Intracochlear Pressure Measurements in Scala Media Inform Models of Cochlear Mechanics

Sushrut Kale* and Elizabeth S. Olson*,†

*Otolaryngology,Head and Neck Surgery, Columbia University, New York City
†Biomedical Engineering, Columbia University, New York City

Abstract. In the classic view of cochlear mechanics, the cochlea is comprised of two identical fluid chambers separated by the cochlear partition (CP). In this view the traveling wave pressures in the two chambers mirror each other; they are equal in magnitude and opposite in phase. A fast pressure mode adds approximately uniformly. More recent models of cochlear mechanics take into account the structural complexity of the CP and the resulting additional mechanical modes would lead to distinct (non-symmetric) patterns of pressure and motion on the two sides of the CP. However, there was little to no physiological data that explored these predictions. To this aim, we measured intracochlear fluid pressure in scala media (SM), including measurements close to the sensory tissue, using miniaturized pressure sensors ($\sim$ 80 μm outer diameter). Measurements were made in-vivo from the basal cochlear turn in gerbils. SM pressure was measured at two longitudinal locations in different preparations. In a subset of the experiments SM and ST (scala tympani) pressure data was measured at the same longitudinal location. Traveling wave pressures were observed in both SM and ST, and showed the relative phase predicted by the classical theory. However, SM pressure showed spatial variations that had not been observed in ST, which points to a relatively complex CP motion on the SM side. These data both underscore the first-order validity of the classic cochlear traveling wave model, and open a new view to CP mechanics.

INTRODUCTION

A physiologically healthy cochlea shows non-linear, sharply tuned basilar membrane responses [**?**]. The active mechanism within the cochlea amplifies responses to low and moderate level sounds in a frequency dependent manner, extending the dynamic range and sharpening the tuning of mammalian hearing. Theoretical models of active cochlear mechanics incorporate outer hair cell electromechanics into a model of the passive mechanics. The classic passive traveling wave model predicts equal magnitude and opposite phase of the pressure on either side of the cochlear partition (CP), where the CP is treated as a simple beamed structure separating scala tympani (ST) and scala vestibuli (SV) [**?**]. However, modern models of passive cochlear mechanics include a multi-compartment CP and predict different frequency-dependent pressure variations on either side of the CP [**?**]. We measured SM and ST pressure in response to pure tone stimulation in gerbil. Presently our preparations are approximately passive (due to the SM cochleostomy) and are useful for testing the predictions of passive cochlear models.

METHODS

Animal use was approved by Columbia University's IACUC. Experiments were performed in young adult gerbils anesthetized with pentobarbital. Surgery was performed to expose the cochlea and a hole of diameter $\sim$ 90 μm was hand-drilled through the cochlear bone in order to access SM and in some experiments ST. In order to penetrate the lateral wall of SM, after opening the bone, a minutiae pin connected to an electric cautery delivered a short pulse of current, resulting in a clean opening. Pure tones at frequencies from 1 to 50 kHz were applied at the ear canal at levels of 40 to 90 dB SPL. Measurements solely in ST showed the nonlinear compression that has been reported previously [**?**]. However, even seemingly atraumatic opening of SM led to linear responses in both scalae, most likely due to loss of endocochlear potential. Pressure sensors were inserted and pressure was measured as the sensor approached the sensory tissue. The micro-pressure sensors used in this study were a modified version of the sensor introduced in [**?**]: light is delivered by a fiber optic to a sensing membrane, whose vibration varies the amount of light returning to a photodetector. The sensors here employed single-mode optical-fiber coupled to a super-luminescent diode. With this design, the outer diameter of the sensor could be reduced to $\sim$ 80 μm. Sensors were calibrated in water and air, and the calibrations were flat in frequency. Their sensitivity extended down to a level of $\sim$60 dB SPL with 1 second of signal averaging. Because of middle ear and intracochlear pressure gain, this corresponds to an ear canal pressure of $\sim$ 35 dB

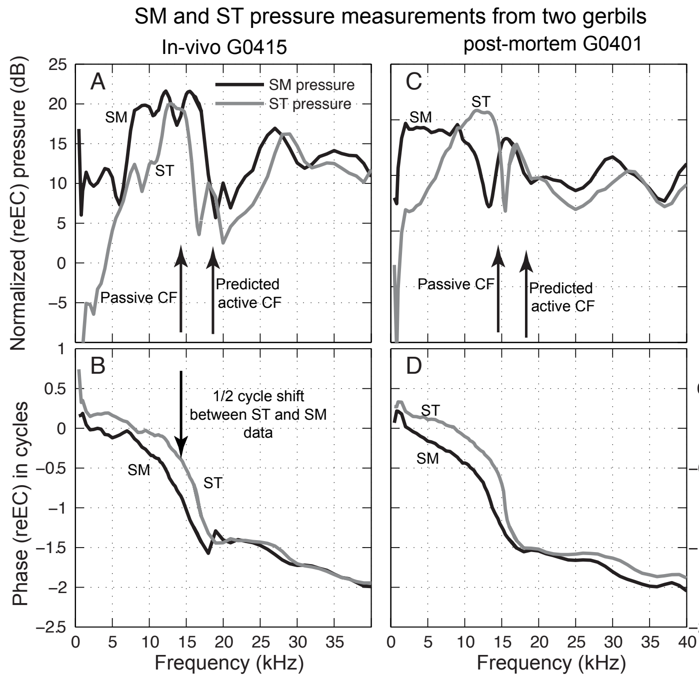

FIGURE 1. Intracochlear pressure measured within 10 um of the cochlear partition in SM and ST. Top row shows cochlear pressure normalized by ear canal pressure. Bottom row shows the phase relative to the stimulus phase in the ear canal. A and B show in-vivo data from gerbil G0415 at 85 dB SPL. C and D show post-mortem data from G0401 at 80 dB SPL. The SM data from G0401 was collected within 2 hours and the ST data within 2.5 hours post-mortem. The pressure level differed by $\sim$ 25 dB in the two preparations, and some of this difference might be due to sensor calibration uncertainty.

SPL or less. Sensor calibrations have a degree of uncertainty, seemingly due to mechanical perturbation to the sensing membrane upon insertion. However, a change in calibration results only in a vertical shift. Once inserted into the cochlea the calibration is usually stable, based on repeated measurements. In experiment G0415 the post-experiment sensor calibration showed 180° phase shift relative to pre-experiment and the SM pressure gain appeared as 20 dB lower than ST, which was likely incorrect, and attributed to inaccurate sensor calibration. The data in Fig. 1A and B are presented with the post-experiment phase calibration, and the SM magnitude was presented shifted vertically.

RESULTS

In two gerbils, the intracochlear pressure was measured first in the SM and then in the ST. The ST pressure (shown in gray) measured in G0415 (Fig. 1A) was tuned to $\sim$ 12 kHz. The pressure appeared to be composed of a traveling wave (TW) component that varied with frequency and a fast mode component that was relatively independent of frequency, as was evident from the response at frequencies above $\sim$ 20 kHz, particularly the phase (Fig. 1B and D). Given that this was a passive, linear preparation, the peak frequency of $\sim$12 kHz was consistent with the longitudinal location of the pressure sensor, corresponding to the $\sim$18-20 kHz characteristic frequency (CF) region in an active, non-linear cochlea (arrows in Fig. 1A and C) [**?**]. The SM pressure showed a similar but broader peak around 12 kHz. Compared to the ST pressure, the SM pressure was relatively flat as a function of frequency, especially at low frequencies (Fig. 1A, C). A prominent notch was observed in the SM pressure measured from G0401 (arrow, Fig. 1C). Either a notch or a peak appeared in all the SM pressure data sets as is discussed below. In the frequency region of the peak, where the phase changed rapidly, there was a half cycle difference between ST and SM pressure phase in both data sets. At higher and lower frequencies the phases were similar in the two chambers (Fig 1B and D).

Figure 2 shows the SM pressure measured in two gerbils from different longitudinal locations, one from a basal location corresponding to $\sim$20 kHz CF (Fig. 2A and B) and the other from a relatively apical location corresponding to $\sim$12 kHz CF (Fig. 2C and D). The data shown is representative of the trends observed in eight gerbils (relatively basal location measurement: three gerbils, relatively apical location measurement: five gerbils). The SM pressure

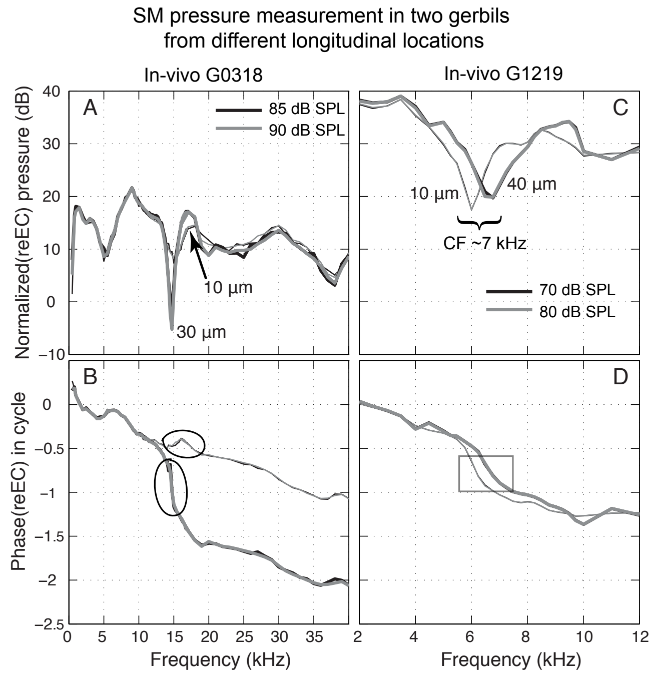

FIGURE 2. SM pressure measured from two different longitudinal locations. A and B: From the location with CF ∼20 kHz. C and D: From the location with CF ∼12 kHz. Thin and thick lines indicate SM pressure relatively near to and far from the CP tissue, respectively. The location of the sensor relative to the tissue is noted in panels A and C. Ovals highlight the different trends in the phase. The square highlights a quarter cycle phase lead shown by the SM pressure near the tissue relative to that away from the tissue. Note the different scale for abscissa in B and D.

showed a notch that was a half to full octave lower than the CF corresponding to the sensor location. Except for the notch, the SM pressure in these data sets was relatively flat with frequency. As the sensor moved from being within 10 μm to within 30 μm from the CP, the notch became deeper (Fig. 2A). A similar notch was observed when the SM pressure was measured from relatively apical locations (Fig. 2C). In the base, the notch frequency decreased slightly with increasing distance whereas in the apical region, the notch frequency increased with the distance from the CP (Fig. 2A, C). SM pressure phase sometimes showed a steep drop associated with the notch whereas in some cases there was a brief phase reversal associated with the notch (ovals in Fig 2B, D). The notch showed spatial dependence (i.e., sensor location relative to CP) but not level dependence (as expected in these passive, linear preparations). These trends suggest that the notch results from the summing of different pressure modes in the cochlea. A distinct peak usually replaced the notch when the velocity was estimated using the difference of two adjacent pressure measurements (Fig. 3). (See [**?**] for velocity calculation.)

Figure 3 shows the CP velocity estimated from the two SM pressure measurements shown in Fig 2A and B. The estimated velocity was tuned to ∼ 15 kHz, slightly above the notch frequency. This was consistent across all the animals from which the SM pressure was measured. The velocity phase varied rapidly through two full cycles at 85 and 90 dB SPL. Interestingly, at the lowest sound level used (70 dB SPL, black line), the phase went through an additional cycle before the fast mode dominated the velocity response. This was observed in one other animal. These results indicate that the traveling wave was dominant at frequencies through an additional cycle at low sound levels, and thus that these preparations retained some nonlinearity.

DISCUSSION

In the present study we measured SM pressure close to the CP at two different longitudinal locations. Although preliminary, this study constitutes the first measurements of this important cochlear mechanical quantity. The ST pressure was measured in addition to the SM pressure in two gerbils, and was similar to previous measurements of passive ST pressure, showing that the hole in SM did not affect passive mechanics. The most consistent feature of

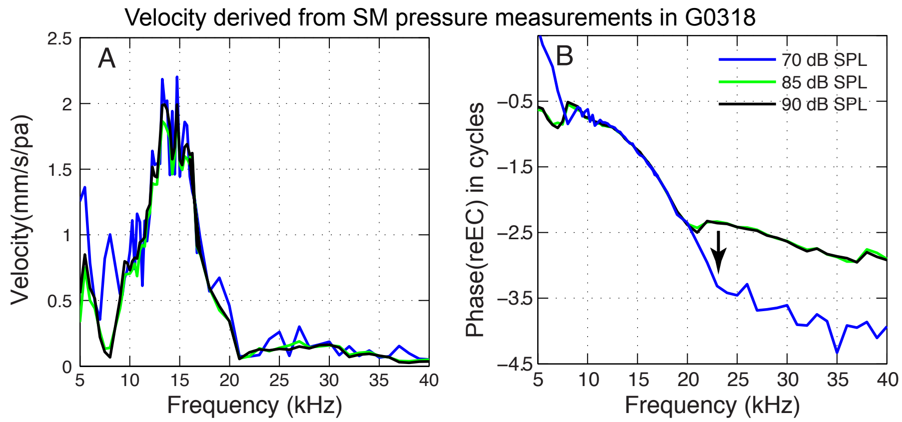

FIGURE 3. Cochlear partition velocity derived from the SM pressure from figure 2A B. A: Velocity magnitude for three sound levels and B: Phase. The arrow indicates the additional cycle for which the TW is dominant at the lower sound level.

the SM pressure was the presence of either a notch or a peak at a frequency a half to full octave below the predicted CF of the sensor location. Based on the anatomical explorations performed before and after the experiments and monitoring of the sensor angle relative to the surface of the external lateral wall of the cochlea we expect that in the SM measurement (1) the sensor was oriented towards the tectorial membrane at a shallow angle (i.e., not perpendicular) and (2) when advancing the sensor, its location varied predominantly in the radial direction and to some extent in the longitudinal direction.

Interaction between fast and slow pressure modes resulted in the notch formation

The SM pressure data presented here had key similarities to the ST pressure measured at high sound levels or in a passive preparation, and the notch is likely due to the sum of a fast mode pressure and a slow, TW mode pressure with roughly equal magnitude and opposite phase [**? ?**]. The ∼1/4 cycle phase shift in the SM pressure with distance (see square in Fig. 2D) and related to the local CF substantiates the theory that the notch depended on the degree to which the sensor was exposed to the TW. The notch was not an artifact of making the SM hole as it (1) moved systematically with the change in the longitudinal location of the sensor, (2) did not disappear or change quantitatively after sealing the SM hole around the sensor and (3) its frequency changed with the location of the sensor in the radial direction along the TM. The notch would be ill-formed or absent closer to the tissue and deepen as the sensor would retract. Moreover, a peak would replace the notch during the same experiment, if the sensor were to be oriented more towards the lateral wall. Given the assumption that the location of the sensing membrane changed along the radial-TM direction, we speculate that (1) the two-mode cancellation was observed only when the sensor was above the part of the TM overlying the tunnel of Corti region (i.e. thick central part) and (2) closer to the lip of the TM or the lateral wall, the TW dominated the two mode interaction, resulting in a peak more similar to the one shown in Fig. 1A.

The observation that the SM pressure was relatively flat with frequency compared to passive ST pressure likely relates to the fact that ST is terminated by the flexible round window membrane, which serves to filter out low frequency pressure. In contrast, the SM measurement was relatively close to the stapes and SV, which has an approximately flat frequency response near the stapes [**?**].

Preliminary data support classical theory of cochlear mechanics plus complexity

Although there was some uncertainty associated with the sensor calibration in animal G0415 (Fig. 1), the data set from G0401 also showed ∼ a half cycle phase difference between ST and SM pressure in the region of rapid phase accumulation. Also, the ST and SM pressure magnitudes were nearly comparable. These results, although preliminary, are consistent with classical models of cochlear mechanics, in which the TW-mode pressure on two sides of the CP is antisymmetric (equal in magnitude and opposite in phase) and the fast-mode pressure on the two sides is symmetric (equal in magnitude and phase) [**?**]. In our data, the TW mode dominates or is substantial in the region of the peak and notch, and the fast mode dominates at higher frequencies. The fluid velocity estimated from the SM pressure measured at two locations 20 μm apart showed a distinct peak at 15 kHz. Considering these results in conjunction with the notch-related data, suggests that we might be seeing the fluid motion along the radial TM direction. Although the passive peak in SM pressure matches closely with the passive peak in ST pressure, the locations of the sensor in SM relative ST is an estimate and the peak in SM might represent a TM resonance below the CF of the corresponding CP location. Also, how the radial fluid motion within subtectorial space would influence the notch is not well understood. Future experiments, along with modeling and anatomical/histological analyses will investigate these questions.

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