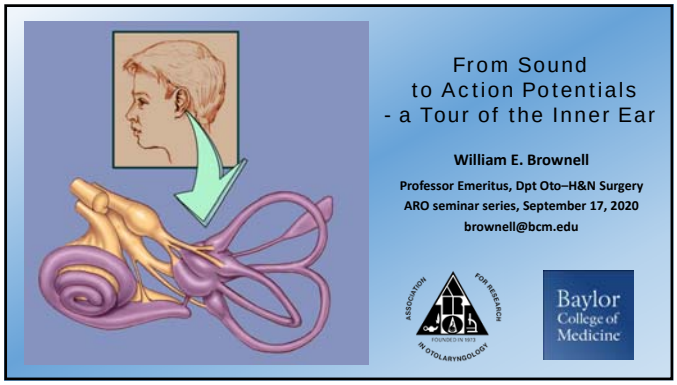

From Sound to Action Potentials - a Tour of the Inner Ear

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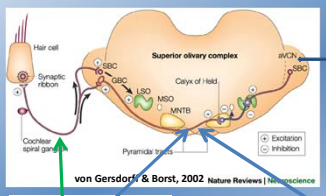
Professor Emeritus, Dpt Oto–H&N Surgery
ARO seminar series, September 17, 2020
brownell@bcm.edu

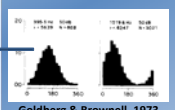
Baylor College of Medicine

1

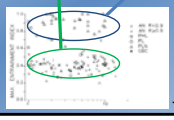
ACTION POTENTIALS in the auditory brainstem



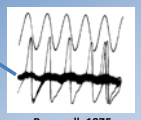
von Gersdorff & Borst, 2002 Nature Reviews | Neuroscience



Goldberg & Brownell, 1973



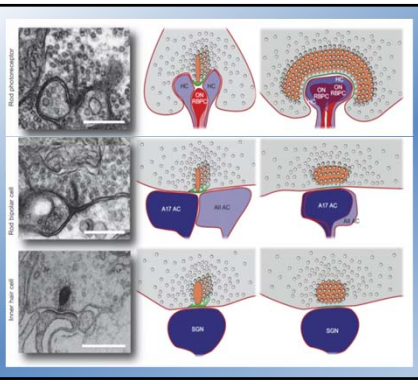
Joris et al, 1994



Brownell, 1975

2

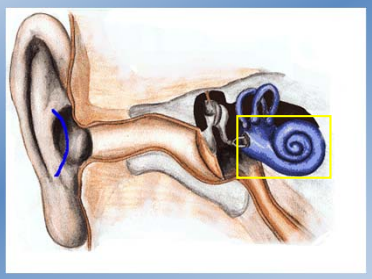
Synaptic Ribbons in Sensory Cells



Moser et al. Physiol Rev. 2020

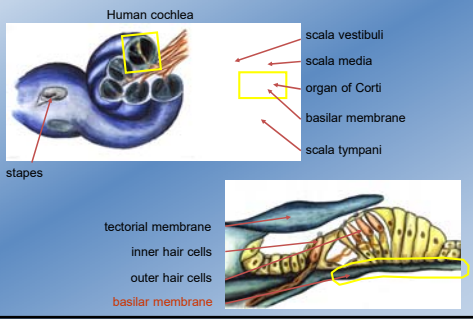
3

Sound enters the human ear



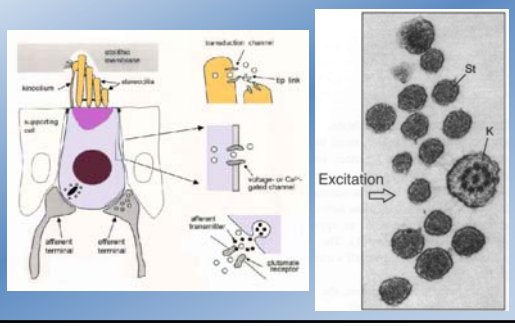
4

The cochlea and the organ of Corti



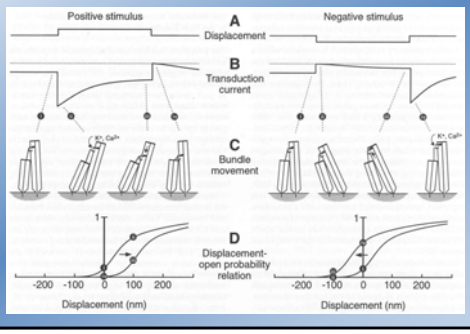
5

Anatomy of a Hair Cell



6

Mechanoelectrical Transduction

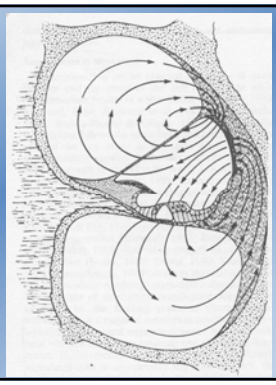


7

Finding the Silent Current

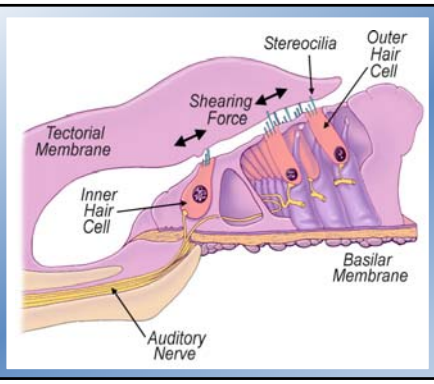
A standing current that powers:

1. mechanotransduction
2. cochlear amplifier



8

Organ of Corti



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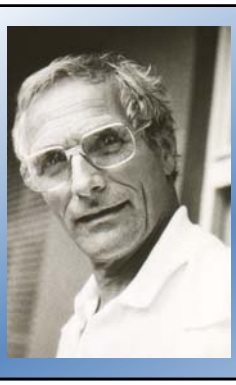
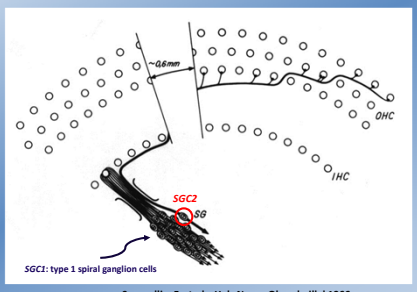


1966 - Heinrich Spoendlin

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

10

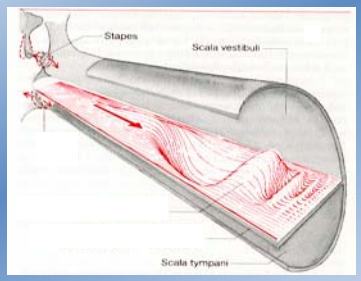
Acoustic world enters via SGC1



Spoendlin, Fortschr Hals Nasen Ohrenheilkd 1966

11

The travelling wave



12

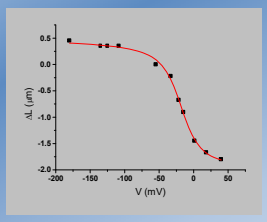
Electromotility & the Cochlear Amplifier

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

13

OHC displacements (ΔL)

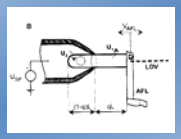
1. ΔL ≠ f (current)
2. ΔL ≠ f (calcium)
3. ΔL ≠ f (ATP)
4. ΔL = f (prestin & small anions)
5. ΔL = f (voltage)



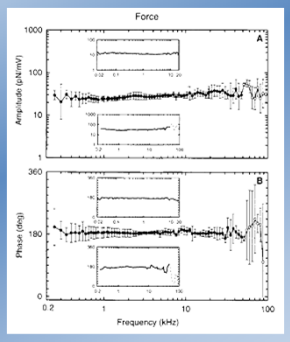
Data of Santos-Sacchi, 1992

14

The OHC generates force at > 80 kHz



Frank et al., 1999



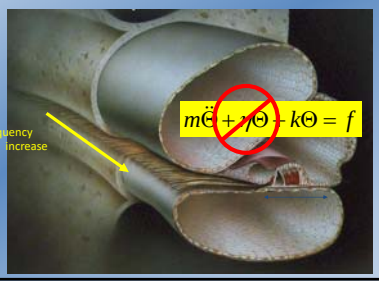
15

The Swing
A Passive Filter

The Swinger
An *Active* Filter

16

Viscosity limits the frequency of cochlear vibrations



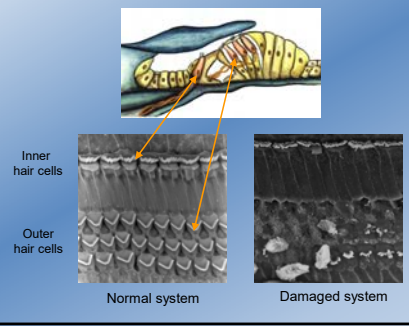
17

3000 Swings

Compton's Interactive Encyclopedia, 1997

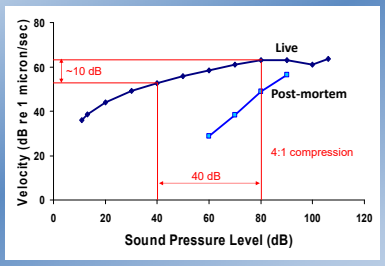
18

Normal versus impaired cochlea



19

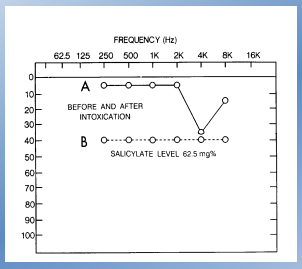
Damage to the outer hair cells



(Ruggero et al., 1997)

20

Aspirin Ototoxicity



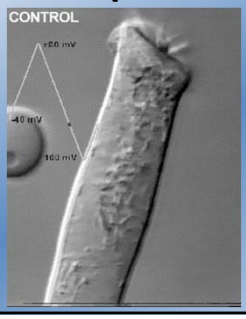
Male (60 yrs) with hearing loss

Myer & Bernstein, 1965

Salicylate blocks otoacoustic emissions - McFaddden & Plattsmier, 1984

21

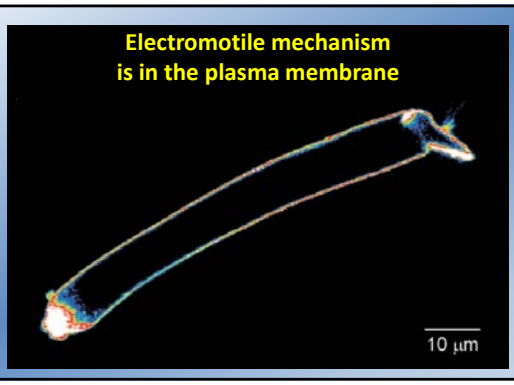
Aspirin Ototoxicity



Salicylate application blocks
OHC electromotility

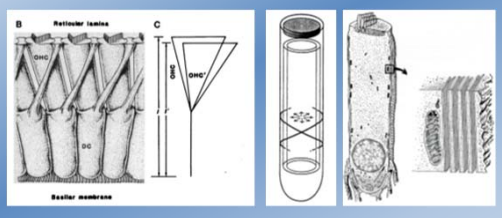
22

Electromotile mechanism is in the plasma membrane



23

OHC is a hydrostat with unusual cytoarchitectonics

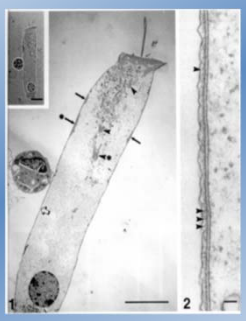


Brownell et al., 1985

Brownell, 1990

24

Plasma membrane folding

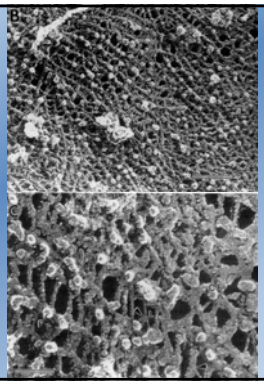


Dieler et al., 1991

25

The Orthotropic Cortical Lattice

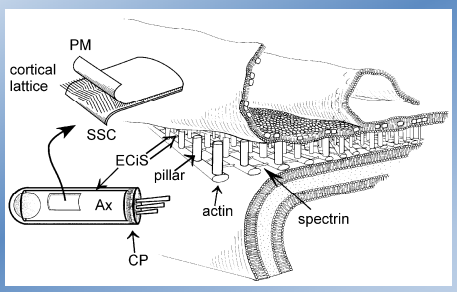
- Actin - circumferential
- Spectrin - longitundinal
- Pillars - radial



Holley et al., 1992

26

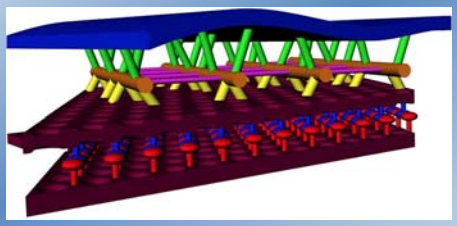
The OHC lateral wall: a trilaminate structure



Brownell and Popel, 1998

27

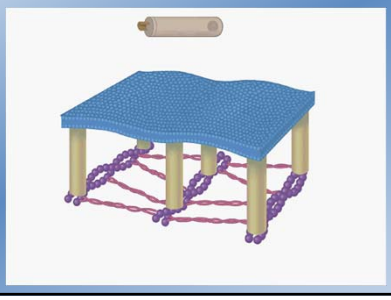
Electron tomography update of lateral wall



Triffo et al Front Cell Neuro, 2019

28

OHC electromotility – voltage induced change in membrane curvature



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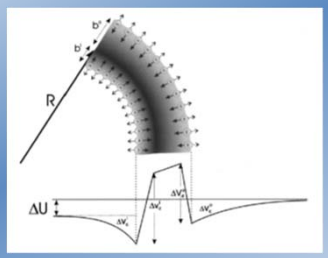
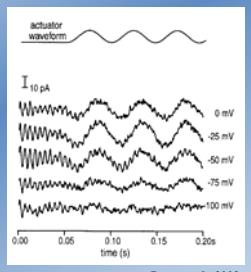
Converse flexoelectricity



Petrov and Sachs, Phys Rev E, 2002

30

Direct flexoelectricity



Dong et al., 2002

31

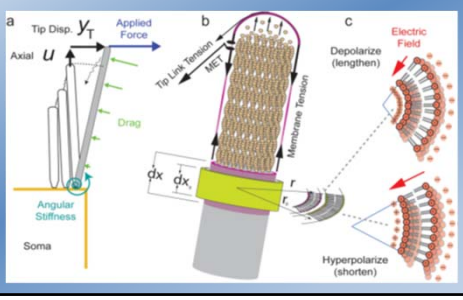
Non mammals have Cochlear Amplifiers but *NO* OHCs

- 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

32

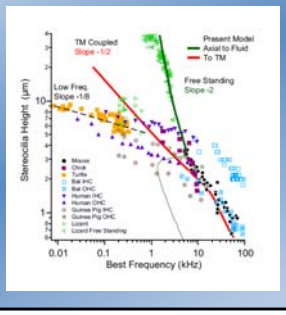
Stereocilia as flexoelectric motors

from: Breneman, Brownell & Rabbitt - 2009



33

Predicts stereocilia length



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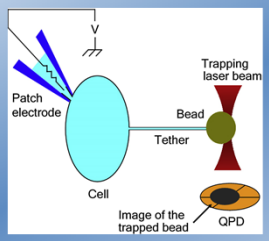
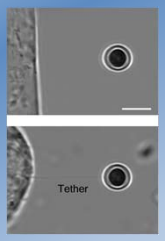
Electromechanics in membrane tethers

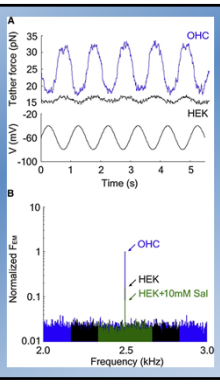




Brownell et al., 2010

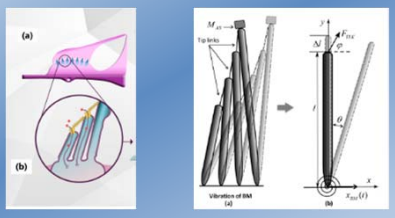
35

Flexoelectric model compatible with optical tweezers results



36

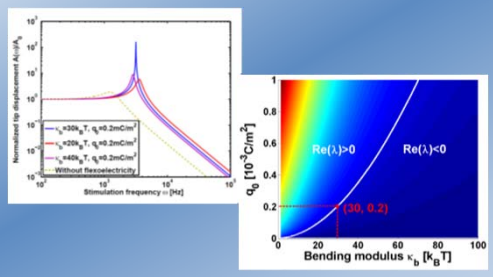
Add an acsessory mass and explicitly include cationic influx through MET



Deng et al., Mech Physics Solids. 2019

37

Selectivity and critical limit cycle



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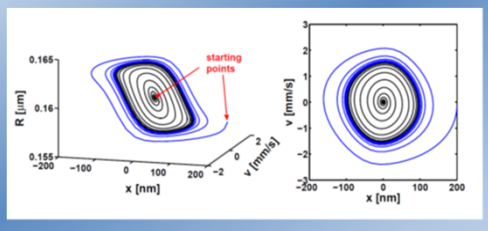
Convergence to a critical limit cycle



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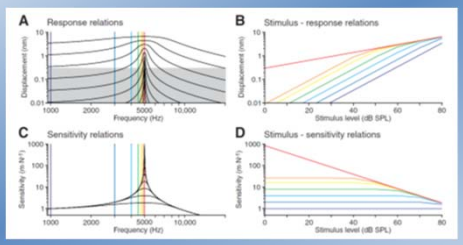
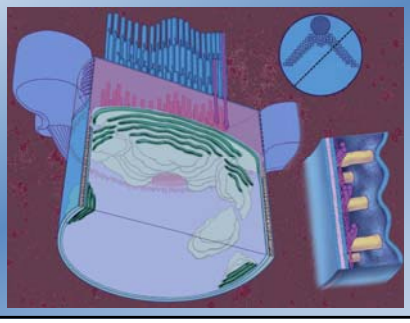
Benefits to hearing



Hudspeth et al, 2010

40

Trilaminate Structures



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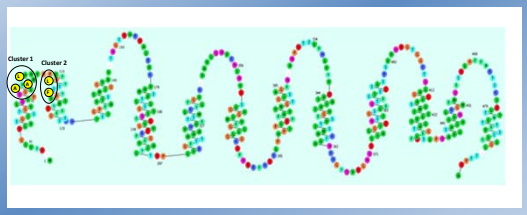
Prestin



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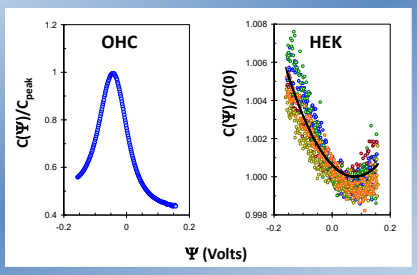
Prestin associated charge movement



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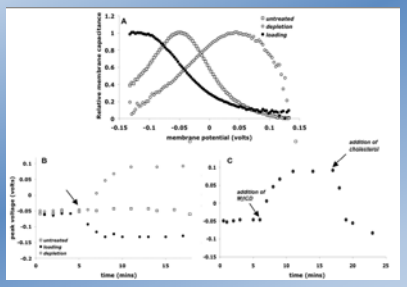
Cholesterol level shifts V_{pkc} in OHCs



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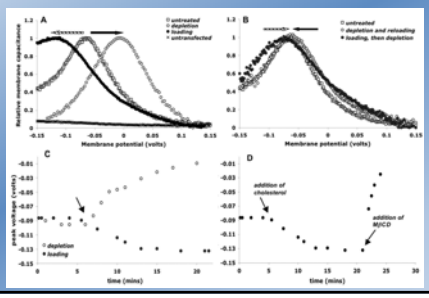
Cholesterol in prestin transfected HEK cells



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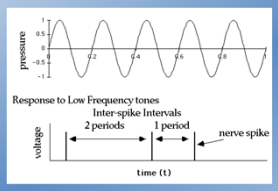
Phase locking & vector strength

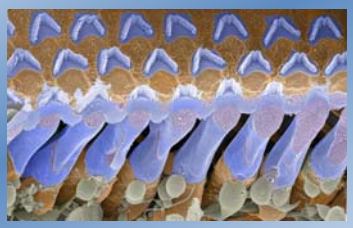


Vector strength: Each spike is represented by a vector of unit length and direction equal to the phase, *p*, of the spikes ($0 < p < 2\pi$) relative to the signal. The sum of these vectors, normalized by the number of spikes, gives the vector strength ***r***. With perfect synchrony, ***r*** =1; if there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

Goldberg and Brown, 1969

48

Outer Hair Cells are surrounded by fluid



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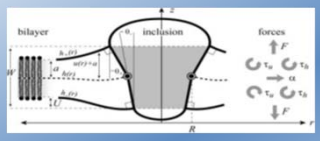
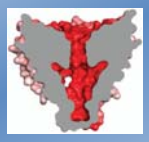
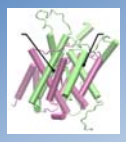
Bilayer-inclusion model



Wiggins & Phillips, 2005



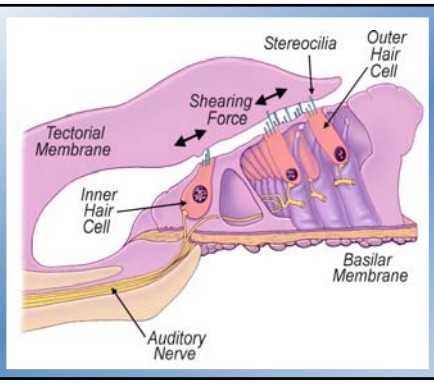
Na $_v$ Channel , Payandeh et al, 2011



Prestin, Gorbunov et al, 2014

50

Organ of Corti



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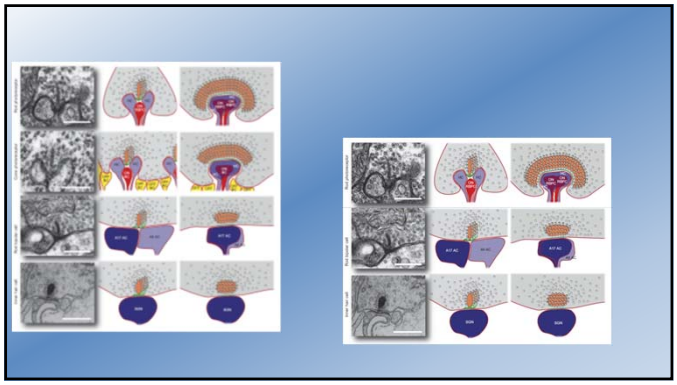

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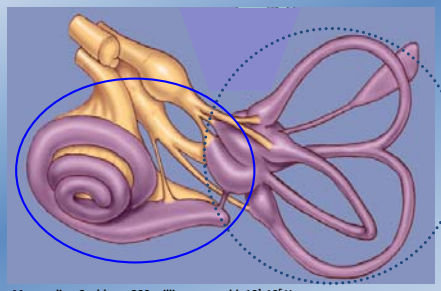
Inner Ear Mechanoreceptor Organs

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



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

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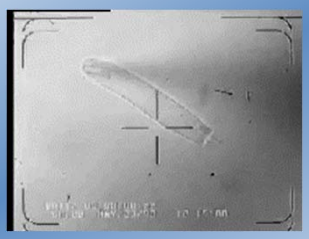
Outer hair cell electromotility



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

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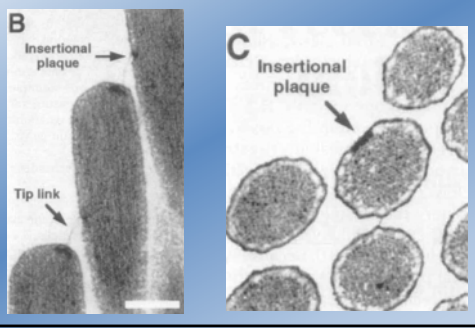
Mechanoelectrical Transduction



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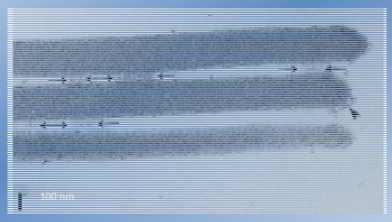
Harnessing membrane EMF by stereocilia



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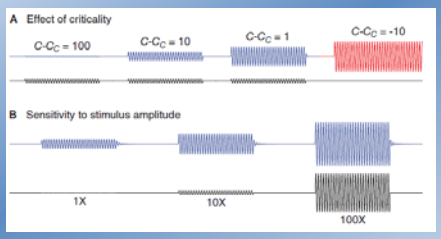
Potential impact on mechanics



Hudspeth et al, 2010

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