Research Article

Localization of the Reflection Sources of Stimulus-Frequency Otoacoustic Emissions

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ABSTRACT

The generation of stimulus-frequency otoacoustic emission (SFOAE) residuals in humans is analyzed both theoretically and experimentally to investigate the relation between the frequency difference between the probe and the suppressor tone and the localization of the residual source. Experimental measurements of the SFOAE residual were performed using suppressors of increasing frequency to separate the otoacoustic response from the probe stimulus. From the response to the probe alone, the SFOAE response was also estimated, using spectral smoothing, and compared with the residuals obtained for different frequency suppressors. A nonlinear delayed-stiffness active cochlear model was used to compute the spatial distribution of the residual sources according to a recent model of the local reflectivity from roughness, as a function of the suppressor frequency. The simulations clarified the role of high-frequency suppressors, showing that in humans, with increasing suppressor frequency, the generation region of the residual is only slightly basally shifted with respect to the case of a near-frequency suppressor, near the basal edge of the peak of the resonant basilar membrane response. As a consequence, the hierarchy among different-delay components correspondingly changes, gradually favoring short-delay components, with increasing suppressor frequency. Good agreement between the experimental and theoretical dependence of the level of otoacoustic components of different delay on the frequency shift between

probe and suppressor confirms the validity of this interpretation.

Keywords: nonlinear cochlear models, local reflectivity, suppression, phase-gradient delay, time-frequency analysis

INTRODUCTION

Stimulus-frequency otoacoustic emissions (SFOAEs) are usually separated from the stimulus tone (at the probe frequency f_p) using a suppressor tone of nearby frequency f_s . The assumed role of the near-frequency suppressor is to strongly decrease the nonlinear gain of the outer hair cell active amplifier in the cochlear region around the tonotopic characteristic place (CP) of frequency f_s , CP (f_s), which is close to CP (f_p), where localized generation of backward traveling waves is predicted by the coherent reflection filtering (CRF) mechanism. The CRF mechanism is sensitive to the local BM displacement level (Zweig and Shera, 1995; Talmadge et al., 1998); therefore, it is commonly assumed that SFOAE residual sources are localized in the tonotopic active region only. Kalluri and Shera (2007) demonstrated that near-frequency suppressors yield SFOAE residual spectra that are equivalent to the SFOAE spectrum estimated using spectral smoothing, without any suppressor. Although sensitive to the arbitrary choice of the smoothing parameters, which could also exclude hypothetical short-delay components, spectral smoothing could be a valid tool for evaluating the true SFOAE emission. Indeed, a residual is, for each frequency, a vector difference; therefore, it could even include hypothetical SFOAE

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components produced by the suppressor at the probe frequency. Recently, it has been demonstrated that significant SFOAE generation may occur slightly basally to the resonant region, within 1–2 mm in humans, corresponding to a relative frequency shift of order 15–30 % (e.g., Moletti et al. 2013). Such near-basal sources should correspond to the short-latency OAE components observed in humans (e.g., Sisto et al. 2013). Significant delay differences are associated indeed to short spatial differences in the high-tuning, sensitive human cochlea.

SFOAE suppression by high-frequency (HF) tones has been experimentally observed by Kemp and Chum (1980), and in chinchillas (Siegel and Charaziak 2015), and interpreted as evidence for correspondingly far-basal SFOAE residual sources. The CRF mechanism may not be in contradiction with basal OAE generation (as shown by Sisto et al., 2015a), if the quality factor is sufficiently low, as it may be the case in animals, particularly at high stimulus levels and at low frequencies. On the other hand, the relation between the localization of the “residual” SFOAE source and a HF suppressor needs further study, to test two common, but not fully demonstrated, assumptions: (a1) a residual obtained using a suppressor of frequency f_s implies OAE generation near (and only near) CP (f_c) and (related to the first one) (a2) suppression residuals from a suppressor whose CP is “far basal” to that of the probe (e.g., a suppressor one octave higher than the probe) should be negligible because it would affect a fully passive region, as regards the probe generators.

In this study, a nonlinear delayed-stiffness model is used to compute how HF suppressors affect the vibration pattern along the basilar membrane, showing that HF suppressors may produce significant SFOAE residuals (contradicting a2), and the generation region of the observed residuals does not necessarily coincide with CP (f_c) (contradicting a1).

From an experimental point of view, to clarify the same issue, SFOAEs have been recorded as a function of f_s , using time-frequency analysis to show the presence of different-delay components, and the dependence of the level of each delay component on f_s has been compared to that predicted by the model. The response to probe alone was analyzed, using spectral smoothing (Kalluri and Shera, 2007) to separate the rotating-phase SFOAE response from the constant-phase stimulus, yielding an estimate of the total SFOAE produced by the superposition of all reflection sources.

Summarizing, the numerical simulations and the assumptions of the local reflectivity model yield the spatial envelope of the whole SFOAE source, which can be converted into a temporal delay distribution of the whole SFOAE, and how this source profile is

affected by suppressors of different f_s , allowing one to predict the delay distribution of the SFOAE residual as a function of f_s . Equivalently, the experimental SFOAE spectra obtained without any suppressor yield the delay distribution of the whole SFOAE, whereas the SFOAE residual spectra obtained with different f_s should contain only the contributions from the regions affected by the suppressor in the real cochlea. This methodology allows one to test the abovementioned assumptions (a1, a2) about the localization of the SFOAE suppression residual generators.

METHODS

Human SFOAEs were recorded in three normal-hearing ears (hearing level better than 20 dB HL), between 2000 and 3000 Hz, using chirp stimuli and suppressors and a double-evoked paradigm (Keefe, 1998; also described in Sisto et al. 2013), for a set of different frequency shifts between probe and suppressor ($\Delta f = f_s - f_p = 100, 200, 300, 500, 1000, 1500, 2000, 2500$, and 3000 Hz). An Etymotic ER10B+ microphone was used to record the OAE signal, while two ER2 loudspeakers were used to deliver the probe and suppressor stimuli. Generation of the stimuli and synchronized acquisition of the response was obtained using a Labview code controlling a PXI NI-4461 24-bit DAQ board. A probe level of 40 dB SPL and a suppressor level of 60 dB SPL were used, calibrated in the ear canal. The chirp frequency rate was 800 Hz/s, yielding a chirp of duration $T = 1.25$ s. Each elementary chirp acquisition was divided into 50 temporal frames of duration 50 ms, with 50 % overlap Hanning windows, so the difference between the central probe frequencies of subsequent frames was 20 Hz. Each frame was Fourier analyzed, measuring the amplitude and phase of the response at its central probe frequency. This acquisition parameter choice ensures that the frequency resolution of the Fourier analysis of each frame (20 Hz) matches that associated with the variation of the chirp frequency between subsequent frames. Least square fit to chirp functions (Long et al. 2008) were also performed on the same data, getting almost identical results. Three elementary acquisitions are obtained: p_1) probe alone, p_2) suppressor alone, p_3) probe and suppressor, with the probe and suppressor chirps delivered by separate loudspeakers. The difference $p = p_1 + p_3 - p_2$ contains in principle the SFOAE residual only. Coherent averages of up to 50 elementary acquisitions were performed to increase the signal-to-noise ratio. An online artifact rejection algorithm was used to exclude noisy frames (based on off-band noise level) and

frames with probable contamination by the probe (based on the size of fluctuations from the average level at the probe frequency) within each elementary acquisition. The total acquisition time was of order 3 min for each value of the frequency difference Δf between suppressor and probe.

The linear acquisitions involving no suppressor, or p_1 , were also separately analyzed, using spectral smoothing (Kalluri and Shera, 2007) to separate the SFOAE response from the probe stimulus. We performed spectral smoothing as a convolution in the frequency domain with a rectangular moving average window of 240 Hz bandwidth.

The complex spectra were analyzed using time-frequency analysis based on the continuous wavelet transform (see, e.g., Moletti et al. 2012), to measure the dependence on Δf of the amplitude of each SFOAE component of given delay. A mother wavelet from Tognola et al. (1997) was adapted to get optimal time-frequency resolution.

A delayed-stiffness nonlinear model of the human cochlea, derived from the linear Zweig (1991) model, was also used, in which gain and phase are dynamically dependent on the stimulus level through the nonlinear dependence of the OHC active force on the instantaneous BM vibration level. The model is discretized using 2000 partitions.

The cochlea is schematized by a box-model, with a tonotopic BM separating two volumes filled by a homogeneous incompressible fluid. The set of equations, which are fully described, e.g., in Sisto et al. (2015a), governing the propagation of the differential pressure p and of the transverse BM displacement ξ along the longitudinal direction x is given by:

$$\begin{cases} \frac{\partial^2 p(x, t)}{\partial x^2} = k_0^2 \sigma_{bm} \ddot{\xi}(x, t) \\ \frac{\partial p(x, t)}{\partial x} = \dot{\xi}(x, t) + \omega_{bm}(x) \delta \dot{\xi}(x, t) + \omega_{bm}^2(x) \xi + \rho \omega_{bm}^2(x) \xi(t - \tau) \end{cases}, \quad (1)$$

where τ is a characteristic delay, which is a function of the local resonance frequency: $\tau(x) = 2\pi \frac{\mu}{\omega_{bm}(x)}$, k_0 is a characteristic inverse length, dependent on the geometrical parameters of the cochlear section, σ_{bm} is the BM surface density, ω_{bm} is the stiffness functions, dependent on x according to the Greenwood map (Greenwood 1990), and $\{\delta, \rho, \mu\}$ are the parameters of the double-pole impedance in the Zweig (1991) model. Cochlear roughness was schematized as a Gaussian randomly spatially distributed fluctuation of the local stiffness, with standard deviation $\varepsilon = 0.005$.

In order to get a dynamical variation of the effective quality factor, with increasing BM velocity,

between two asymptotically linear regimes with, respectively, $Q_3 = Q_{act}$ and $Q_3 = Q_{pass}$, we set:

$$Q_3 = Q_{pass} + (Q_{act} - Q_{pass}) \left(1 - \tanh \left(\frac{\xi^2(x, t)}{\xi_{sat}^2} \right) \right) \quad (2)$$

where the tuning Q_3 is defined here as the ratio between the angular frequency and the bandwidth of the BM frequency response at the CP, measured at 3 dB below the peak level. In this study, we used $Q_{act} = 18$, and $Q_{pass} = 3$. An important feature of the model is that, according to the local and instantaneous BM transverse velocity (in the time domain, involving therefore all frequency components), each cochlear place responds with a different tuning $Q(x, t)$. Therefore, the attenuation of the traveling wave at the probe frequency along its forward path is sensitive also to the local BM excitation level at the suppressor frequency.

From the simulations, the BM response to a pure tone of frequency $f_p = 2500$ Hz was computed along the longitudinal coordinate x . This way, it was possible to compute the spatial envelope of the local SFOAE source function (Sisto et al., 2015a). The actual local cochlear reflectivity is the coherent result of the vector sum of all backward wavelets associated with each localized reflection source; therefore, it shows, under this wide envelope dependent on the local BM response level, a multiple-peak spatial structure, dependent on the individual roughness pattern, which corresponds to a multiple-delay structure in the time domain. In a real cochlea, the temporal structure of the SFOAE residual response is indeed modulated by the spatial position of the peaks of the actual local reflectivity function (Sisto et al., 2015a), but the relative amplitude of the different-delay peaks changes with stimulus level as the envelope of the local reflectivity function, which is proportional to the square of the local BM displacement. The local reflectivity function was analytically computed in Sisto et al. (2015a) using the WKB approximation:

$$R_{local}(f, x) \approx \frac{1}{\Delta x} \int_0^\infty g(x' - x, \Delta x) \varepsilon(x') \xi^2(f, x') dx', \quad (3)$$

where $g(x' - x, \Delta x)$ is a Gaussian window function centered at x , of width Δx ($f, x \approx v_g(f, x)/f$), and v_g is the local group velocity at frequency f , which can be estimated from the computed phase of the local BM response. In this study, as the roughness function that determines the actual position (or delay) of the peaks of the SFOAE source function in a given ear is unknown and varies among ears, only the envelope of the local reflectivity function was computed with

the model. Under this universal envelope, each different roughness function inserted in the model would yield a slightly different peak configuration (as in Fig. 2 of Sisto et al., 2015a), similar to the experimental delay distributions (see Fig. 2 of the present study), but it would be impossible (and useless) to match the exact peak configuration of a given ear by trying different roughness functions. The comparison between model and experiment is more easily performed by measuring the delay of the experimental peak and computing how the envelope of the theoretical SFOAE source function (which is independent of the roughness pattern) changes with Δf at the cochlear place corresponding to that delay value. This dependence on Δf can be compared to that of the level of the corresponding experimental peak.

The effect of a suppressor was computed as the change in the amplitude of the local SFOAE source at the probe frequency along the BM, with respect to the probe-only case, as a function of the difference Δf between f_s and f_p . As in the experiments one measures a residual SFOAE, the difference between the local source function with and without suppressor is the relevant quantity, directly reflected in the envelope of the delay function of the SFOAE residual.

For each nonlinear model simulation, a correspondent simulation was run using a linear Zweig model of constant Q . As in a linear model one does not expect

any suppression, the results of these simulations provided a measure of the background “residual” level associated with the computational uncertainties and with the finite resolution of the Fourier analysis, which could be not negligible for small Δf . Only results exceeding these computational uncertainties will be discussed.

RESULTS

Experiments

In Figure 1, the SFOAE experimental residual response, normalized to the maximum, is shown for ear MML in the time-frequency domain, for three different values of Δf (100, 500, and 1500 Hz, respectively, in panels a, b, and c). The amplitude of the wavelet coefficients is shown on an arbitrary dB scale, shown in the color bar. As usual, SFOAE energy clusters in spots in the time-frequency domain. For each ear, the position of these spots is independent of the suppressor frequency shift. Increasing the suppressor frequency has two effects: (1) decreases the overall residual amplitude and (2) gradually modifies the hierarchy among different-delay spots in each frequency range, increasing the relative weight of the short-delay components. The total SFOAE response (d), estimated by spectral smoothing of the “probe

FIG. 1. Time-frequency plot of the experimental SFOAE response of ear MML, between 2000 and 3000 Hz, for three different suppressor frequency shifts: $\Delta f = 100$ Hz (A), $\Delta f = 500$ Hz (B), and $\Delta f = 1500$ Hz (C). With increasing Δf , the level decreases less rapidly for the shorter-delay components than for the longer-delay

ones, but the delay and frequency of each SFOAE spot do not significantly change. The t-f distribution of the total SFOAE estimated using spectral smoothing is also shown (D) for comparison.

alone” response p_1 , is almost coincident with the residual obtained in the near-frequency suppressor conditions (a, b).

Double-reflection SFOAE components (reflected at the cochlear base, and then again near the resonant region) appear with twice the phase-gradient delay of the single-reflection components, whereas hypothetical nonlinear distortion components would have zero delay in a scaling-symmetric cochlea. Some zero-delay component appear indeed in Figure 1, but their intensity and frequency varies quite randomly with Δf (see also Fig. 2), suggesting that they are not real SFOAEs, but, more likely, spurious residuals associated with fluctuations of the probe level between intervals 1 and 2 of the double-subtraction paradigm. Indeed, stimulus contamination or probe nonlinearity may yield significant residuals. This is particularly true at high probe levels because, in this case the reflectivity is low, so small relative fluctuations of the probe level may be of the order of the SFOAE residual level.

By integrating over the whole frequency band, one can compute the delay distribution of the wavelet coefficients, shown in Figure 2 for the same ear of Figure 1, for the SFOAE residuals obtained with nine different values of Δf , and for the SFOAE response evaluated with spectral smoothing (dashed line). Although for the largest values of Δf the signal to noise ratio (SNR) is rather poor, the multiple-peak

FIG. 2. Experimental delay distribution of the SFOAE amplitude of ear MML in a 1 kHz bandwidth centered at 2.5 kHz, for $\Delta f = 100, 200, 300, 500, 1000, 1500, 2000, 2500$, and 3000 Hz (respectively, black, red, orange, green, cyan, blue, magenta, violet, and gray). Dashed line represents the SFOAE response evaluated with spectral smoothing without any suppressor. SFOAE components with stable delay are clearly visible across stimulus levels between 3 and 8 ms. Focusing on the two main peaks, with increasing suppressor frequency, the residual SFOAE level decreases more rapidly for the long-delay component. The other two examined ears show similar patterns, with short-delay peaks around 3.5–4 ms and long-delay peaks around 6–6.5 ms. The actual delay of each peak depends on the random roughness function of the each ear.

SFOAE delay structure is generally visible, and one may appreciate that: (1) the typical delay of each peak is independent of Δf , and (2) the decrease of the peak amplitude with increasing f_s is faster for the long-delay than for the short-delay peaks.

Simulations

The simulations show how the BM response profile at frequency f_p (Fig. 3A) is modified by the presence of a suppressor of frequency f_s . Of course, near-frequency suppressors yield the largest changes, but even suppressors about one octave higher in frequency than the probe (the blue and magenta curves) suppress the response at the probe frequency in the peak region by about 1 dB. Such a small relative change is not negligible where the response is high. Indeed, although the maximum *relative* suppression (shown in dB units in Fig. 3B) occurs, for each f_s , near its characteristic place CP (f_s), the envelope of the SFOAE residual source (which is proportional to the *absolute* difference between the local BM displacement squared with and without suppressor) is always peaked within the resonant region (Fig. 3C), also for very high-frequency suppressors. With increasing f_s , the overall intensity of the SFOAE residual source drops rapidly, and the maximum moves slightly towards the base, approaching the basal edge of the resonant response peak (the BM response at frequency f_p without any suppressor corresponds to the highest line in Figure 3A).

By estimating the SFOAE phase-gradient delay as twice that of the BM at each place x , the simulated SFOAE residual source spatial density profile may be converted into a delay profile of the corresponding SFOAE components. By multiplying by the local group velocity, one gets a quantitative estimate of the envelope of the expected delay density profile (Fig. 3D). Indeed, the temporal density of the SFOAE residual source is given by:

$$R(\tau) = R(x) \frac{\partial x}{\partial \tau} = R(x) v_g(x) \quad (4)$$

This profile, which can be compared with experimental results, is broadly peaked at a typical delay that slowly decreases with increasing Δf . At a given delay, the predicted SFOAE level rapidly decreases with increasing Δf , slightly more rapidly for long-delay than for short-delay components, as graphically shown in Figure 3D.

As shown by Sisto et al. (2015a), introducing in the numerical simulation a particular random roughness profile, one gets a multiple-peak spatial distribution of the SFOAE source function, (whose envelope is

FIG. 3. Numerical simulation of the spatial profile of the BM response to a 40-dB SPL tone at frequency f_p , with a 60-dB SPL suppressor of $\Delta f = (100, 200, 500, 1000, 1500, 2000, 3000 \text{ Hz})$ (respectively, *black, red, orange, green, cyan, blue, magenta thin solid lines*, in all panels) and without suppressor (*thick black dashed line*) (A). Decreasing Δf increases the effect of the suppressor on the BM response level and, consequently, on the SFOAE source function. The relative difference between BM response with and without suppressor is peaked near the suppressor CP (B), but the difference between the BM responses squared, expressed in linear

units, which is theoretically proportional to the envelope of the residual SFOAE source function, is always peaked within the resonant region (C). This spatial source function may be represented along the delay axis, by associating to each place x the SFOAE delay estimated as twice the local BM phase-gradient delay, as computed by the model, and finally, the SFOAE source density along the delay axis is computed by further multiplying by the local group velocity (D).

shown in Fig. 3C) which corresponds to a delay distribution (whose envelope is shown in Fig. 3D). The spatial (or temporal) position of the peaks depends instead on the roughness pattern, which is obviously different for each ear. As these positions are not predictable, no roughness was introduced in the simulations, and only the envelope function was computed (Fig. 3D). One can compute from Figure 3D the dependence on Δf of a SFOAE component of any given delay and compare it with that experimentally measured in the real ears for the corresponding-delay SFOAE components, as those shown, e.g., in Figure 2. At the probe frequency used in this study, $f_p = 2.5 \text{ kHz}$, the two components have peaks of variable delay in the different ears, respectively, around 3.5–4 and 6–6.5 ms. A lower peak at twice the delay of the short-delay component is visible in Figure 2 (at about 8 ms delay), which is

likely due to double intra-cochlear reflection, although single reflection from the apical edge of the peak region cannot be ruled out. Focusing on the two main peaks in Figure 2, which we will call short-delay and long-delay, one may compute the dependence on Δf of the short and long-delay SFOAE component levels in the experiment and compare with that predicted by the model at the delay of each experimental peak, using Figure 3D. We remark again that, adding a specific roughness pattern to the model, under the envelope function shown in Figures 3C and 3D, a few main peaks would appear, as shown in Sisto et al. (2015a). In Figure 3D, these peaks would occur at random delays, so it was chosen to compute the dependence on Δf of the SFOAE source function near the typical delays of the short-delay (4 ms) and long-delay (6 ms) experimental peaks.

Comparison between Experiment and Model

In Figure 4, the level difference with respect to the near-frequency suppressor case is shown, for clarity, for the three examined ears and for the model, as a function of Δf . In the experiment, the SNR was >0 dB for all ears only up to $\Delta f = 2$ kHz, so Figure 4 is limited to this value. This comparison shows that the model slightly underestimates the experimental slope of both components (by about 20 %). This problem could be cured by fine-tuning the model, but this would not be useful to improve our understanding of the OAE phenomenology. What is more interesting is that, both in the model and in the experiment, the level decays slightly faster with increasing suppressor frequency for the long-delay SFOAE components (average slope 12.9 dB/kHz in the experiment and 10.9 dB/kHz in the model) than for the short-delay components (respectively, 9.8 and 7.8 dB/kHz). The model seems therefore to be able to provide a reasonably good estimate of the dependence on Δf of both SFOAE components, considering the variability among different ears shown in Figure 4. Part of this variability is due to the different roughness pattern of each ear, which implies that the delay of the short-delay and long-delay peaks may be different.

FIG. 4. Dependence on Δf of the level of short- (red) and long-delay (blue) SFOAE residual components, relative to the near-frequency case. Shaded thick lines: estimated from the source amplitude computed in the numerical simulations (Fig. 3D) at 4 and 6 ms. Symbols: actually measured in the three ears (different symbols for different ears) at the delays corresponding in each ear to the two main peaks (e.g., 3.5, and 6 ms, respectively, for the ear of Fig. 2, and very similar delays for the other ears, within 0.5 ms).

In the experiments, the typical delay ratio between the long- and short-delay peaks was of order 1.5–1.7 (see Fig. 2). This apparently large factor corresponds, in the model, to a rather narrow and apical spatial region for the corresponding SFOAE residual generators due to the sharp slowing down experienced by a TW of given frequency approaching its own resonant region. From Figure 5, one may appreciate that, in the model, the SFOAE delay, estimated as twice the BM phase-gradient delay at the generation place, varies by a factor of 2 over a longitudinal distance of order 0.7 mm ($\Delta CF(x)/f_p = 0.1$ in Figure 5).

DISCUSSION

This study was meant to contribute to the ongoing discussion about SFOAE generation by high-frequency suppressors (e.g., Berezina-Greene and Guinan, 2015). The above results show that, in humans, the dependence of the SFOAE suppression residuals on the suppressor frequency is consistent with the predictions of a nonlinear delayed-stiffness cochlear model. The main result of the study is that, although the SFOAE reflectivity obviously drops rapidly with increasing f_s , the barycenter of the generation region of the SFOAE residual is tightly bound to the f_p resonant region, and only slightly shifts towards the base while f_s is increased over a wide frequency range. On the other hand, this relatively small spatial shift has significant consequences on the SFOAE delay distribution. Due to the sharp dependence of SFOAE delay on the source longitudinal position within the resonant region, relatively small spatial shifts correspond indeed to large delay differ-

FIG. 5. Relation between SFOAE delay at 2.5 kHz and position of the source along the BM, estimated from the nonlinear theoretical model as twice the local BM phase-gradient delay. Within the resonant region, large delay difference may occur over a short longitudinal distance.

ences, easily measurable with time-frequency analysis. As a consequence, the decrease with increasing f_s of the SFOAE residual level associated with relatively basal sources (near the basal edge of the peak region) is significantly slower than that of the sources near the apical edge of the peak region.

The simulations clearly show (Fig. 3) that a high-frequency suppressor affects the BM response at frequency f_p also in the region between CP (f_s) and the resonant region CP (f_p), and that the main effect in terms of SFOAE residual source density is always within the resonant region because the absolute BM response change is largest there. The apparently surprising effectiveness of high-frequency suppressors is related to two model features: (1) the time-domain instantaneous nonlinearity, which implies that a BM perturbation at f_s near CP (f_s) also slightly attenuates the forward TW at f_p along its path, decreasing its peak amplitude; (2) the fast quadratic dependence of the local SFOAE source function on BM displacement, which implies that even small *relative* BM displacement changes (1 dB) in the peak region cause significant *absolute* decrease of the SFOAE generation and, therefore, significant residuals.

This study indirectly suggests that increasing the stimulus level might increase the relative weight of basal sources in the SFOAE response (or in the residual) more effectively than using high-frequency suppressors. Indeed, in the first case, as demonstrated in several modeling and experimental animal studies, the envelope of the whole SFOAE source distribution is widened and shifted towards the base, whereas in the second case only the residual source distribution is basally shifted, but it remains locally bound to the peak region of the SFOAE source profile, which, at low stimulus levels, is sharply localized. Further experimental and theoretical studies should address this particular issue. This also means that, once one chooses a high stimulus level, getting SFOAE response from a wide cochlear region, it is not possible to fully disentangle contributions from different regions using suppressors of different frequencies because the residual regions almost completely overlap.

All these phenomenological pattern is coherent with theoretical models and experimental evidence and suggests that, from a clinical application viewpoint:

- 1) SFOAEs may be effectively measured using near-suppressor paradigms or spectral smoothing, getting similar results, confirming the experimental findings of Kalluri and Shera (2007);
- 2) The main SFOAE generation region is close to the characteristic place, typically within the resonant peak of the BM response;
- 3) The localization of the SFOAE residual sources is related to the width of the SFOAE source function (i.e., of the BM response), and only weakly

depends on the suppressor frequency. Therefore, measurements at moderate probe levels seem necessary to provide more frequency-specific diagnostic information.

Summarizing, experiments and simulations suggest that, in humans, due to the peaked nature of the SFOAE source function, suppression paradigms essentially produce SFOAE residuals generated within the resonant region of the BM response. HF suppressors are obviously less effective than near-frequency suppressors as residual emission generators, but, as long as a residual is concerned, the peak of the generation region is only slightly basally shifted as the suppressor characteristic place moves towards the cochlear base. In animals, the results could be different because, due to the much lower quality factor of the cochlear resonances, the spatial width of the envelope of the SFOAE source function is much larger. This means that high-frequency suppressors can suppress SFOAE components of very short delay, coming from the basal edge of wide resonant regions.

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