Cochlear Mechanics: A Sideways Look

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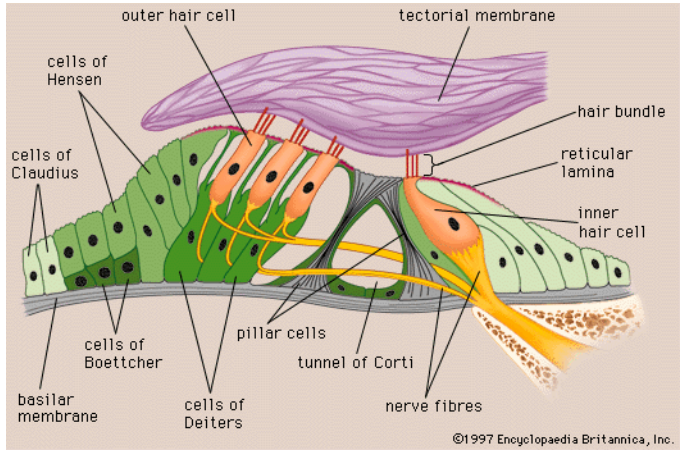


These are issues that arise in viewing the cochlear mechanics literature. Given the complexity of this literature, they may initially appear simplistic. But the challenge to dismiss them or answer them should be worthwhile.

1. The extent of intrinsic damping

Gold's model [1] of viscous damping of a miniature piano string in aqueous fluid is not very appropriate for the basilar membrane (BM). Passive damping of the resonance of a small elastic region separating two aqueous chambers may actually be much more consistent with observed critical bandwidths [2]. This raises the possibility that active mechanisms, combined with what looks rather like an enhancement of viscous damping due to the structural features of the organ of Corti, may serve to modulate damping and provide a trade-off between frequency selectivity and transient resolution, rather than simply to counter viscosity.

2. The nature of the inertial mass

The density of most BM structures cannot greatly exceed that of the fluids, so the effective inertial mass in BM resonance is substantially a function of the pattern of surrounding fluid flow. Contributions to effective mass are proportional to the square of local fluid velocity, and for divergent flow are therefore dominated by the varying size and shape of the local zones of maximum displacement around the BM and within a travelling wave. This introduces non-linearities and means that local effective mass and resonant frequency may drop for a travelling wave that is slowing down and approaching its resonant point, leading to sharpening of the activation peak.

3. The consequence of Outer Hair Cell (OHC) depolarisation

Though BM displacement towards scala media is generally agreed to cause OHC depolarisation, it seems unclear whether the result of this depolarisation and consequent shortening of OHCs will shift fluid in the same or opposite direction to the stimulus. Even an attempt to answer this directly [3] seems equivocal, since imposed current across the BM into scala media will (as observed) have depolarised the apical OHC membranes, but will simultaneously have hyper-polarised the basal portions to an uncertain extent.

4. The role of active negative stiffness

It is tempting to regard negative stiffness of BM structures (in which an active internal mechanism produces force in the same direction as displacement [4,5]) as providing amplification. The internal force adds to the effect of external force at frequencies below resonance. However, without a phase shift this internal

force (in phase with the displacement) does not do work and add energy to the system: the increased energy of displacement comes from greater work done by the external force. This is the opposite of the active energy feed into a travelling wave that is required to produce cochlear amplification. A phase delay is in fact inevitable as soon as such a mechanism operates at increased frequency, but with a negative active stiffness this leads to extraction of energy from the system, similar to viscous energy dissipation. To achieve negative damping and energy feed into a BM disturbance (true amplification) an active force must act with positive stiffness and a phase delay $\leq \pi$ (optimally $\pi/2$). The physiological role of active negative stiffness must surely be something different. The benefits from positive active stiffness (which - subject to the uncertainties of the previous paragraph - may be generated by OHC prestin mechanisms) can arise in two ways [6]: firstly by reducing the energy loss from a travelling wave as this passes over basal regions of the BM that are actively stiffened for frequencies below local resonance, and secondly by feeding energy into the wave as the resonant point is approached, due to an increasing phase lag.

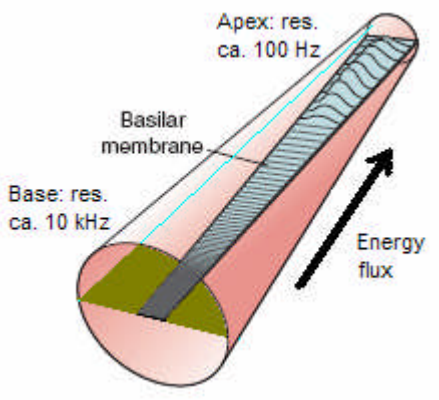
5. The significance of OHC membrane capacitance

In considering the possible role of OHC membrane potential changes and the prestin motor in cochlear amplification, the attenuation at audio frequencies due to the membrane capacitance is often considered a serious problem. However, if the effect of OHC prestin is actively to stiffen the BM in response to low frequency pressure changes, then it is this capacitance that can provide the phase lag needed to feed energy into the travelling wave displacement at frequencies approaching resonance. Critical parameters are two local ratios: that of the OHC membrane time constant τm to the time constant for passive viscous damping of energy in free oscillations ($=\alpha$), and that of the (low frequency) active to passive stiffness ($=\beta$). Calculations under typical conditions show that amplification increases with α up to a point where α is comparable to β, above which instability may occur. An interesting possibility is that the value of τm (and hence the amplification) may drop significantly when there is increased channel conductance due to large amplitude stimuli, thereby introducing a degree of compressive non-linearity.

1. Gold T (1949) Proc R Soc Lond B Biol Sci 135, 492-8
2. Gardner-Medwin AR (2006) Proc Physiol Soc 3, DC2 [also 7]
3. Mammano F & Ashmore JF (1993) Nature 365, 838-41
4. Martin P, Mehta AD & Hudspeth AJ (2000) PNAS 97, 12026-31
5. Kennedy HJ, Crawford, AC & Fettiplace R (2006) Nature 433, 880-3
6. Gardner-Medwin AR (2007) Int J Audiology 46, 652 [also 7]
7. see further details at: http://www.ucl.ac.uk/~ucgbarg/pubres.htm#cochlea

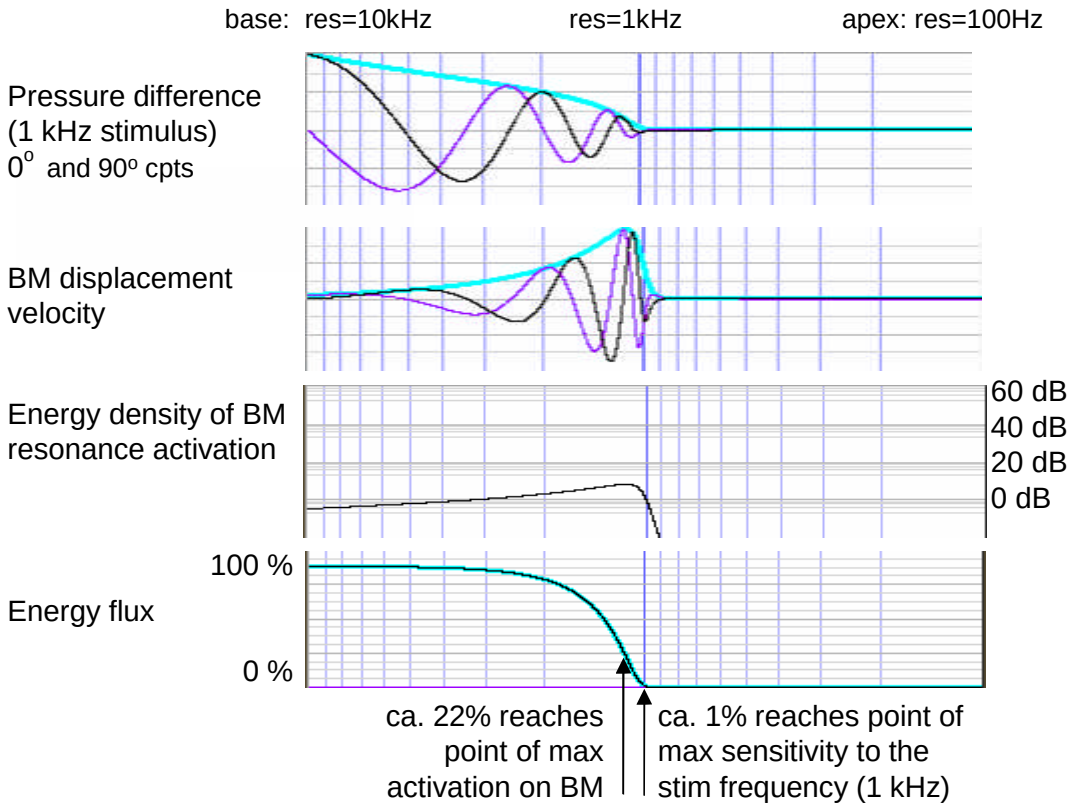
Travelling waves on a resonant transmission line:

The issues addressed here and the simulations employed only treat the BM as a simple 1-dimensional structure: a resonant transmission line. Of course the Organ of Corti is more complex in ways that are doubtless important, but these need not be introduced here.

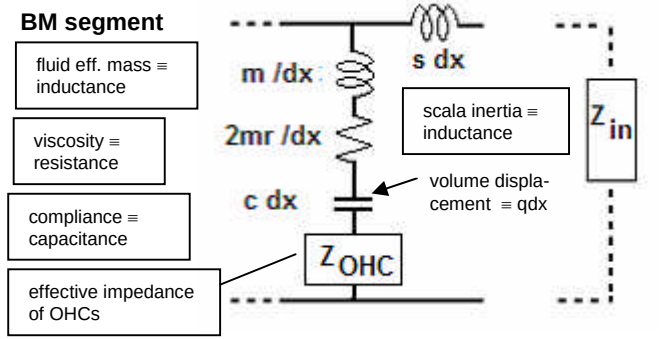


Simulation treats a continuous transmission line (resonance f=10 kHz to 100 Hz) as below. The time constant for passive amplitude decay is generally set uniformly at 2 ms (r=0.5 ms^{-1}).

What happens to the energy fed in at the base? [Passive cochlea, stimulus 1 kHz]



Equivalent circuit



Disturbance travels from left (base) to right (apex)
q = vol displaced / unit length : m^2 [≡ C/m]
c = compliance = q / pressure : m^2/Pa [≡ F/m]
m = generalised mass for transverse flow
= 2 energy / $(dq/dt)^2$: kg m^{-3} [≡ Hm]
s = series mass = 2 energy / $flow^2$: kg m^{-5} [≡ H/m]
r = rate constant for resonance decay : s^{-1} [≡ Ω/H]

Countering energy loss from the travelling wave

Energy is progressively absorbed from a passive travelling wave before the resonant point is reached. The most sensitive part of the cochlea may be exposed to less than 1% of stimulus energy.

Early after stimulus onset (less than the time constant for viscous energy dissipation), lost energy goes into building up BM displacements in the basal cochlea. Once a steady state is reached, the lost energy dissipates by viscosity. If OHCs act to stiffen the BM between stapes and the resonant point, energy loss can be reduced.

Frequency-independent stiffening

If the basal cochlea were rendered wholly stiff to all disturbance, energy delivery could in principle increase 100-fold (20 dB). Simulation (below) shows that a 15 dB increase could be achieved with just a 50% increase in stiffness.

Though substantial, this increase is much less than the OHCs are believed to account for. The mechanism would also be highly non-linear.

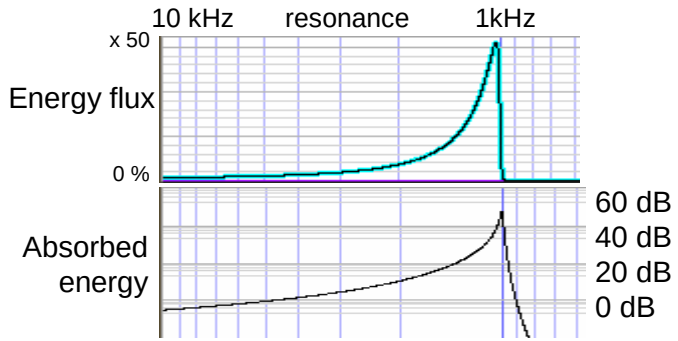
Note that the abrupt change of stiffness here causes standing waves by reflection.

Stiffening by OHC negative feedback

If the OHCs **<u>oppose</u>** BM movement with force proportional to displacement (a linear homeostatic mechanism), this effectively stiffens the local BM up to a limiting frequency. The high frequency roll-off has 2 desirable consequences:

1. stiffening is greatest for low frequency components for which the energy needs to be transmitted further apically

2. the phase lag results in energy feed, amplifying the energy sent forward in the travelling wave



Negative feedback (stiffness at low freq x 4.1 everywhere), with uniform 3dB roll-off at 100 Hz (1st order filter, time constant 1.5 ms). Stimulus: 1 kHz. Viscosity x2 to reduce sharpness of the activation peak. There is a ca.50-fold (17 dB) increase in energy flux and ca. 40dB increase of peak sensitivity compared with the passive model.

Mechanism

Active BM stiffening in this model enhances sensitivity by 3 mechanisms:

(i) Concentration of energy delivery to the region most sensitive to each frequency component

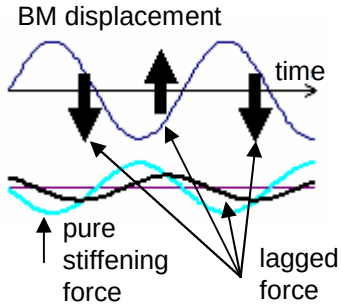
(ii) Energy feed into the travelling wave, amplifying the stimulus energy

(iii) Negative damping at the resonance point, allowing activation to build up for longer times

Comparable increases may arise from each source, depending on model parameters. To achieve enhancement of the order of 40 dB as suggested experimentally for the contribution of OHCs, it is probably not sufficient just to make the basal Organ of Corti more rigid in response to a detected stimulus (left panel above, (i) alone).

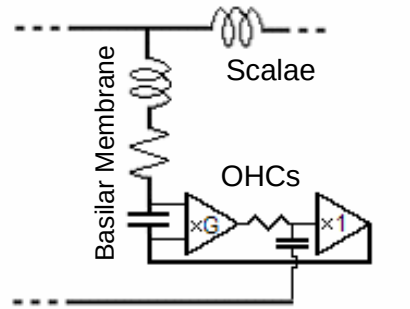
The effect of lag

Mechanisms (ii), (iii) arise naturally if OHCs attempt to oppose detected movements of the BM, since there are intrinsic delays and phase lags. A lagged stiffening force has a component that is in phase with velocity, feeding energy into the travelling wave and opposing viscous drag.



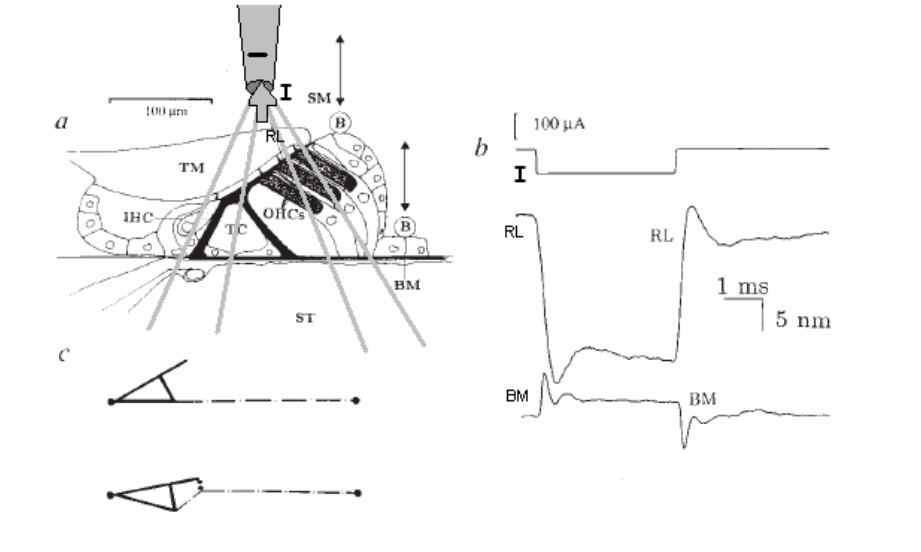
Equivalent Circuit

The simplest equivalent circuit is shown below. At low frequencies this reduces the effective BM capacitance (analogous to compliance) by a factor 1+G, equivalent to introducing a series capacitance C_{BM}/G. The effect of the OHC filter is to increase the series capacitance at higher frequencies and introduce a negative series resistance.



Conclusion

*Most cochlear models assume OHCs enhance rather than oppose BM displacement at low frequencies. Surprisingly, the issue seems somewhat unclear experimentally. Mammano & Ashmore ('93) showed that extracellular current causing apical depolarisation of OHCs (as occurs with upward displacement of the BM) led to downward movement of the Reticular Lamina (**RL**) and a smaller upward movement of BM. This might be taken to support conventional models, but there is some uncertainty about whether the basal end of the OHCs may have been significantly hyperpolarised in these experiments. Undoubtedly the RL and BM are squeezed together with OHC depolarisation, expanding the tissue radially. This could have unexplored consequences, including possible downward pressure on the attached BM and a reduced mass of fluid moving perpendicular to the BM.*


a
100 µm
I
SM
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RL
TM
IHC
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OHCs
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c
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100 µA
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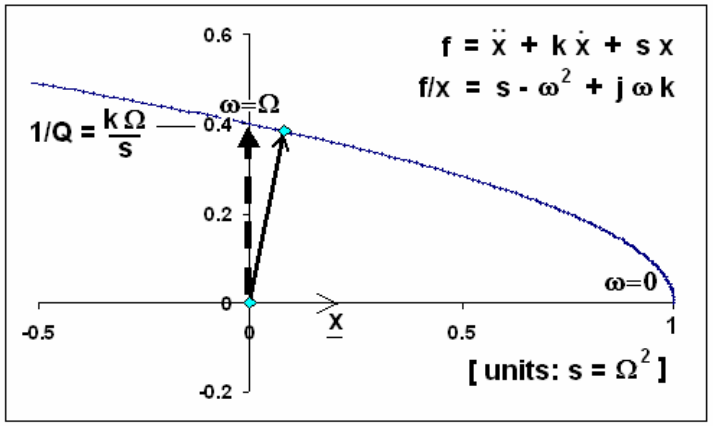
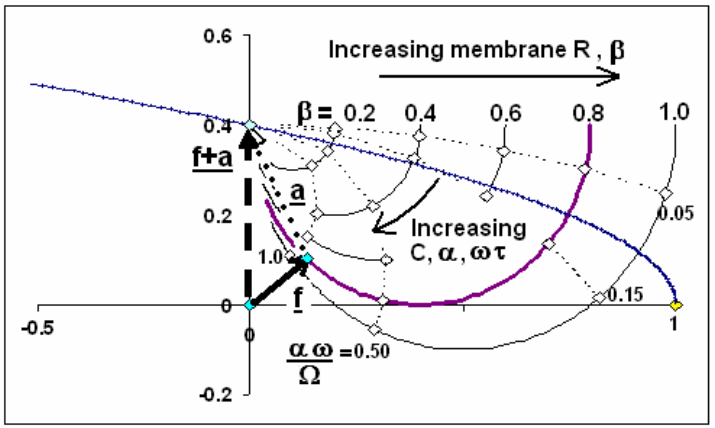
RL
1 ms
5 nm
BM
BM

Response of a local BM resonator:



Passive resonance:
Argand plot of the force required per unit displacement at frequencies (ω) from zero to well above resonance.
DASHED ARROW: force at nominal resonance ($\omega=\Omega=(s/m)^{0.5}$).
FULL ARROW: minimum force (corresponding to maximum gain) achieved at frequency $\omega=0.95\ \Omega$.
The passive quality factor Q is taken as 2.5 ($k=0.4\ \Omega$)

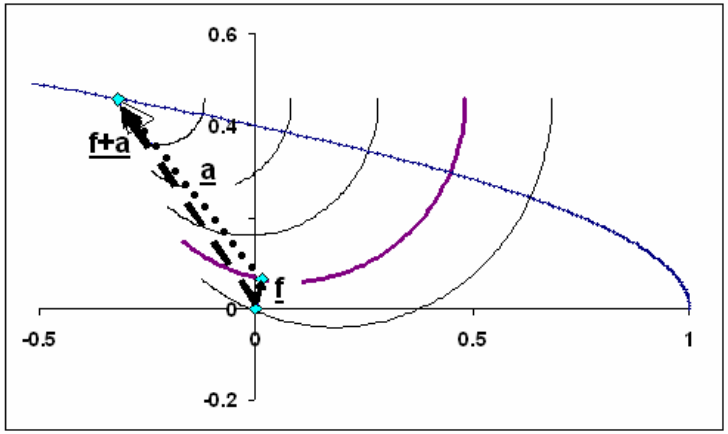
[For simplicity, mass is normalised: m =1 and f/x is plotted relative to passive stiffness s. The displacement vector (x) is horizontal.]



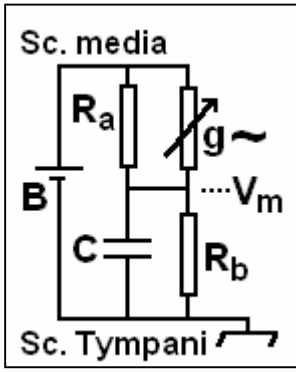
The effect of active stiffness:
Net force per unit displacement (f+a) is the sum of external force (f) and an internal active force a . Active stiffening increases passive stiffness (s) by βs at low frequency and is attenuated with a phase lag at higher frequencies, due to a membrane time constant $\tau = \alpha / k$ (see below).

Semicircular loci show the origin of the vector a for given values of β . Dotted loci show the origins for indicated values of $\alpha\omega/\Omega$. The illustrated forces are for $\omega=\Omega$, $Q_{passive}=2.5$, $\beta=0.8$, $\alpha=0.9$.

High gain corresponds to a short vector length | f |, achievable with $\beta \simeq 2/Q_{passive}$ and $\alpha \simeq \beta$. The illustrated gain (for clarity) is increased only 2.4x here, though larger β can yield arbitrarily large gains or instability (unless α is reduced).



Behaviour at frequencies >Ω:
Max gains occur with $\omega>\Omega$. With $\beta=0.8$ and $\alpha=0.52$ the passive Q=2.5 is increased to Q=15, with the peak resonance at $\omega=1.15\Omega$.



Equivalent OHC circuit:
Active force a is assumed proportional to ΔVm caused by sinusoidal conductance fluctuations Δg , in phase with displacement Δx. Membrane time constant τ =RC where 1/R= 1/Ra+1/Rb. The ratio of τ to the viscous damping t.c. (1/k) is defined as $\alpha = \tau k$.