# New methods for analyzing high-multiple spontaneous otoacoustic emissions: no spectral periodicity but binaural mirroring

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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 previously unexploited opportunity to explore these questions are the occasionally found high-multiple spontaneous OAEs (SOAEs) in humans, because of their large number of adjacent small 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) statistical analysis of adjacent small intervals; (b) comparison of real vs. simulated, random-generated, interval data. Results: (a) The mean difference between adjacent small intervals is unexpectedly large, i.e. 26 % of the preferred minimum spacing. (b) The variation between adjacent small intervals is not significantly different between real and simulated, random-generated, data. (c) Binaural frequency mirroring occurs significantly more often in the real than in the simulated, random-generated, data ($P < 0.0001$) and ca 20 % of all SOAEs take part in above-chance binaural mirroring. In conclusion, there is no spectral periodicity of SOAEs, and thus no indication for spatial periodicity in the cochlea. The finding of binaural SOAE mirroring replicates earlier results derived by a different method and further emphasizes the strong role of neural influence on the formation of SOAE frequency loci.

Keywords: Human; Spontaneous otoacoustic emission; Cochlea; Binaural; Acoustic frequency interval.

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Abbreviations: OAE, otoacoustic emissions; SOAE, spontaneous otoacoustic emissions; PMD, preferred minimum distance; ST, semitone.

## 1. Introduction

Is OAE generation related to, or even caused by, phenomena of spatial periodicity in the cochlea? 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. Talmadge et al. (1993) were the first to suggest the possibility of some kind of equal spacing in the cochlea that caused the PMD. However, Braun (1997) found in a large-scale statistical analysis of inter-SOAE spacings that there was a strong peak in the interval distribution at PMD but not at the multiples of PMD, as the equal spacing hypothesis would predict. Despite of this counter evidence, numerous mathematical models of OAE generation and cochlear function of the past 20 years were based on concepts of spatial periodicity in the cochlea. It is the declared aim of the present investigation not to take part in the discussion of these mathematical concepts (for a recent example, Siegel et al., 2011, pp. 312-313), but to answer a simple empirical question. Is SOAE spacing periodic, i.e., are small adjacent intervals of similar size a typical observation?

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

OAE amplitudes are influenced by descending neural signals to the cochlea (reviewed in Braun, 2006), but as yet there is no theory that could explain the many diverse effects that have been observed. Binaural effects are of particular interest, because they implicate a central auditory influence. Concurrently-measured covariations of bilateral SOAEs were reported by Penner et al. (1994), and accurate binaural mirroring of SOAE frequencies by Braun (1998). High-multiple SOAEs in both ears of one subject provide a unique and again previously unexploited opportunity to increase our knowledge on possible efferent influences on OAE generation.

## 2. Material and methods

There are two preconditions for the collection of a relevant number of high-multiple SOAEs: 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 subject 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 semitones (ST) with a fine-graded scaling of 0.01 ST (1 octave = 12 ST). 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. For all *adjacent* intervals with this quality, the size variation from interval to interval was computed and analyzed statistically, separately per ear.

Each of the eight given SOAE distributions per ear was paired 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.

The probabilistic low-side limit of ~ 0.5 ST for intervals between adjacent SOAEs (see above) 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. It should be noted that the purpose of the simulation was to generate a stochastic interval distribution for the given conditions of each individual ear. The PMD at 1 ST was not simulated, because it only has a small and negligible effect on interval variation (see results section). The necessary further constraints that underlie the PMD phenomenon in real ears are an important but separate issue (see section 4.3). The eight simulated SOAE distributions were then analyzed in the same way as the eight real distributions. Finally, the difference between the results from the real and the simulated ears was tested on significance, for each of the eight pairs separately and in cumulation.

Binaural frequency mirroring of SOAEs was determined for each of the four subjects. If the interval between a right-ear SOAE and a left-ear SOAE was <= 0.16 ST (equivalent to a frequency deviation of 0.9 %), it was considered a mirroring incident. Unavoidably, this value had to be set arbitrarily, because of our limited understanding of OAEs. It seemed reasonable, however, because it is also the value of largest deviation from optimum consonance in the standard (equal temperament) tuning of all keyboard instruments and the guitar (re intervals of minor third and major sixth). The difference between the ratio of mirroring incidents in the real and in the simulated ears was tested on significance, for each of the eight pairs separately and in cumulation.

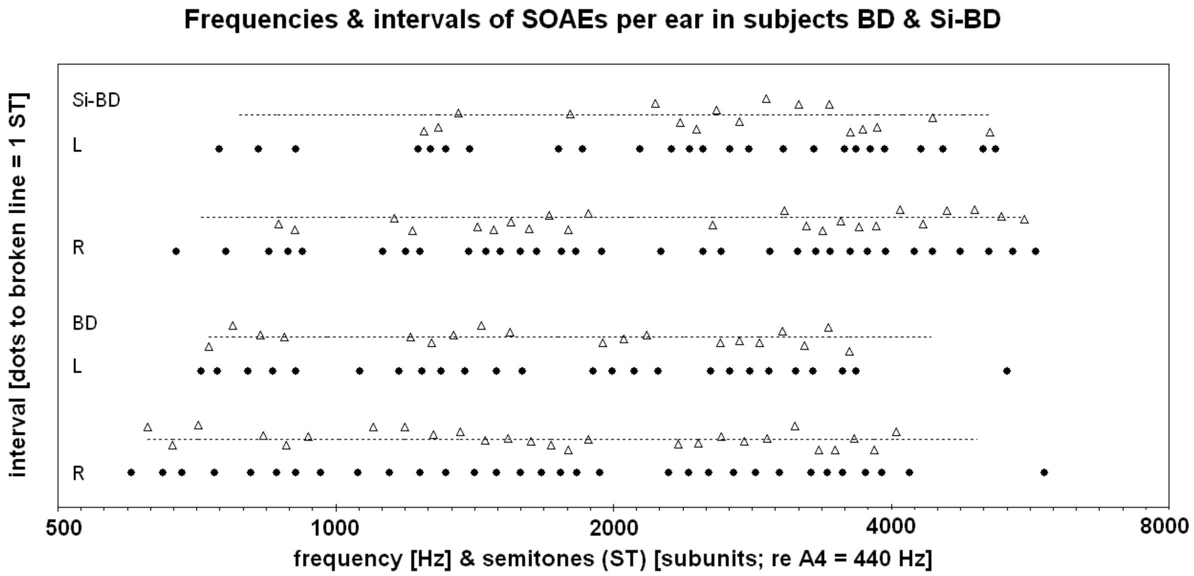


Fig. 1. Frequency spacing of all 57 SOAEs from subject BD. Lower half: real data (BD). Upper half: simulated data (Si-BD). R = right ear; L = left ear. Triangles mark position and size of all intervals that have a size between 0.5 ST and 1.5 ST. Distance between each line of SOAE dots and parallel broken line above it is equivalent to PMD = 1 ST.

## 3. Results

The lower half of Fig. 1 shows the spectral SOAE distribution in the two ears of subject BD on a logarithmic, ST-graded, frequency scale. At the first glance, the two lines of filled circles may appear partly quasi-periodic. However, at the second glance this impression becomes doubtful. Therefore the exact size of all small intervals in the 0.5 to 1.5 ST range was marked by triangles above the respective interval. This technique has now made 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 I). In each of the five ears it was close to 0.25 ST, and across all eight ears it was 0.26 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. 1 shows the simulated SOAE distribution for subject BD. Concerning the question of apparent periodicity, the similarity to the real distribution is striking. Close inspection reveals only a single slight difference. The marked intervals tend to be a tiny bit smaller in the simulated data. This difference appears to be due to the simple cut-off at 0.5 ST or 0.6 ST in the simulation, whereas the real data are consistent with a gradual cut-off between ~ 0.9 ST and ~ 0.5 ST (see discussion section). Fig. 1 makes it clear, however, that this tiny difference only has a negligible effect on size variation between adjacent intervals. The statistics showed that seven of the eight simulated 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 5A & 6A of Table I). The mean across all eight simulated ears was slightly larger than the one across all real ears (0.32 ST vs. 0.26 ST). Statistical tests (line 7B of Table I) showed that the difference between real and simulated data never reached the level of significance ($P > 0.1$ in each test).

Fig. 2 shows both the real and the simulated SOAE distribution of subject DZF7A. Incidents of binaural mirroring, as defined in the methods section, are marked. Table I (lines 8, 9, 8A, 9A,

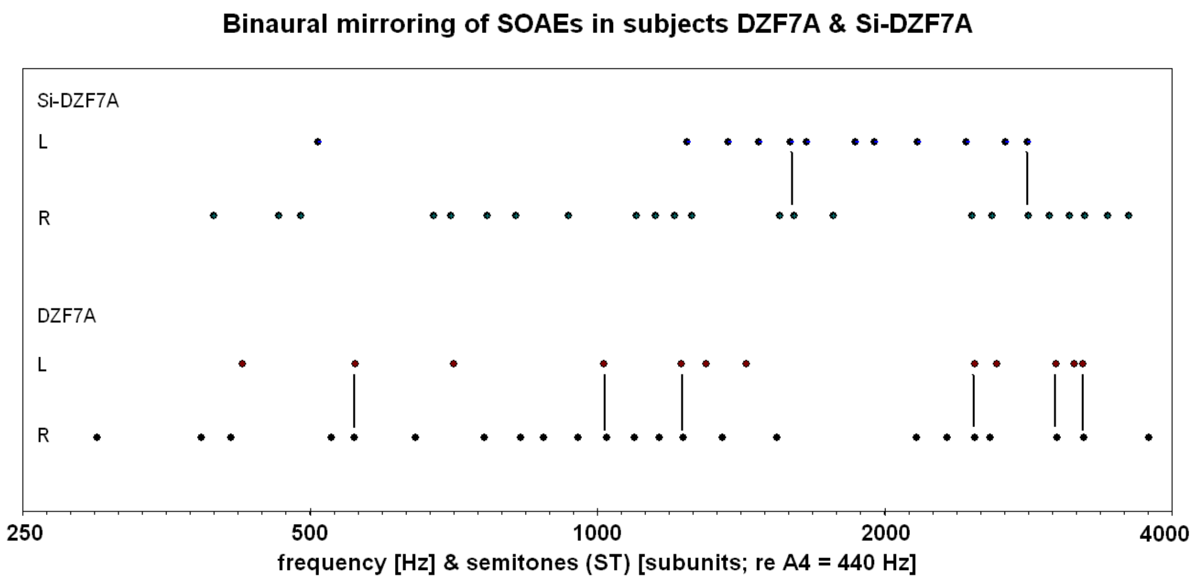


Fig. 2. Frequency spacing of all 35 SOAEs from subject DZF7A. Lower half: real data (DZF7A). Upper half: simulated data (Si-DZF7A). R = right ear; L = left ear. Binaural intervals <= 0.16 ST (see text) are marked by vertical lines.

and 9B) shows that the real data show a much higher ratio of mirroring incidents than the simulated ones. The difference is highly significant (*P* < 0.0001).

**Table 1**
**Characteristics 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 |
| 8 | Binaural tone mirroring | 10 | 10 | 6 | 6 | 6 | 6 | 5 | 5 | **54** |
| 9 | (8) in % of (3) | 31 | 40 | 26 | 29 | 26 | 50 | 29 | 33 | 32 |
| 1A | **Simulated subjects** | Si-BD | | Si-JK | | Si-D… | | Si-M… | | **Si-Total** |
| 2A | Ear | R | L | R | L | R | L | R | L | |
| 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 |
| 7B | t-test of (6) vs (6A) | **NS** | **NS** | **NS** | **NS** | **NS** | ---- | ---- | ---- | **NS** |
| 8A | Binaural tone mirroring | 7 | 7 | 1 | 1 | 2 | 2 | 1 | 1 | **22** |
| 9A | (8A) in % of (3A) | 22 | 28 | 4 | 5 | 9 | 17 | 6 | 7 | 13 |
| 9B | $Chi^2$ test of (8)/(3) vs (8A)/(3A); *P* | NS | NS | < 0.05 | < 0.05 | NS | < 0.10 | < 0.10 | < 0.10 | **< 0.0001** |

## 4. Discussion

4.1. Why was the absence of SOAE periodicity not reported earlier?

All earlier analyzes of SOAE frequency spacing, from the first one (Schloth, 1983) to the most recent one (Bergevin et al., 2012), applied one identical method of data presentation, the histogram of frequency intervals. This method is simple, transparent, and successful. It shows an outstanding peak at the interval of 1 ST and a range from 0.5 ST to 1.5 ST at the base of the distribution mode. The histogram technique, however, provides no information on the question of a possible periodicity in SOAE spacing. While it shows that intervals close to 1 ST are the most common ones, the variation (corresponding to the 0.5 to 1.5 ST range) between adjacent small intervals in a given ear may, or may not, be consistent with periodic spacing. Despite this lack of knowledge, the variation of SOAE spacing from one interval to the next in one ear has never before been published. This course of events is surprising, considering the strong and longstanding interest in periodicity in the cochlea in the context of mathematical concepts of membrane-based traveling waves (section 4.3).

### 4.2. Binaural mirroring

Binaural mirroring of SOAE frequencies had earlier been found in the statistics of 9555 binaural SOAE pairs from a large number of subjects (Braun, 1998). There, the possibilities that this phenomenon was caused by artefacts in measuring or analyzing, acoustic cross-talk, genetics, or developmental factors were examined by specific empirical and statistical sub-studies. It turned out that all of these factors had to be excluded as possible causes. The only surviving hypothesis was that time-locking, which is known to occur in the medial olivocochlear system (Gummer et al., 1988), can spread bilaterally and have a long-term effect upon the cochlear outer hair cells. In case of same best frequency, and thus same electromechanical resonance, these cells would respond very similarly, across both ears, upon period information that is encoded in the inter-spike intervals of efferent input.

The present study shows that only four subjects with high-multiple SOAEs in both ears are sufficient to reveal the phenomenon. Further, the new results allow for the first time a reliable estimate of the probability for a human SOAE to be mirrored in the opposite ear. The simulated data showed a mirroring ratio of 13 % (Table I, line 9A) and the real data one of 32 % (Table I, line 9). Therefore we can estimate that the ratio of above-chance mirroring in human SOAEs is about one in five. This is not a negligible quantity and it should be considered both in theory (section 4.3) and in medical diagnosis (section 4.4).

4.3. Implications for OAE generation and cochlear function

The mean variation between adjacent small intervals was found to be 26 % of PMD. The same value would also apply to any spatial variation within the cochlea that might be related to SOAE generation, such as in anatomy or in standing waves of vibrating membranes. For the latter cases it is instructive to express the deviation as phase difference. 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°.

Even more important than the absence of periodicity in SOAE spacing may be the apparent stochastic nature of spacing above the low-side probability limit at 0.5 ST. Both the PMD of ~ 1 ST and the low-side probability limit of ~ 0.5 ST can be explained by a mutual suppression of oscillating emission generators. Suppression would lead to such results, if it affected intervals <~ 0.9 ST and became progressively more effective as intervals decrease from ~ 0.9 ST to ~ 0.5 ST, the probabilistic low-side limit of interval existence. The suppression may be similar to the one suggested by van Hengel et al. (1996).

When taking together the indications of (a) absence of periodicity, (b) a stochastic element, (c) binaural coupling, and (d) further efferent influence (Braun, 1997 and 2000), one can summarize that SOAE generation apparently is not related to spatial periodicity in the cochlea. Instead, it appears to be related to stochastic order and mutual interaction of potential emission sources, which additionally are influenced by descending neural input. As candidates for SOAE generators, the outer hair cells of the mammalian cochlea would fit the observed constraints.

4.4. Consequences for medical diagnosis

Currently the main application of OAEs in medical diagnosis is restricted to checking the status of normal hearing, particularly in newborns, who cannot answer questions. One can expect, however, a much larger potential of OAEs in the context of highly complex disorders, such as tinnitus or Ménière's disease. Tinnitus occurs in various, strikingly different, forms, which often are difficult or even impossible to verify objectively. The diagnosis of Ménière's disease is so complex and difficult that usually several years pass between the first symptoms and a conclusive diagnosis. While there is already a considerable body of research that explores the potential of OAEs in these respects (e.g., Geven et al., 2012, for tinnitus, and Avan et al., 2011, for Ménière's disease), it is evident that the chances for a breakthrough would increase with more knowledge on the origin of OAEs.

In particular, the central auditory neural influence on OAEs (Norena et al., 2002) has not yet been explored very well. A more widespread awareness of OAE generation by neurally influenced cellular generators is likely to direct more research also into this direction.

## 5. Conclusions

SOAE spacing is not periodic but consistent with stochastic order. The only observable general constraint for stochastic order is compatible with a mutual suppression of nearby frequency neighbors where suppression starts at ~ 0.9 ST and then progressively increases toward a probabilistic coexistence limit of ~ 0.5 ST. Additional order in SOAE spacing, such as binaural frequency mirroring and binaural low-integer frequency ratios (Braun, 2000), which may affect more than 20 % of measured SOAEs, can only be attributed to descending neural influence. The new observations on SOAE spacing are in agreement with the concept of outer hair cells in the mammalian cochlea as the sources of OAE generation.

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