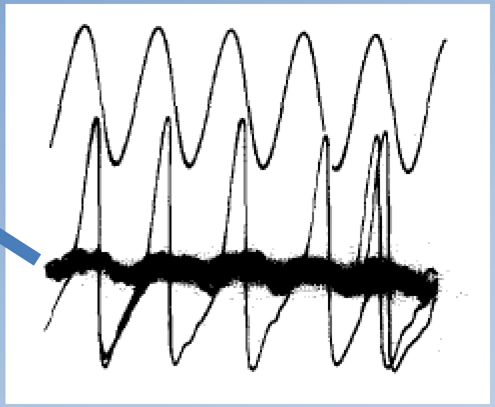
von Gersdorff & Borst, 2002



Goldberg & Brownell, 1973

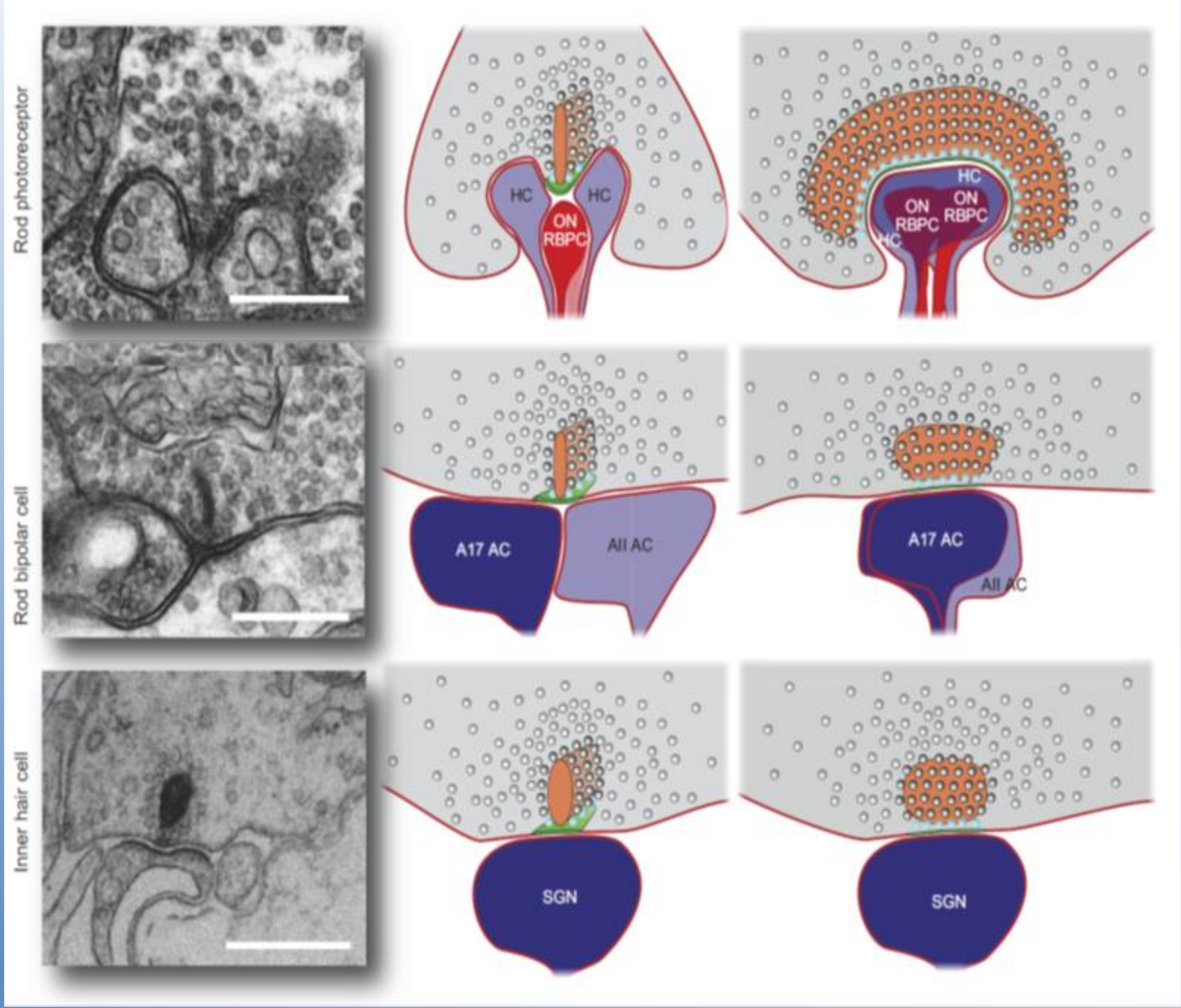


Joris et al, 1994



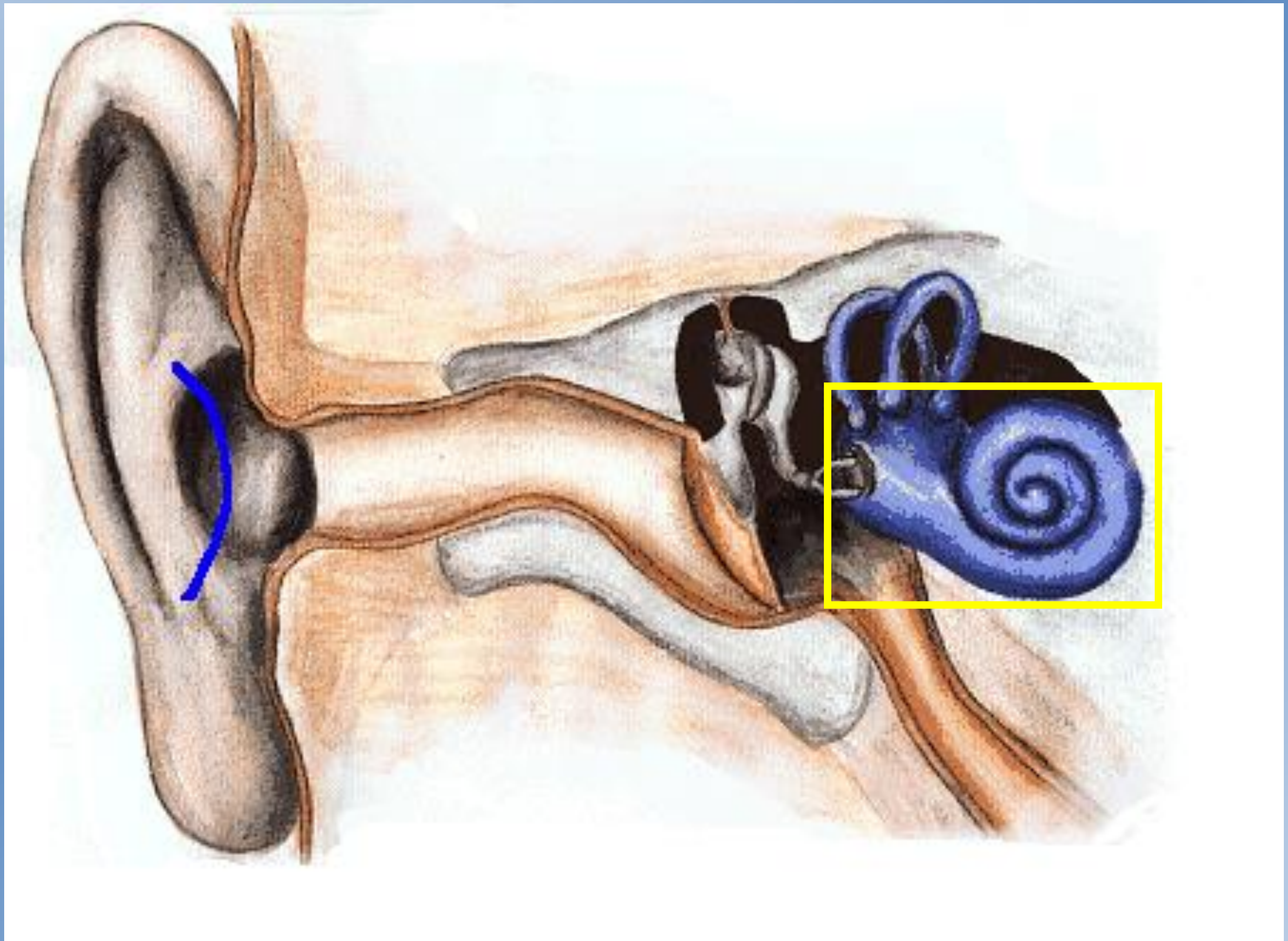
Brownell, 1975

Synaptic Ribbons in Sensory Cells



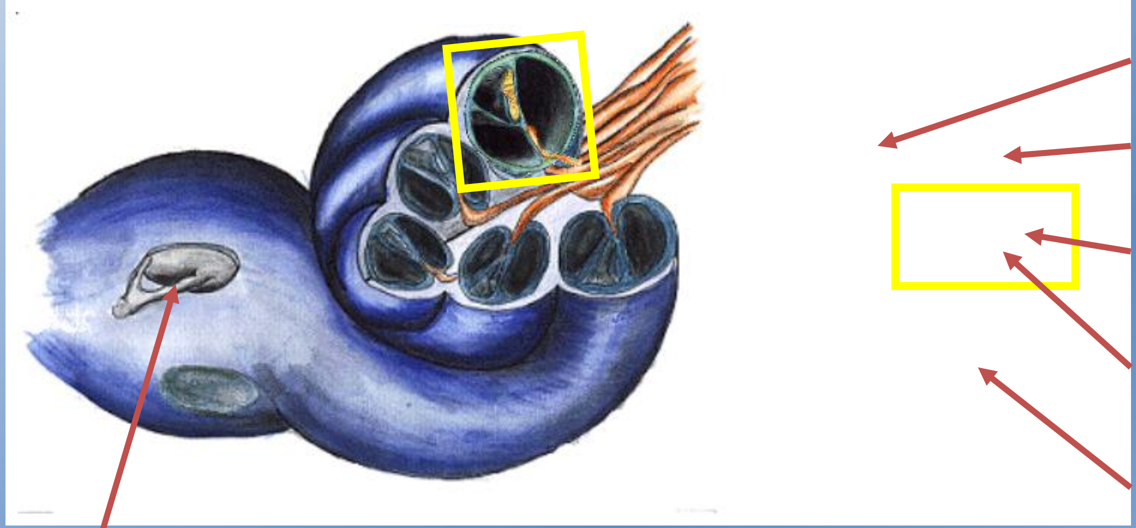
Moser et al. Physiol Rev. 2020

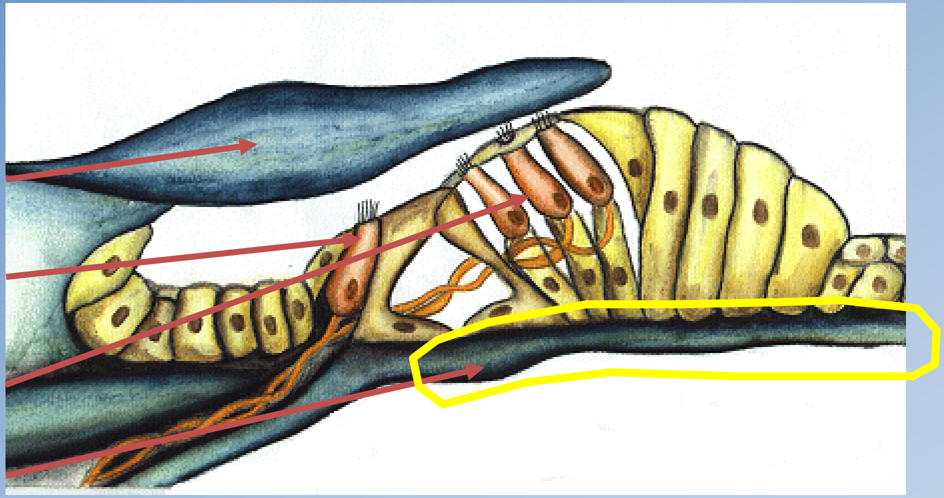
Sound enters the human ear



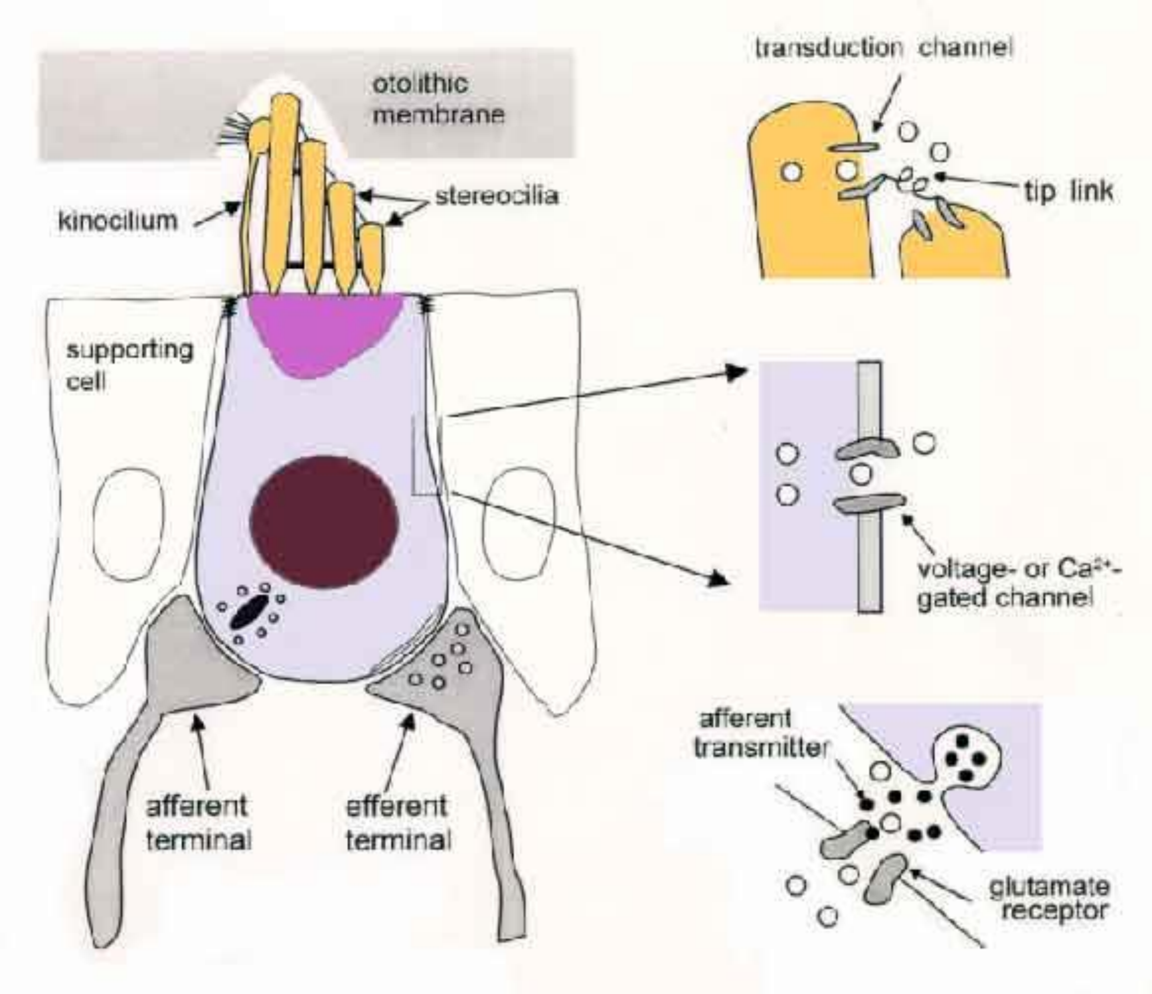
The cochlea and the organ of Corti

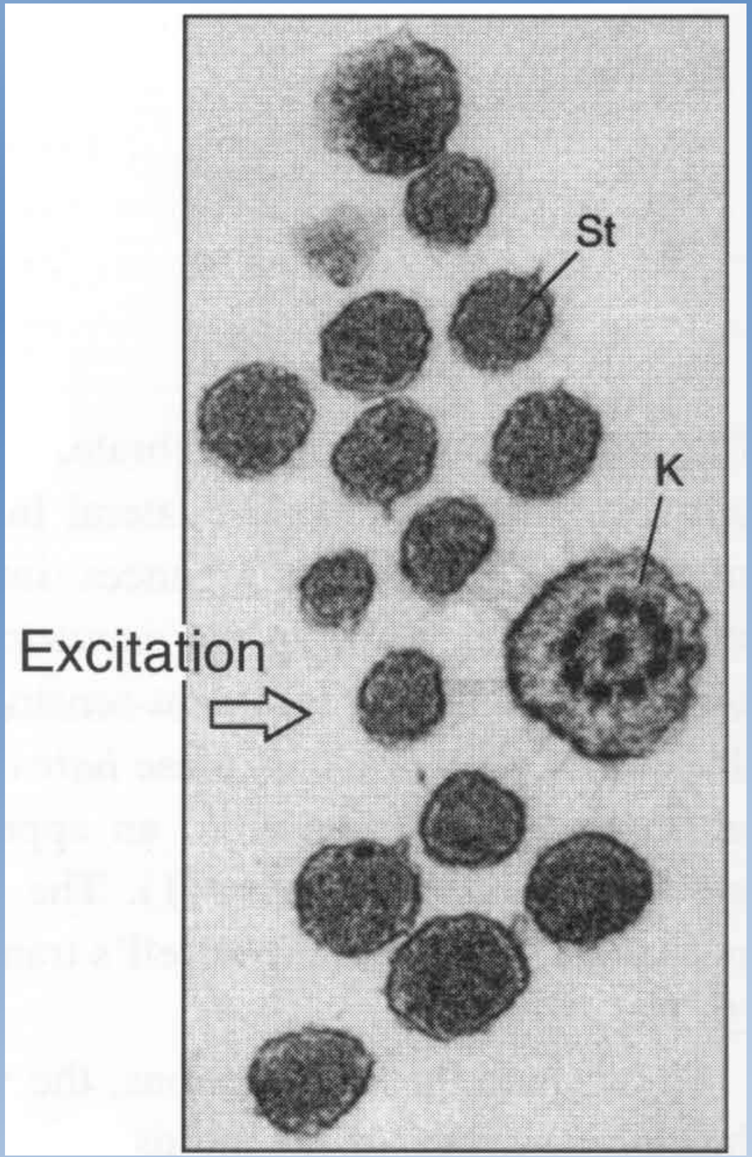
Human cochlea



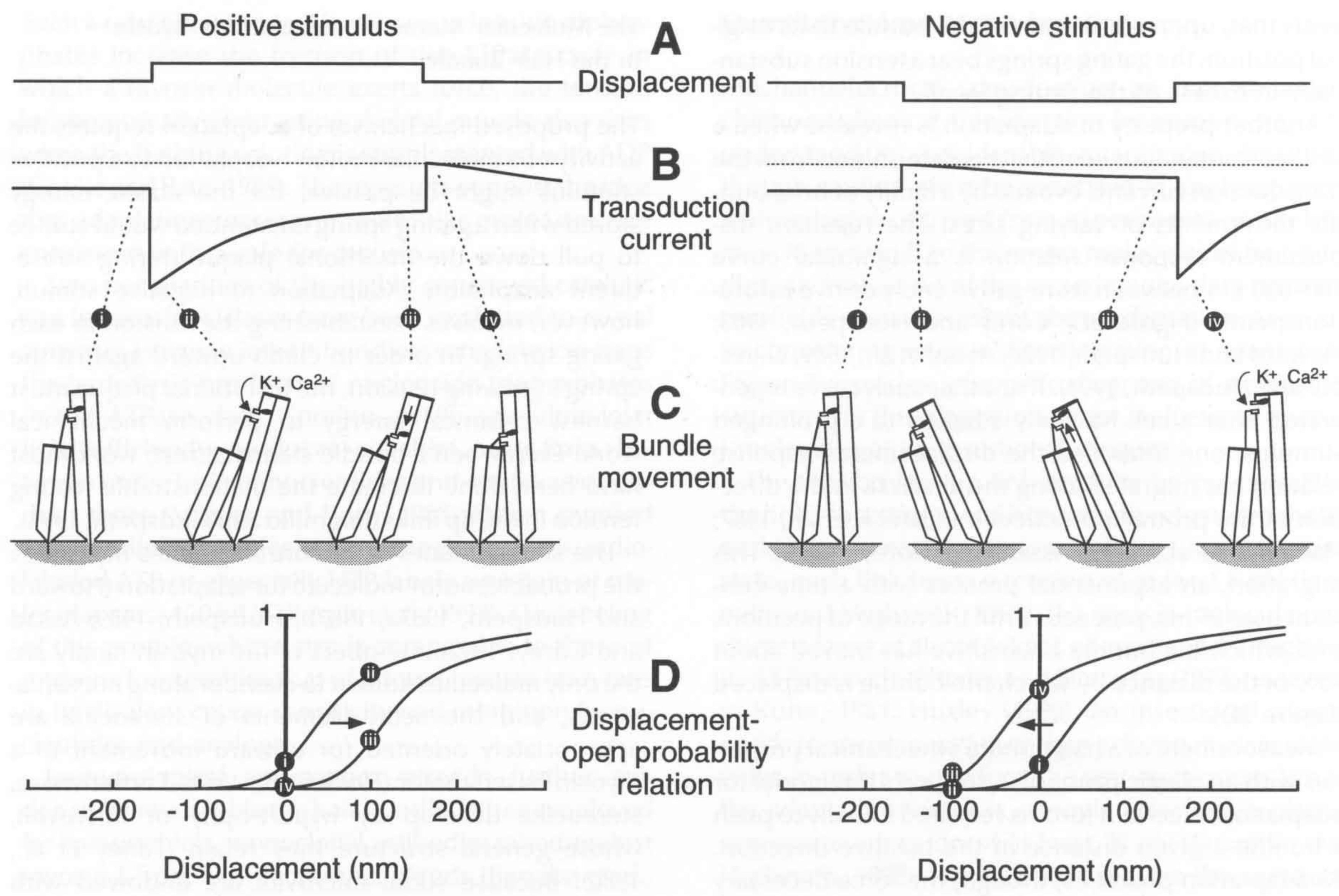


Anatomy of a Hair Cell





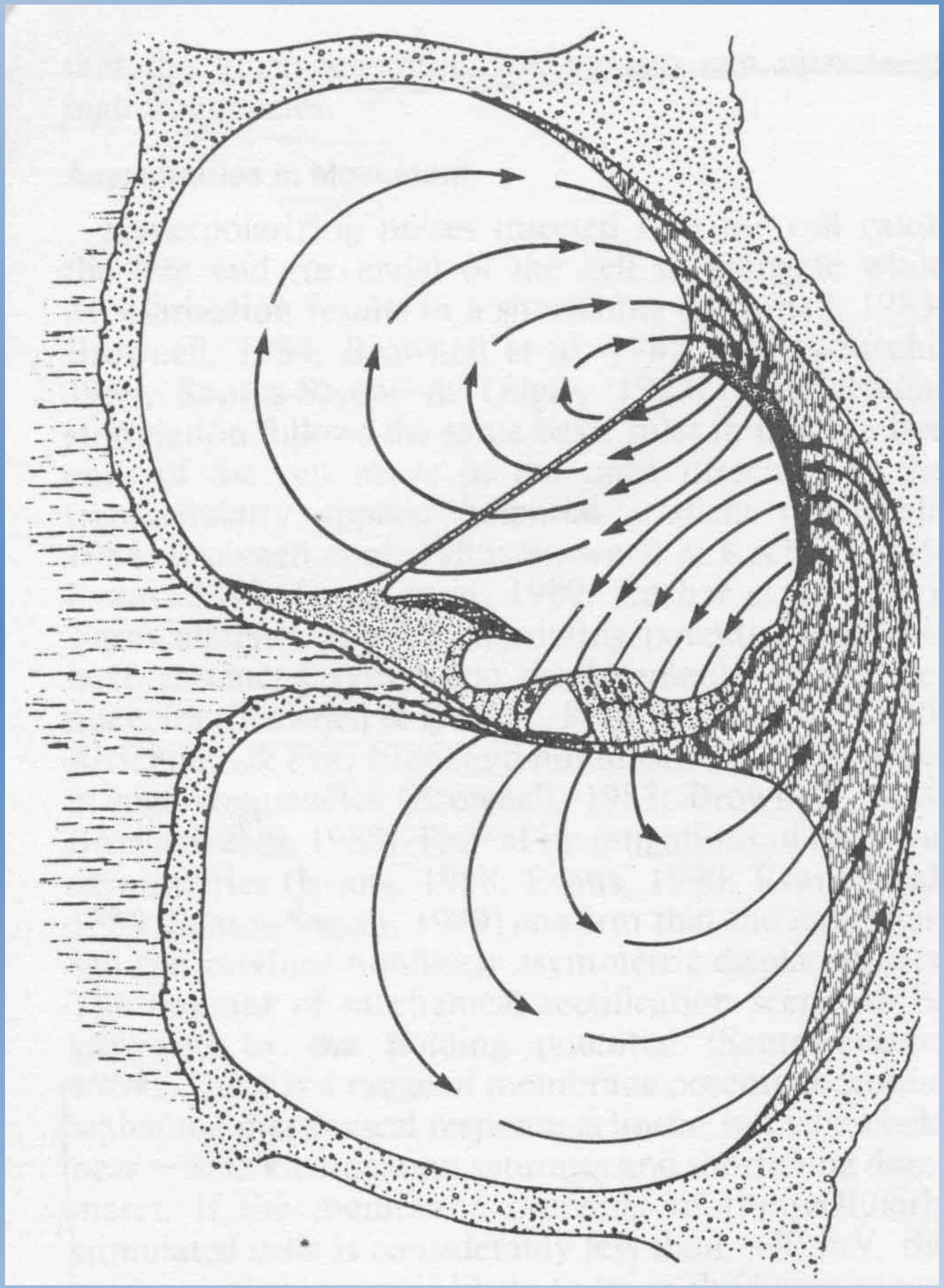
Mechanoelectrical Transduction



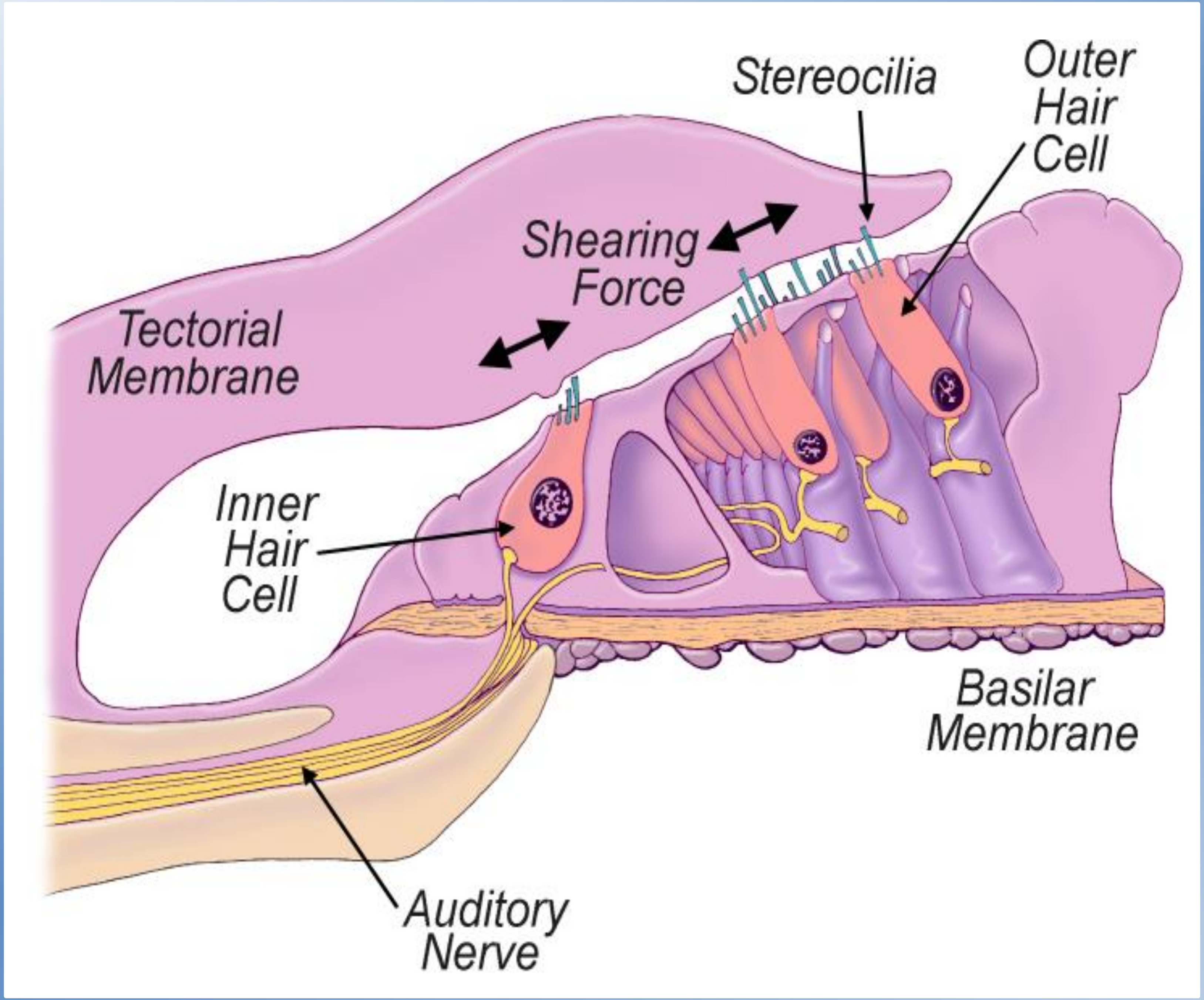
Finding the Silent Current

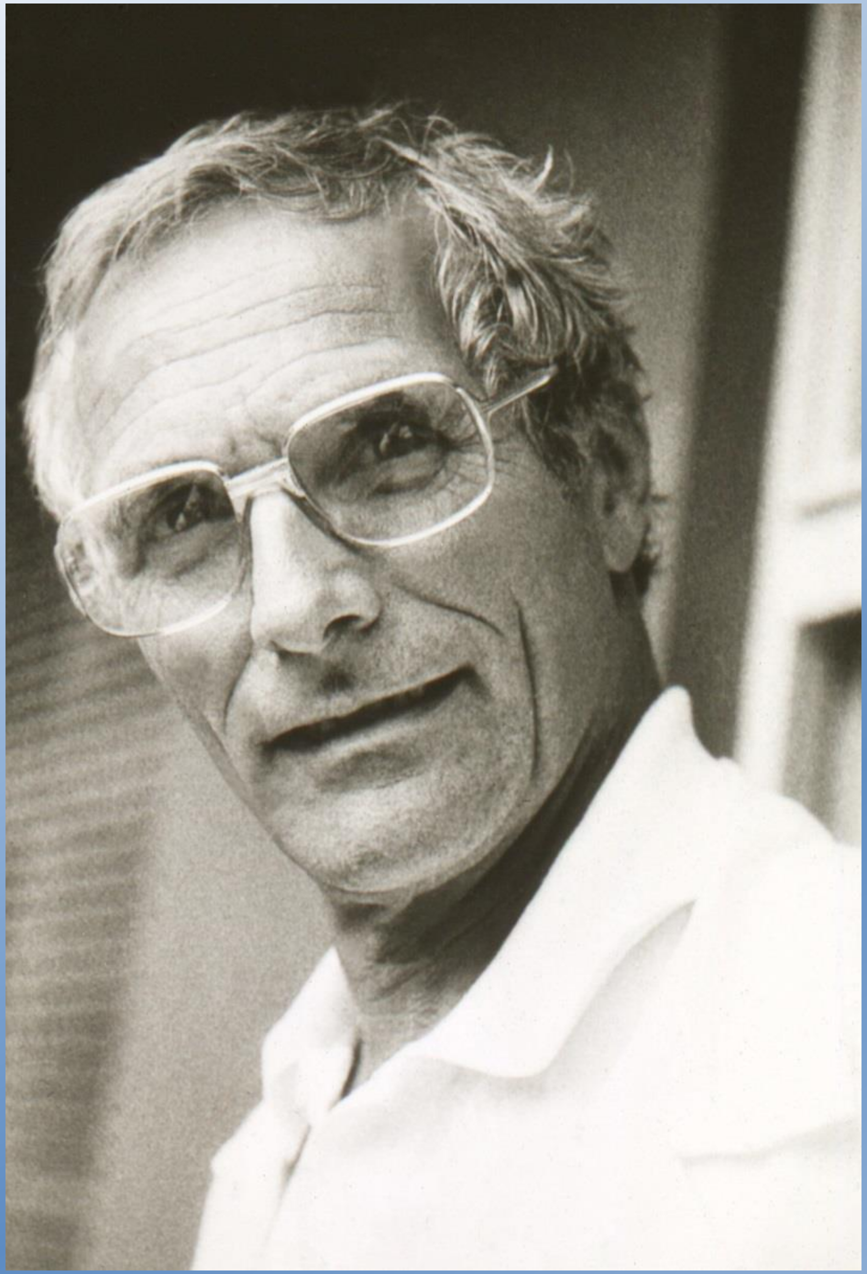
A standing current that powers:

1. mechanotransduction
2. cochlear amplifier



Organ of Corti

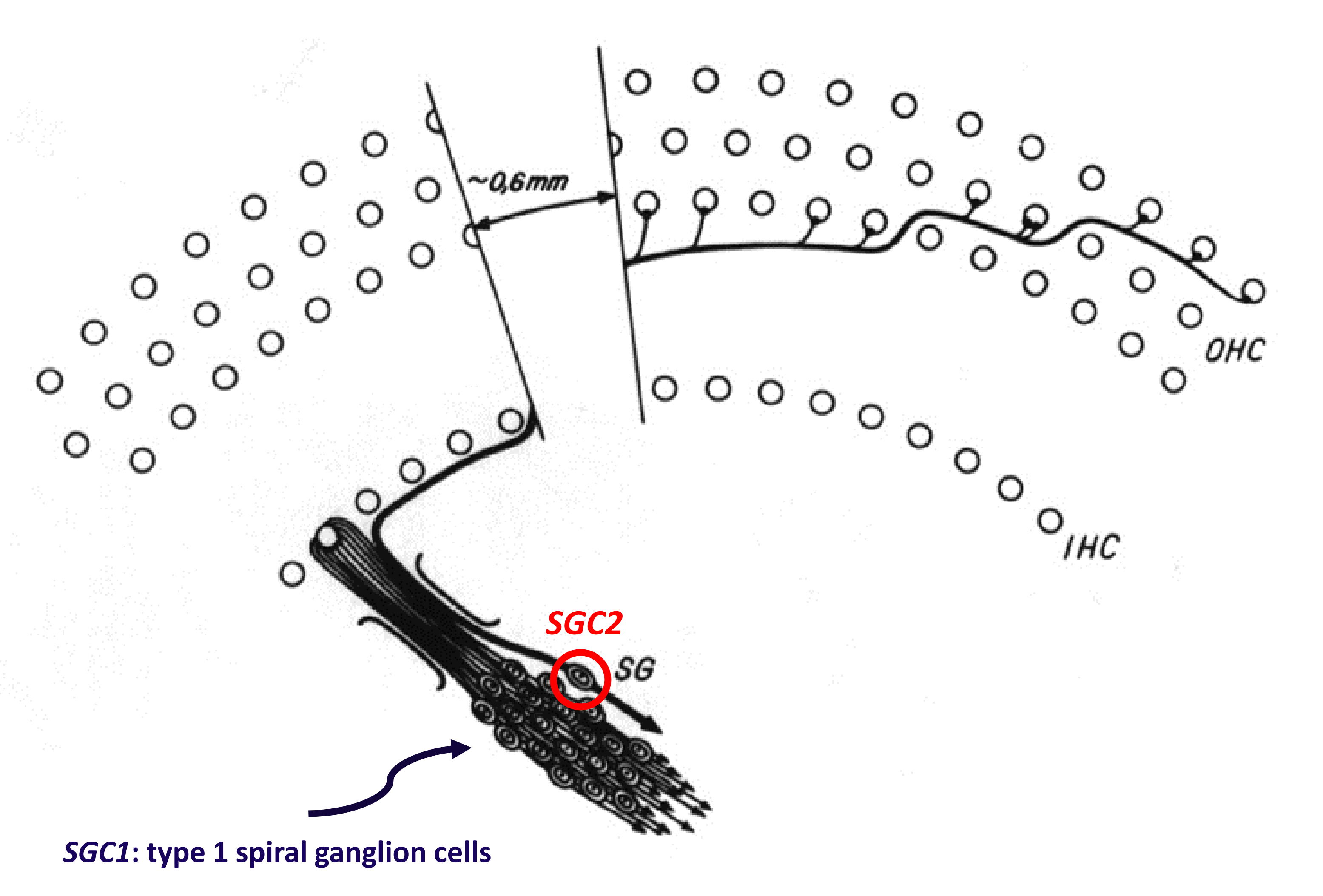




1966 - Heinrich Spoendlin

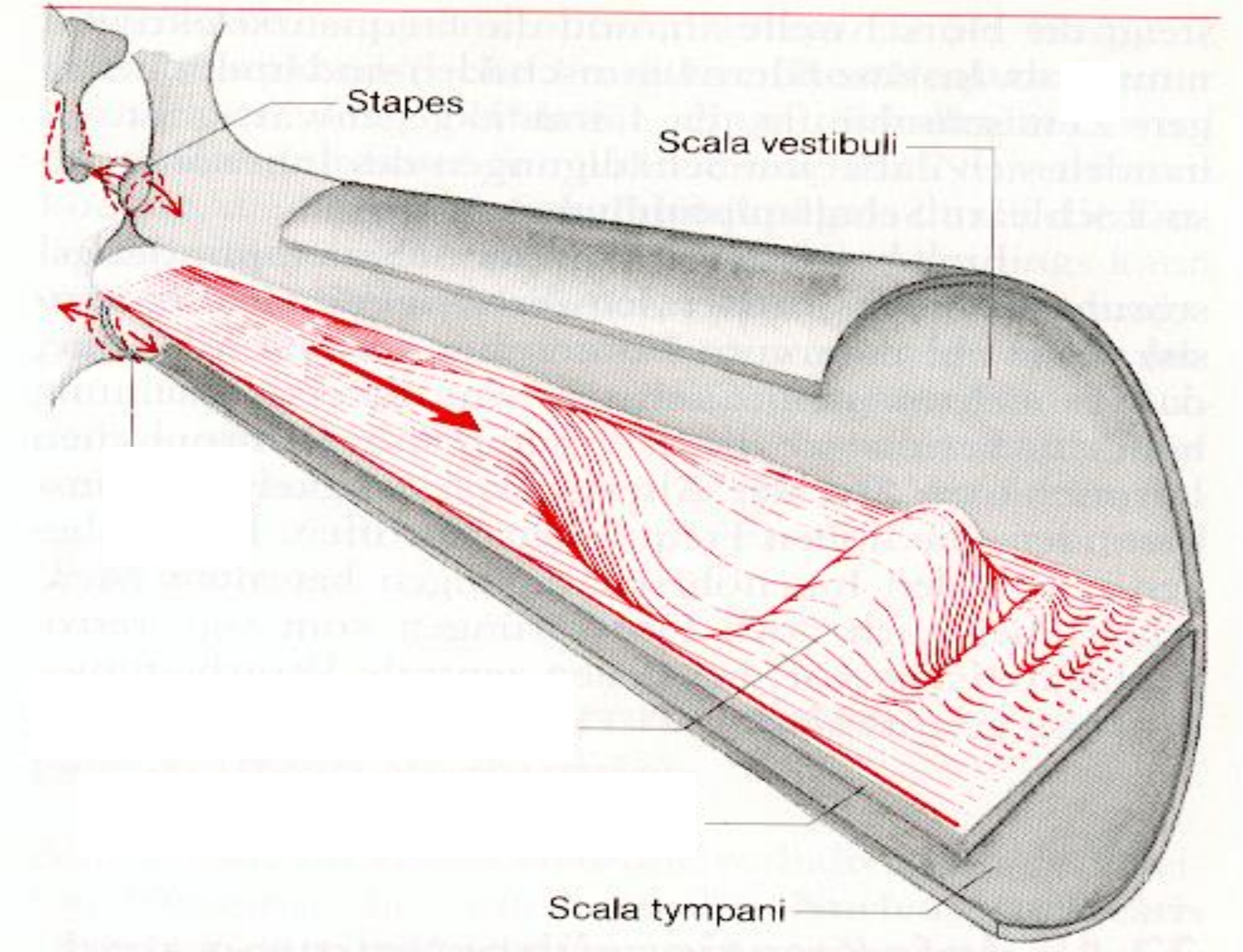
discovers that up to 95 percent of auditory nerve fibers terminate on the inner hair cells

Acoustic world enters via SGC1



Spoendlin, Fortschr Hals Nasen Ohrenheilkd 1966

The travelling wave

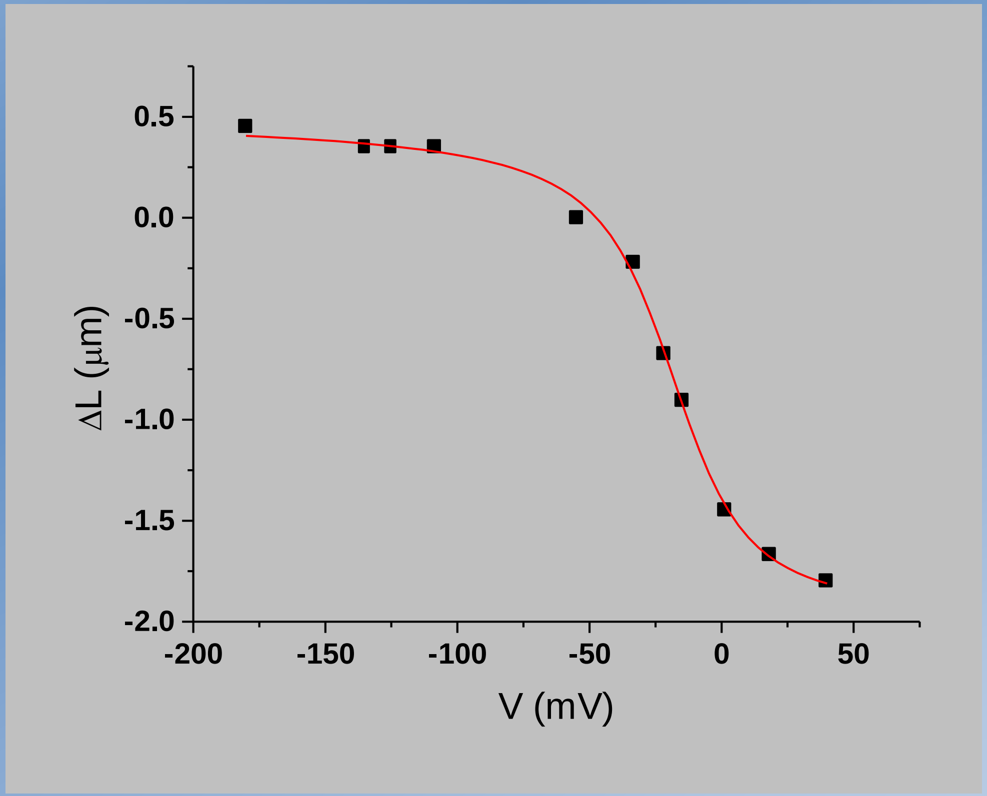


Electromotility
& the Cochlear Amplifier

200 msec pulses from a holding potential of –60 mV. Initial pulse is hyperpolarizing and each successive pulse +10 MV from that.

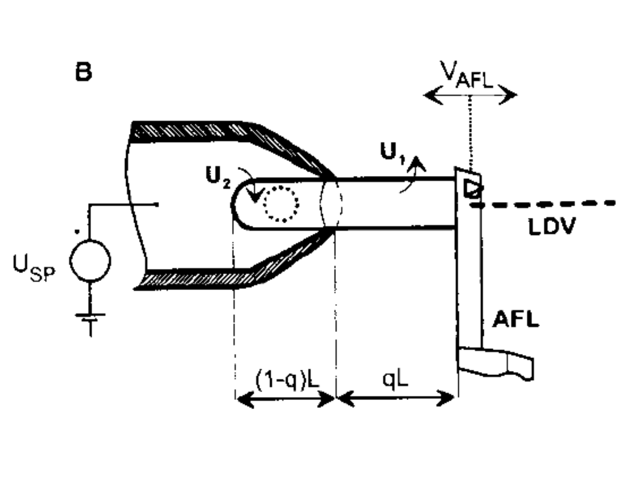
OHC displacements (ΔL)

1. ΔL ≠ f (current)
2. ΔL ≠ f (calcium)
3. ΔL ≠ f (ATP)
4. ΔL = f (prestin & small anions)
5. ΔL = f (voltage)

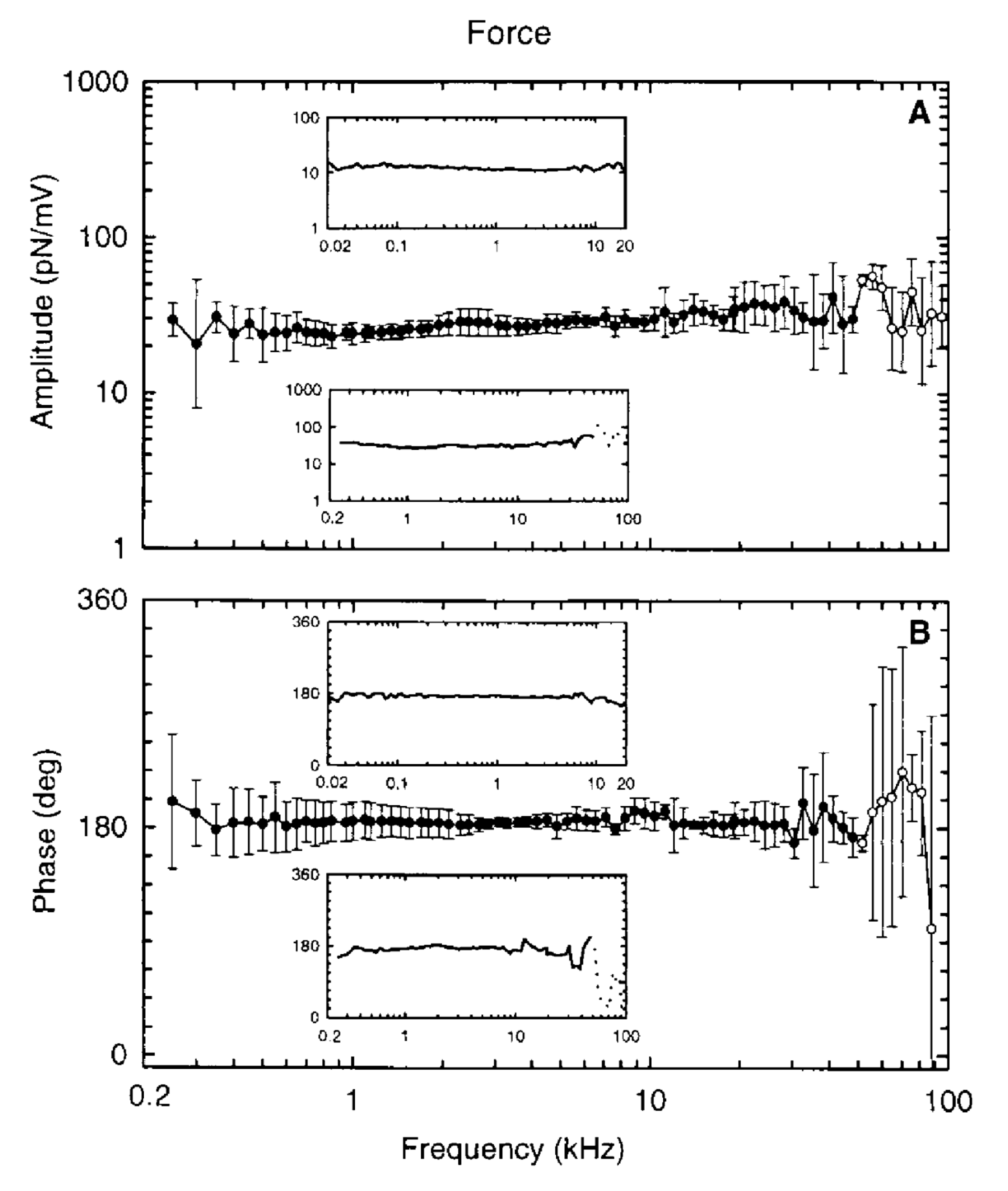


Data of Santos-Sacchi, 1992

The OHC generates force at > 80 kHz

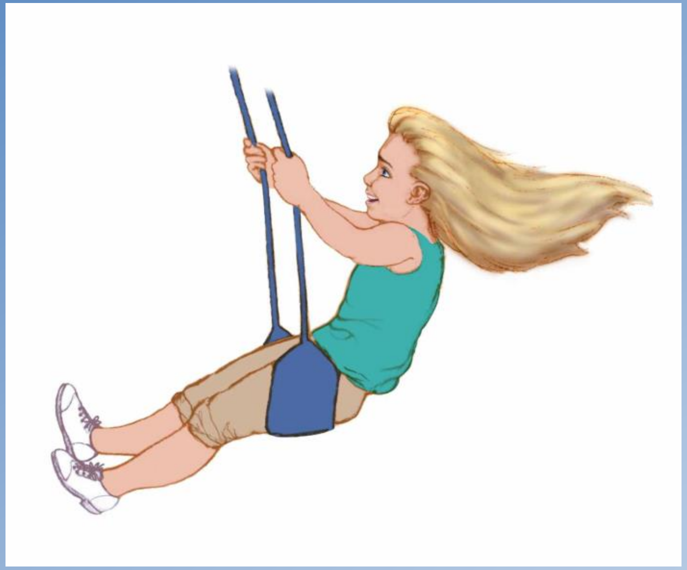


Frank et al., 1999

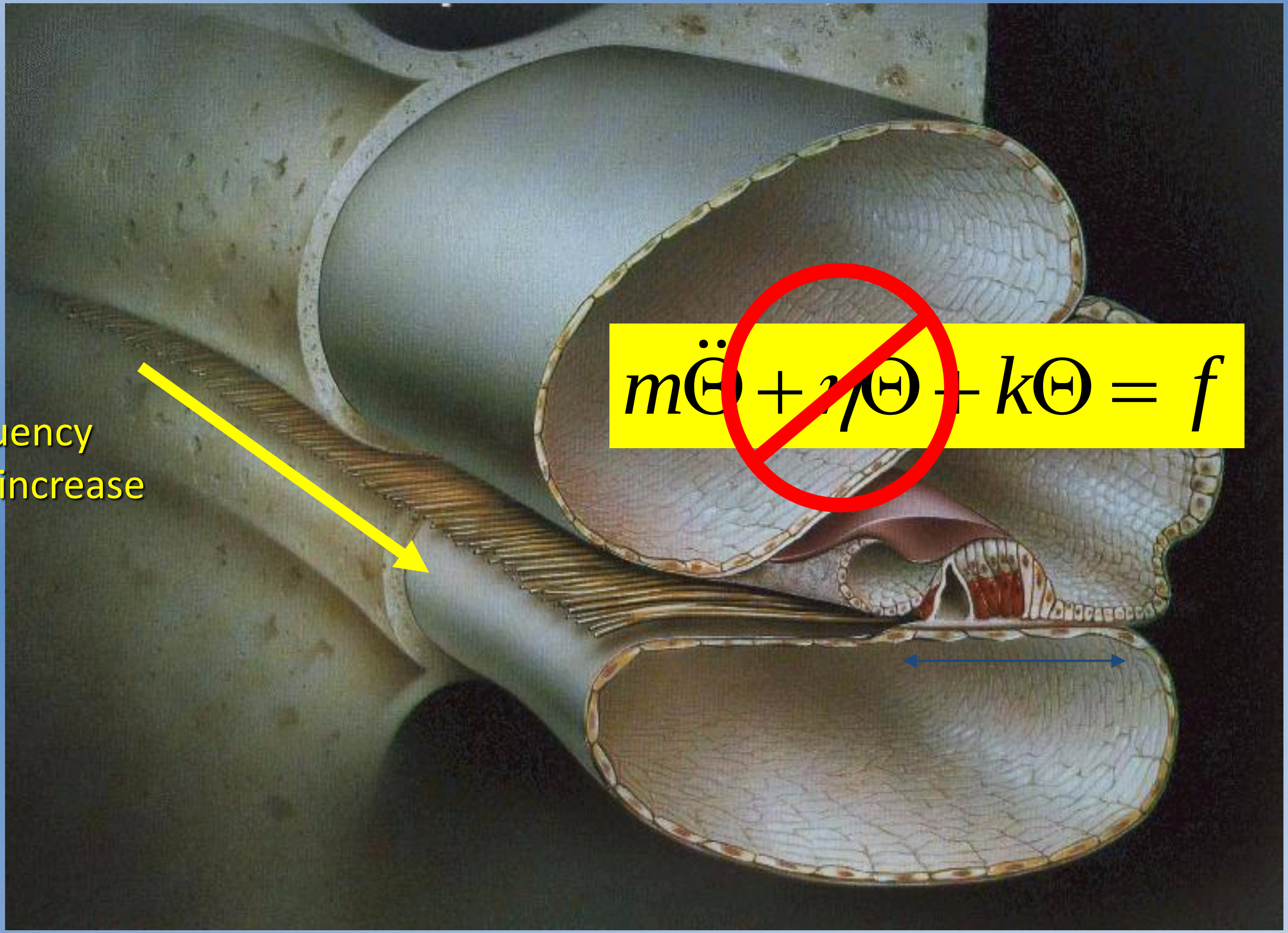


The Swing
A Passive Filter

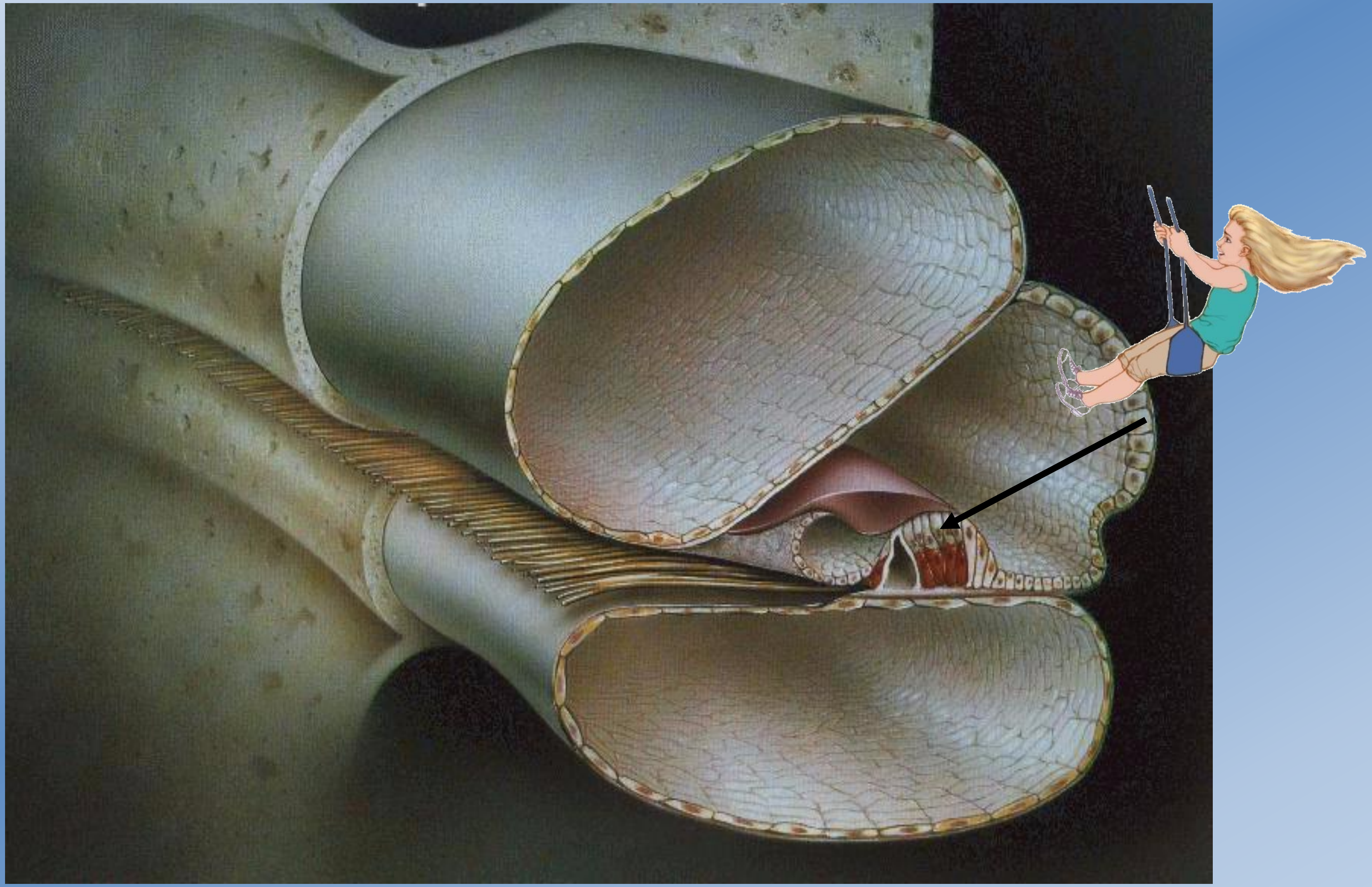
The Swinger
An ***Active*** Filter



Viscosity limits the frequency of cochlear vibrations

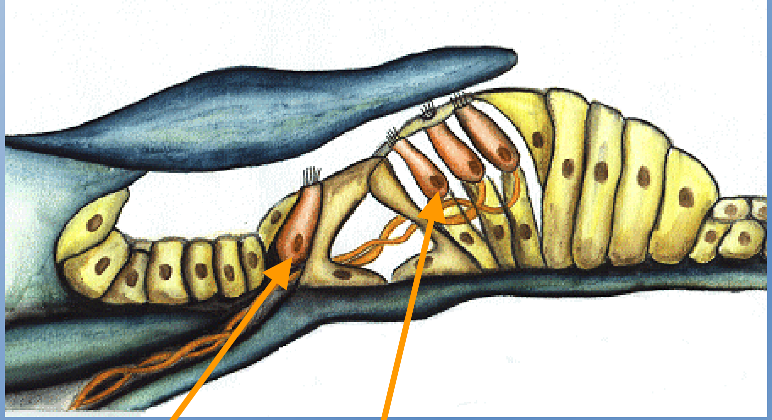


3000 Swings



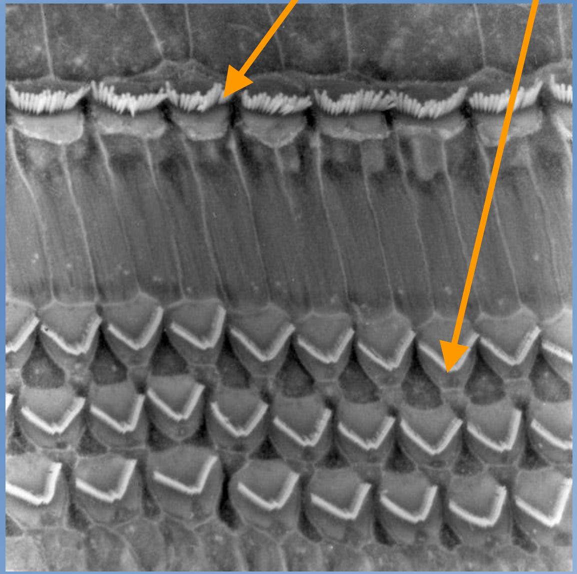
Compton's Interactive Encyclopedia, 1997

Normal versus impaired cochlea

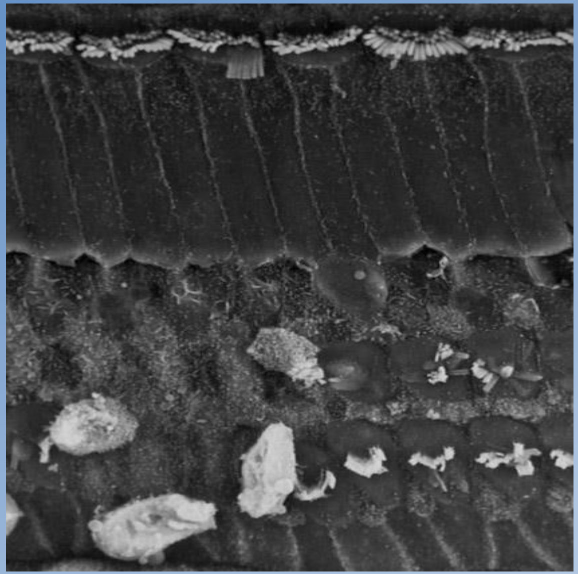


Inner
hair cells

Outer
hair cells

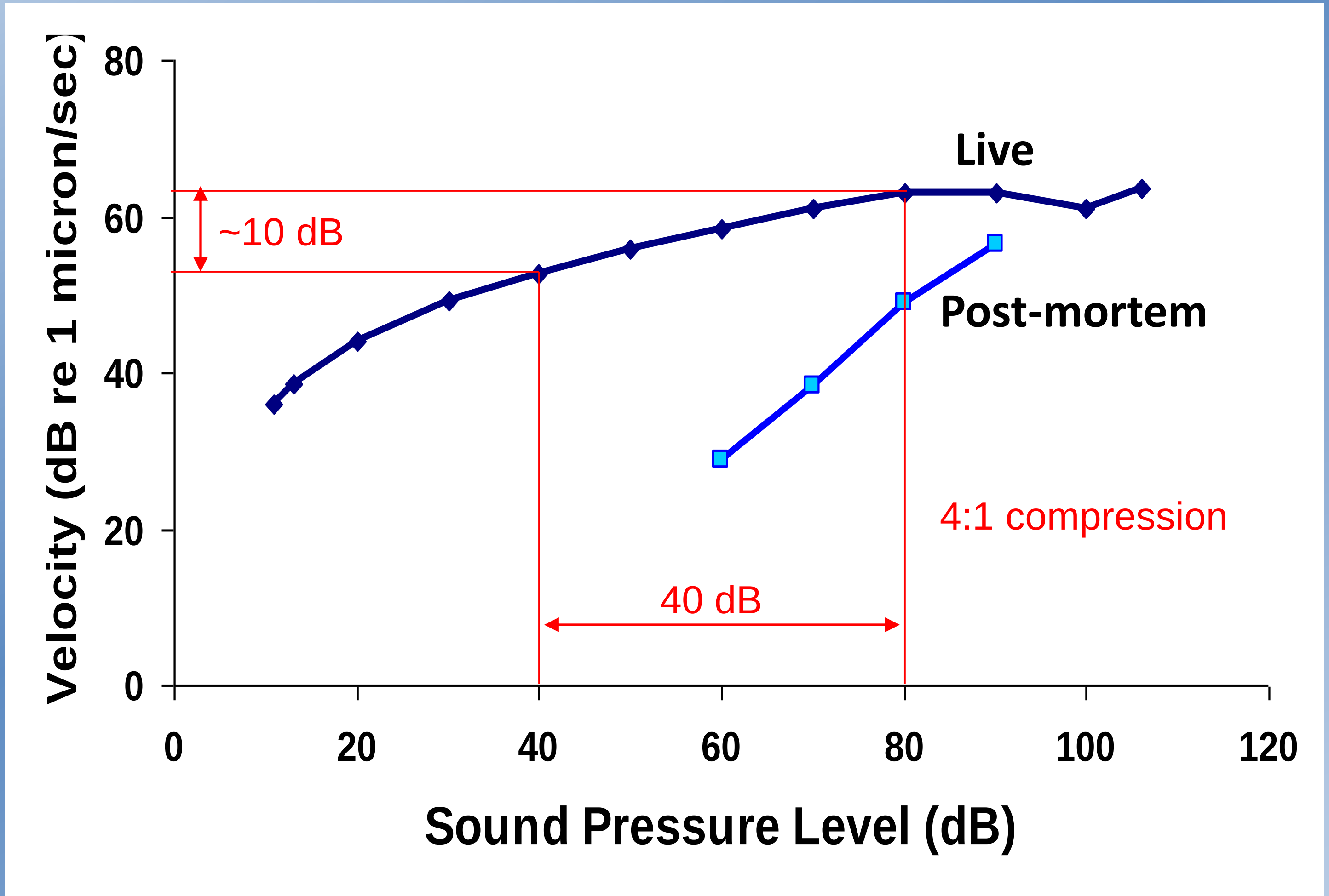


Normal system



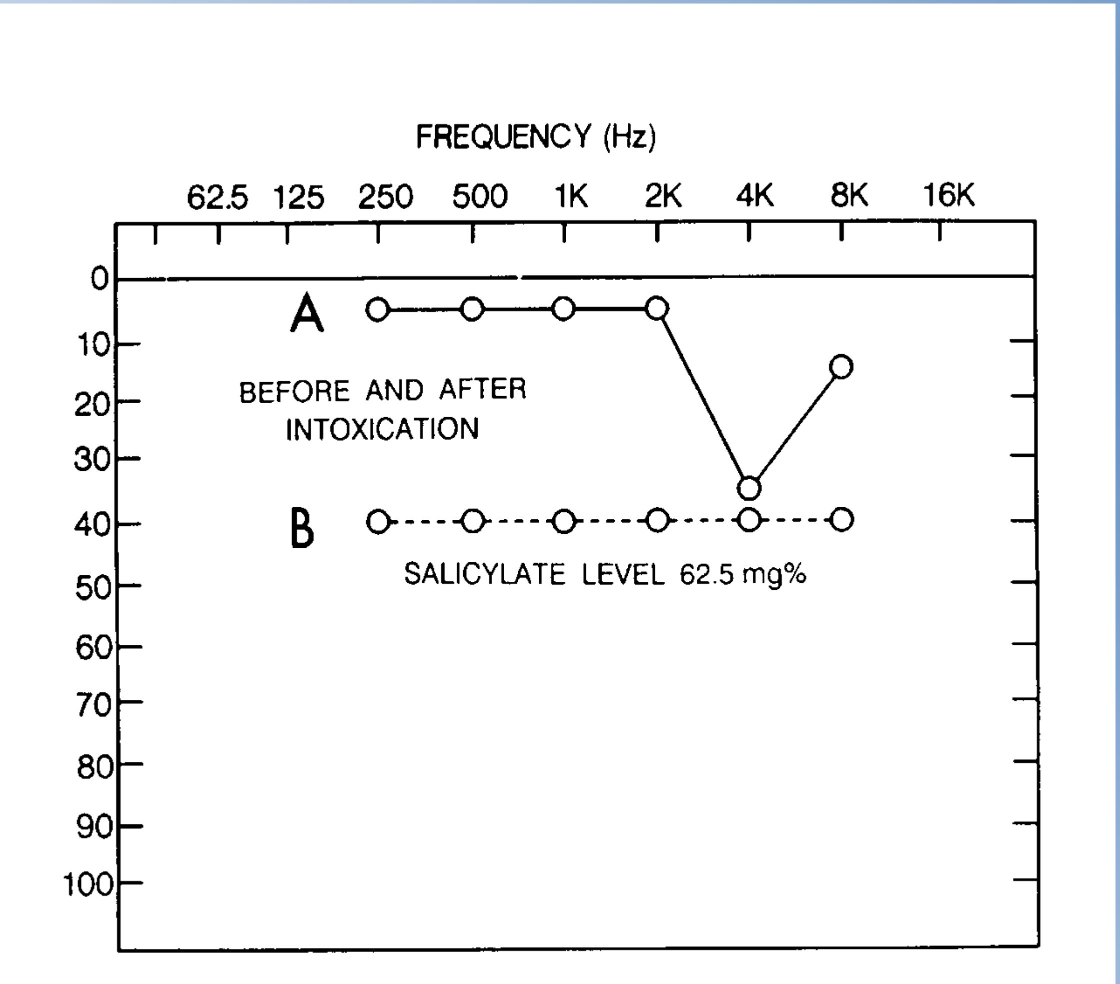
Damaged system

Damage to the outer hair cells



(Ruggero et al., 1997)

Aspirin Ototoxicity

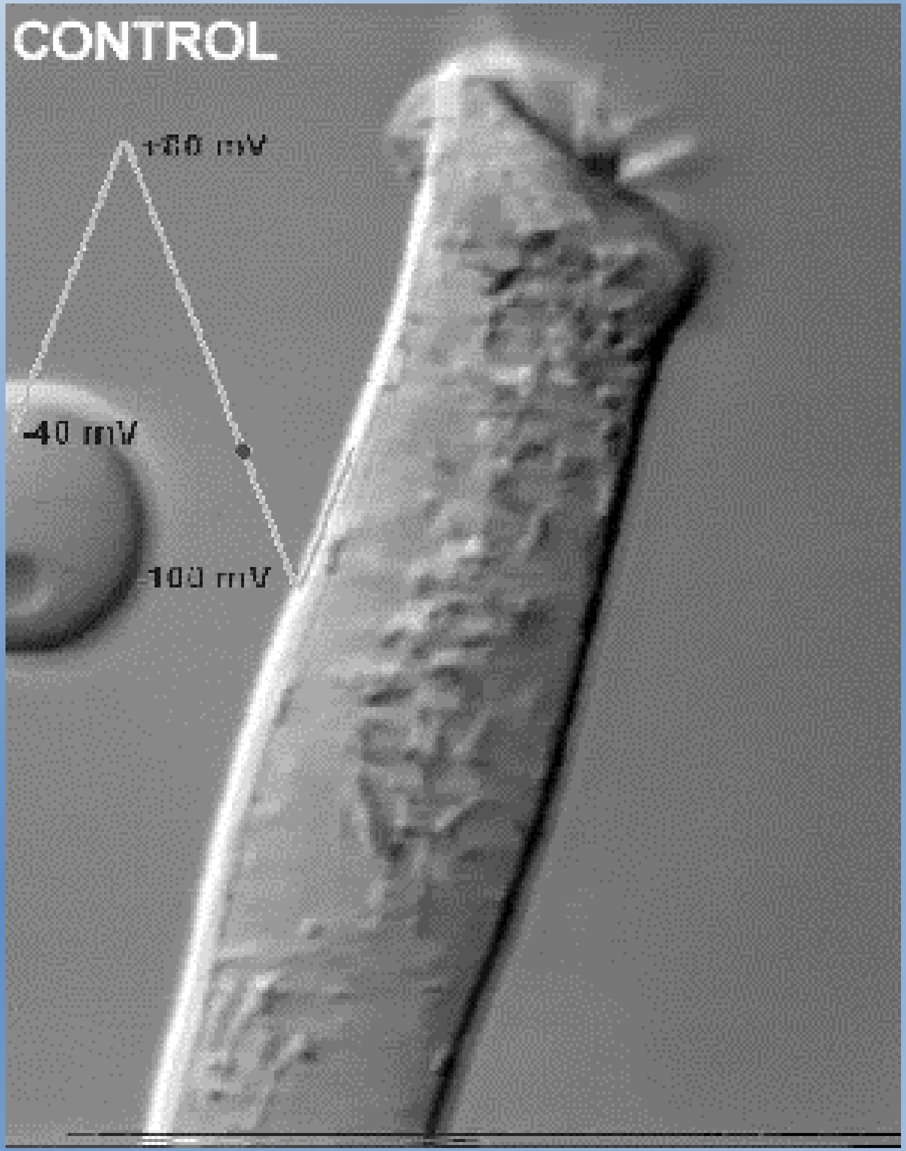


Male (60 yrs) with hearing loss

Myer & Bernstein, 1965

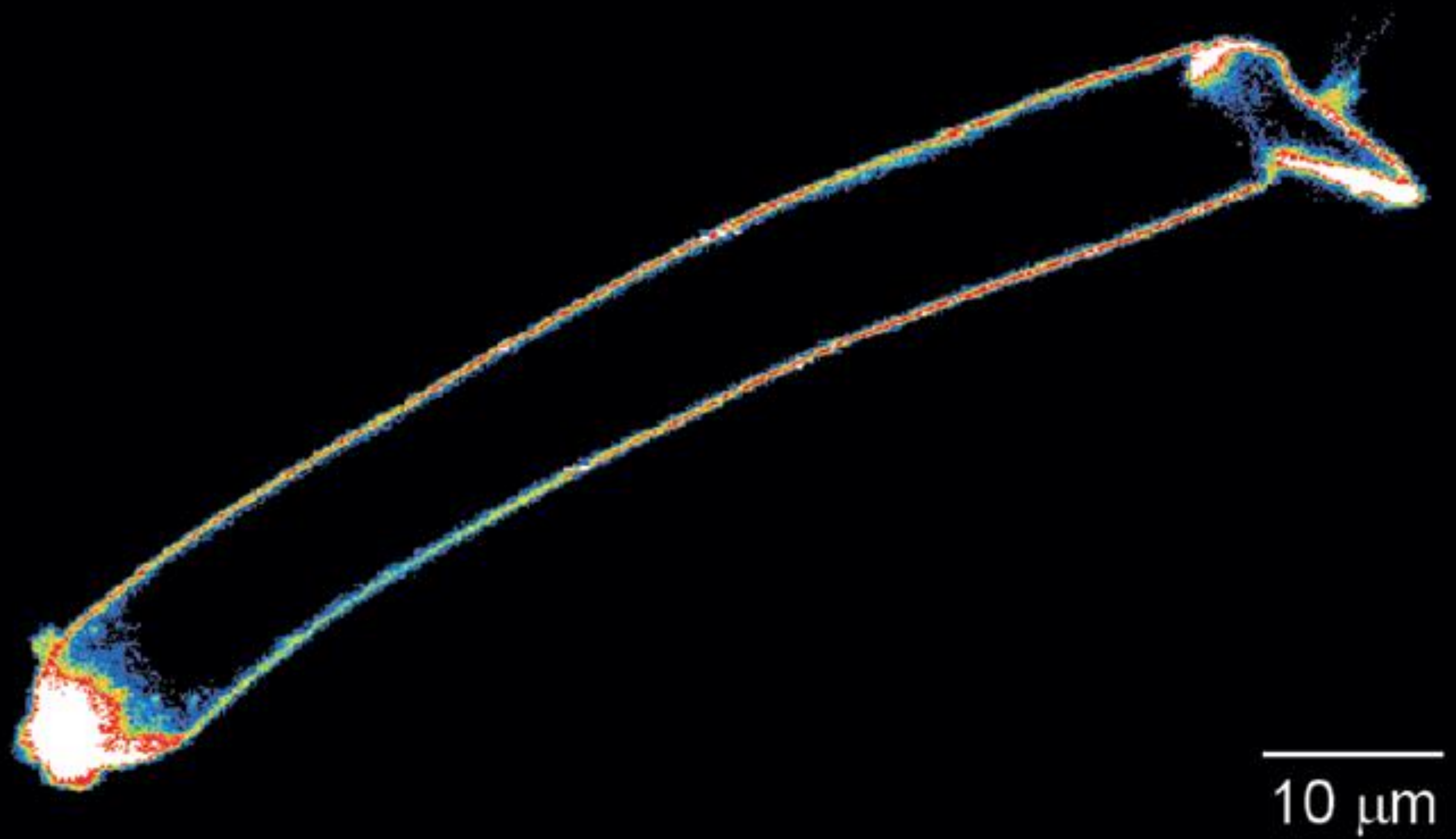
Salicylate blocks otoacoustic emissions - McFaddden & Plattsmier, 1984

Aspirin Ototoxicity

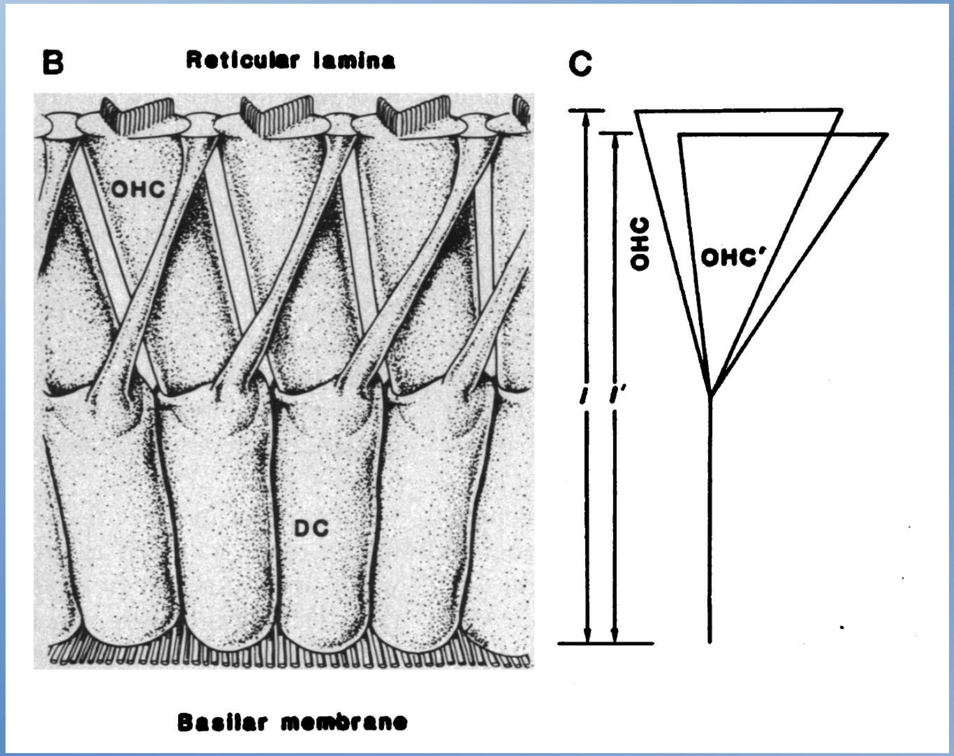


Salicylate application blocks OHC electromotility

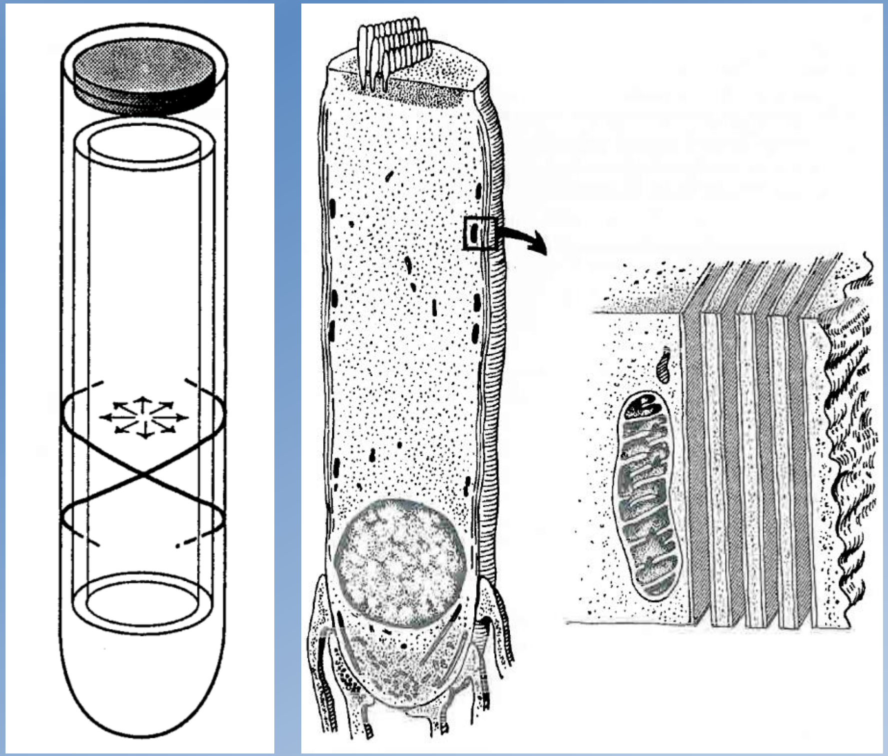
Electromotile mechanism is in the plasma membrane



OHC is a hydrostat with unusual cytoarchitectonics

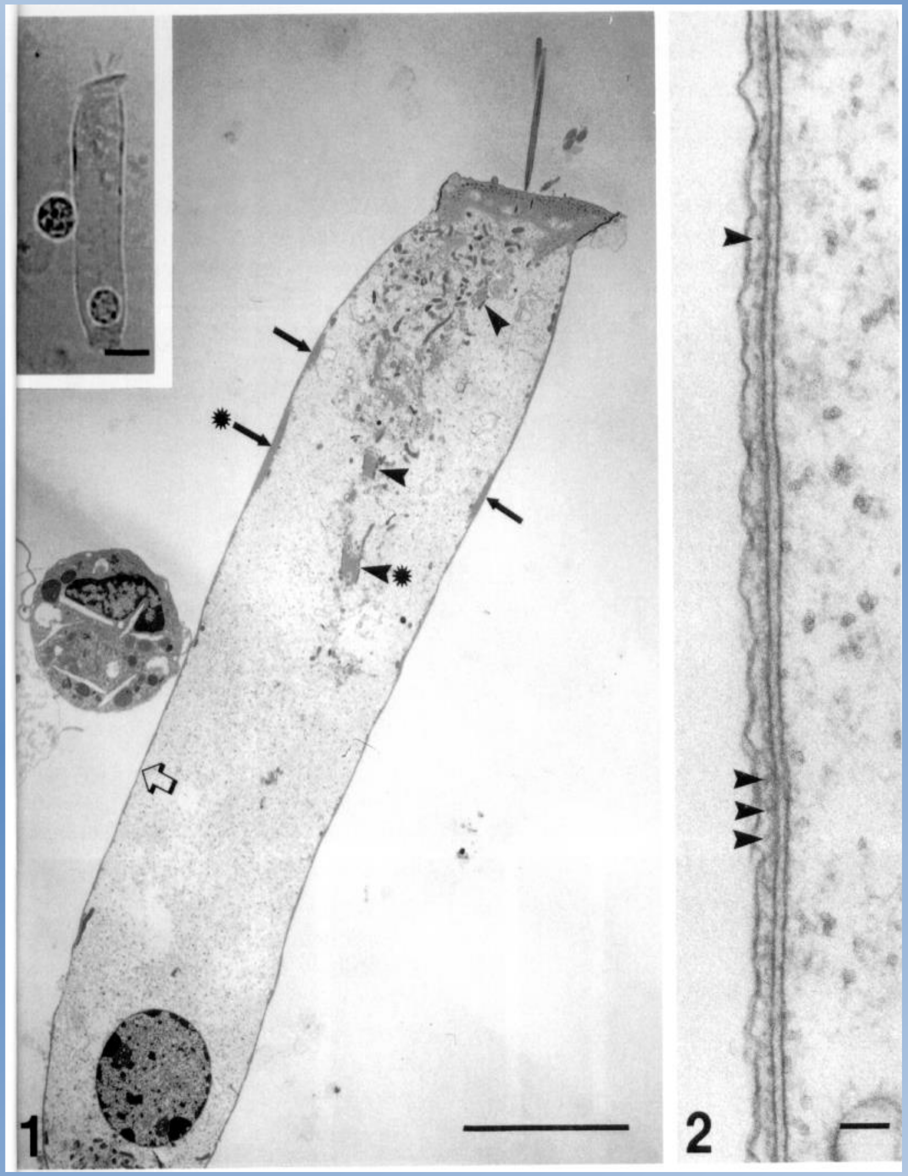


Brownell et al., 1985



Brownell, 1990

Plasma membrane folding

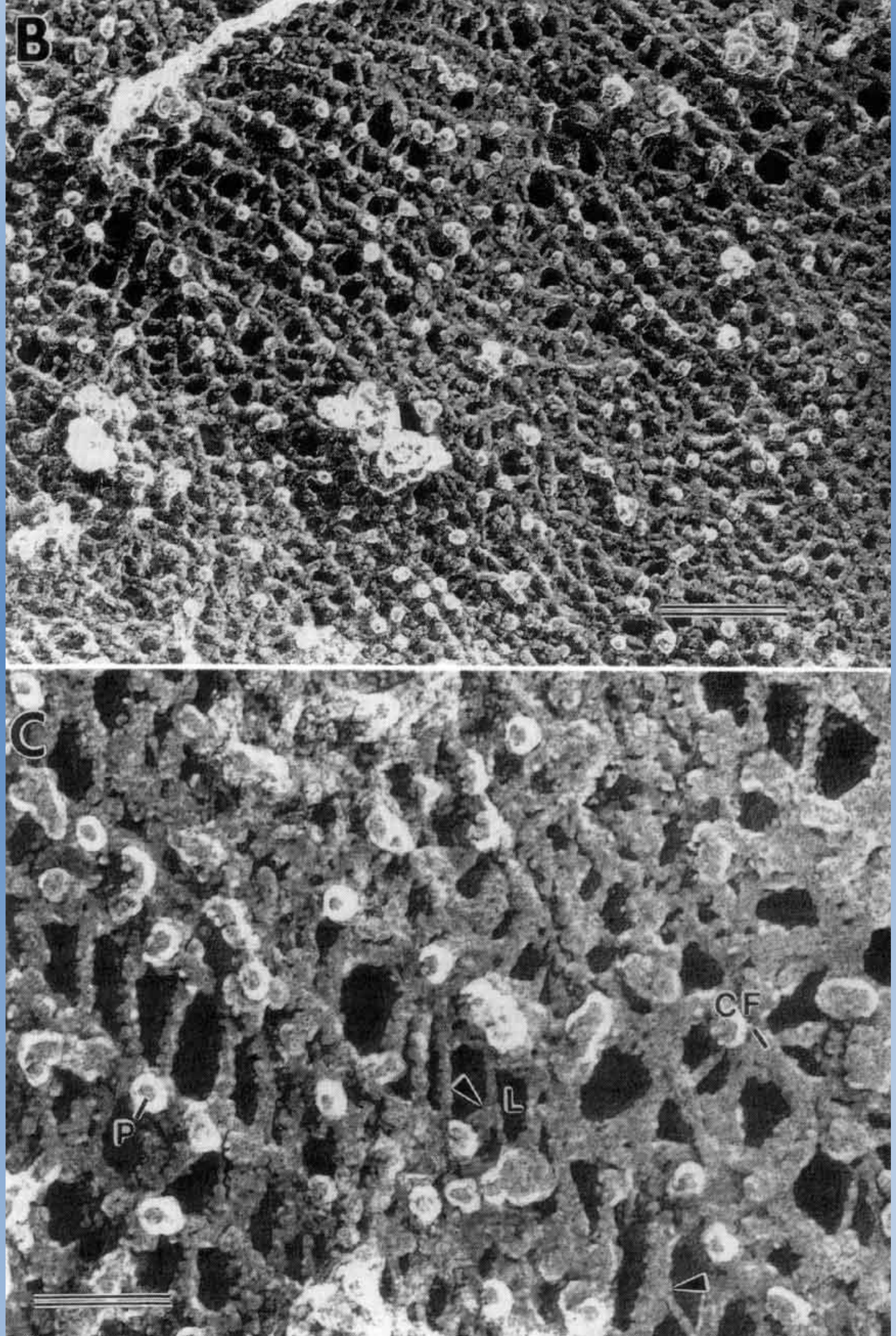


Dieler et al., 1991

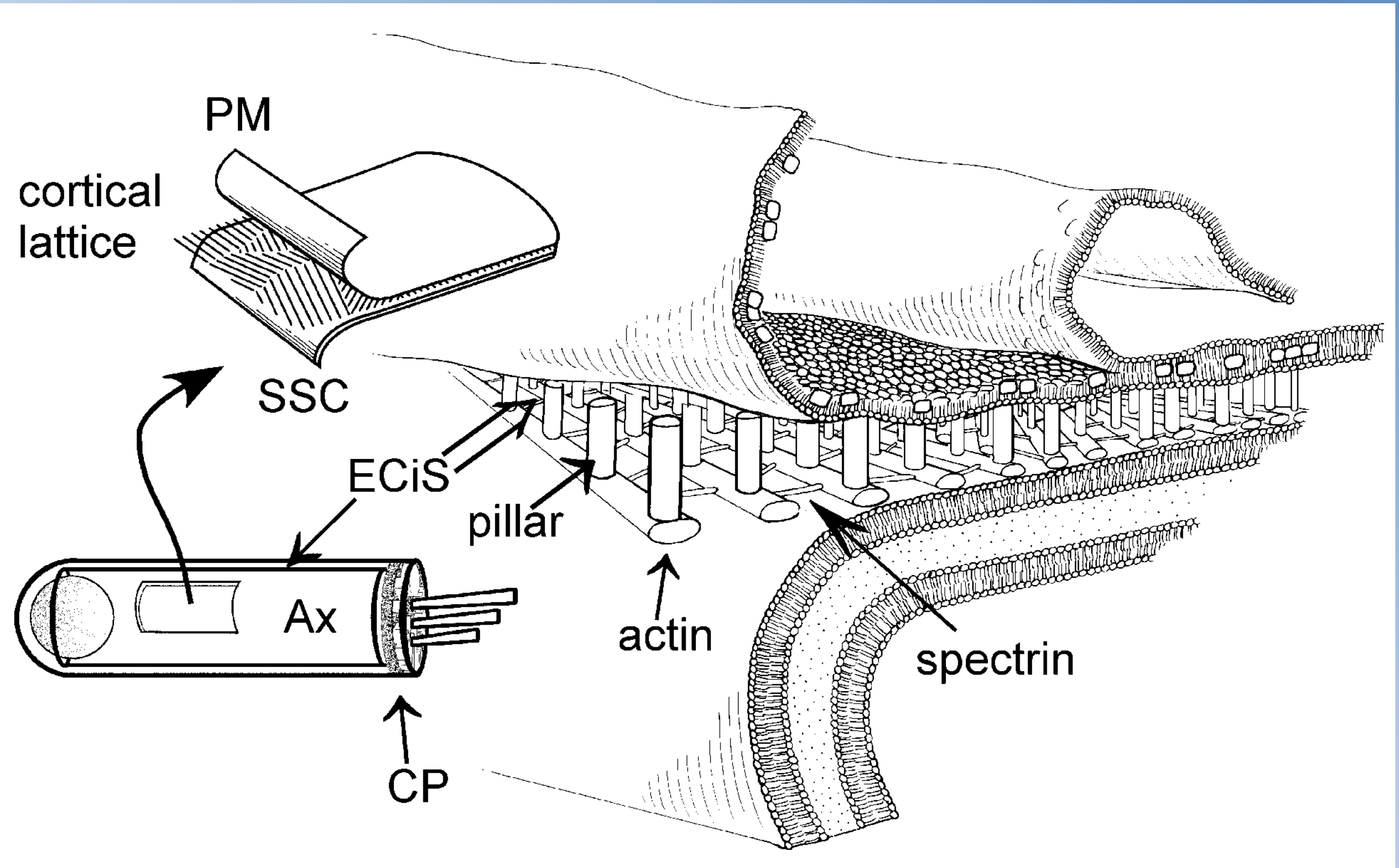
The Orthotropic Cortical Lattice

- Actin - circumferential
- Spectrin - longitundinal
- Pillars - radial

Holley et al., 1992

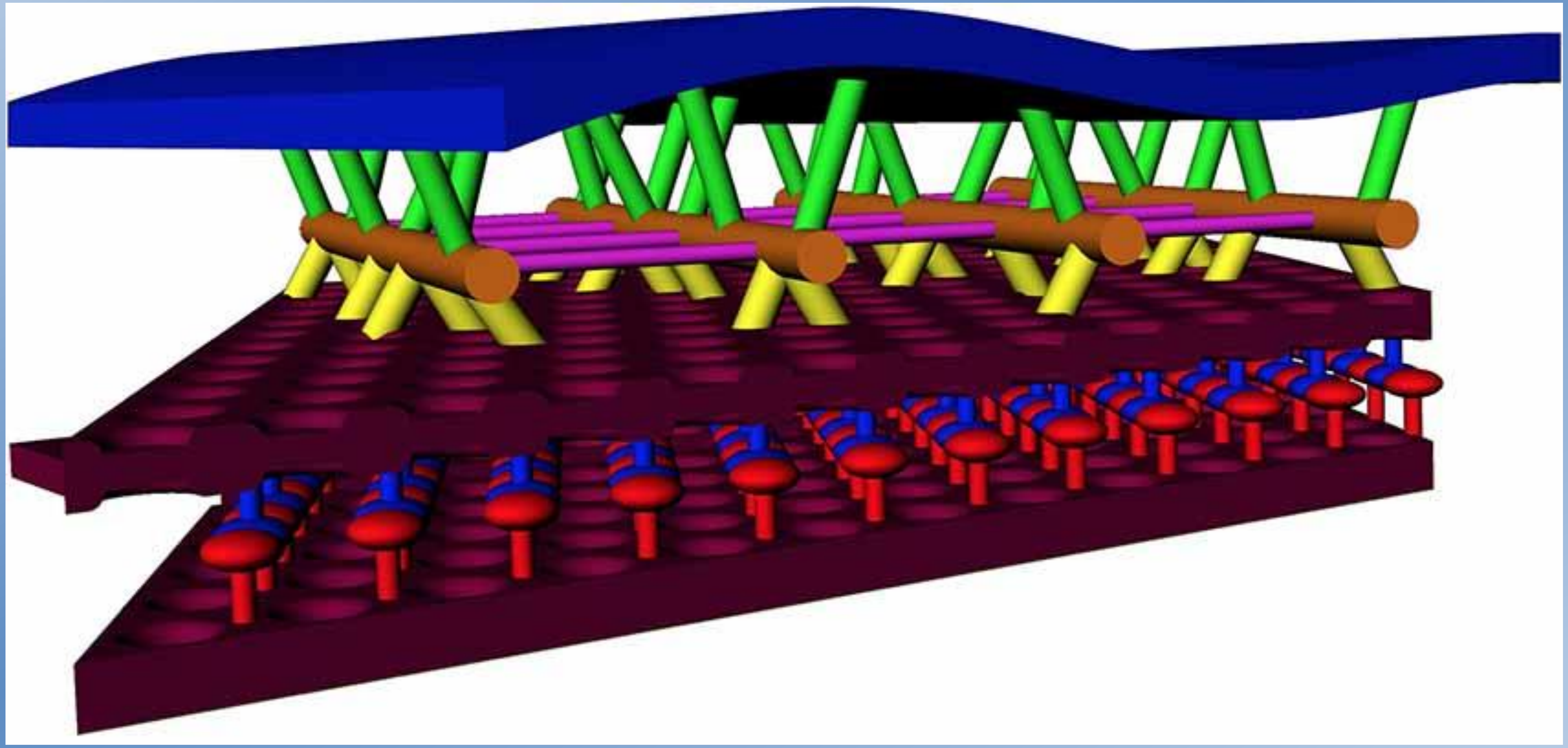


The OHC lateral wall: a trilaminate structure



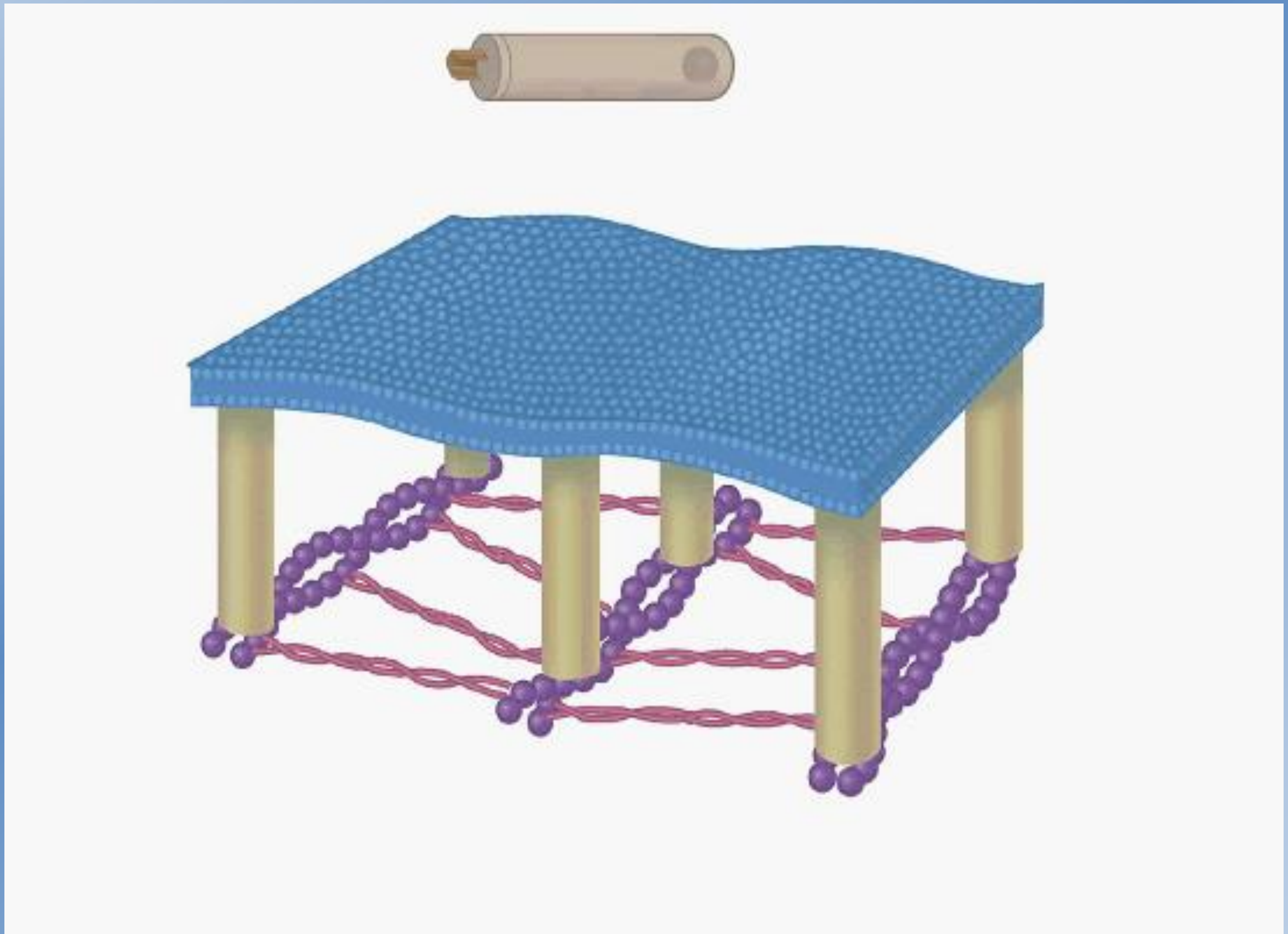
Brownell and Popel, 1998

Electron tomography update of lateral wall

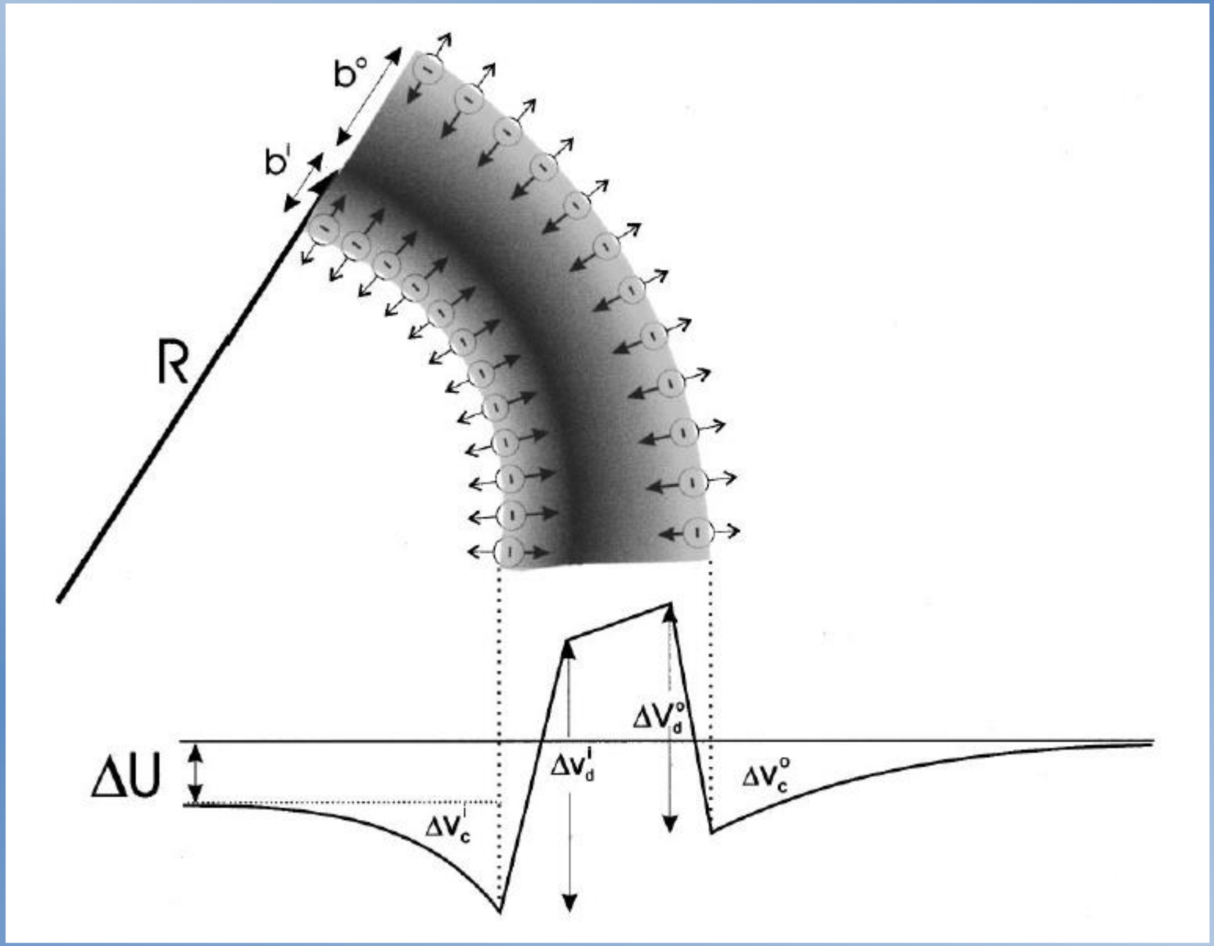


Triffo et al Front Cell Neuro, 2019

OHC electromotility – voltage induced change in membrane curvature

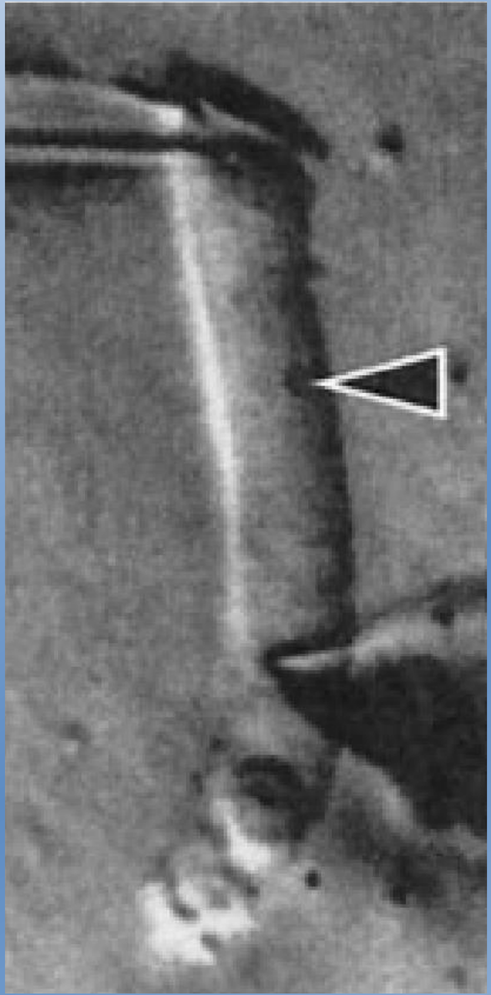


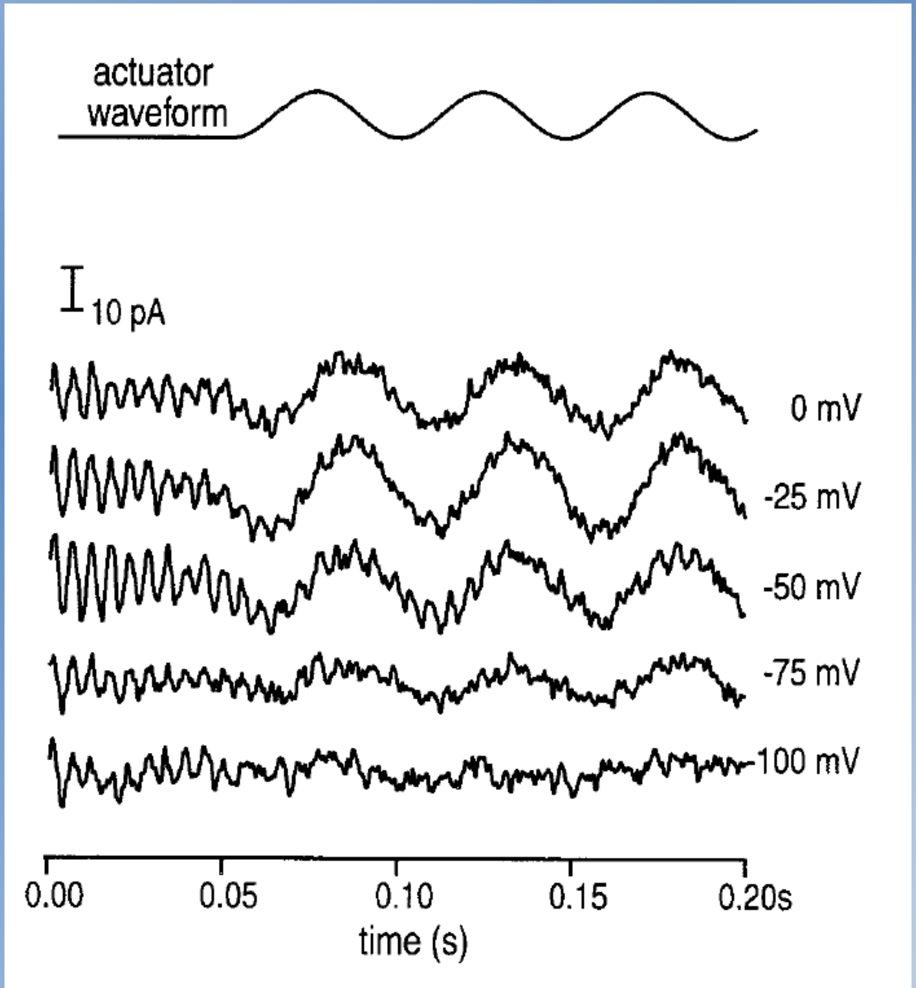
Converse flexoelectricity



Petrov and Sachs, Phys Rev E, 2002

Direct flexoelectricity





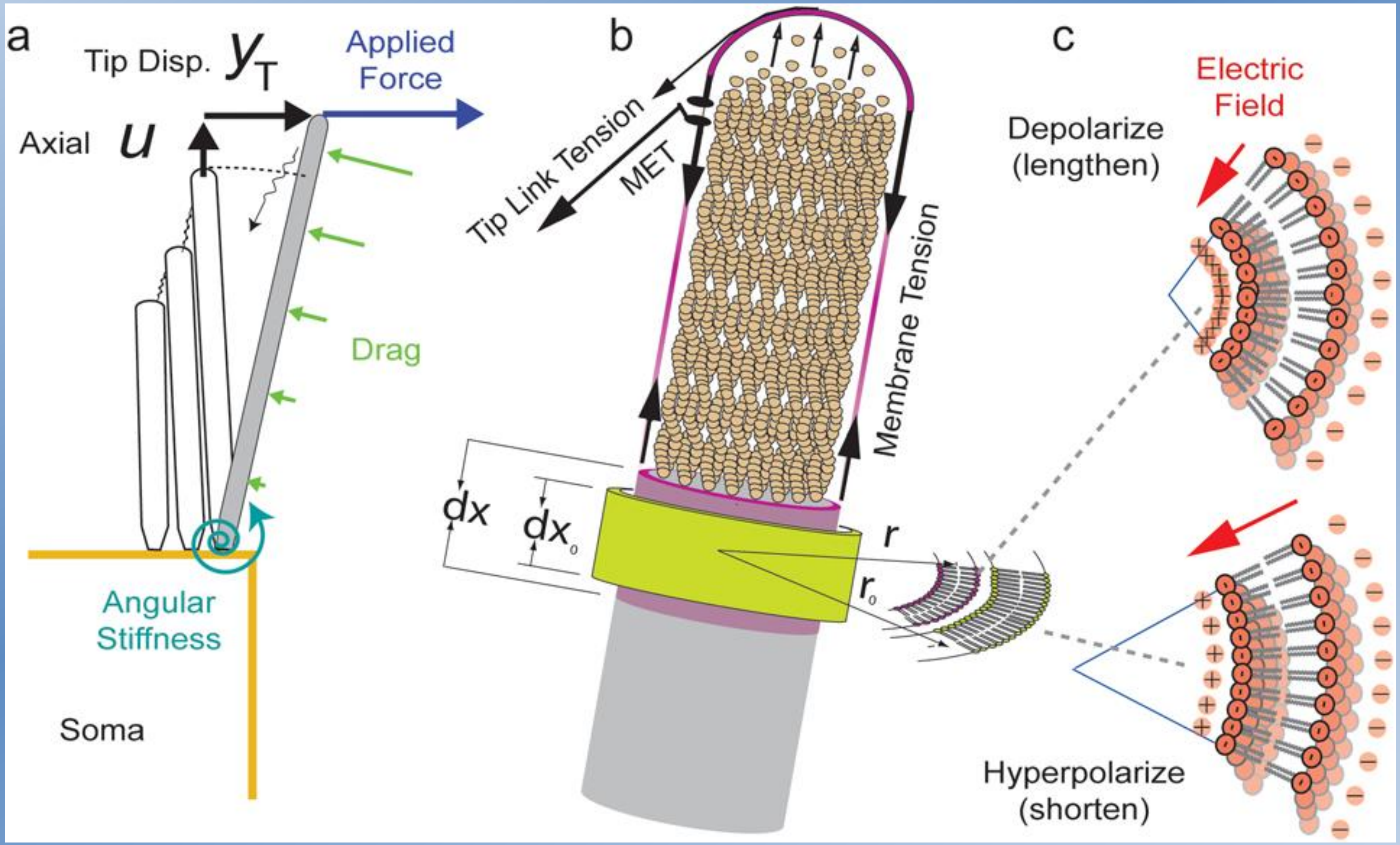
Dong et al., 2002

Non mammals have Cochlear Amplifiers but ***NO*** OHCs

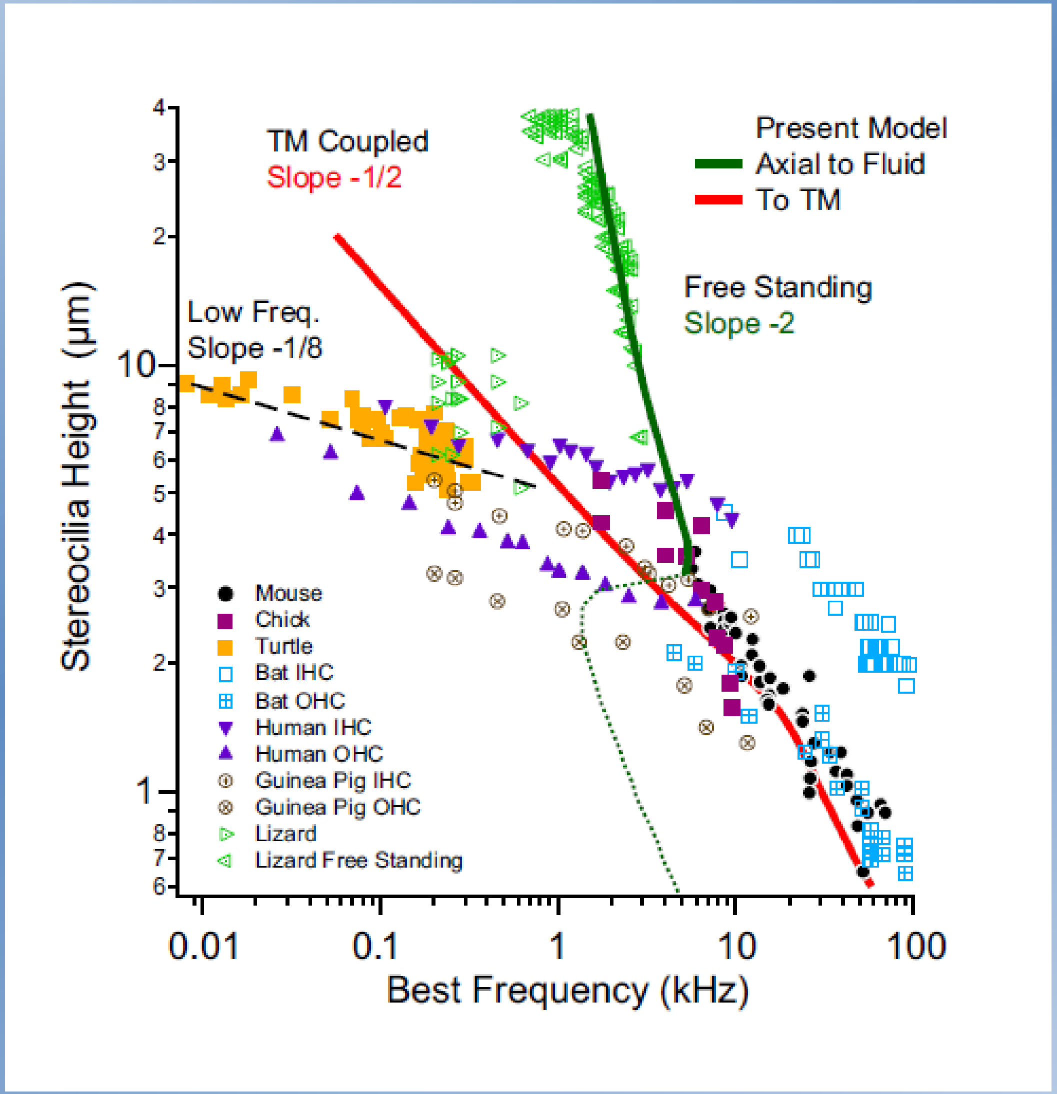
- They do have otoacoustic emissions
- Their hair cells do not have somatic motility
- Amplifier is postulated to originate in stereocilia
- A form of electromotility/adaptation occurs in hair cell stereocilia bundles

Stereocilia as flexoelectric motors

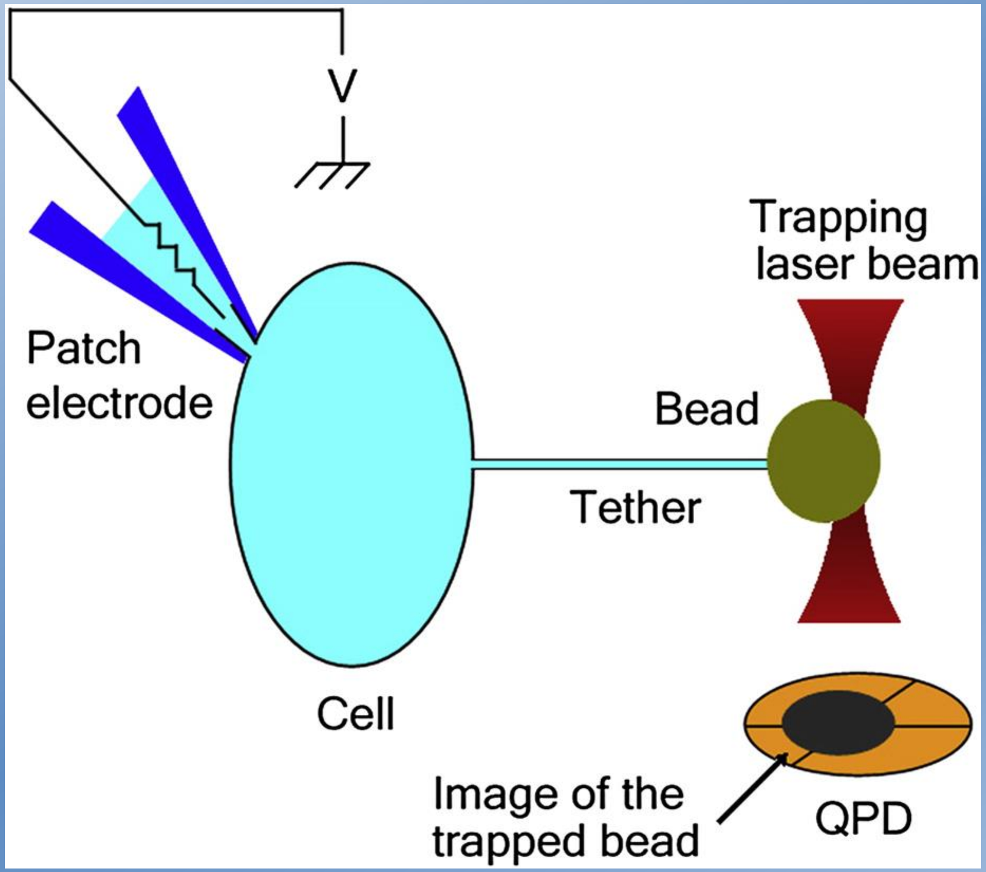
from: Breneman, Brownell & Rabbitt - 2009

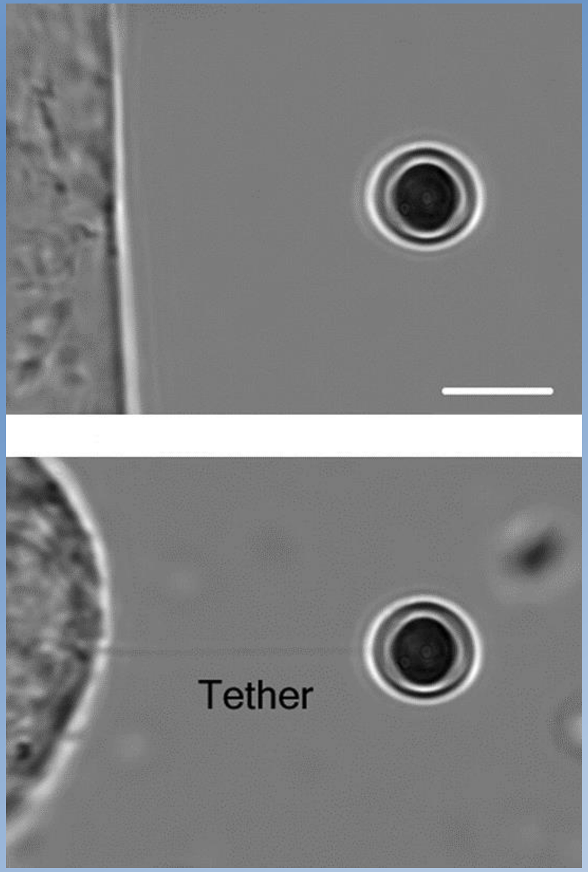


Predicts stereocilia length



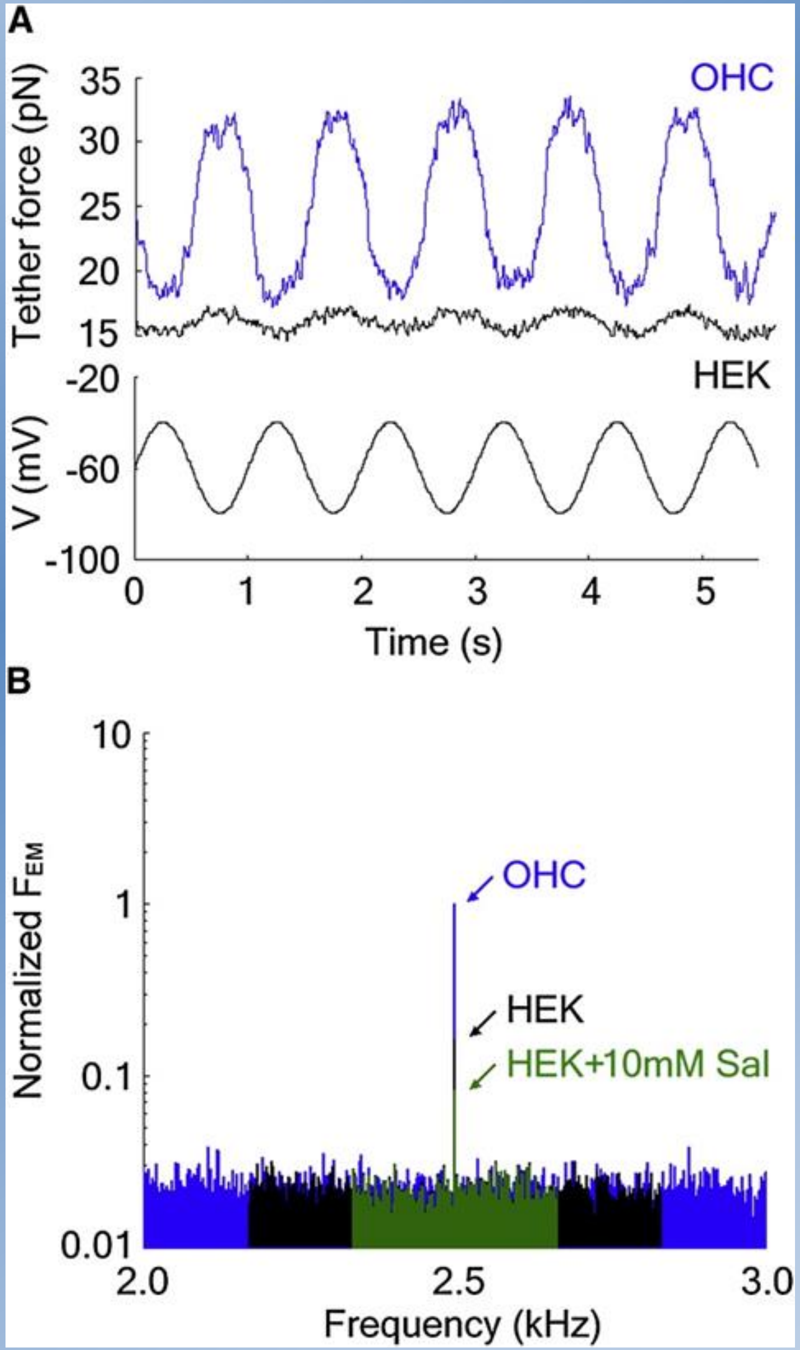
Electromechanics in membrane tethers



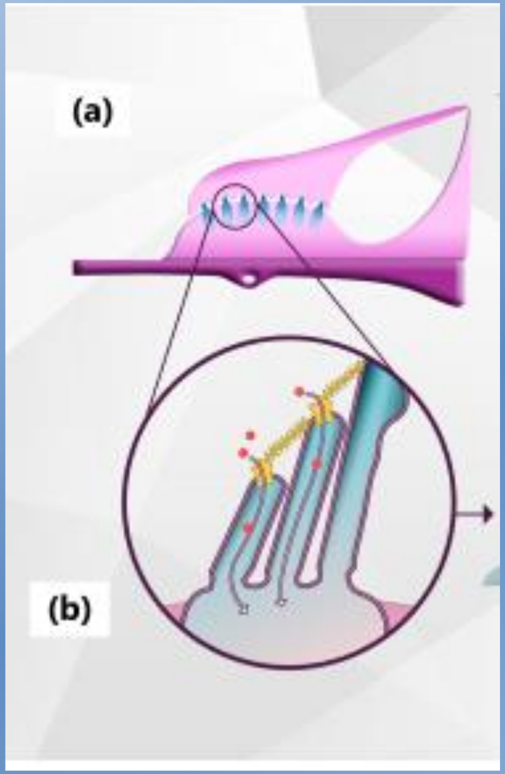


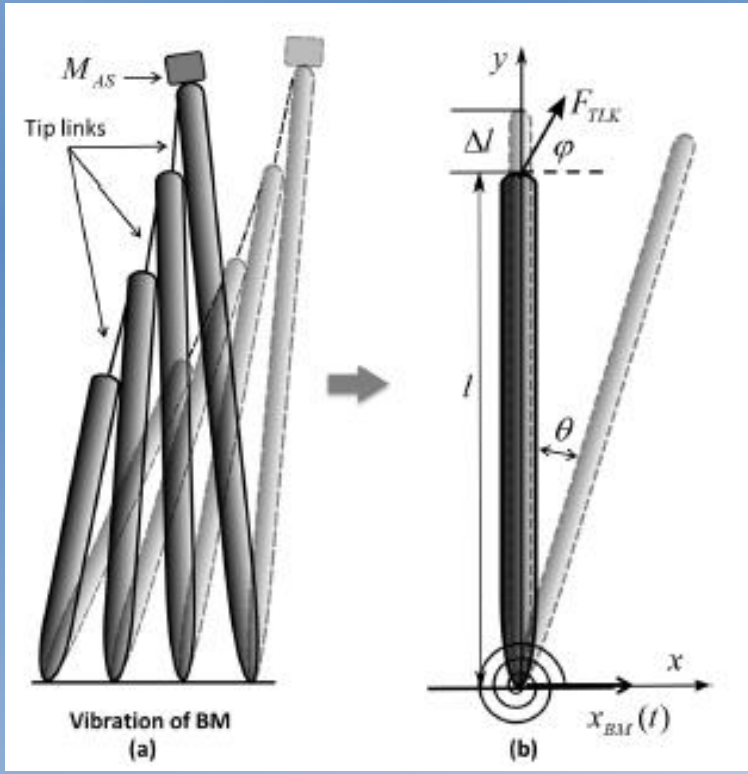
Brownell et al., 2010

Flexoelectric model compatible with optical tweezers results



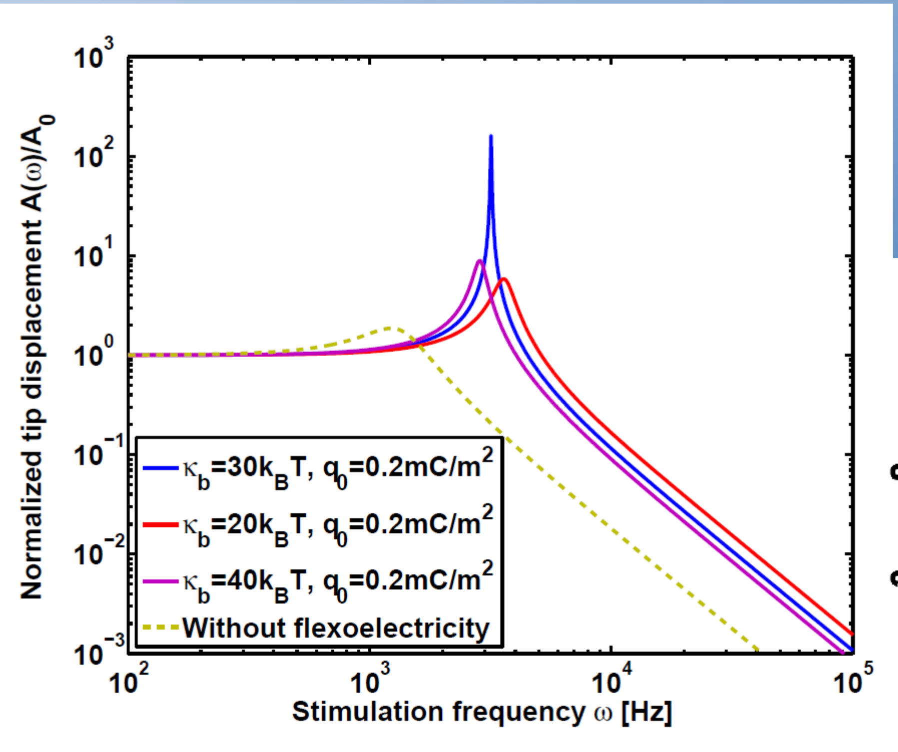
Add an acsessory mass and explicitly include cationic influx through MET

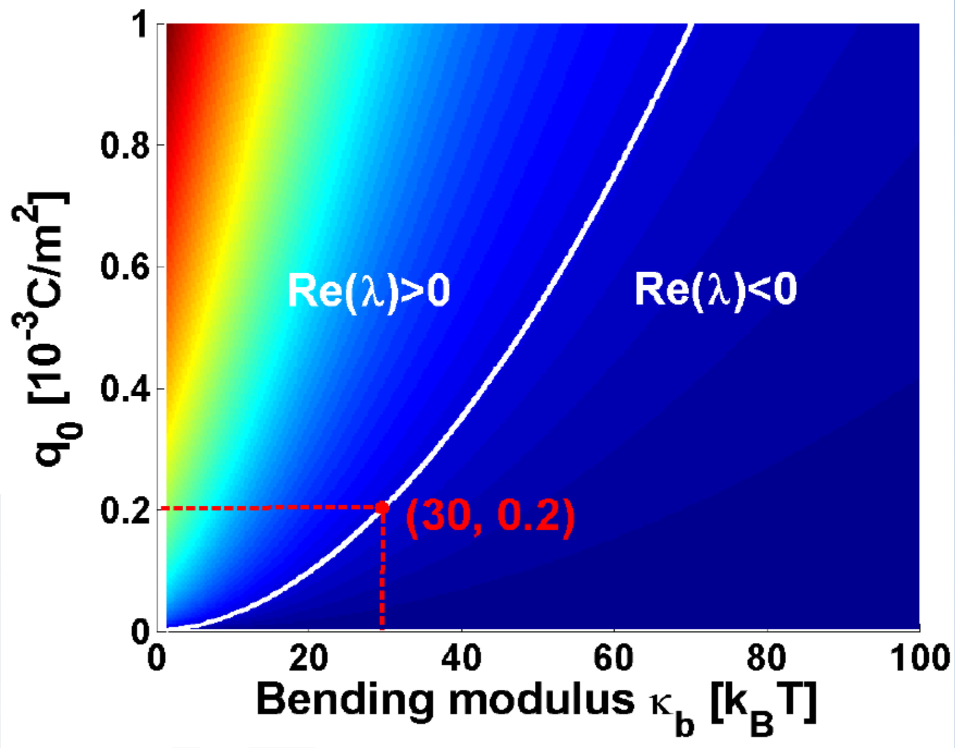




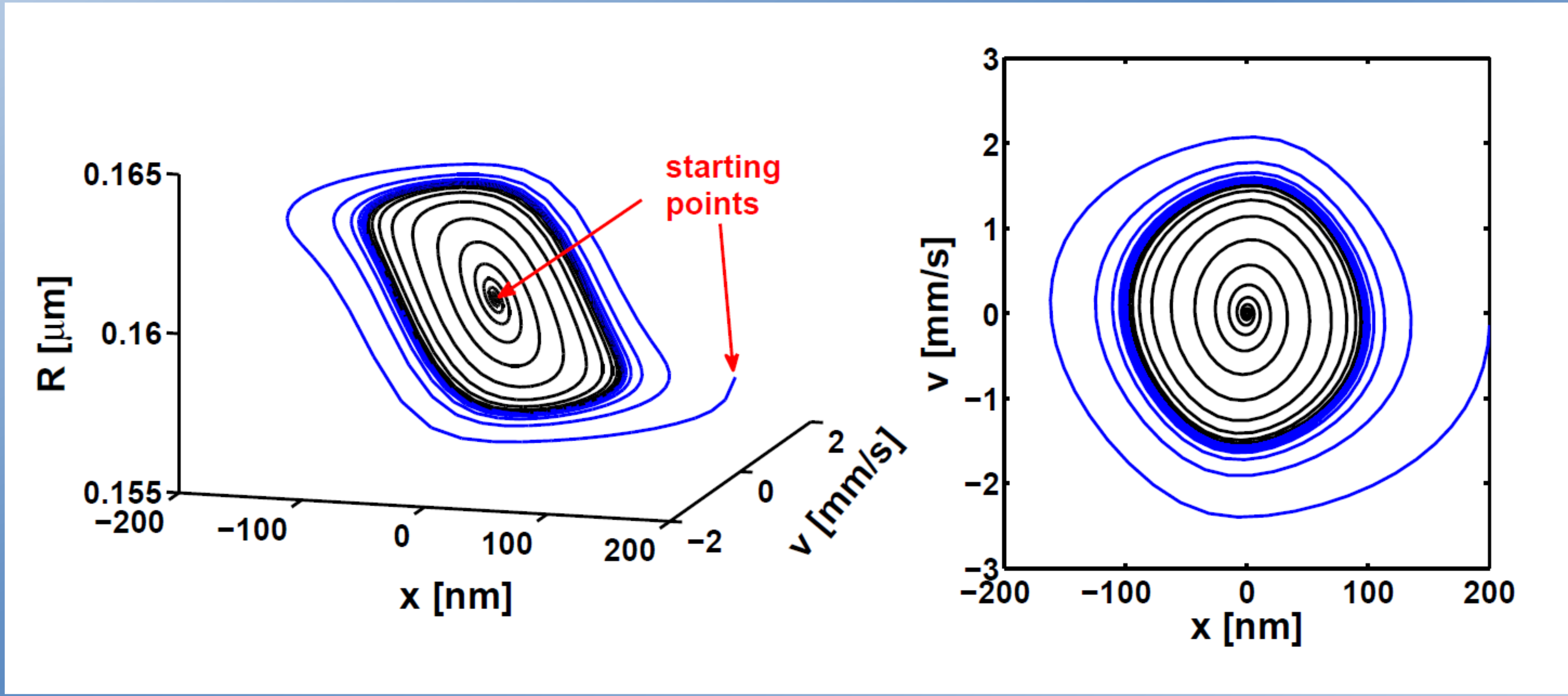
Deng et al., Mech Physics Solids. 2019

Selectivity and critical limit cycle

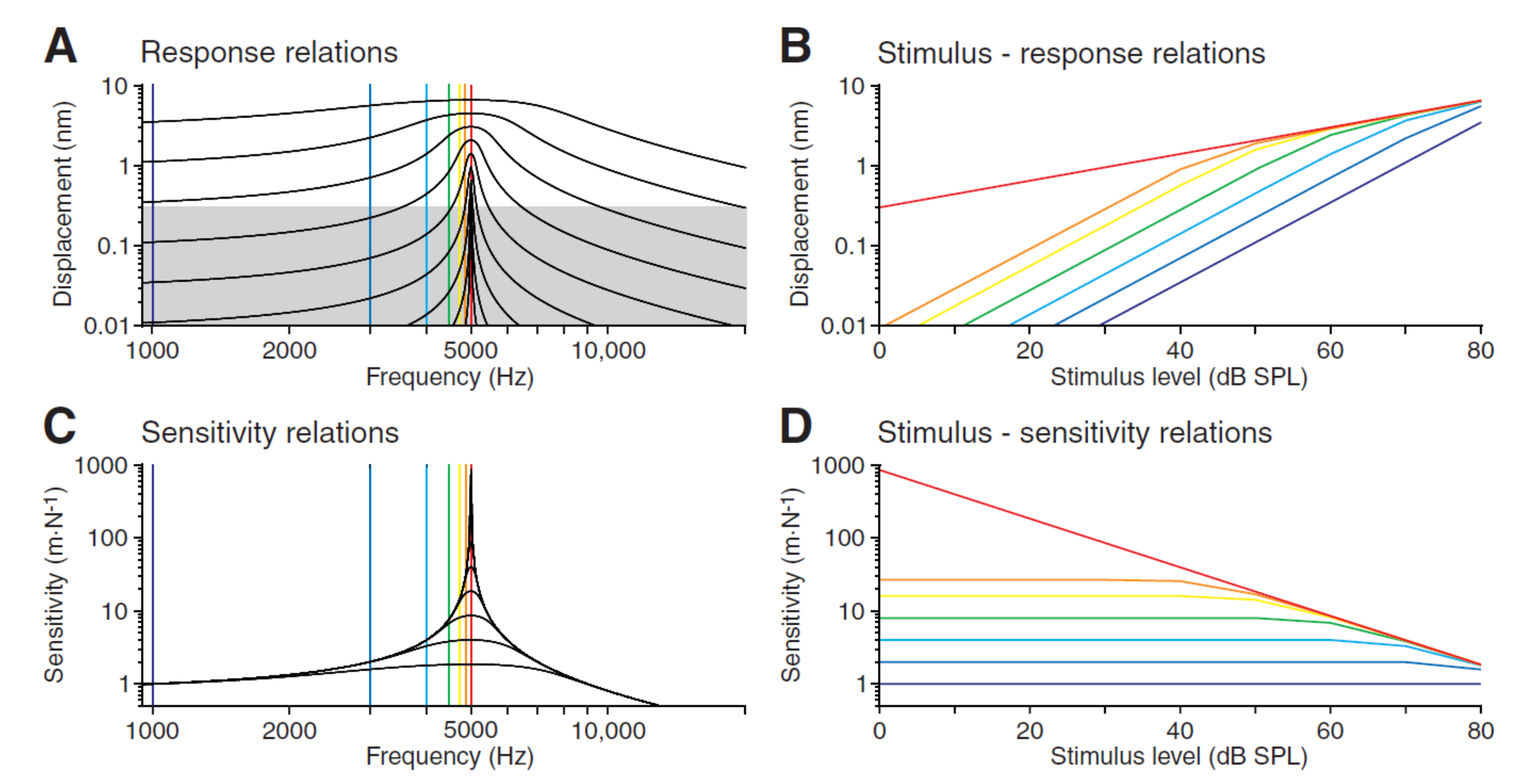




Convergence to a critical limit cycle

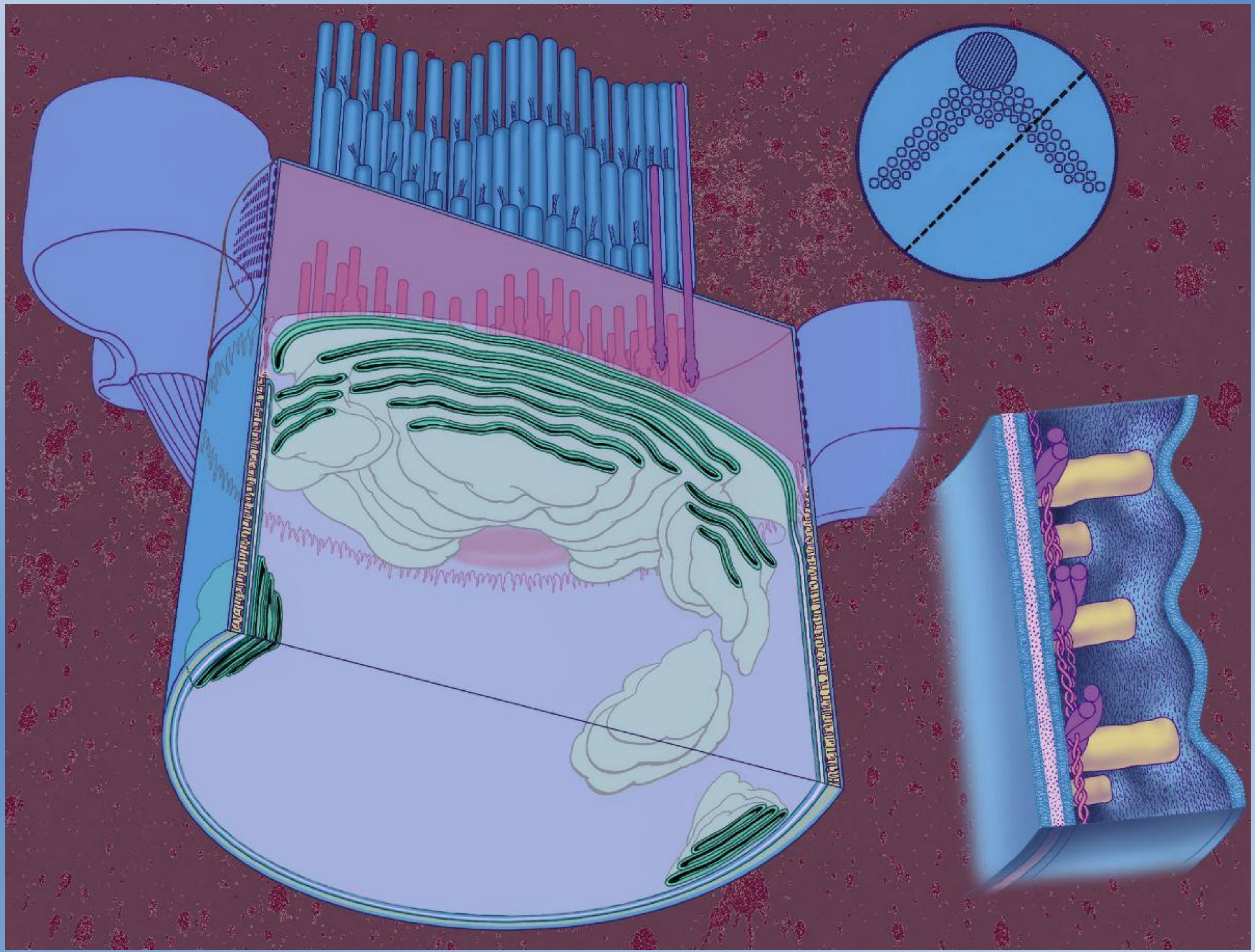


Benefits to hearing



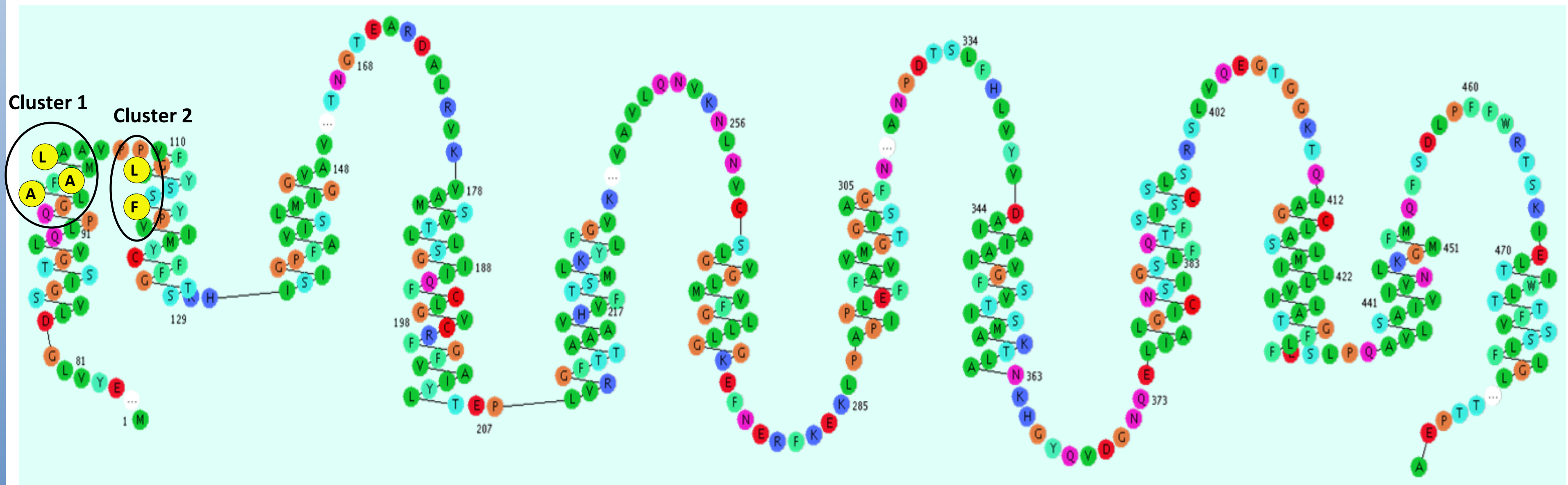
Hudspeth et al, 2010

Trilaminate Structures

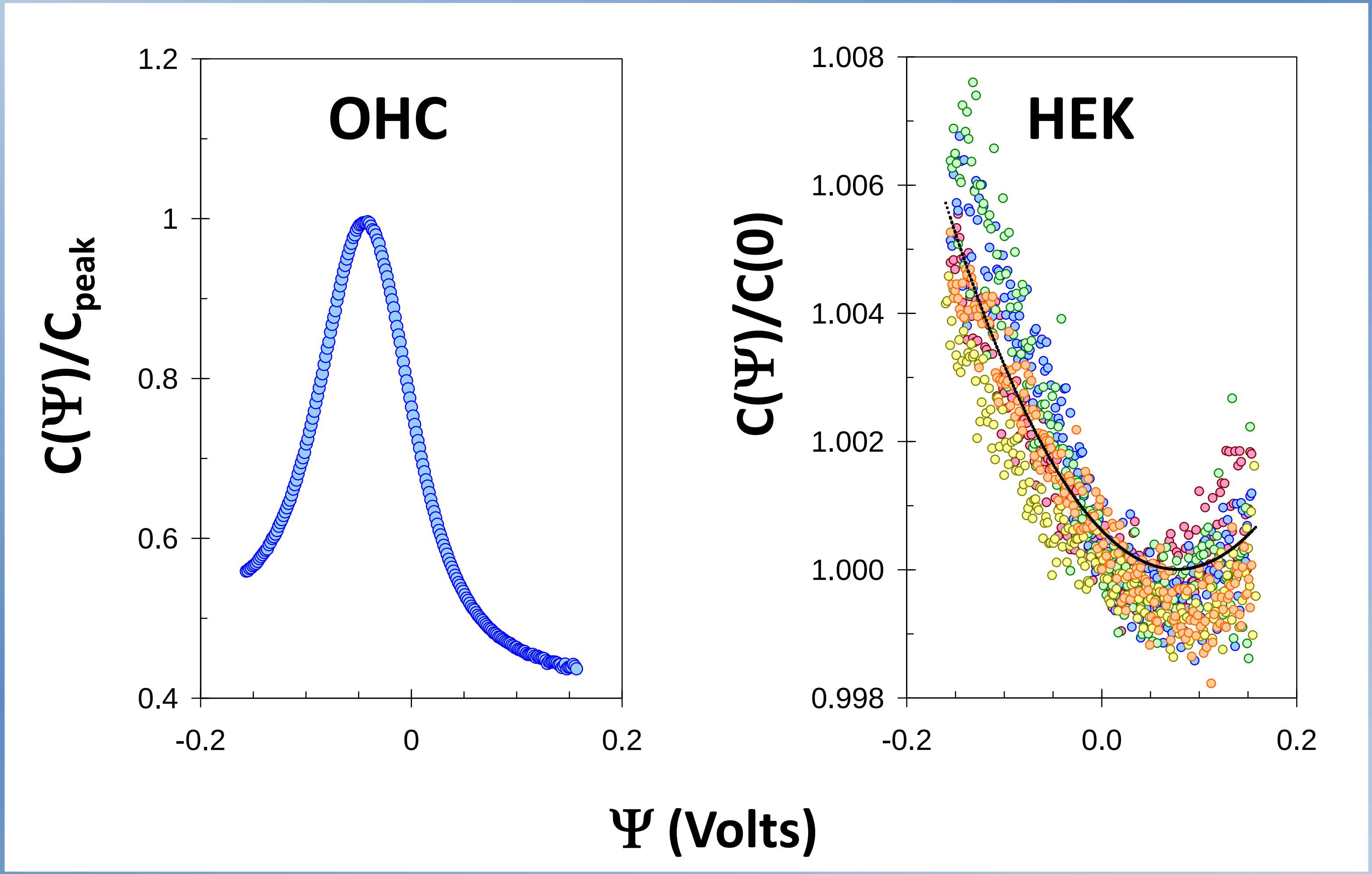



5781

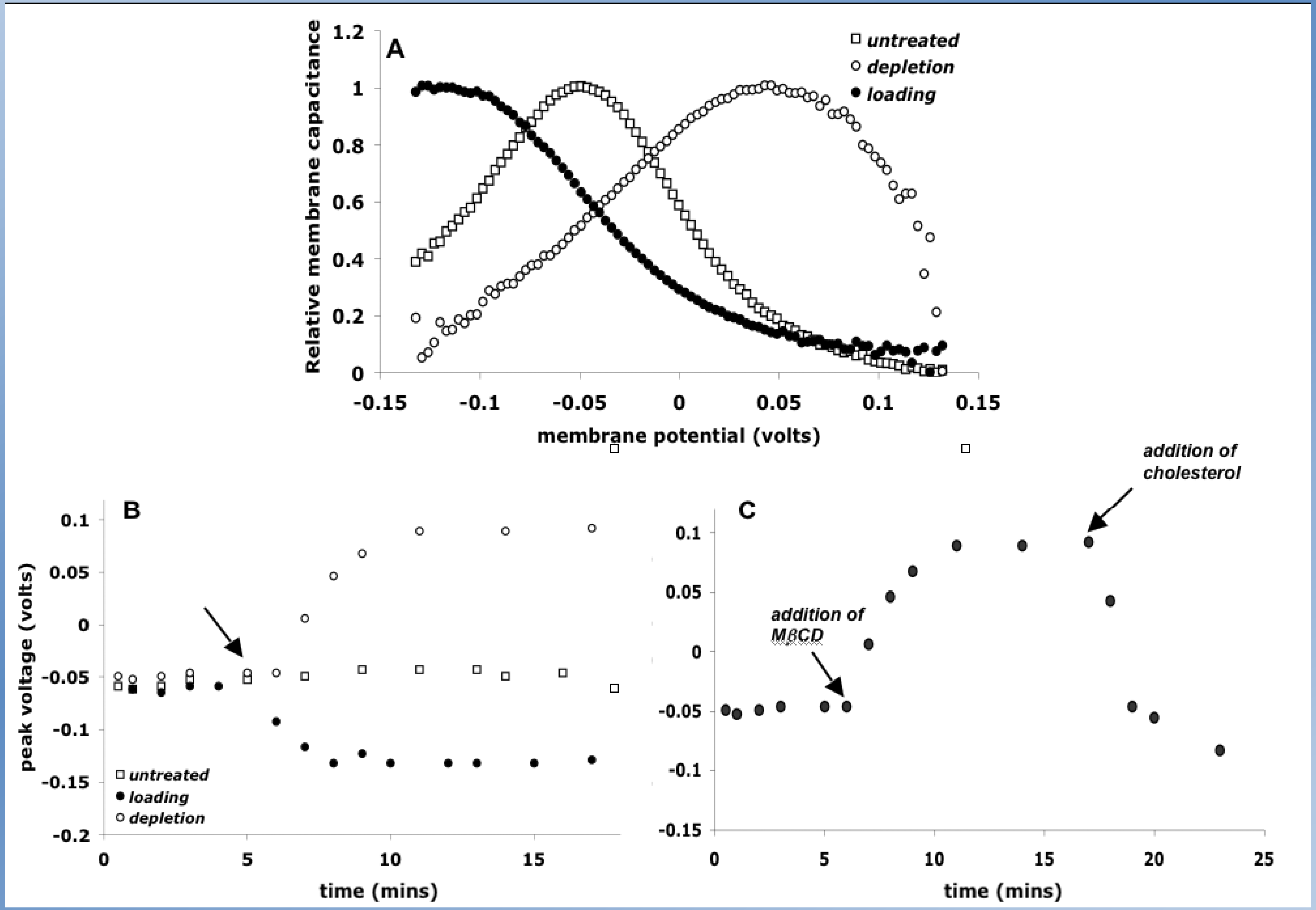
Prestin



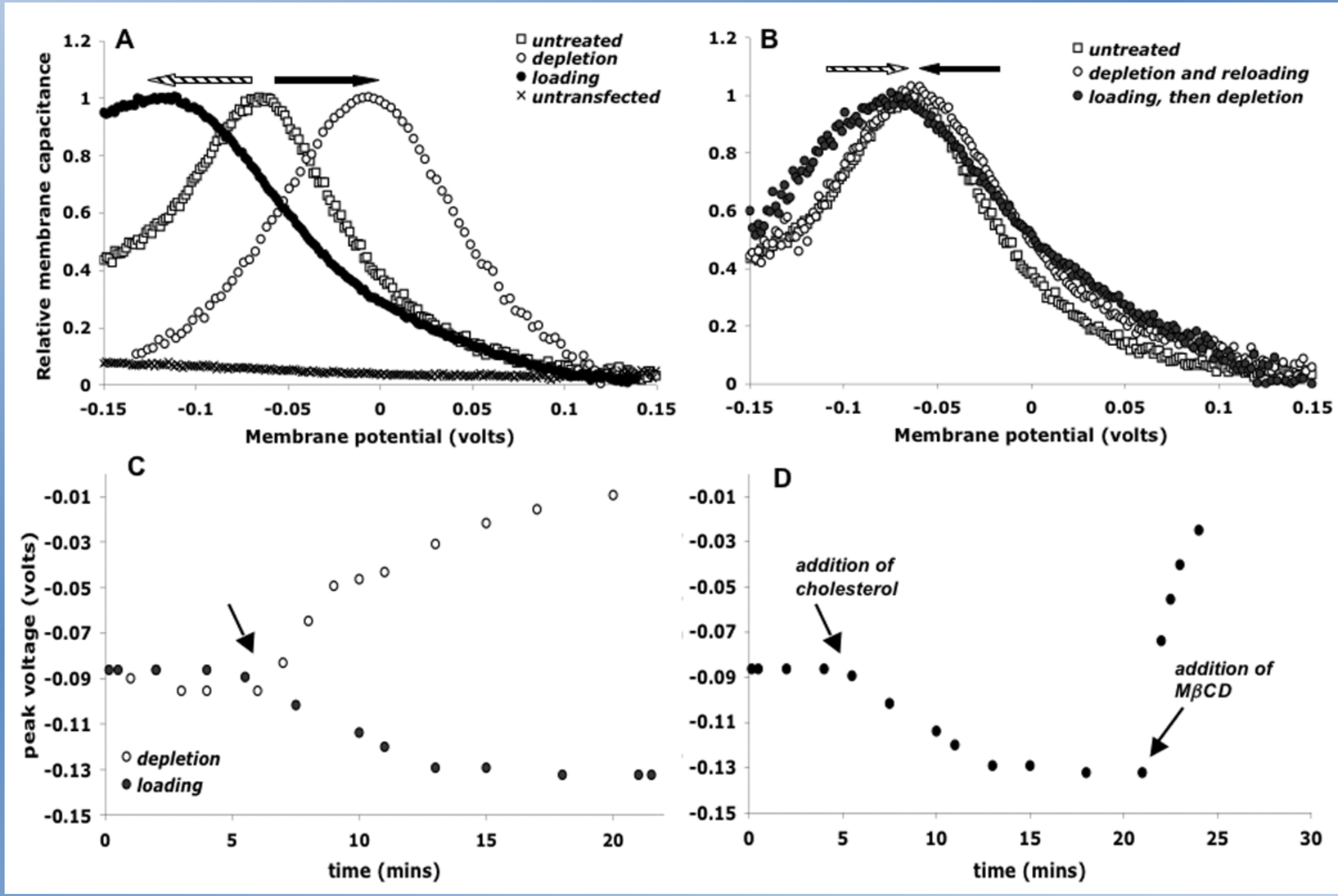
Prestin associated charge movement



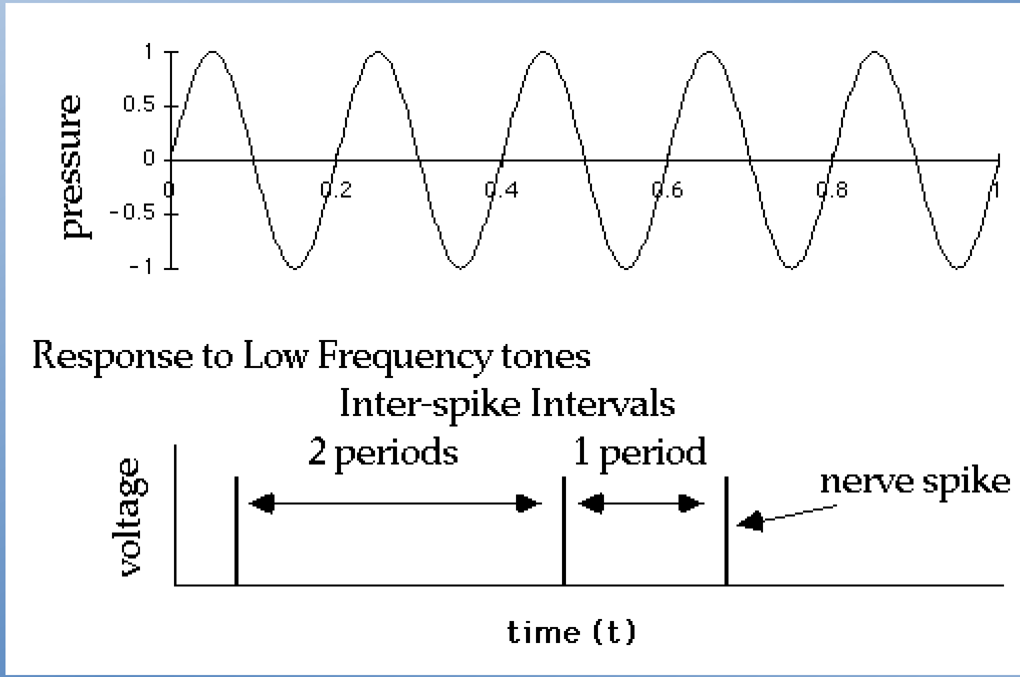
Cholesterol level shifts V_{pkc} in OHCs



Cholesterol in prestin transfected HEK cells



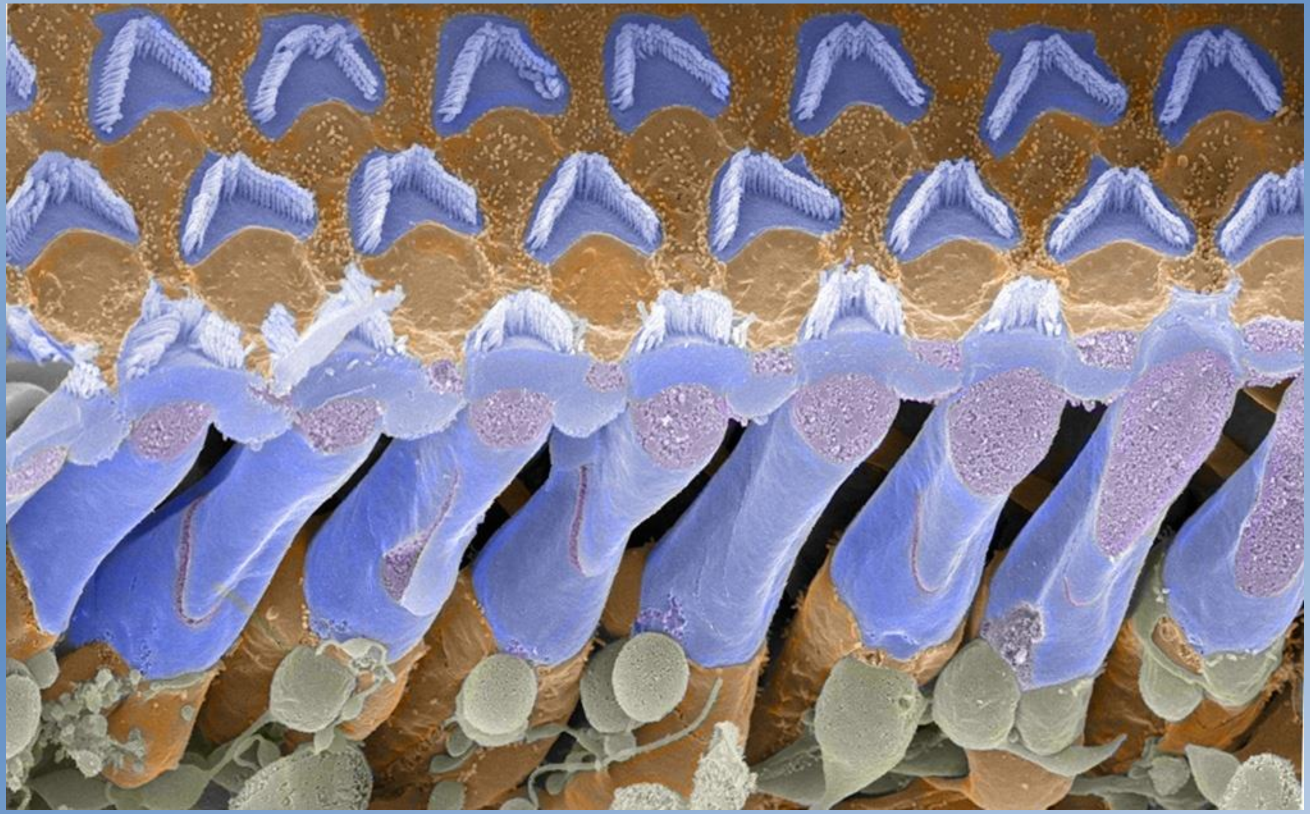
Phase locking & vector strength



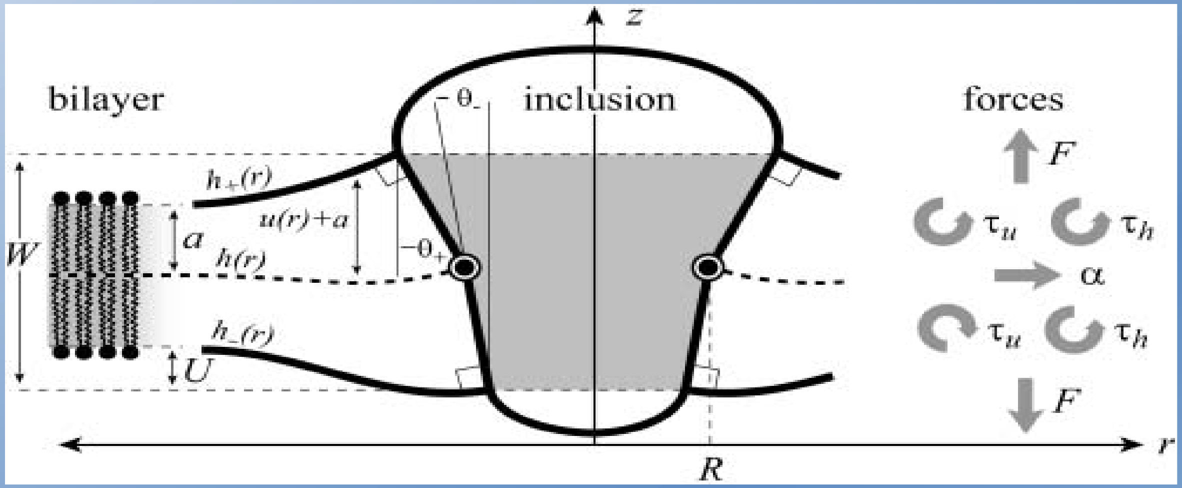
Vector strength: Each spike is represented by a vector of unit length and direction equal to the phase, *p,* of the spikes ($0 < p < 2\pi$) relative to the signal. The sum of these vectors, normalized by the number of spikes, gives the vector strength ***r***. With perfect synchrony ,***r*** =1; if there is no phase locking, ***r*** = 0.

Goldberg and Brown, 1969

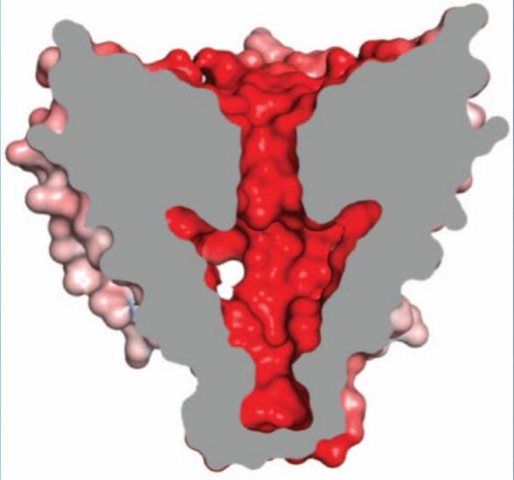
Outer Hair Cells
are surrounded by fluid



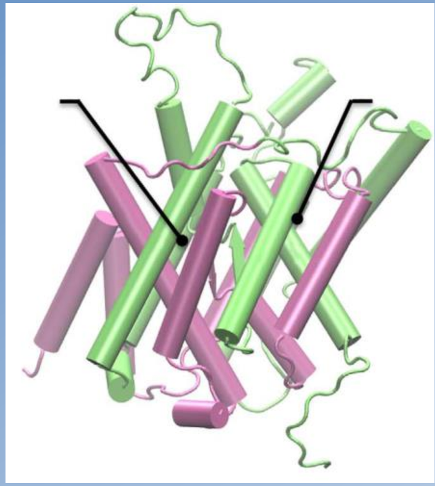
Bilayer-inclusion model



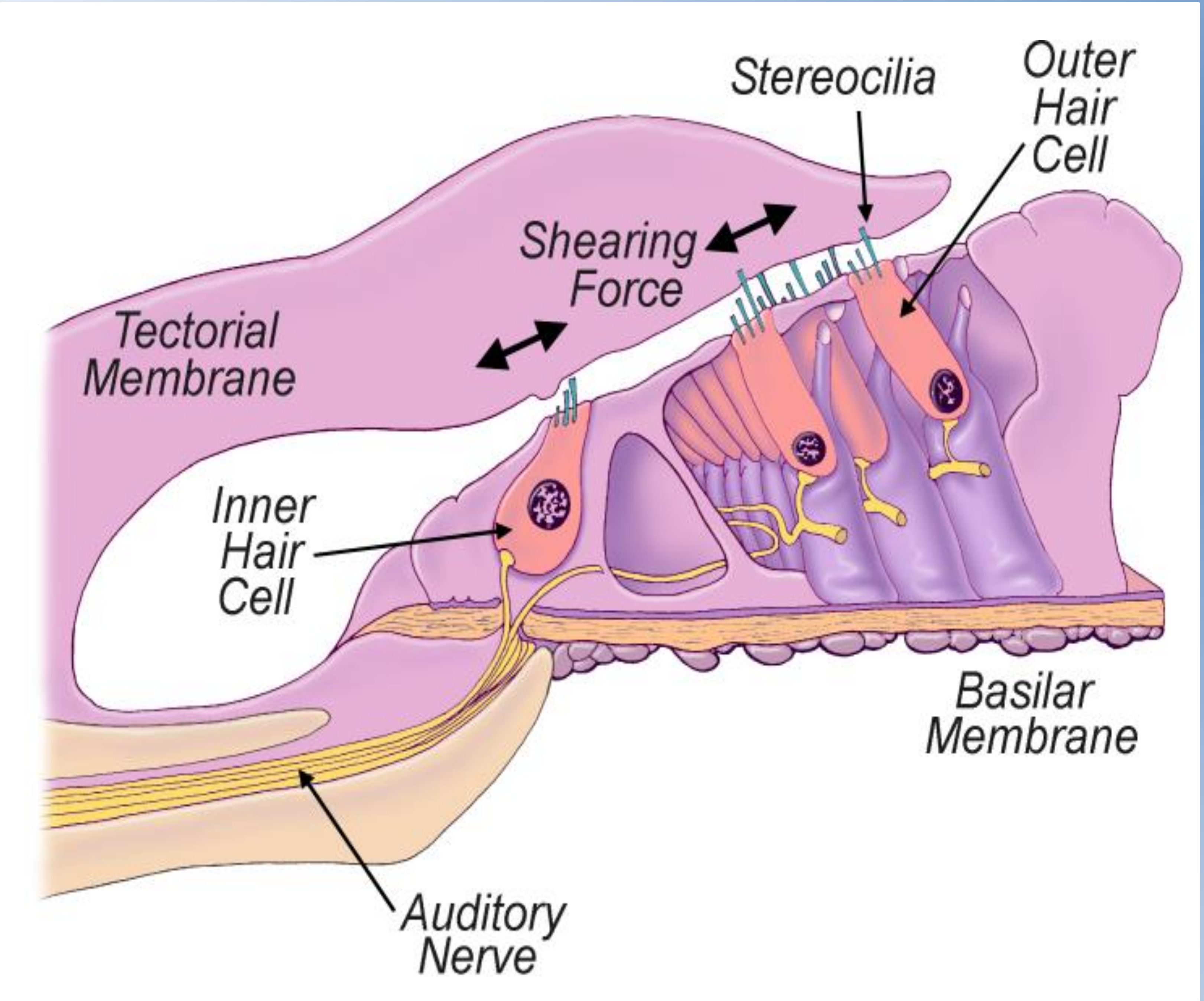
Wiggins & Phillips, 2005



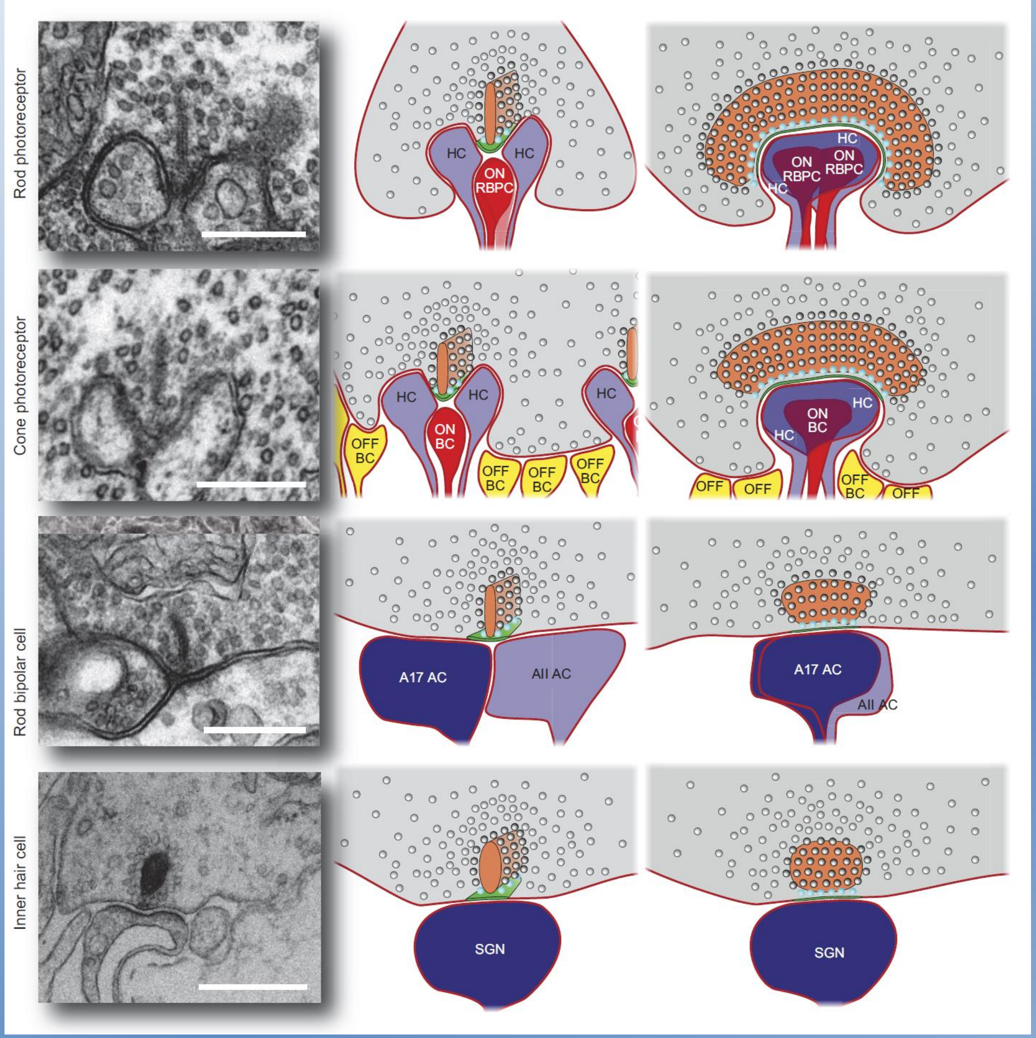
Na_V Channel , Payandeh et al, 2011

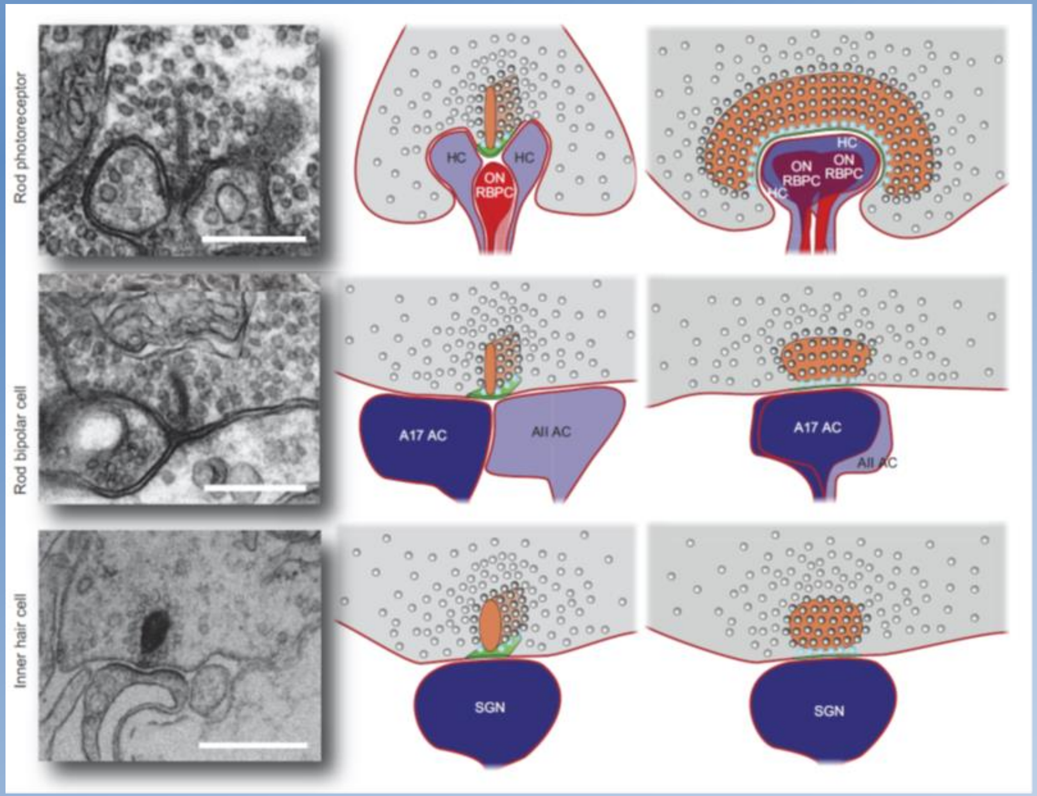


Prestin, Gorbunov et al, 2014



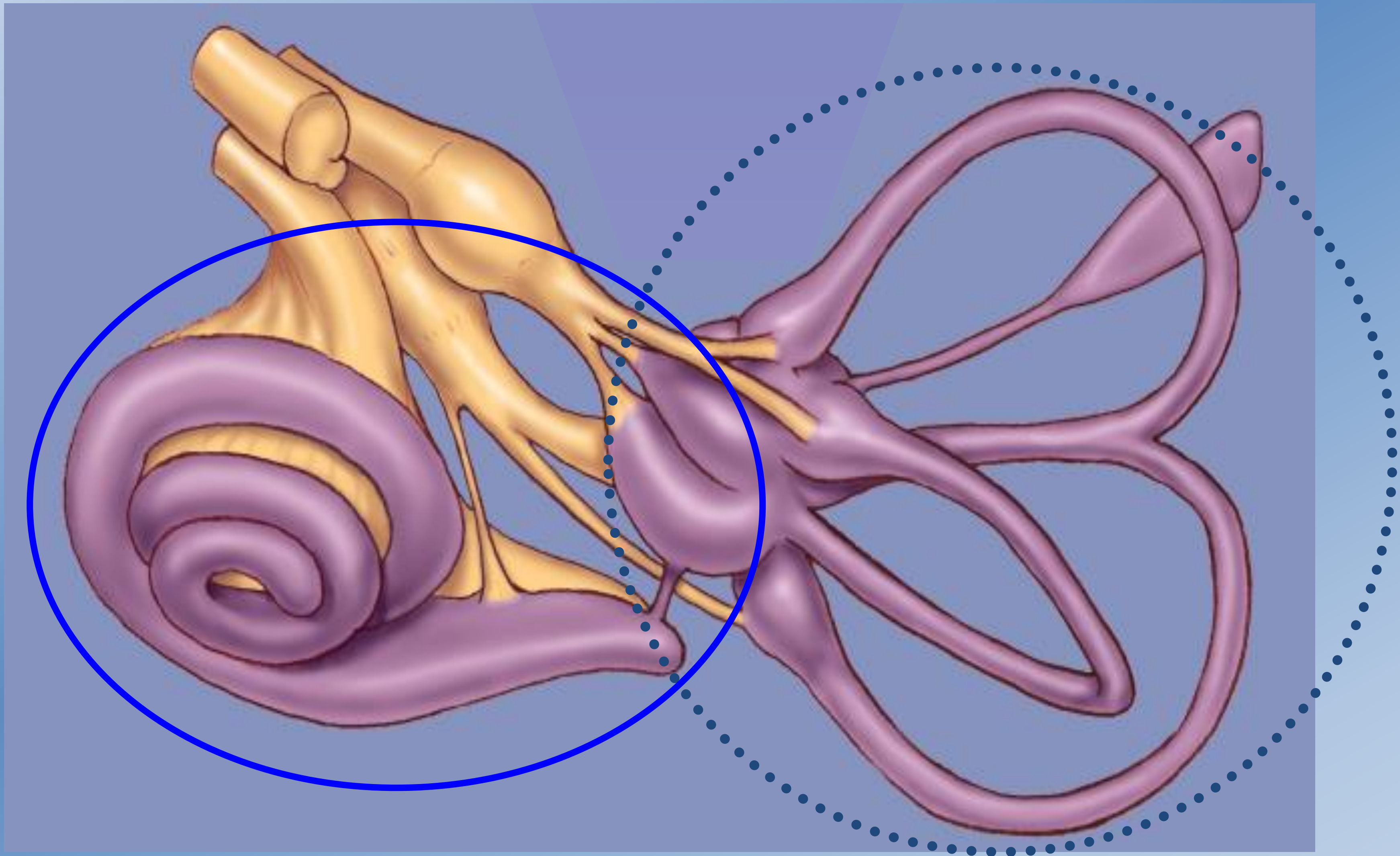
Organ of Corti


Rod photoreceptor
Cone photoreceptor
Rod bipolar cell
Inner hair cell
HC
ON RBPC
ON BC
OFF BC
OFF
A17 AC
AII AC
SGN


Rod photoreceptor
Rod bipolar cell
Inner hair cell
HC
ON RBPC
A17 AC
AII AC
SGN

Inner Ear Mechanoreceptor Organs

Vestibular system > 400 million years old 0-10^2 Hz

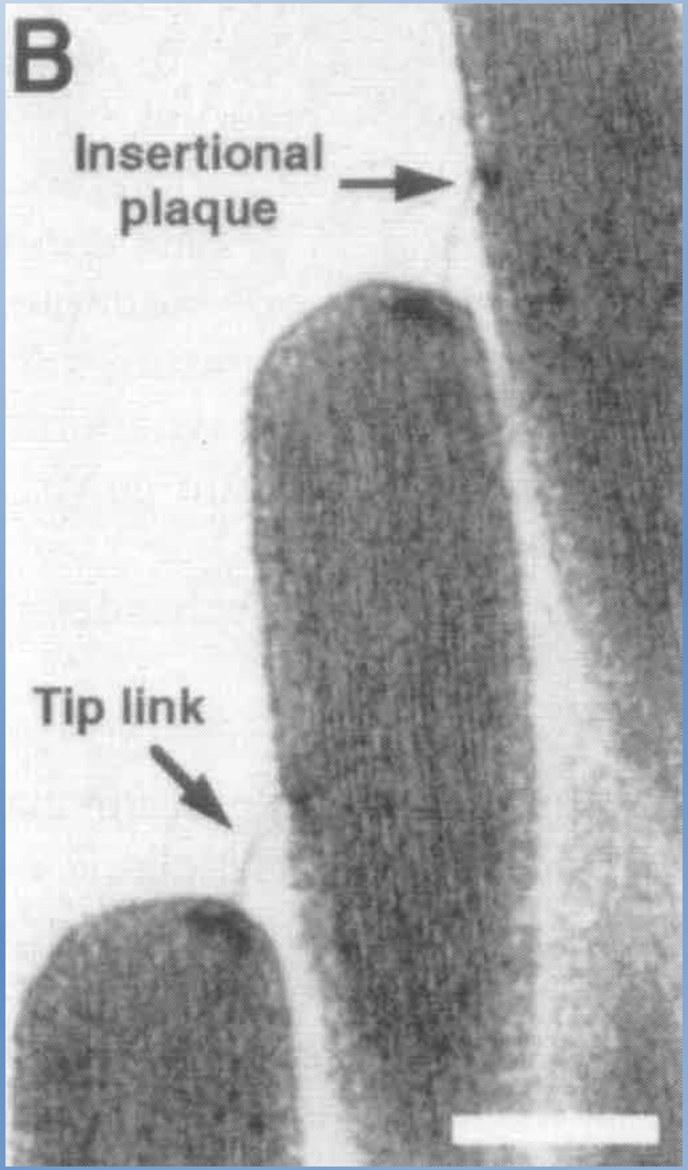


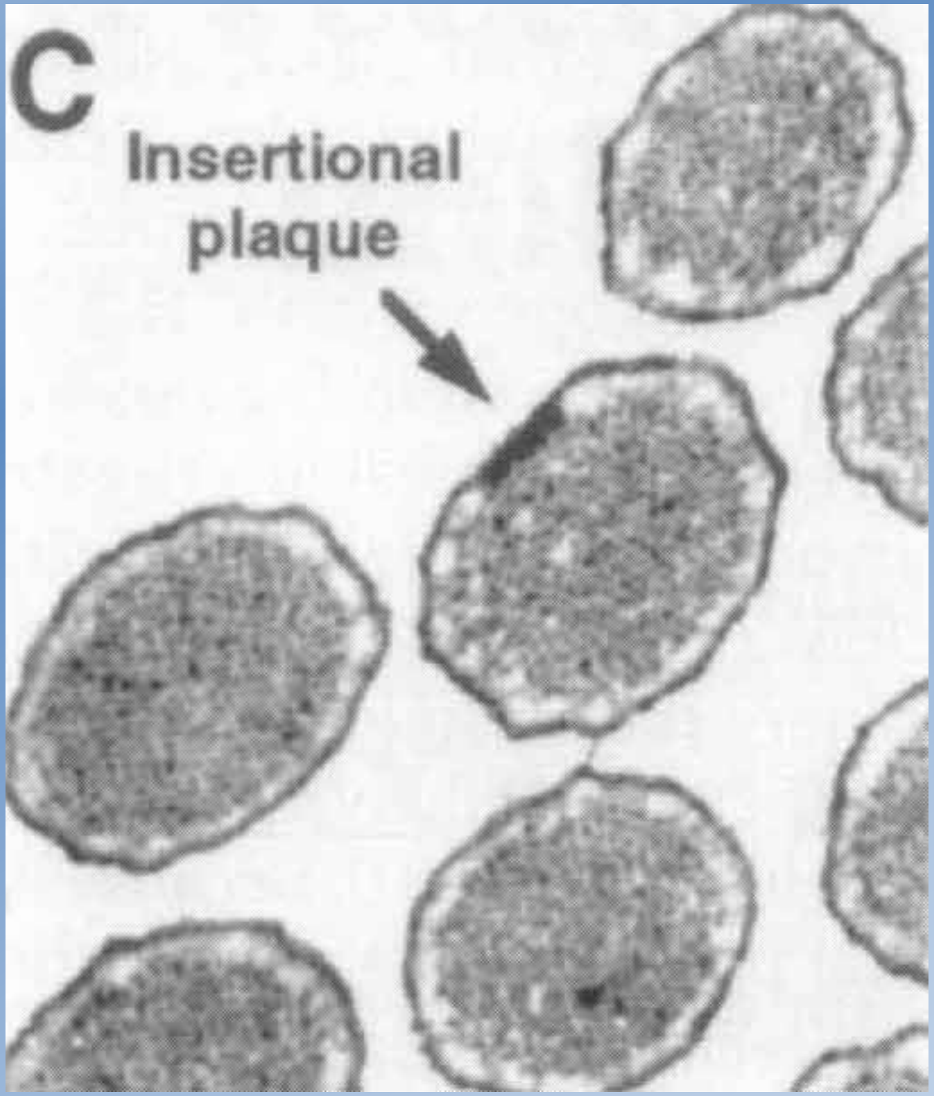
Mammalian Cochlea ~ 200 million years old, 10^1-10^5 Hz

Outer hair cell electromotility

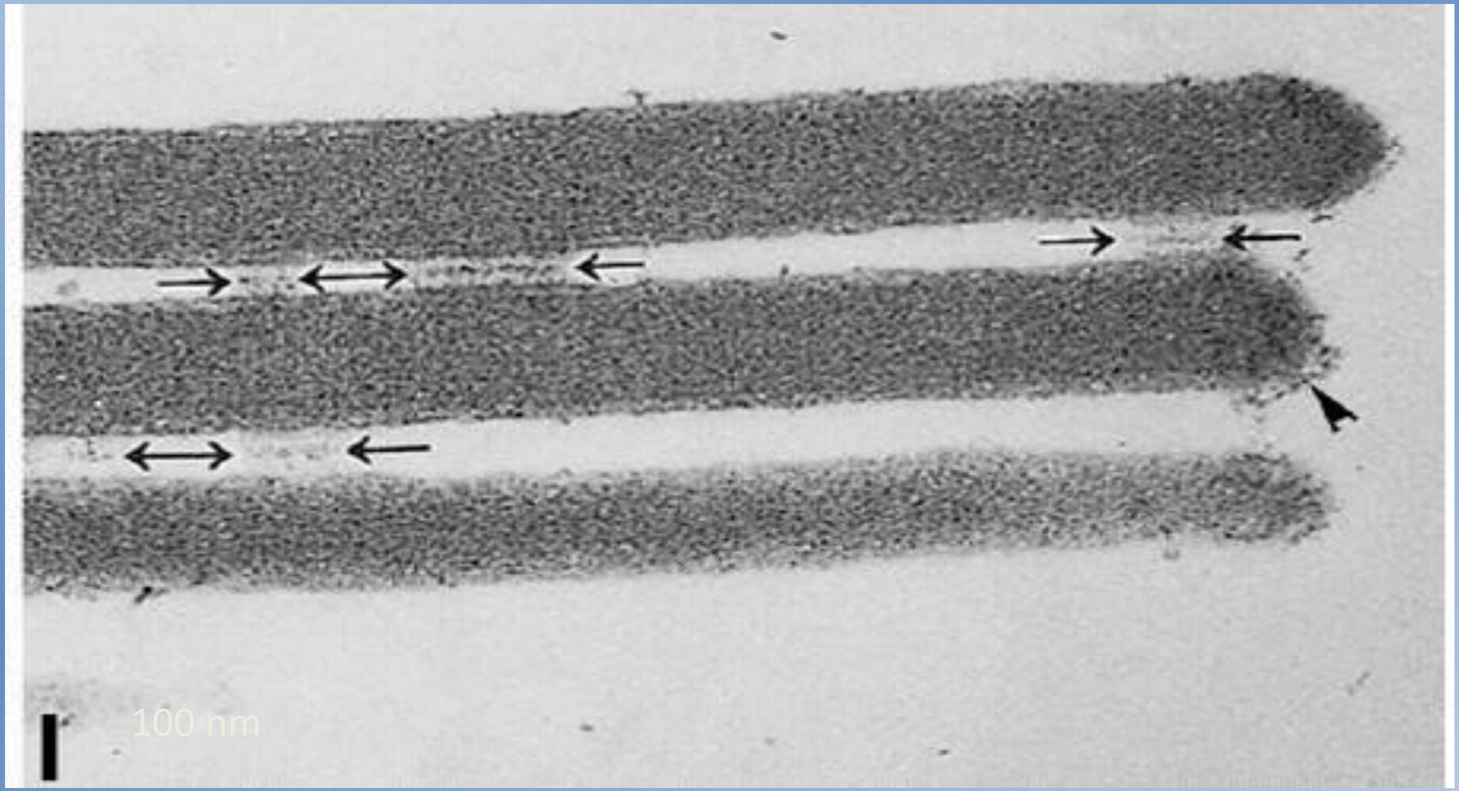
200 msec pulses from a holding potential of –60 mV. Initial pulse is hyperpolarizing and each successive pulse +10 MV from that.

Mechanoelectrical Transduction

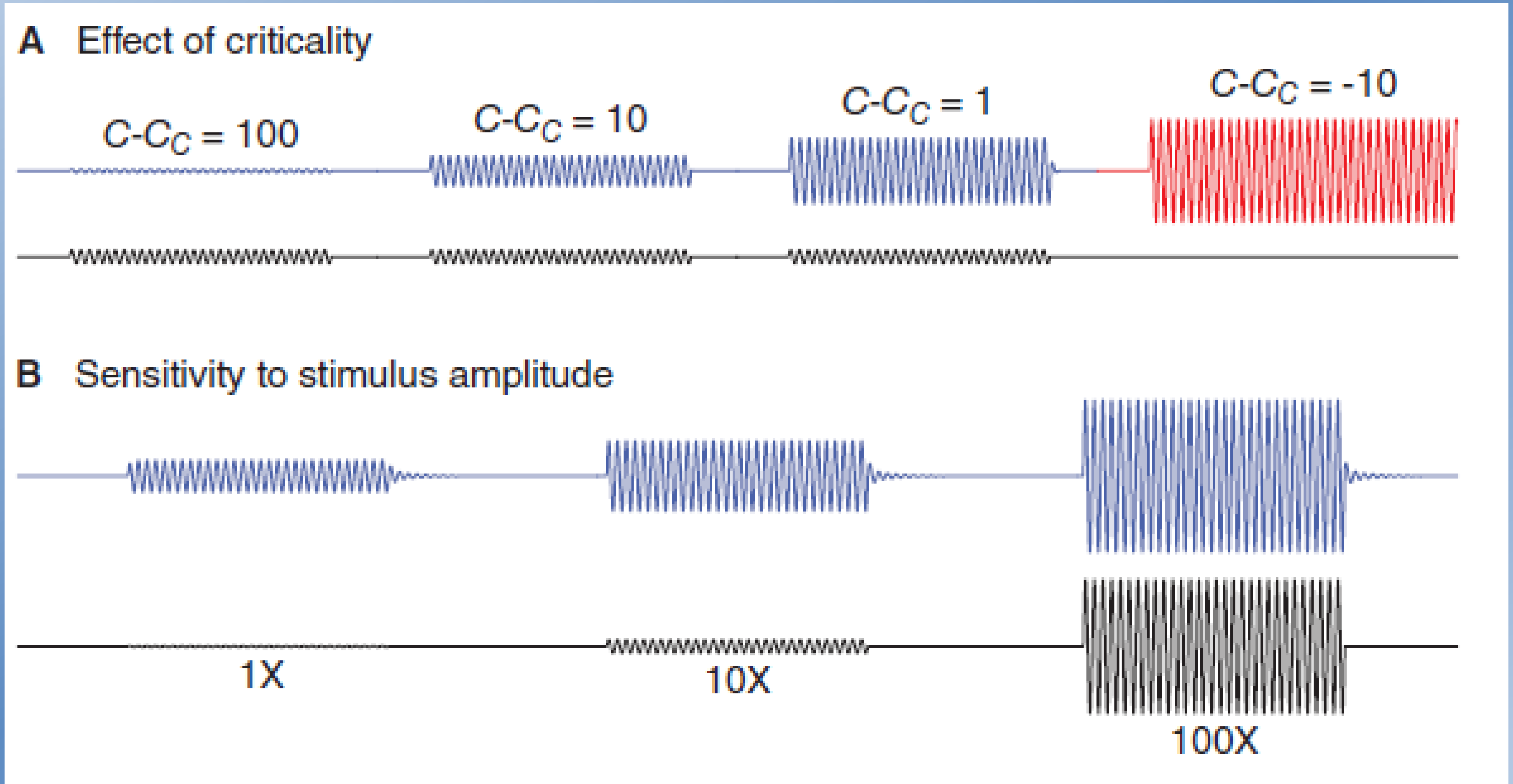




Harnessing membrane EMF by stereocilia



Potential impact on mechanics



Hudspeth et al, 2010