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ABSTRACT

R, C and RC in Outer Hair Cells : What aspects of function do they constrain?

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Two recent papers (1,2) challenge a concept that is widely cited in OHC literature: the supposed 'RC problem' where OHC membrane time constants (τ=RC) exceed 1/(2π x the local characteristic frequency (CF)), especially in the basal (h.f.) cochlea. This, it has often been argued, is a problem because it reduces the stimulus to prestin, and hence the amplification of signals at CF. The recent papers point out that this is really a 'C problem' not an 'RC problem' because only lowering of C (not R) can increase the OHC potential changes (ΔV_m). This is easily derived from a simple R,C model. The transfer function (T) for V_m changes due to a sensor current (I) with angular frequency $\omega=2\pi f$ fed into the cell is:

$T = \Delta V_m/I = R/(1+j\omega RC)$; $|T| = R/\sqrt{(1+(\omega RC)^2)}$

If $RC=5/\omega_{CF}$, the absolute transfer gain |T| at CF is 98% of its maximum possible value ($1/\omega_{CF}C$). If R is reduced, |T| drops to 71% with $\omega_{CF}RC=1$, and 20% with $\omega_{CF}RC=0.2$. This makes intuitive sense because reducing R introduces a conductive shunt that diverts sensor current away from its useful job charging and discharging the capacitance (with V_m phase lag $\pi/2$) to oppose damping and enhance vibration.

Clearly, high frequencies and high C both constrain the transfer gain of OHCs, as is well known. Just how much, and the significance of non-linear and piezoelectric factors are focuses of attention. But what constraints are set by R? As shown above, it should not be much less than $1/\omega_{CF}C$ to avoid limiting OHC negative damping at CF. But data suggest it is not much higher than this value, especially in l.f regions. Raised R ($>1/\omega_{CF}C$) would lower the frequency below which ΔV_m becomes predominantly in phase with I, which would restrict a second (l.f.) benefit of OHC function. This is the negative compliance (stiffening) that can reduce power loss from l.f. components of the cochlear travelling wave - yet to reach their zones with matching CF. Where a phase lag leads to negative damping, in phase forces should (at least in simple models) produce the necessary negative compliance.

1. M van der Heijden, A Vavakou (2022), Hearing Res, 423, 108367 Rectifying and sluggish: Outer hair cells as regulators rather than amplifiers
2. A Altoè, CA Shera (2023), J Assoc Res Otolaryngol, 24,129–145. Long Outer-Hair-Cell *RC* Time Constant: A Feature, Not a Bug, of the Mammalian Cochlea

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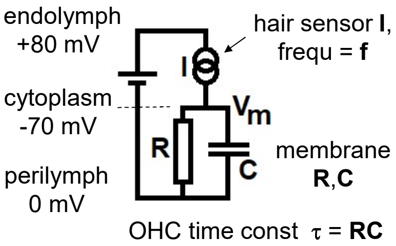


What is the ‘RC Problem’ ?

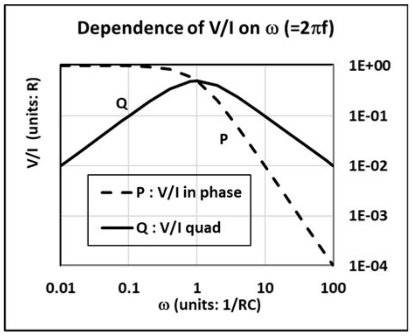
The OHC time constant **RC** can be >>**1/2πF** at the local char. frequ. (CF) in basal cochlea, supposedly too large for h.f. Vm changes to support prestin motility and resonance amplification.

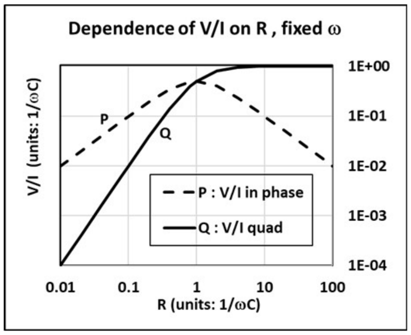
What are the OHC inputs & outputs?

- $\mathbf{V_m}$ changes affecting prestin are caused by hair current **I** at frequency **f**
- **I** is essentially independent of **R,C** – driven by a large **V** gradient & small $\mathbf{\Delta g_m}$
- The transfer function **T** = **V/I** = $\mathbf{R}/(1+(\omega \mathbf{RC})^2)\ (1\text{-}j\ \omega\mathbf{RC})$ where ω=**2πf**
- **T** has in-phase (**P**) and quadrature (**Q**) components with different roles in motility
- **P** increases stiffness, reducing l.f. energy loss. **Q** generates negative damping.

Is the OHC a low-pass filter?

- Yes, the transfer function **T** (=**V/I**) has a ‘corner’ frequency ω=1/**RC** above which **P** & **Q** components fall with increasing ω.
- Below this frequency, **P** is dominant (enhancing l.f. stiffness), while above it **Q** is dominant, providing –ve damping.
- At corner frequency **Q**=**P**=0.5**R**=0.5/ω**C**.
- Low-pass favours l.f. energy retention
- **V/I** at high frequencies requires low **C** (the “C problem” in Refs. 1,2).





ωCR>>1 increases Q transfer

- Given ω & **C,** raising **R** always increases the **Q** component of **V/I**, even if ω**CR**>>1.
- If ω**CR=1** at local resonant frequency and **R** is raised to give ω**CR=10,** then **Q** increases ×2 and **P** falls ×0.2.
- The same change brought about by raising **C** would lower both **Q,P** (**Q**×0.2, **P**×0.02).

Combining a simple resonant system with OHC feedback

- In a simple resonant system, force **z** required to produce displacement **x** at ang. freq. ω is **z = (s - mω^2- j kω)x**
- The in-phase **z** component opposes stiffness (**s**) and generates acceleration (**mω^2**)
- The quad component (phase advanced) opposes viscous drag.
- OHC force driven by Vm (with **I** $\propto$ **x**) yields additional stiffness (in phase with **x**) and negative drag.
- Combining the two means that stiffness below resonance is effectively enhanced and drag is reduced or eliminated.
- NB graphs show **z/x** (force/displacement). Both in phase & quad components must be small at the same freq. for a resonance peak (with large |x/z|).

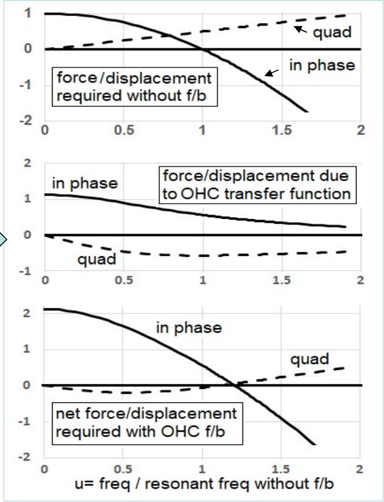
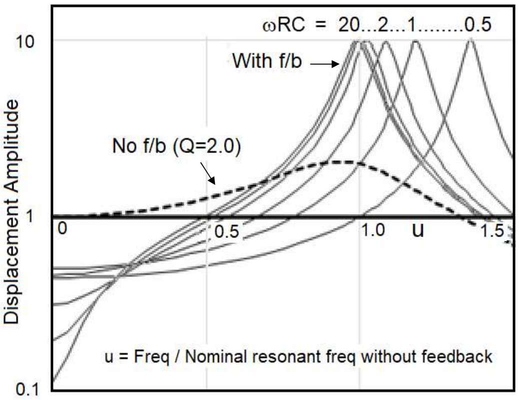


Illustration is for a simple mechanical resonance with $\omega_{CF}=\sqrt{(\mathbf{s/m})}$, k=0.5**s**/$\omega_{CF}$ (i.e. **Q**=2). OHC f/b is with ω**CR**=1 at CF and with f/b strength set to 90% of what would yield instability. Peak resonance with f/b has **Q**=19.5 at a frequency 20% above CF without f/b (musically, a shift of about a minor third).

High R, C, ωRC ? Are they good or bad?

- High **ωC** increases sensor currents required to produce OHC Vm changes. Low **C** is important at high frequencies.
- High **R** (ω**CR>1** at CF) increases the quad Vm changes important for –ve damping.
- **ωRC>1** ensures that the resonance peak with OHC f/b does not shift to significantly higher frequencies than the basic mechanical resonance.
- High **R** may not be compatible with other aspects of OHC membrane physiology.



"High C bad, High R good" is a mantra that makes some simple intuitive sense, since a major function of sensor hair current is to produce V changes on the OHC capacitance **C**, and this is not aided by diverting some of that current through an increased membrane conductance.