New methods for analyzing high-multiple spontaneous otoacoustic emissions: short-range but no long-range spacing order

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Abstract

Three decades after their discovery, otoacoustic emissions (OAEs) are today widely used in medical diagnosis. Where, how, and why they are generated, however, is still fiercely debated, which severely impedes further medical applications. A key issue that has remained unresolved for 30 years is extent and origin of spacing order of multiple spontaneous OAEs (SOAEs) in one ear. Two mutually exclusive theories of spacing order are currently discussed, the standing-wave theory of SOAE generation and the theory of mutual suppression of adjacent local emission generators. A previously unexploited opportunity that might help settle this controversy lies in the occasional phenomenon of high-multiple SOAEs in human ears, which entail a large number of adjacent small frequency intervals. Here, the frequency distribution of 168 SOAEs from eight healthy ears of four subjects (12 to 32 SOAEs per ear) is analyzed by two newly developed methods: (a) a comparison of the real SOAE data with simulated ones that are random-generated under realistic conditions of close-range mutual suppression, and (b) a statistical analysis of adjacent small intervals. Results: (a) The histograms of interval distribution from two sets of differently simulated SOAE data have nearly the same shape as the one based on the real data. (b) The mean difference in size between adjacent small intervals is unexpectedly large, i.e. 26 % of the preferred minimum distance. (c) The variation between adjacent small intervals is not significantly different between real and simulated data. In conclusion, (a) the SOAE simulations show that mutual interaction of adjacent emission generators would be sufficient to explain the observed spacing order, and (b) the absence of multiples of the preferred minimum distance and the large variation between adjacent small intervals indicates that there is no long-range spacing order, such as predicted by the standing-wave theory of SOAE generation.

Keywords: Human; Cochlea; Acoustic frequency interval; Frequency spacing order.

1. Introduction

Currently the main application of OAEs in medical diagnosis is restricted to checking the status of hearing. One can expect, however, a much larger potential of OAEs in the context of highly complex disorders, such as tinnitus (Geven et al. 2012) or Ménière's disease (Avan et al. 2011). Certainly, the chances for a breakthrough in this respect would increase with more knowledge on the origin of OAEs.

What does the phenomenon of spacing order of multiple SOAEs in one ear tell us about the mechanism of SOAE generation? This question has remained unresolved since Schloth (1983) and Dallmayr (1985, 1986) reported the finding of a preferred minimum distance (PMD) between spectrally neighboring SOAEs. All later studies replicated this result, and Braun (1997) determined on the basis of a pool of 5245 intervals of human SOAEs that the mean PMD amounts to almost exactly 1 semitone (ST) = 1/12 of an octave. Currently there are two theories of SOAE generation, and each has its own sub-theory to explain the PMD.

According to the first theory, SOAEs are products of self-sustained oscillations of outer hair cells (OHCs) in the inner ear. This view has been supported by numerous empirical studies, e.g., by van Dijk et al. (1994) after analyzing short-term amplitude and frequency fluctuations of SOAEs. Based on this oscillator theory, van Hengel et al. (1996) used a mathematical cochlear model to test the effect of frequency distance on mutual suppression of SOAEs. They concluded (p. 3570): "The resulting suppression profile leads to natural minimal distances of effective emissions, without any necessity of additional assumptions about the mechanics of the cochlea."

According to the second theory, SOAEs are caused by cochlear standing waves (Shera 2003). Here, SOAE spacing order is determined by the parameters of the standing waves, as described by its author (p. 259): "… the characteristic SOAE spacing can be traced to the value of the wavelength of the traveling wave …"

The first theory describes SOAE generation as local, because of its assumed origin in autonomous cellular oscillators. The second theory describes it as global, because of its assumed origin in cochlear traveling waves. The local-global dichotomy also extends to the corresponding sub-theories of SOAE spacing order. The local-oscillator theory explains the PMD as a short-range effect of mutual suppression of too close oscillators. The global standing-wave theory explains the PMD as a long-range effect of the wavelengths of cochlear traveling waves. The latter dichotomy has the advantage that it can be tested fairly directly by experimental data. Here, the simple empirical question is, can short-range and/or long-range effects be observed in measured SOAE data?

High-multiple SOAEs (>10) in each ear of normal hearing human subjects are occasionally found in large screenings. Because of their large number of adjacent small SOAE intervals, these ears provide a unique and previously unexploited opportunity to examine the question of SOAE spacing order, and thus also the question of SOAE generation.

2. Material and methods

There are two preconditions for the collection of a relevant number of high-multiple SOAEs: the screening of many subjects (>100), and the best possible techniques for recording and signal analysis. Several survey studies were carried out in the early 1990s, when the principal aim was to establish prevalence conditions of SOAEs in humans. The ones that collected the largest numbers of SOAEs were those of Russell (1992) and Talmadge et al. (1993). These authors applied similar advanced techniques, which is reflected in the similar statistical results that they reported. Here, from each of these two studies the data from the two subjects presenting the highest numbers of SOAEs were investigated by newly developed techniques. The four subjects, BD, JK, DZF7A, and MZF13A were all adult females, healthy, and normal hearing. At their ages of 34, 20, 21, and 21 they presented 57, 44, 35, and 32 SOAEs, respectively.

For each of the eight ears, all frequency intervals between adjacent SOAEs were calculated into values of the logarithmic Cent scale [100 Cent = 1 semitone (ST); 12 ST = 1 octave]. Then the intervals of the 168 SOAEs of the eight ears were pooled and their size distribution was calculated for bins of 10 Cent = 0.1 ST and displayed in a histogram.

The possible effects of mutual suppression of adjacent SOAEs on spacing order were investigated by using two different simulations. The first simulation applied a simple low-side limit of interval size for each ear, i.e., intervals that were smaller than a given value were excluded. The second simulation applied a progressive range of existence probability on the low-end side of interval size, i.e., the probability of small intervals decreased progressively toward the given smallest interval. Both simulations had in common that each of the eight real SOAE distributions per ear was mirrored by an individually simulated, random-generated distribution. The RANDBETWEEN function of the software package Microsoft Excel was used to generate simulated SOAE frequencies, randomly with equal occurrence probability, from within the SOAE frequency range of the real ear. For example, for the simulation of the right ear of subject BD, 32 SOAE frequencies were generated from within the range of 629 Hz to 6140 Hz.

In the first simulation, the empirically observed general low-side limit of ~ 0.5 ST for intervals between adjacent SOAEs (Braun 1997) was simulated as follows. First, the smallest interval in the real ear was determined, e.g., 0.67 ST in the right ear of subject BD. Second, from this value a low-side limit for the simulated intervals of this ear was derived by using the nearest low-side multiple of 0.10 ST as the exclusion criterion, thus rejecting intervals < 0.61 ST for this ear. Third, after random generation, the higher SOAE frequencies of all intervals that fell into the rejection zone, i.e. were too small, were deleted and replaced by new random-generated SOAE frequencies. Fourth, the replacement procedure was repeated until the low-side criterion was satisfied for all intervals of this ear, e.g., no interval was < 0.61 ST.

For ears BD-R, JK-L, DZF7A-R, and MZF13A-R the exclusion criterion was < 0.61 ST. For the other four ears it was < 0.51 ST. When determining the exclusion criteria, the extremely small interval of 0.11 ST in MZF13A-R was neglected as an extreme outlier and the equally untypical interval of 0.36 ST in DZF7A-L was taken to justify the lower of the two typical limits, i.e. < 0.51 ST. For the 168 simulated SOAEs of the eight simulated ears the interval distribution was analyzed in the same way as for real SOAEs.

In the second simulation, the results from the first simulation were reprocessed in order to take into account the gradual decrease of intervals between 0.9 ST and 0.5 ST in the real data. The progressive decrease of intervals towards the smallest one was simulated by using several limits at steps of 0.1 ST, with each limit mirroring the real data. For example, in the right ear of subject BD the four 0.1 ST bins between 0.5 ST and 0.9 ST show 0, 4, 0, and 5 cases, respectively. These numbers were taken as maximum in the corresponding bins in the second simulation, and the same deletion and replacement procedure as in the first simulation was applied until all maximum-per-bin conditions were satisfied. It should be noted that the number of simulated intervals could in the end be below the given maximum of some bins, because each deletion and replacement of a random-generated SOAE frequency leads to a reordering of the complete chain of SOAE frequencies per ear. Further, it was not possible to add an interval to a bin, because random generation does not permit this. Therefore, the data of the second simulation unavoidably showed slightly less small intervals below 0.9 ST than the real data.

Possible long-range effects in SOAE spacing order were investigated by computing the size variation between adjacent small intervals. Because PMD amounts to almost exactly 1 ST with a range from ~ 0.5 ST to ~ 1.5 ST at the base of the distribution mode (Braun, 1993 and 1997), all intervals between 0.5 and 1.5 ST entered into the analysis. The interval size variation was analyzed statistically, separately per ear, and the differences between the variation in the real and the simulated data were tested on significance.

3. Results

3.1. Short-range spacing order

The histogram of size distributions of frequency intervals between adjacent SOAEs (Fig. 1A) shows a peak with three characteristics: a mode at 100 Cent = 1 ST, symmetrical slopes between 0.6 and 1.4 ST, and a more shallow slope between 1.4 and 1.9 ST.

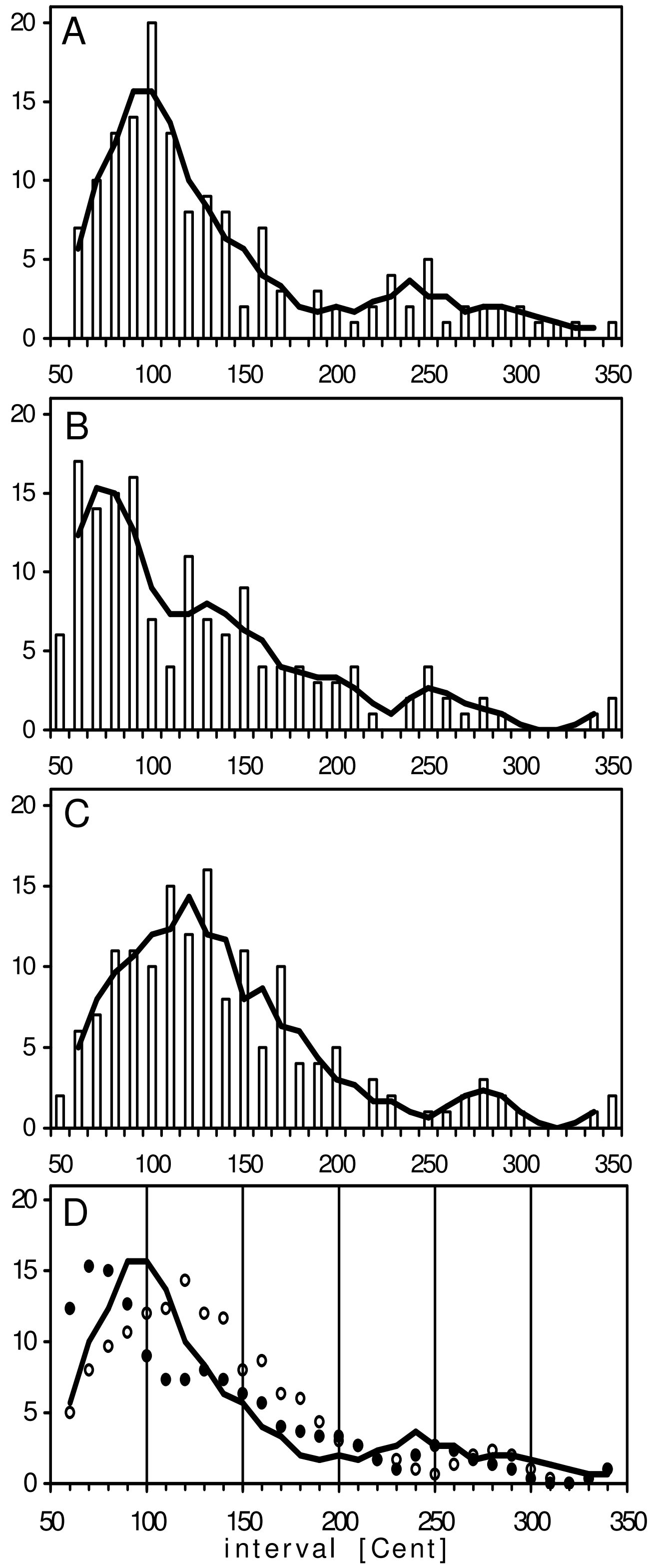

Fig. 1. Distribution of frequency intervals of all 168 SOAEs of the eight ears, displayed on the logarithmic Cent scale [100 Cent = 1 semitone; 12 semitones (ST) = 1 octave]. X-axis: interval

size in 10-Cent bins, where each bin is centered around the given scale step. Y-axis: number of intervals per bin. Columns: cases per bin. Lines: 3-point smoothing across bins. A. Real data. B. Data of first simulation (Sim1). C. Data of second simulation (Sim2). D. Lines from A-C in one plot: line: real data; filled circles: Sim1 data; open circles: Sim2 data.

The corresponding histogram of the data from the first simulation (Fig. 1B) shows the same three characteristics, but at different values: a mode at 75 Cent = 0.75 ST, symmetrical slopes between 0.5 and 1.0 ST, and a more shallow slope between 1.0 and 2.2 ST.

Also the second simulation (Fig. 1C) showed the same characteristics and at different values, again: a mode at 120 Cent = 1.2 ST, symmetrical slopes between 0.7 and 1.7 ST, and a more shallow slope between 1.7 and 2.3 ST.

Considering the single 0.1 ST bins across the three histogram, a conspicuous difference between real and simulated data appears. The real data show a clear 1-bin mode, whereas the simulations show wider modes of 4 and 3 bins. Comparison of the smoothed data (Fig. 1D), however, shows that height and shape of the three peaks are very similar. Also the more shallow slope sections of the three curves run in parallel.

3.2. Long-range spacing order

Besides the mode at 1 ST there is no further peak in Fig. 1A. In particular, it is important to note that at the multiples of 1 ST, i.e. at 2 ST and 3 ST, the distribution density is flat. Further, as Fig. 1D shows, above 2 ST the real data closely resemble the random-generated data of the two simulations.

The lower half of Fig. 2 shows the spectral SOAE distribution in the two ears of subject BD. The exact size of all small intervals in the 0.5 to 1.5 ST range is marked by triangles above the respective interval. This technique makes it evident that not only the large intervals (>1.5 ST), but also the small ones, vary considerably from one interval to the next.

Five of the eight ears had a sufficient number of adjacent intervals in the 0.5 to 1.5 ST range for the calculation of a reliable mean difference (lines 5 & 6 of Table 1). In each of the five ears it was close to 0.25 ST, and across all eight ears it was 0.26 ST (SD = 0.19 ST; range 0.00 ST to

0.84 ST). Because PMD ~ 1 ST, it follows that the mean variation between adjacent small intervals was 26 % of the PMD.

The upper half of Fig. 2 shows the simulated SOAE distribution for subject BD from the second simulation (Sim2). The similarity to the real distribution is obvious. Both real and simulated data show sections of strongly or moderately fluctuating interval size. The statistics of interval variation is shown in Table 1. Statistical tests (lines 8A and 8B of Table 1) show that the difference between real and simulated data never reaches the level of significance ($P > 0.1$ in each test).

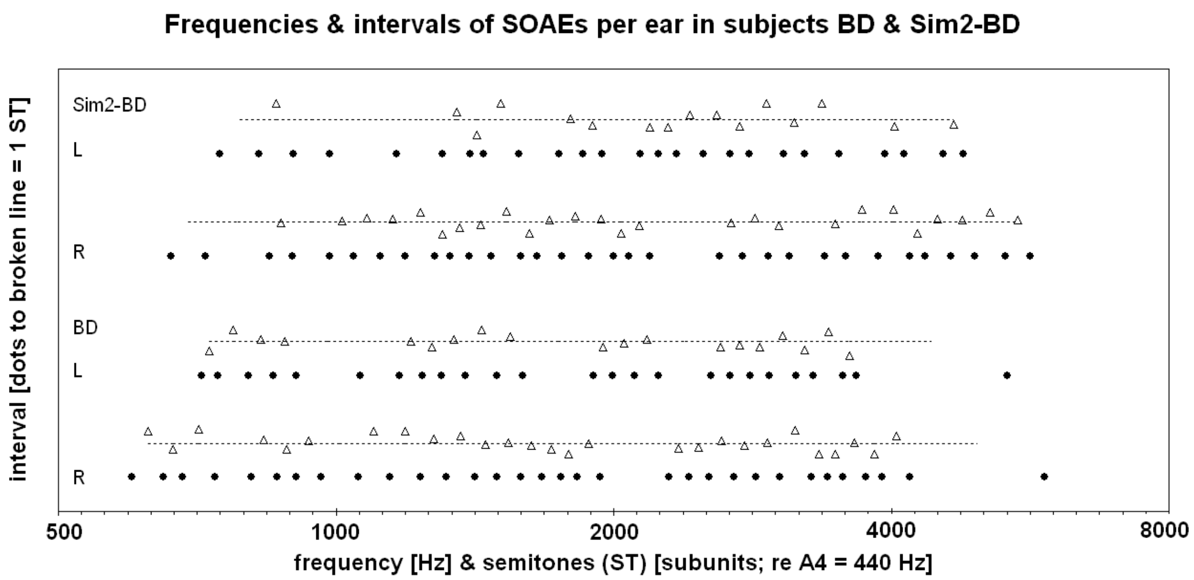

Fig. 2. Frequency spacing of all 57 SOAEs from subject BD. Lower half: real data (BD). Upper half: data from second simulation (Sim2-BD). R = right ear; L = left ear. X-axis: octave scale, expressed both in frequency [main units, in Hz] and semitones [subunits: 12 semitones = 1 octave]. Y-axis: interval size: distance between each line of SOAE dots and parallel broken line above it is equivalent to PMD = 1 ST. Filled circles (dots): spectral location of SOAEs. Triangles: spectral location and size of all intervals that have a size between 0.5 ST and 1.5 ST.

Table 1. Frequency spacing of high-multiple SOAEs in humans

1	**Subjects**	BD		JK		DZF7A		MZF13A		**Total**
2	Ear	R	L	R	L	R	L	R	L	
3	SOAEs	32	25	23	21	23	12	17	15	168
4	Intervals > 0.5 & < 1.5 semitones	27	19	18	11	13	3	6	7	**104**
5	Adjacent intervals from (4)	23	15	14	5	8	0	1	3	**69**
6	Mean difference between adjacent intervals of (5) [in semitones]	0.24	0.28	0.25	0.24	0.26	----	0.16	0.43	**0.26**
7	Standard deviation re (6)	0.20	0.21	0.14	0.11	0.22	----	----	0.41	0.19
1A	**First simulation (Sim1)**	BD-1		JK-1		DZF7A-1		MZF13A-1		
3A	SOAEs	32	25	23	21	23	12	17	15	168
4A	Intervals > 0.5 & < 1.5 semitones	24	17	17	9	14	5	12	10	**108**
5A	Adjacent intervals from (4A)	19	12	14	5	8	2	10	5	**75**
6A	Mean difference between adjacent intervals of (5A) [in semitones]	0.26	0.33	0.32	0.28	0.24	0.36	0.35	0.58	**0.32**
7A	Standard deviation re (6A)	0.16	0.27	0.22	0.20	0.25	0.44	0.31	0.28	0.24
8A	t-test of (6) vs (6A)	**NS**	**NS**	**NS**	**NS**	**NS**	----	----	----	**NS**
1B	**Second simulation (Sim2)**	BD-2		JK-2		DZF7A-2		MZF13A-2		
3B	SOAEs	32	25	23	21	23	12	17	15	168
4B	Intervals > 0.5 & < 1.5 semitones	26	16	14	9	10	5	12	10	**102**
5B	Adjacent intervals from (4B)	22	10	8	5	5	2	8	6	**66**
6B	Mean difference between adjacent intervals of (5B) [in semitones]	0.27	0.43	0.26	0.37	0.19	0.36	0.22	0.46	**0.31**
7B	Standard deviation re (6B)	0.21	0.30	0.21	0.23	0.13	0.44	0.20	0.25	0.24
8B	t-test of (6) vs (6B)	**NS**	**NS**	**NS**	**NS**	**NS**	----	----	----	**NS**

4. Discussion

4.1. Short-range spacing order

The two simulations have shown that a low-side limit of interval size alone leads to a strong distribution peak slightly above the limit. In the real data the difference between limit and peak is 0.5 ST. In the first simulation (Sim1) it is 0.25 ST, and in the second simulation (Sim2) it is 0.7 ST. These differences are the logical and transparent results of the respective simulation conditions, and they provide interesting information. The peak in the real data cannot be the result of a simple threshold for suppression. In that case it would be closer to the low-side limit of 0.5 ST, as demonstrated by the effect of a simple threshold in Sim1. However, it can be the result of progressive suppression, as shown by the effects of Sim2. In other words, Sim1 overestimated mutual suppression by a too sharp low-side cut-off, and Sim2 underestimated it by a too moderate progressive cut-off range. From these results one can conclude that appropriate suppression conditions that lie between Sim1 and Sim2 quite naturally will produce a peak at 1 ST, as seen in the real data.

The sharpness of the peak in the real data, however, is not reproduced in the simulations. This means that mutual suppression alone cannot be a sufficient cause of the PMD phenomenon. A possible solution would be additional mutual facilitation of close-range oscillators. At a certain frequency difference two oscillators can reach a stability between facilitation and suppression resulting in an increased probability of self-oscillation. The coexistence of the sharp distribution peak at 1 ST (Fig. 1A) and the large variation in interval size of adjacent SOAEs (Fig. 2) may have its origin in the coexistence of geometrical order and slight irregularities in the anatomy of the organ of Corti.

3.2. Long-range spacing order

The absence of distribution peaks at the multiples of 1 ST (Fig. 1A) was reported before (Braun 1997). In that study, however, all possible intervals per ear (all-order intervals) were analyzed, not just intervals between adjacent SOAEs (first-order intervals). This led to doubts (Shera 2003) if chains of several adjacent small intervals around 1 ST really would add up to multiples of 1 ST, or, due to their size variation, rather would cumulate to such broad peaks in the distribution histogram that they would disappear in the noise floor. The same doubts cannot be put forward against the present results, because here only intervals between adjacent SOAEs (first-order intervals) were analyzed.

The missing multiples of 1 ST mean that the standing-wave theory of SOAE spacing order is difficult to uphold. If the wavelength of a cochlear standing wave influences the probability of frequency spacing from one SOAE to its neighbor, it should also influence the spacing to its second next and third next neighbors. The reason is that the standing waves are conceptualized as extending from the cochlear frequency place that corresponds to an SOAE frequency down to the stapes. Over such a long distance the wavelength of a standing wave seems unlikely to vary from one node to the next to such an extent that multiples of the wavelength would disappear into the noise floor of a histogram.

The size variation between adjacent SOAE intervals, as shown in Fig. 2 and Tab. 1, provides similar consequences for the standing-wave theory of SOAE spacing. The mean variation between adjacent small intervals was found to be 26 % of PMD. In the context of standing waves it should be instructive to express interval variation as the corresponding phase variation. Concerning a full circle rotation that might be related to SOAE spacing (e.g., Siegel et al. 2011, p. 312) it would be 360° x 0.26 = 94°. Concerning a half circle rotation it would be 180° x 0.26 = 47°. Such variation appears to be too large to be related to the rotation in a standing wave.

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