The outer-hair-cell RC time constant: A feature, not a bug, of the mammalian cochlea

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Abstract The cochlea of the mammalian inner ear includes an active, hydromechanical amplifier thought to arise via the piezoelectric action of the outer hair cells (OHCs). A classic problem of cochlear biophysics is that the long resistance-capacitance (RC) time constant of the hair-cell membrane produces an effective cut-off frequency much lower than that of most audible sounds. The long RC time constant implies that the OHC receptor potential—and hence its electromotile response—decreases by several orders of magnitude over the frequency range of hearing. This “ RC problem” is often invoked to question the role of cycle-by-cycle OHC-based amplification in mammalian hearing. Here, we use published data and simple physical reasoning to show that the RC problem is, in practice, a relatively minor physical issue whose importance has been unduly magnified by viewing it through the wrong lens. Indeed, our analysis indicates that the long RC time constant is actually beneficial for hearing, reducing noise and distortion while increasing the fidelity of cochlear amplification.

Introduction

To boost the sensitivity and dynamic range of hearing, the mammalian inner ear embeds a physiologically vulnerable active process that amplifies sound-evoked motions as they propagate as waves along the cochlear spiral (Shera, 2007). Although operation of the cellular amplifiers requires prestin-based somatic outer-hair-cell (OHC) electromotility (Brownell et al., 1985; Zheng et al., 2000; Liberman et al., 2002; Dallos et al., 2008), serious doubts persist about whether the piezoelectric mechanism can respond with the speed and vigor necessary to boost the power carried by waves of high frequency. This vexing subject has been the focus of much research and debate, starting shortly after the discovery of OHC electromotility (Santos-Sacchi, 1992; Housley and Ashmore, 1992) and continuing to the present day (Vavakou et al., 2019; van der Heijden and Vavakou, 2021; Santos-Sacchi and Tan, 2018). There are two distinct and largely independent issues. One concerns the kinetics of prestin, which may not be fast enough to support high-frequency electromotility (Santos-Sacchi and Tan, 2018).

The second issue, more widely appreciated, arises because OHC electromotility is driven by transmembrane voltage (Santos-Sacchi and Dilger, 1988). Electrically, the OHC membrane consists primarily of a resistance (R) and a shunt capacitance (C) that combine to create a low-pass filter with time constant $\tau = RC$. With one exception (Johnson et al., 2011), both direct (Housley and Ashmore, 1992) and indirect (Vavakou et al., 2019) observations indicate that in the basal, high-frequency region of the cochlea, the time constant τ is much larger than the characteristic oscillation period

of the basilar-membrane (BM) mechanical response. Equivalently, the cutoff frequency of the OHC low-pass filter is much lower than the maximum frequency of hearing. Consequently, the low-pass filtering is presumed to render the oscillatory component of the OHC receptor potential too small to subserve high-frequency amplification. Dubbed the outer-hair-cell “RC time-constant problem” (Ashmore, 2008)—or, more compactly, the “RC problem” (Vavakou et al., 2019)—the dilemma has prompted the search for compensatory mechanisms (Nobili and Mammano, 1996; Lu et al., 2006; Dallos and Evans, 1995; Ospeck and Iwasa, 2012) while challenging the biophysical relevance of “cycle-by-cycle” electromotility to cochlear amplification (Santos-Sacchi, 1992; van der Heijden and Vavakou, 2021). Ultimately, any definitive evaluation of the significance of these two issues awaits a more complete understanding of OHC dynamics *in situ*, as the mechanical load greatly influences their electromechanical properties (Ashmore, 1987; Mountain and Hubbard, 1994; Liu and Neely, 2009; Iwasa, 2017; Rabbitt, 2020).

In this paper we side-step the issue of prestin kinetics and deal solely with the RC problem. In effect, we follow classic results about the speed of the OHC “motor” (Frank et al., 1999), although these have recently been questioned (Santos-Sacchi and Tan, 2018). To bring the RC problem maximally to the fore, we play devil’s advocate and purposely ignore the many proposed avenues for ameliorating the problem. These include the entirely plausible possibilities that (i) dynamic interactions with realistic mechanical loads (Iwasa, 2017; Rabbitt, 2020), (ii) the tonotopic variation of OHC electrical properties (Johnson et al., 2011), and (iii) the voltage-dependence of OHC basolateral currents (Housley and Ashmore, 1992; Perez-Flores et al., 2020) may all make beneficial contributions to high-frequency electromotility, both individually and in combination. Thus, we consciously inflate the RC problem to its maximal size. Nevertheless, our analysis of this artificially grim, worst-case scenario reveals that, despite its rather long RC time constant, the OHC still produces high-frequency (>50 kHz) motile responses comparable to or greater than the motion of the basilar membrane (BM) measured at moderately high sound levels. These results are consistent with recent *in vivo* recordings from the 10 kHz region of the mouse cochlea, which indicate that high-frequency OHC electromotile responses can be large compared to the motions of the surrounding tissue (Dewey et al., 2021).

Furthermore, we draw on functional analogies with existing electronic circuits to elucidate multiple ways that the long OHC-membrane time constant appears beneficial for hearing. Among these benefits are significant reductions in the distortion and noise that are the inevitable byproducts of active, nonlinear OHC-based amplification.

A linearized model of the OHC membrane

To illustrate the ostensible problems that arise from the electrical properties of the OHC, we outline a simple, albeit over-linearized treatment of the generic electrical model of the OHC shown in Fig. 1(a). Our treatment follows that of studies that argue against the significance of cycle-by-cycle OHC amplification. Briefly, mechanically-gated mechanoelectrical transduction (MET) channels drive the electrical response of the OHC basolateral membrane. The electrical impedance of the basolateral membrane is determined primarily by (i) outward K^+ currents, whose action is collectively represented by a voltage-dependent resistor (Johnson et al., 2011); (ii) the membrane capacitance; and (iii) a complex impedance that captures the electrical effects of the mechanical load on the OHC (Iwasa, 2017). Motion of the OHC stereocilia modulates the ionic current that flows through the MET channels:

$$I_{\text{MET}} = g(\mu)(V_M - V_{\text{EP}}), \quad (1)$$

where μ is the stereocilia displacement, $g(\mu)$ is the transduction function (units of $[\Omega]^{-1}$), V_{EP} the endocochlear potential, and V_M the OHC membrane potential. For simplicity, we ignore the still unresolved effects of adaptation (Caprara et al., 2019) on μ and g . Accounting for such effects in a linearized model amounts to high-pass filtering the model input and does not modify our conclusions.

89 Rewriting V_M as the sum of the resting (V_{REST}) and receptor (V_{REC}) potentials yields

$$I_{MET} = g(\mu)(V_{REST} + V_{REC} - V_{EP}) . \quad (2)$$

90 In the small-signal limit ($|V_{REC}| \ll |V_{REST} - V_{EP}|$), the dependence of I_{MET} on V_{REC} can be neglected, and
91 I_{MET} becomes proportional to the transduction function, $g(\mu)$. When the stereocilia displacement
92 μ is a sinusoid of amplitude A and frequency f , Taylor expansion of $g(\mu)$ leads to

$$I_{MET} \approx I_{MET}(0) + \bar{I}_{MET}(A) + \tilde{I}_{MET}(A) \sin(2\pi f t) + O(A^2) , \quad (3)$$

93 where $\bar{I}_{MET}$ and $\tilde{I}_{MET}$ represent, respectively, the DC and AC components of the MET current. The
94 DC component arises from the quadratic term in the series expansion and reflects the possible
95 asymmetry of the transduction function around $\mu = 0$.

108 **Figure 1. (a)** Simplified model of the OHC
109 membrane potential. **(b)** Over-linearized model of
110 the OHC receptor potential often used to illustrate
111 the RC problem (e.g., *Vavakou et al., 2019*). **(c,d)**
112 Magnitude of the electrical impedance [Z , Eq. (4)]
113 of the RC circuit in panel (b). Panel (c) plots $|Z|$ vs
114 frequency for various values of the RC time
115 constant ($\tau = RC$) when the capacitance (C) is kept
116 fixed; in this case, τ varies linearly with R .
117 Conversely, panel (d) plots $|Z|$ when R and C are
118 covaried with their product, τ , held constant.
119 Together, the two panels demonstrate graphically
120 that at frequencies above the low-pass cut-off
121 frequency, $|Z|$ depends entirely on the
122 capacitance and not on the time constant
123 [Eqs. (4,5)].

To highlight the problem of the OHC time constant in its most severe form, we now (over-)linearize the model of the OHC membrane. For example, we ignore the voltage-dependent activation of basolateral currents (*Housley and Ashmore, 1992; Perez-Flores et al., 2020*). When properly linearized, these introduce inductances in parallel with the capacitance, thereby reducing the hair-cell reactance (*Altoè et al., 2018*).¹ In addition, we ignore the possible salutary effects of the mechanical load [Z_{load} in Fig. 1(a)], which may help reduce the effective membrane capacitance *in vivo* (*Iwasa, 2017*). With these simplifications, the OHC membrane appears as the parallel combination of a resistance and capacitance, driven by a (MET) current generator [Fig. 1(b)]. In this worse-case scenario, the electrical impedance of the OHC membrane becomes equivalent to an RC (low-pass) filter:

$$Z(f) = \frac{R}{1 + i2\pi f RC} , \quad (4)$$

whose associated 3-dB cut-off frequency is $f_c = [2\pi RC]^{-1}$.²

For what follows, we find it convenient to introduce a second current generator, in parallel with the MET current, to quantify the effects of various form of noise on the OHC output.

121 The time constant RC matters less than R and C

122 Figure 1(c,d) shows the magnitude of the OHC impedance [Eq. (4)] for various values of R and C .
123 The resulting curves represent the magnitude of the OHC receptor potential produced by a sinu-
124 soidal MET current of unit amplitude. Figure 1(c) shows the value of the impedance when C is fixed

¹Because it ignores leading-order linear terms that emerge when properly linearizing the basolateral K^+ currents (see *Koch, 2004*), this “straightforward linearization” (*Vavakou et al., 2019*) is not a true linearization of the OHC membrane model. Nonetheless, the simplification appears to capture the OHC motile response *in vivo* reasonably well (*Vavakou et al., 2019; Dewey et al., 2021*).

²In the literature the resting MET conductance is sometimes included in the value of R (e.g., *Johnson et al., 2011*). The definition of the RC time constant requires a linearized model, and linearization when the input of the model is the vibration of the stereocilia leads to representing the MET channels as a current generator [Fig. 1(b)]. We therefore find it more informative to exclude the MET resting conductance from the calculation of R . Indeed, while the MET resting current indirectly contributes to the filtering property of the OHC (by determining resting potential and hence the resting basolateral conductance), once this conductance is determined and “fixed” in the model, the oscillating (AC) component of the OHC potential is independent of the MET resting current.

and R is varied. Although the RC time constant decreases (the cut-off frequency increases) with R , the magnitude response at high frequencies does not change. Equation (4) implies that decreasing R increases the cut-off frequency by reducing the impedance at low frequencies, while leaving it unaltered at high frequencies. (Recall that the cut-off frequency is defined as the frequency where the magnitude falls to 3-dB below its maximum value.) Although one can increase the cut-off frequency arbitrarily by decreasing the response at low frequencies, where $|Z|$ is the largest, such manipulations do not improve the high-frequency response—as recently highlighted by *van der Heijden and Vavakou (2021)*. As a well-known corollary (*van der Heijden and Vavakou, 2021*), “solutions” to the RC problem based on mechanisms that effectively lower the value of R , do not help with the high-frequency operation of the OHC—they simply disable the OHC at lower frequencies.

Figure 1(d) illustrates the complementary scenario in which the RC time constant is held constant while varying the values of R and C . Although the cut-off frequency remains fixed, the response amplitude changes dramatically at all frequencies, depending on the relative value of R and C . In this scenario, $|Z|$ increases in proportion to R or, equivalently, inversely with C . These examples make clear that simply knowing the value of the RC time constant reveals little about the magnitude of the OHC response at high frequencies. This observation has important consequences for OHC biophysics: In OHCs, the membrane capacitance C is small (a few pF) and the resistance R is large (dozens of MΩ).

OHCs in the high-frequency regions of the cochlea operate well above the cut-off imposed by their RC time constant. In this case, the current flowing through the resistance R becomes small compared to that flowing through the capacitor C . Therefore, the AC receptor potential becomes

$$\tilde{V}_{\text{REC}}(f) \approx \tilde{I}_{\text{MET}}/(i2\pi fC) . \quad (5)$$

Equivalently, the MET current required to achieve a given “target” value ($\tilde{V}_{\text{REC}}$) of the OHC receptor is

$$|\tilde{I}_{\text{MET}}(f)| = 2\pi fC|\tilde{V}_{\text{REC}}| . \quad (6)$$

In other words, the so-called “ RC problem” that supposedly limits the high-frequency operation of the OHC reduces to the problem of charging a capacitor to a certain potential: the C problem (© *van der Heijden and Vavakou, 2021*).

Little seems enough: Worst-case parameters yield realistic displacements

To explore whether the membrane capacitance limits the high-frequency operation of the OHC, we apply Eq. (5) to estimate the magnitude of OHC electromotility at the highest frequencies for which systematic mechanical recordings of BM and organ-of-Corti motions are available [namely, in the ~50 kHz region of the mouse cochlea (*Ren et al., 2016b*)]. Again, our focus on the RC problem allows us to ignore possible limits imposed by prestin dynamics. Additionally, we side-step the many unknowns concerning OHC force production by comparing estimated limits on OHC length-changes with BM displacements recorded *in vivo*. The argument goes as follows: if the electrical drive to the OHC can produce motile responses comparable to or larger than the measured motion of the BM (and surrounding structures), then the AC response of the OHC is evidently “large enough,” and membrane filtering does not preclude functionally relevant high-frequency operation.

Again, we suppress any bias towards wishful thinking by perversely imagining a worst-case scenario. Consider, for example, the well-known tonotopic variation in OHC properties. Whereas OHC length and capacitance increase systematically along the cochlear spiral, the MET-channel conductance decreases with position (*Beurg et al., 2006; Johnson et al., 2011; Soons et al., 2015*). For a given AC receptor potential, long OHCs elongate more than short ones (*Frank et al., 1999*). On the other hand, short cells have smaller capacitance, and are therefore more easily charged. The MET conductance determines the amplitude of the MET current, and hence the magnitude of the OHC electromotile response. Since our goal is to make unfavorable parameter choices, we

171 take our hypothetical murine OHCs at the 50-kHz place to be simultaneously (i) short and therefore
172 limited in their ability to elongate and (ii) endowed with membrane capacitance and MET currents
173 representative of OHCs from more apical locations with a much lower CF (*Johnson et al., 2011*). In
174 a nutshell, we not only neglect the known tonotopic variations, we purposely counteract them to
175 inflate the apparent severity of the *RC* problem.

176 Based on the micro-chamber experiments of *Frank et al. (1999)*, we assume that short OHCs ex-
177 pand and contract by ~ 1 nm/mV at frequencies close to 48 kHz. Although the voltage-displacement
178 relation depends on the OHC's mechanical load—which may not be the same in the micro-chamber
179 as it is *in situ*—this estimate is in good agreement with *in situ* values obtained using electrically
180 evoked responses in the excised temporal bone of the guinea pig (see Fig. 2 of *Nowotny and Gum-*
181 *mer, 2006*). We also assume that the available AC MET current is on the order of 1.5 nA—half of
182 the available MET current measured in gerbil OHCs at the 10-kHz place (*Johnson et al., 2011*)—and
183 assume that the OHC capacitance is ~ 4 pF, also based on data from the 10-kHz place in gerbil
184 (*Johnson et al., 2011*).

185 Using these values, we find [Eq. (5)] that our worst-case OHC is capable of elongating on the
186 order of 1.25 nm at 48 kHz. For comparison, vibrational data from the 48-kHz region of the mouse
187 cochlea (*Ren et al., 2016b*) indicate that *in vivo* mechanical movements are close to this value at
188 sound levels of 60–70 dB dB SPL (at 48 kHz, BM and RL responses at 70 dB SPL are less than 3
189 nm). In these experiments, both BM and RL gain at CF decrease with level above 30 dB SPL (where
190 BM motion is ~ 0.2 nm) and are dramatically reduced above about 70 dB. That is, our approximate
191 numerical bound on the magnitude of the OHC electromotile response (1.25 nm) is much larger
192 than the BM displacements measured at low sound levels, where amplification is strongest, and
193 is comparable to BM displacement at moderately high levels, where amplification is greatly re-
194 duced. Note that if this comparison had come out differently—if our approximate upper bound
195 on OHC electromotility had been much less than the displacement of the BM and surrounding
196 structures—then assertions that cycle-by-cycle somatic motility appears too weak to influence in-
197 tracochlear motions at high frequencies would be intuitively compelling. As it turns out, however—
198 and notwithstanding a number of unfavorable assumptions—the comparison demonstrates that
199 the low-pass filtering of the OHC membrane does not, in practice, impose intrinsic limitations on
200 the cell's high-frequency response that compromise its ability to make significant contributions to
201 measured cochlear amplification.

202 For a complementary perspective, we can run the analysis “in reverse” using Eq. (6). Although
203 it is not easy to determine, on theoretical grounds, how much the OHCs need to elongate and
204 contract in order to provide the required wave amplification, we can infer the voltage and current
205 required to drive OHC motile responses comparable in magnitude to the BM vibrations observed
206 at sound levels near the threshold of hearing. Linear extrapolation of the reference data (*Ren*
207 *et al., 2016b*) indicates that a 48-kHz tone at 10-dB SPL—a sound level somewhat smaller than
208 the threshold of the most sensitive auditory-nerve fibers (*Taberner and Liberman, 2005*)—evokes
209 BM responses of ~ 20 pm, requiring voltage swings on the order of 20 μ V, and corresponding MET
210 currents on the order of 25 pA. This current is on the order of the AC current mediated by one or two
211 MET channels.³ Recent *in vivo* recordings from the 10-kHz region of the mouse (*Dewey et al., 2021*)
212 indicate that OHC electromotile responses are approximately 4 times larger than BM vibrations
213 near CF. Assuming that this relationship also holds at higher CFs, the simple model implies that
214 OHC near-CF AC potentials in the 50 kHz region must be ~ 80 μ V near threshold, requiring a driving
215 current equivalent to that mediated by roughly 4–8 MET channels.

216 Following *van der Heijden and Vavakou (2021)*, we note that BM nonlinearities and amplification
217 are observed at frequencies where BM (and RL) responses are ~ 20 dB smaller than at CF (*Ren*

³*Beurg et al. (2006)* report that a single MET channel in the mid-turn of the rat cochlea mediates a current of ~ 12 pA and that the channel conductance increases with CF. If there are approximately 100 MET channels per OHC (*Beurg et al., 2006*), then a single channel in a 10-kHz gerbil cell mediates a current of ~ 3 nA/100 = 30 pA (*Johnson et al., 2011*). Not knowing the single-channel current in the 50-kHz region of the mouse cochlea, we use these two values as proxies.

218 *et al., 2016b*). At these frequencies, the simple OHC model implies, conservatively, that AC receptor
219 potentials on the order of few (2–8) μV are sufficient to elicit OHC displacements comparable to or
220 greater than the near-threshold motion of the BM.

221 These values appear small, although they are somewhat larger than the receptor potentials (<1
222 μV) extrapolated by *van der Heijden and Vavakou (2021)* from *in vivo* intracellular recordings at the
223 16 kHz region of the guinea pig (*Cody and Russell, 1987*). Note, however, that the validity of this
224 extrapolation is unclear. It has long been known that the perforation produced by the microelec-
225 trode *in vivo* has a major impact on hair-cell electrodynamics (*Kros and Crawford, 1990*), with the
226 likely result being an underestimate of the true physiological range of AC receptor potentials (see
227 *He et al., 2004*). Furthermore, the invasive approach adopted in such experiments likely results
228 in reduced cochlear sensitivity. Indeed, *Cody and Russell (1987)* report that in their experiments,
229 OHC responses (AC, near-CF) at sound levels near neural threshold are roughly 10–30 μV , a range
230 of values that compares favorably to the results presented above.

231 **The long RC time constant reduces noise where it matters most**

232 Do such small voltage excursions and the resulting motile responses have any functional relevance
233 in the presence of noise? Multiple noise sources contribute to the OHC transmembrane voltage,
234 including various forms of hydro-mechanical noise that influence the motion of the stereocilia (*Sas-*
235 *mal and Grosh, 2018*). Although the magnitudes of these noise sources are not yet fully character-
236 ized, their effects can be explored in the model by introducing a current source whose output
237 represents the sum of the various forms of white (flat power spectral density), pink ($1/f$), and
238 brown ($1/f^2$) noise expected to be present in the cochlea. These noise sources include, but are
239 not limited to, the thermal noise associated with the OHC membrane resistance, pink noise associ-
240 ated with the kinetics of K^+ transport, stochastic gating of the MET channels, and mechanical and
241 background noise contributing to stereocilia displacement.

242 Note that the OHC membrane filters these noise sources in the same way that it filters the
243 driving MET current, a quantity otherwise known as the “signal” (Fig. 1c). Consequently, the signal-
244 to-noise ratio (SNR) measured in small frequency bands around the stimulus frequency mirrors the
245 ratio of the stimulus-driven MET current to the noise current. Simply put, at any given frequency,
246 the signal-to-noise ratio at the OHC output *is independent of the membrane filtering*.

247 Details of the power spectral density of the inherent electrical noise (i.e., thermal noise and the
248 flickering of MET channels) depend on OHC parameters (e.g., the fraction of MET channels open
249 at rest) for which there is as yet little agreement in the literature. In Appendix 1, we estimate that
250 the inherent electrical noise corresponds to a broadband current source whose root-mean-square
251 (RMS) amplitude is on the order of that mediated by 1–5 MET channels. Interestingly, this range
252 of values closely matches that required to elicit OHC motions near the threshold of hearing (see
253 above). But note that there are generally three OHCs at each CF location. Simple mathematical
254 reasoning (coherent signal, incoherent noise) implies that if each of the three contributes equally,
255 this architecture could boost the signal-to-noise ratio of the cochlear amplifier by roughly 5 dB.
256 Additionally, whereas tonal stimuli have narrow bandwidths, the noise power of the current source
257 is uniformly distributed over a broad frequency range. Thus, the inherent electrical noise at the
258 hair-cell input—and, consequently, the output—is therefore relatively small.

259 Importantly, the long RC time constant means that noise at the OHC output is significantly at-
260 tenuated at high frequencies. Indeed, low-pass filtering by the membrane not only reduces the
261 overall noise power at the OHC output but also confines it to a region where it cannot do much
262 harm. According to prevailing theory (e.g., *Shera, 2007*), the OHCs amplify traveling waves by locally
263 pumping small amounts of power into the adjacent fluids. The coherently emitted⁴ power accu-

⁴A prominent feature of theories of cochlear wave amplification is that the amplification of spatially distributed intracochlear sources, such as the motions produced by OHCs, requires some form of spatial coherence (*Zweig and Shera, 1995; Talmadge et al., 1998; Shera and Guinan, 2007*). Since incoherent noise sources do not satisfy these conditions, the criticism raised by *van der Heijden and Vavakou (2021)*—namely, that the responses of active models inevitably succumb to the catastrophic

264 mulates spatially and boosts the amplitude of the traveling pressure wave and thereby the motion
265 of the BM. Coherent wave amplification is most effective in the so-called “short-wave region” that
266 extends roughly 0.5–1 octave basal to CF, depending on species and tonotopic location (see *Altoè*
267 *and Shera, 2020b*, and Fig. 3d).⁵ Indeed, *in vivo* measurements demonstrate that OHC electrical ac-
268 tivity in the gerbil (*Dong and Olson, 2013*) and OHC mechanical activity in the mouse (*Dewey et al.,*
269 *2019*) are effectively coupled to the traveling wave only in frequency ranges spanning about 0.5
270 and 1 octave below CF, in excellent agreement with the theory. Furthermore, electrically-evoked
271 mechanical responses *in situ* appear broadband near the apical surface of OHCs but narrowband
272 on the BM (*Ren et al., 2016a*).

273 In a nutshell, the OHC low-pass filter attenuates the OHC response to noise at frequencies
274 where it would otherwise couple strongly to the traveling wave. By decoupling OHC noise from
275 the hydromechanical action of the cochlear amplifier, the long *RC* time constant renders the noise
276 band different from the amplification band. Additionally, present understanding suggests that the
277 inner-hair-cell (IHC) stereocilia are driven primarily by fluid velocity, which is inevitably high-pass
278 filtered relative to the displacement of the surrounding tissue (for a review, see *Guinan, 2012*).
279 Thus, the long *RC* time constant reduces noise at frequencies where it would interfere most with
280 the operation of the primary sensory cells, at least in the base of the cochlea.

281 **Tonotopic variations, scaling, and operation at higher frequencies**

282 What about operation at even higher frequencies? Simple arguments suggest that our results,
283 derived from data at ~50 kHz, extend further. With fixed parameters, the model predicts that the
284 OHC motile response decreases in a manner inversely proportional to frequency. But the same is
285 true both for the expected displacement of the sensory tissue and for the noise at the OHC output
286 (see above). Figure 2 demonstrates that the logarithm of near-CF BM displacement in the mouse
287 decreases almost linearly with frequency.⁶ That is, the estimated frequency-dependence of the
288 OHC response-limit mirrors that of BM displacement.

289 In the real cochlea, OHC properties vary systematically along the tonotopic axis. Nevertheless,
290 many prominent variations in cochlear responses (such as the change in tuning with CF) can be
291 reasonably accounted for by models where the action of the OHCs is assumed scaling symmetric
292 and thus essentially identical at all locations (*Altoè and Shera, 2020a*), with possible deviations
293 at the extreme apex near the helicotrema (*Sasmal and Grosh, 2019*). We note that a principal
294 functional consequence of the tonotopic gradient of OHC length (*Soons et al., 2015*)—reduced
295 OHC motion at higher CFs—is effectively counteracted by the gradients of OHC capacitance and
296 MET current (*He et al., 2004; Johnson et al., 2011*), which act to increase OHC motion at higher
297 CFs. Thus, an assumed scaling symmetric (or “one-size-fits-all”) phenomenology of OHC action is
298 perhaps not unreasonable. Note also that systematic variations of MET-channel sensitivity (*He*
299 *et al., 2004*) and cytoarchitectural geometry (*Soons et al., 2015*) may serve to help equalize OHC
300 functionality along the tonotopic axis, and not necessarily differentiate it, as often assumed.

“cascaded” amplification of distributed, incoherent noise sources—appears puzzling.

⁵In their recent critique of the cochlear amplifier, *van der Heijden and Vavakou (2021)* claim that their own theoretical speculations differ from most models in that they focus on the abrupt transition between long- and short-wave regions. In particular, the authors interpret the abrupt transition as the locus where cochlear waves convert from propagating without substantial loss to a mode where energy dissipates via mechanical vibrations within the sensory epithelium. Their criticisms, however, mischaracterize existing theories and appear at odd with the modeling literature (see e.g., *de Boer, 1981, 1983; Shera et al., 2005; Zweig, 2015; Altoè and Shera, 2020a*). Indeed, we have recently demonstrated that the long-to-short wave transition region found in active models is abrupt enough that one can obtain good approximate solutions to the model equations using a “shotgun wedding” that matches long- and short-wave solutions at a seam (*Altoè and Shera, 2020b*).

⁶Simple, hand-waving arguments might reassure the skeptical reader that near-CF BM displacement can reasonably be expected to decrease with increasing frequency. The acoustic power carried by the traveling wave is proportional to the fluid velocity (necessary equal to BM velocity near the BM), and the power delivered from the middle ear to the cochlea is largely independent of frequency (*Lynch et al., 1982; Shera and Zweig, 1991*). Therefore, an approximately constant acoustic power entering the cochlea can be expected to produce approximately constant BM velocity at the peak of the traveling wave, even for a passive cochlea where there is no OHC amplification (*Zweig et al., 1976*). Constant velocity, however, implies that the corresponding displacement decreases as $1/f$, consistent with the data in Fig. 2. Thus, the observed scaling with frequency is neither a dubious assumption of byzantine models or an inexplicable peculiarity of the murine cochlea.

301 As a corollary, note that the assumption of
302 approximate functional invariance of the OHCs
303 along the cochlea implies that near-CF OHC ve-
304 locity, like the peak velocity of the BM (see Fig. 2),
305 is independent of location. Because the mechan-
306 ics of the tissue surrounding the OHC are likely
307 to be viscous-dominated [rather than stiffness-
308 dominated, as recently assumed by *Vavakou*
309 *et al., 2019*] at frequencies extending several oc-
310 taves below CF (*Scherer and Gummer, 2004*), the
311 force that OHCs deliver to the sensory epithe-
312 lium (and consequently the power injected to the
313 traveling wave) is also approximately indepen-
314 dent of CF. This is precisely what active, scaling-
315 symmetric models (e.g., *Zweig, 1991*) have imple-
316 mented since the dawn of cochlear amplification
317 (*Kemp, 1978*).

Figure 2. Scaling of BM displacement in the mouse cochlea. The symbols give BM displacement measured using CF tones of 20 dB SPL (where BM responses are approximately linear) at CFs of 9 kHz (*Dewey et al., 2019*), 22 kHz (unpublished data courtesy of J. B. Dewey), and 48 kHz (*Ren et al., 2016b*). The trend is well captured by a function inversely proportional to frequency (dashed line).

318 The long *RC* time constant reduces dis- 319 tortion

320 We now employ analogies with existing electronic circuits to illustrate how much the *RC* problem
321 has been magnified over the years by an excessive focus on the mental construct of the low-pass
322 filter. We first turn attention to a basic building block of analog electronics: the triangle-core oscilla-
323 tor, a simple circuit whose somewhat abstracted representation is shown in Fig. 3a. The operation
324 of this oscillator is straightforward. A constant positive current charges a capacitor. When the ca-
325 pacitor voltage reaches a desired maximum value, an auxiliary circuit inverts the current polarity,
326 discharging the capacitor over time. When the capacitor voltage reaches a desired minimum value,
327 the current polarity is again inverted, back to positive, and the capacitor is recharged. And so on.
328 The voltage output of the circuit is a triangular waveform whose fundamental frequency depends
329 on the strength of the current source, the capacitance to be charged, and the desired voltage swing.
330 Although theoretically infinite, the time constant of the charging element (the capacitor) is limited
331 in practice by parasitic conductances in the capacitor and by other non-ideal circuit components.
332 This simple circuit provides a concrete, real-life example of a system whose high-frequency op-
333 eration, like that of the more exotic OHCs, is not limited by the *RC* time constant of its charging
334 element. Indeed, like the OHCs, this circuit operates above the cut-off frequency (theoretically zero)
335 imposed by its *RC* time constant. But perhaps the analogies do not end here.

336 For example, regarding the OHC as a filter driven by a sinusoidal input may overlook important
337 aspects of OHC function. It is now a classic result that the MET transduction function is a highly
338 nonlinear and saturating function (e.g., *Russell et al., 1986; He et al., 2004*), implying that the MET
339 current approaches a square wave for sufficiently large excursions of the stereocilia. When the
340 *RC* time constant is much larger than the period of the local CF, the response remains “clean” de-
341 spite the highly distorted input (Fig. 3b). Thus, in the same way that the capacitor in the electronic
342 oscillator transforms a square current into a triangular voltage, the OHC low-pass filter increases
343 the fidelity of the hearing organ by reducing harmonic distortion. Indeed, a recent study (*Peterson*
344 *and Heil, 2020*) proposed an analogous role for the low-pass filtering present in the IHC mechano-
345 to-neural transduction machinery. Just as in our simple OHC model [Fig. 3b], IHC low-pass filtering
346 reduces the distortion introduced by the saturating MET nonlinearity, thereby increasing the fi-
347 delity and temporal precision of auditory-nerve responses (*Peterson and Heil, 2020*).

Figure 3. (a) Schematic illustration of a current-controlled oscillator, whose operation has important analogies with the OHC [see text and panel (b)]. (b) Simple model elucidating the effect of OHC low-pass filtering for improving the fidelity of the hearing organ. From left to right: The input is assumed to be a sinusoidal deflection of the OHC stereocilia. This vibration is converted into MET current via an asymmetric, saturating sigmoidal nonlinearity. The OHC voltage is derived from the MET current by low-pass filtering, in accordance with the model adopted for our analysis of the RC problem. The oscillating (AC) component of the OHC voltage is obtained by high-pass filtering the OHC voltage. Whereas the MET current becomes highly saturated and distorted as the stereociliary input increases, the OHC voltage remains much less distorted, and the AC response is nearly sinusoidal. This same model has recently been shown to capture the mechanical distortions measured near the OHCs in the organ of Corti (Dewey et al., 2021). (c) Example of AC coupling in a textbook signal amplifier. The signal at the output terminal (collector) of the transistor is the sum of the amplified version of the input signal and a DC bias. The series capacitor at the output terminal acts as a high-pass filter, removing the DC bias from the amplified signal. The capacitance value is selected to couple the amplified signal in a relevant range of frequencies. (d) In analogy with the signal amplifier of panel (b), OHC forces are AC coupled to the traveling wave on the BM. This panel compares the magnitude of OHC forces and amplification of BM response, quantified as the ratio between BM displacement in both the presence and absence of active forces (i.e., postmortem) in a 3-D model of the mouse cochlea (Altoè and Shera, 2020b). Whereas OHC forces are broadband, BM amplification retains a prominent high-pass characteristic, so that low-frequency OHC activity has a negligible effect on the BM response. In this simple model, OHC forces are active (i.e., amplifying and in phase with BM velocity) at all frequencies; the prominent frequency dependence of BM amplification is brought about by the short-wave hydrodynamics.

OHCs as regulators?

The analogy with electronic circuits allows one to analyze, with minimal complexity, the recent proposal that the OHCs serve primarily as sluggish regulators rather than as the motors for cycle-by-cycle power amplification (Vavakou *et al.*, 2019). The hypothesis is that because their response near DC is large and nonlinear, OHCs act as envelope detectors whose role in cochlear mechanics must be that of somehow modulating the traveling wave by serving as automatic gain controllers (AGCs). Although AGC theories of cochlear mechanics have been criticized and found wanting on other grounds (Altoè *et al.*, 2017), a simple analogy with AC- and DC-coupled electronic circuits raises additional theoretical and empirical concerns.

Very low frequency (near-DC) biases introduced by electronic circuits in the signal path are often undesirable (e.g., in radio and audio applications). The problem is commonly solved by connecting a capacitor (or a transformer) in series with the output (or input). The capacitor acts as a high-pass filter, removing the DC component of the signal (Fig. 3c). Using this simple but effective strategy, multiple circuits can be chained together without worrying about the potentially deleterious side-effects of DC biases (or low-frequency noise) in the signal path. Circuits that include these coupling capacitors (e.g., radio receivers and the inputs and outputs of most audio signal processors) are said to be AC-coupled. Conversely, circuits that are designed to generate or process DC or very low-frequency signals (e.g., on/off thermostats) exclude coupling capacitors and are said to be DC-coupled. Basic physics implies that in the mammalian cochlea both slow and compressional pressure waves are AC coupled to the motions of the sensory epithelium (Peterson and Bogert, 1950; Lighthill, 1981; Shera and Zweig, 1992). Additionally, OHC activity is theoretically (Fig. 3d) and empirically found to couple to the traveling wave predominantly in a narrowband region below CF (see Dong and Olson, 2013; Dewey *et al.*, 2019, and “The long RC time constant reduces noise where it matters most”).

Thus, OHC motions appear strongly AC coupled to the traveling wave, the primary means of energy transport in the cochlea. Forms of DC coupling between OHC motions and the traveling wave—necessarily more indirect than the known AC coupling—have not been identified and proposed models are at odds with the experimental data (Altoè *et al.*, 2017). Indeed, theories that propose a central, regulating role for the DC response of the OHC are fundamentally similar to the “impedance-reduction” hypothesis of Kolston *et al.* (1990). This hypothesis posits that the OHCs act to regulate the reactive and/or resistive impedance components of the cochlear partition (i.e., its stiffness and/or damping), without boosting the energy carried by the traveling wave (see Allen, 2001; van der Heijden and Vavakou, 2021). Kolston himself ultimately determined that impedance-reduction models do not fit the data (Kolston, 2000). In particular, Kolston demonstrated that impedance-reduction models tailored to replicate the BM-magnitude response predict excessive phase accumulation, incompatible with the data. He concluded that the measured BM phase response implies some form of energetic boost to the BM wave. As it turns out, this result is no mere model-dependent speculation: the real and imaginary parts of the wavenumber—which determine the phase and energy accumulation, respectively—are not independent of one another, but obey dispersion relations imposed by causality (see Shera, 2007). Furthermore, we have recently demonstrated (Altoè and Shera, 2020b) that significant level-dependencies of the partition damping and stiffness cannot easily be reconciled with the approximate level-invariance of the fine-time structure of the BM click-response and the biological robustness of this phenomenon (for a review, see Shera, 2001; Zweig, 2016). Indeed, the problem would be particularly acute were the level-dependence to mirror OHC activity and occur in extended regions basal to the peak of the traveling wave (see Appendix A of Altoè and Shera, 2020b).

The results of our simple model (see “The long RC time constant reduces noise where it matters most”), taken together with the inevitability of noise sources having $1/f$ (or $1/f^2$) spectral densities, leave little doubt that the noise at the OHC output must be substantially larger at low (near-DC) frequencies than at high. When the noise sources are white, the SNR at the OHC output measured

in narrow frequency intervals for a given oscillatory MET current is fairly independent of frequency. But in the real world, where many noise sources are pink and brown, the SNR is expected to decrease significantly at low frequencies. Unfortunately, providing more quantitative statements about the effects of noise in alternative “gain-control” scenarios remains difficult in the absence of concrete, mechanistic proposals. However, physical intuition suggests that the low-pass nature of physical and biological noise can only render noise more problematic for mechanisms based on the DC response of the OHC (Vavakou *et al.*, 2019; van der Heijden and Vavakou, 2021) than for existing theories where OHCs are AC coupled to the traveling wave.

The RC problem and OHC tuning

A classic problem associated with the OHC membrane circuitry is that low-pass filtering is a nuisance when attempting to produce sharply tuned OHC forces. Although solutions to this problem have been proposed (e.g., Lu *et al.*, 2006), we argue that the 3-D nature of cochlear hydrodynamics renders the problem moot. To compensate for the oversimplified hydrodynamics (Shera *et al.*, 2005), sharply tuned OHC forces acting on the BM are indeed necessary in cochlear models with zero- or one-dimensional fluid coupling. (Examples of zero- and one-dimensional models include filter-bank/critical-oscillator and transmission-line models, respectively.) However, models that incorporate two- or three-dimensional fluid coupling can produce realistic narrowband BM amplification without resorting to sharply tuned OHC forces. This is nicely illustrated by a recent 3-D model that replicates BM data well—and provides intuitive explanations for a number of other observations—while employing phenomenological OHC forces that are low-pass filtered relative to the BM (see Altoè and Shera, 2020b, and Fig. 3d). Similar results are found in the data. Indeed, a recent study in the ~9 kHz region of the mouse (Dewey *et al.*, 2021) demonstrates that the OHC motile response *in vivo* appears low-pass filtered relative to that of the BM; the cut-off frequency associated with such low-pass filtering is suspiciously similar to OHC corner frequencies reported in the literature. Despite the prominent low-pass filtering, the cycle-by-cycle OHC response is larger than that of the BM, even at CF and at stimulus levels of 70 dB SPL, corroborating the analysis presented above, as well as its conservative character.

We conclude by noting what is now obvious from the literature: detailed, physics-based cochlear models that include OHCs with membrane time constants similar to those reported in the literature have no problem producing realistic wave amplification (e.g., Sasamal and Grosh, 2019). Arguments suggesting that the low-pass filtering action of the OHC membrane precludes effective cycle-by-cycle wave amplification in the cochlea evidently fall prey to the fallacy of composition—mistaking the parts (an isolated OHC) for the whole (the cochlear amplifier). For example, one can easily obtain high-, band-, and low-pass transfer functions by cascading multiple low-pass filters and mixing their responses, with or without the introduction of feedback loops.⁷ In a similar way, the cochlear amplifier can be thought of as emerging from the “mixed” responses of multiple OHCs. Mixing occurs hydrodynamically, via the fluids and other coupling mechanisms, and each coupling mechanism has its own frequency (or wavelength) dependencies. Thus, it should not be surprising that the frequency-dependence of cochlear amplification differs from that of the isolated OHC. Indeed, while OHC responses are low-pass filtered relative to that of the BM, they are band-pass relative to the cochlear input [whether that input is considered to be the pressure near the tympanic membrane or the vibration of the stapes (Lee *et al.*, 2016; Ren *et al.*, 2016b; Dewey *et al.*, 2021)], a direct consequence of the tuned mechanical drive to the OHC stereocilia. Despite a mischievous grin that has taunted the field for decades, the RC problem, like the Cheshire cat, appears effectively to have vanished from view in both modern theories and experiments.

⁷Cascading N low-pass filters and mixing their responses (i.e., computing a weighted sum) is equivalent to producing a filter with $N - 1$ zeros and N poles, where the pole locations are determined by the poles of the individual filters and the zeros depend on the mixing coefficients. Mixing the result with the input signal increases the number of zeros to N . When feedback loops are included, the system of cascaded low-pass filters becomes a general purpose, zero-pole model of order N . Such models are commonly used in system identification, signal processing, and physical modeling applications (e.g., Choi, 2012).

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579 Appendix 1

581 Estimate of electrical noise

582 Electrical noise is conveniently modeled as a current generator driving the OHC membrane
583 (Fig. 1b). The equivalent thermal noise current source has power spectral density

$$584 S_{I,TN} = 4k_b T / R \quad [A^2/Hz], \quad (7)$$

586 where k_b is the Boltzmann constant, T the absolute temperature and R the OHC resistance.
587 Note that this current generates a voltage at the OHC output with RMS amplitude $\sqrt{k_b T / C}$
588 and bandwidth $1/4RC$. At body temperature, and assuming a resistance R of approximately
589 10–20 MΩ, Eq. (7) indicates the noise current power in the frequency band of 0–50 kHz is
590 the same as that produced by a sinusoidal current of ~10 pA, which is on the order of that
591 mediated by a single MET channel (Beurg et al., 2006).

593 The “shot” noise (van der Heijden and Vavakou, 2021) associated with the random open-
594 ing and closing of MET channels is not so easy to estimate. Regardless of the assumed
595 stochastic behavior of MET-channel gating, the shot-noise spectral density—with units of
596 A²/Hz—is proportional to qI_{MET} , where q is the charge mediated by a single opening event.
597 Unfortunately, q is hard to estimate from published experiments without making a number
598 of assumptions. If the MET channels open and close independently of one another, the
599 root-mean-square (RMS) noise current is on the order of

$$600 i_{RMS,SN} \sim p\sqrt{N}i_o \quad [A], \quad (8)$$

602 where p is the channel open-probability, N the number of MET channels, and i_o the cur-
603 rent mediated by a single channel. Although the value p “at rest” remains controversial—
604 *in vitro* estimates range from roughly from 10–50% (Russell et al., 1986; Johnson et al.,
605 2011)—relatively strong rectification and even-order harmonics are observed in mechan-
606 ical responses from the OHC region in both the base and apex of the mouse (Dewey et al.,
607 2021; He and Ren, 2021), and in the base of the gerbil as well (Vavakou et al., 2019), suggest-
608 ing that p is relatively small (i.e., $\leq 20\%$). The number of MET channels is on the order of 100
609 [~60 tip-links, with on average of 1.65 channels per tip-link (Beurg et al., 2006)]. With these
610 values, Eq. (8) implies an RMS shot-noise similar to the current mediated by a small number
611 of channels [0–5 for $p \in (0, 0.5)$].

612 As an interesting aside, note that this simple analysis points out that the degree of rec-
613 tification (i.e., the value of p at rest, or equivalently the asymmetry in the MET transduction
614 function) controls the OHC susceptibility to shot noise, with smaller values of p reducing the
615 noise at the OHC input and, consequently, at the OHC output. On the other hand, in the
616 absence of noise, the OHC is maximally sensitive to small stereocilia vibrations when $p = 0.5$
617 and the transduction nonlinearity is perfectly symmetric (Johnson et al., 2011). Therefore,
618 the asymmetry of the MET transduction function (i.e., the value of p)—and its possible sys-
619 tematic tonotopic variation (Nam and Guinan, 2016)—may play an important role in control-
620 ling the effective OHC sensitivity in the presence of noise. Although $p = 0.5$ optimizes signal
621 detection in idealized, noiseless models, the same is not true in the presence of shot noise.