DISCRIMINATION OF TREMOR DISEASES BY INTERACTIVE SONIFICATION

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ABSTRACT

We introduce an interactive sonification approach for the discrimination of tremor diseases. Following up to our previous research, we developed two new sonification methods of measured 3-axes acceleration data of patient's hands. Prior to sonification, the data is conditioned by Principal Component Analysis (PCA) in order to separate translational and rotational components of the movement. The first sonification implements a vocoder-based method in which energies of relevant frequency bands are used to control individual amplitudes of harmonically tuned oscillators.

The second sonification approach is based on Empirical Mode Decomposition (EMD). The input signal is decomposed into Intrinsic Mode Functions (IMFs) whose frequencies and amplitudes control an oscillator bank.

In order to enhance the distinct rhythmic qualities of tremor signals in the output, additional amplitude modulation based on various instantaneous energy measures has been applied for both sonifications.

An intuitive interface allows to switch interactively between both sonifications and control critical parameters in order to listen to specific aspects of the observed tremor. The results of a pilot study indicate that both sonification methods are able to provide relevant information on tremor data and represent a useful and complementary addition to already available diagnostic tools.

1. INTRODUCTION

Tremor is a movement disorder which produces involuntary rhythmic oscillation movements of a body part [1]. As it can be caused by various neurological diseases [2], a correct diagnosis is needed as fast as possible to choose the right therapy. Each of those diseases evokes a specific movement pattern which can be recognized visually by specialized neurologists. This visual diagnosis, however, is unreliable and common approaches for additional ex-post analysis of videos or measured sensor data are time-consuming and can not be easily integrated into daily clinical practice. Real-time sonification of tremor movement data could therefore become a promising extension to already available diagnostic tools [3].

Similar to [3] we concentrate on the three tremor diseases parkinsonian tremor, essential tremor, and psychogenic tremor, which are sometimes difficult to distinguish by traditional methods. Following up to our previous research [3], we developed two new sonification methods for tremor analysis. These are supposed to be used interchangeably dependent on tremor characteristics and personal preference. The presented sonification interface is targeted at interactive use in the presence of the patient, acting as a supplementary medical tool in order to improve diagnostic quality.

This article is structured as follows. First, in Sec. 2, we describe the technical setup as well as some basic data conditioning steps, such as automatic gain control and Principal Component Analysis. Afterwards, two different tremor sonification methods are presented: Vocoder-based (Sec. 3) and EMD-based (Sec. 4). These sonifications are integrated in an interactive audiovisual interface, which is described in Sec. 5. In order to evaluate both sonifications and the interface, a pilot study has been carried out, which is presented in Sec. 6. Finally, in Sec. 7, we summarize our findings and give an outlook on future work.

Accompanying sound examples can be found on the project web page [4]. These include stereo recordings of both sonifications with two patients of each tremor type.

2. DATA AQUISITION AND CONDITIONING

Movement data is recorded by 3-axis accelerometers[1] attached to the patient's hands and sampled at 1 kHz. The acceleration signal is processed by a DC removal and low pass filter at 70 Hz in order to cover the typical frequency range of pathological tremor (predominantly 3 – 15 Hz). Both left and right arm sensors are individually sonified.

As strong amplitude variations can occur between different measurements, Automatic Gain Control (AGC) is applied to the input signal at different stages in both sonifications.

The measurement data is further conditioned by a Principal Component Analysis (PCA). This method from multivariate statistics facilitates the evaluation of high-dimensional data sets. After finding the principal components, it is possible to divide the movement into translational and rotational components [3], [5]. In the context of the presented sonifications only the first principal component $PCA_1[n]$ is used for sonification. It contains only translational components and describes a projection of the three-dimensional data onto a one-dimensional vector.[2]

In both sonifications, however, the ratio between rotational and translational components can be optionally made audible through an additional chorus effect – a slightly delayed playback of the sonification signal (see Sec. 3.1 and 4.2). While this shows no effect for purely translational signals, an increasing amount of rotational components results in an increased amplitude of the duplicate signal, up to a strong chorus effect for purely rotational signals.

[1] Biometrics ACL300 (mass: 10 g, range: ±10 G, accuracy: ±2% FS): http://www.biometricsltd.com/accelerometer.htm

[2] A detailed description of the PCA implementation can be found in [3].

3. VOCODER SONIFICATION

The first sonification implements a vocoder-based method in which energies of relevant frequency bands are used to control individual amplitudes of harmonically tuned oscillators. Eventually, the amplitude of the summed output is modulated by the envelope of the original input signal to reproduce the specific rhythmic behavior of the tremor.

3.1. Implementation

Sonification 1 can be divided into the following functional blocks:

1. *Data Preconditioning: bandpass filtering, AGC, PCA*
2. *Division into frequency bands*
   The signal is divided into 5 frequency bands by using a sliding window FFT:
   2–4 Hz, 4–6 Hz, 6–9 Hz, 9–13 Hz, and 13–20 Hz.
   The lower frequency bands are chosen to be relatively narrow, as they are expected to contain most energy. The center frequencies and bandwidths were selected based on experience with the spectra of different tremor types.
3. *Energy distribution in the bands*
   The energy signals in each band are computed and normalized.
   Eventually, by using a variable exponent p, their dynamic range is expanded (p>1) or compressed (p<1).
4. *Oscillator bank*
   The processed energy values control the amplitudes of five sinusoidal oscillators tuned harmonically to each other, i.e., following the harmonic series (f_0 , $2 \cdot f_0$, etc.).
   - A Frequency Modulation (FM) with the smoothed and half-wave rectified input signal $HW\{PCA_1[n]\}$ can be applied optionally. This results in a time-varying fundamental frequency of $f_i(t)$ instead of a constant f_0.
   - A slightly detuned duplicate oscillator bank is used for the optional chorus effect.
5. *Summing and Amplitude Modulation (AM)*
   The sum of the five oscillator signals is finally amplitude modulated by the variably smoothed and half-wave rectified input signal $HW\{PCA_1[n]\}$.

3.2. Sound characteristics

Overall, the sonification sounds result in a harmonic complex evoking a clear, optionally time-varying pitch percept (compare sound examples [4]). The time-varying timbral character resembles vocal formants whereas the overall amplitude modulation adds a rhythmic dimension. The three different tremor types lead to different sound characteristics:

A distinct characteristic of the parkinsonian tremor is the very regular and stable rhythm. Also strength, i.e.amplitude of $PCA_1[n]$ and rhythmic base frequency show only small fluctuations. Due to peakedness of the tremor signal, the energy fluctuations of the different frequency bands are well synchronized and provide a rich timbre.

The essential tremor shows similar rhythmic behavior as the parkinsonian tremor; however, the rhythm is a bit more irregular. Also the frequency of the main peak is less stable and slightly varies around the center frequency. In contrast to the parkinsonian tremor, often only one or two fluctuating harmonics are distinguishable.

The movement pattern of the psychogenic tremor can be seen as a mixture of both other tremors. Consequently, this applies for its sound characteristics.

4. EMD SONIFICATION

The second sonification approach is based on Empirical Mode Decomposition, as was already suggested in [3].

4.1. Empirical Mode Decomposition

EMD was originally developed by Huang, Shen, Long, *et al.* [6] to analyze non-stationary and non-linear signals. Complex data sets can be decomposed into a finite (and often small) number of so-called Intrinsic Mode Functions (IMFs). Each IMF represents one mode of the signal.

In contrast to the Fourier analysis, where a signal is decomposed into a set of pre-defined base functions, the EMD obtains the base functions adaptively from the signal. A perfect reconstruction of the original signal is possible via summation of the contained IMFs and the resulting residual signal (see Eq. 1).

The basic EMD algorithm is explained in [6]–[9]. To be able to define an extracted function as IMF, two conditions must be fulfilled:

1. The number of maxima and the number of zero crossings must be equal or only different by one.
2. The (current) average, determined through the envelope of the maxima and minima, must be zero.

The sifting process

The process of finding the IMFs $x_i[n]$ ($1 \leq i \leq N$) from the original signal $x[n]$ is called sifting. The input signal is iteratively decomposed into a finite number of N IMFs. The sifting process is structured as follows:

1. *Upper and lower envelope generation*
   Generate the upper and lower envelope based on the local maxima and minima.
2. *Envelope subtraction*
   Subtract the average of both envelopes $m_i[n]$ from the original signal $x[n]$: $h_i[n] = x[n] - m_i[n]$
3. *Validity check*
   Check $h_i[n]$ on the validity of the two conditions for IMF.
   - If these are fulfilled, $h_i[n]$ is an intrinsic mode function $x_i[n]$.
   - If not, a sifting takes place, which means that steps 1 to 3 are repeated with $h_i[n]$ as new input signal.
4. *IMF subtraction*
   Compute residual signal: $r_i[n] = x[n] - x_i[n]$
5. *Termination criterion*
   - If $r_i[n]$ is either a constant or a monotonic function, the sifting is complete.
   - If not, $r_i[n]$ provides the new raw material for the further decomposition process (go to step 1).

The decomposed signal $x[n]$ can now be written as:

$$x[n] = \sum_{i=1}^{N} x_i[n] + r_N[n] \tag{1}$$

Hilbert-Huang Transform (HHT)

For each individual IMF, the instantaneous phase, frequency, and amplitude can be obtained from the Hilbert transform. In conjunction with the EMD, this is called the Hilbert-Huang Transform (HHT) [6].

The HHT carries several advantages compared to other transforms, which have made the EMD a powerful analytic tool. Firstly, it makes a perfect lossless reconstruction of the original signal possible, while no prior knowledge on the signal qualities (stationary, non-stationary, etc.) is needed. Further, it provides an illustration of the "physical world". Finally, instantaneous attributes can be determined through the Hilbert transform.

Typical applications of the HHT, amongst others, are medical tools, damage detection at structures, and analysis of climate data, earthquakes, or quote time series in financial mathematics [10]. The HHT has been proposed for tremor analysis in recent studies, e.g., [11]–[13].

4.2. Implementation

In sonification 2, the first five intrinsic mode functions of $PCA_1[n]$ are determined via empirical mode decomposition. As the first, $IMF_1[n]$, does not contain much relevant information of the tremor it is rejected and only the remaining four $IMF_2[n]$ to $IMF_5[n]$ are used as an input signal for the sonification. The higher the number of IMFs, the more low-frequency components are included. Eventually, these IMFs are individually leveled by AGC.

Each IMF then controls the frequency and amplitude of an individual sinusoidal oscillator. Although the instantaneous amplitude and frequency can be computed at any time by using the Hilbert transform, we used a different approach which provided better sonification quality.

The instantaneous frequencies are determined by generalized zero-crossing [14], as a computation from the HHT was found to provide instable results. The determined frequencies are then multiplied by a user-controlled constant factor to map the low tremor frequencies (about 2 – 15 Hz) to the audible range. Instead of using the IMF envelope as an amplitude modulator, as proposed by the original EMD algorithm, each oscillator is then individually amplitude modulated by the by the smoothed and half-wave rectified IMF signal $HW\{IMF_i[n]\}$ itself, in order to display the original tremor frequency range as a superposition of rhythmic structures.

Similar to sonification 1, a slightly detuned oscillator bank for the optional chorus effect can optionally be added.

Finally, the output signal of the sonification is formed by the sum of these four signals.

4.3. Sound characteristics

Due to the specific time-varying characteristics of the tremor signals, the sonic result of the EMB-based sonification resembles the sound of singing birds (compare sound examples [4]). The register of each "bird" is dependent on the frequency and amplitude of the corresponding IMF. The impression of different tempos of the individual chants is determined by the AM. Different sound characteristics can be observed for the examined tremor types:

The parkinsonian tremor leads to singing with constant rhythm and very stable, and often low, pitch. One IMF often dominates – only one bird is singing.

In case of the essential tremor, the rhythmic pattern is very similar to the parkinsonian tremor; still, with the addition of some rhythmic disturbances. The audible frequency of the main peak is less stable and fluctuates around the center frequency. This leads to the impression of eagerly chatting birds at different registers. Compared to the parkinsonian tremor, the dominant bird/IMF is more intensely accompanied by others.

As with sonification 1, the psychogenic tremor is hard to identify due to the sound characteristics of both other tremors mixed.

5. INTERACTIVE USER INTERFACE

The interactive sonification interface is implemented in Pure Data (Pd). Apart from the sonic representation of the tremor data, a simple visualization is provided (see Fig. 1).

On the one hand, it shows various visual information, such as waveform view, oscillogram, level meter, FFT spectrum, ratio between rotational and translational movement as well as band intensities and IMF frequencies for the individual sonifications.
On the other hand, apart from standard controls, such as volume, it features interactive access to a selection of sonification parameters. Globally for both sonifications, the smoothing of the AM modulator signal as well as the optional chorus effect can be controlled. In addition, each sonification allows individual access to oscillator frequency, dedicated gains for left and right arm sensors, and optional FM (only sonification 1).

As we have described, the presented sonification system implements various analysis methods of the tremor input signal. This tool, however, aims not at providing definite answers nor a final diagnosis of the disease. Rather, it is employed to extract relevant features of the tremor signal, which are exposed aurally by the developed sonification algorithms. The resulting feature space is high dimensional and therefore predestined for aural rendering in preference to visual representations.

A metaphor for this approach could be the use of the microscope in medical context. By adjusting the magnification and focus, or by adding contrasting agents, it helps exposing and collecting different characteristics of the sample, which would not be accessible otherwise. These characteristics can then be connected in order to form a coherent picture. The diagnosis is, and probably has to be, left to the doctor.

Similarly, the developed sonification interface, whilst aurally rendering the whole complex feature space, provides fast means for contrasting specific features of the tremor against others, e.g., by zooming in or out on a particular subset of characteristics. Our intention is not to break down the complex structure of the input signal to a lower dimensional or more simple representation, but rather to facilitate the construction of a coherent picture based on the observed phenomena in order to make informed decisions. We think that the interactive change of the sonification parameters is paramount for this to happen.

The proposed interactive sonification tool tries to accomplish this task by combining both visual and aural representations; providing an apt number of toggles and parameters to the user, which have an immediate effect on the visual and aural display and allow rapid switching and comparison between different settings.

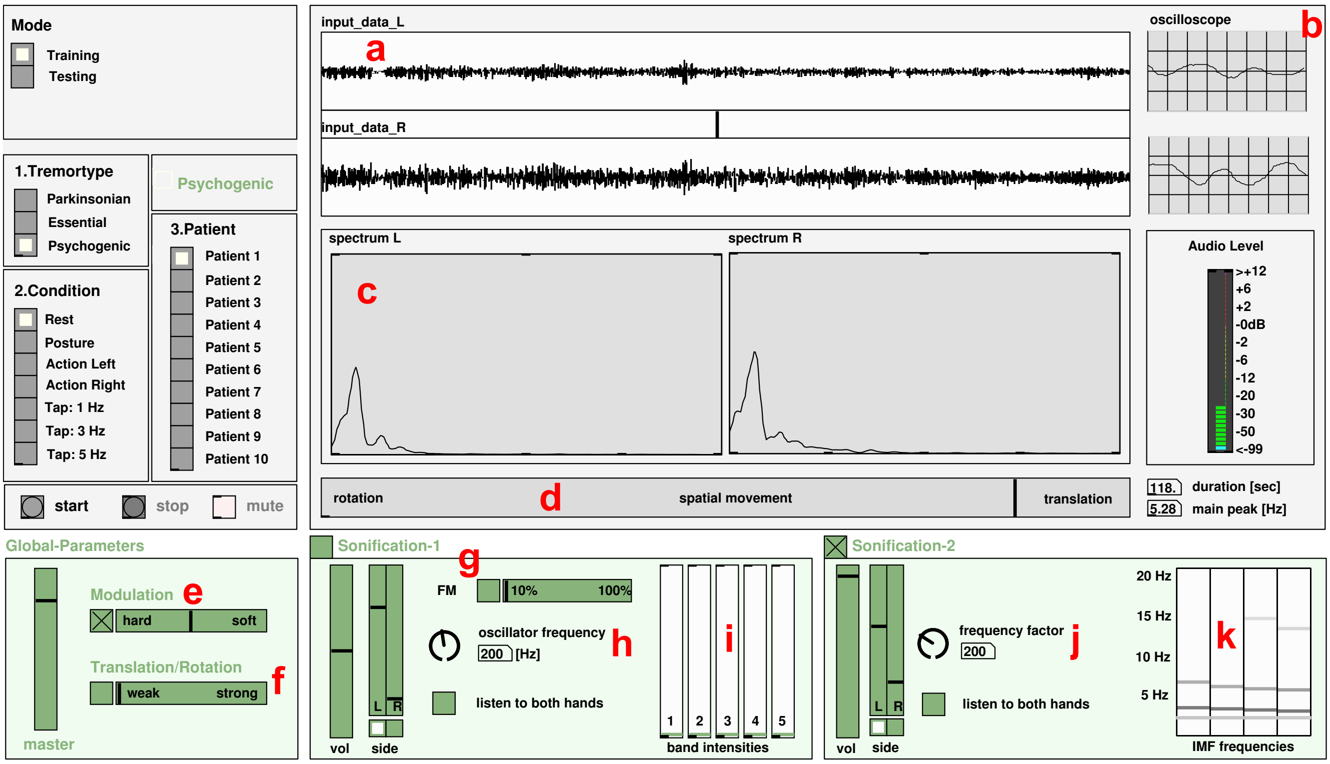

Figure 1: *Graphical user interface (here in training mode). Annotations in red letters. Visual feedback: a) waveform view, b) oscilloscope, c) FFT spectrum, each for left and right arm sensor, d) indication of the current ratio between rotational and translational components. Global parameters: e) compression/expansion of the AM modulator, f) chorus effect. Sonification 1: g) FM modulation, h) oscillator fundamental frequency, i) visualization of band intensities. Sonification 2: j) oscillator frequency factor, k) visualization of IMF frequencies.*

6. PILOT STUDY

The presented sonification methods as well as the interactive interface were evaluated in a pilot study. Under three conditions (see Tab. 1), five test participants (three neurologists, two audio professionals) were asked to identify diseases through sonification alone: At first, the vocoder-based and the EMD-based sonification were tested individually, while in the third case participants were allowed to switch interactively between both sonifications. Test participants obtained prior training to differentiate the specific sound characteristics and become accustomed to the software interface. The resulting sound was presented via headphones.

During the experiment, all available parameters (see Sec. 5) could be altered freely and interactively; however, no data about this interaction has been collected. It is important to note that especially the comparison between left and right arm sensor signals revealed critical information on the observed tremor type, e.g., when listening to both channels simultaneously in stereo. This is due to the fact that different tremor diseases led to different synchronicity/intensity between both hands. In particular, both arms are usually similarly affected by essential and psychogenic tremor, but can show strong asynchronous behavior in case of the parkinsonian tremor [2].

Recorded movement data[3] of 30 patients were equally divided into three different groups of diseases (10× parkinsonian tremor, 10× essential tremor, and 10× psychogenic tremor). This reference diagnosis was made by means of common clinical diagnosis criteria.

[3]The clinical tremor data was collected by the Medical University of Graz in 2012. Signals were recorded with CED 1401 interface in Spike software and pre-processed in Matlab.

Table 1: *The different evaluation types and groups of diseases in the experiment.*

Evaluation	1	Sonification 1 (Vocoder)
	2	Sonification 2 (EMD)
	3	Interactive switch between Son. 1 and 2
Disease	1	Parkinsonian tremor (Par)
	2	Essential tremor (Ess)
	3	Psychogenic tremor (Psy)

Each evaluation type was tested in two separate runs. In each run, the data of all 30 patients was presented in random order. Participant could only proceed to the next patient after submitting a diagnosis. Afterwards, it was not possible to go back or change a previous diagnosis. Each started run had to be finished completely (all 30 patients), otherwise the gathered data was invalidated. For every diagnosis, participants had to specify their confidence on a scale reaching from 1 to 100. Additionally, the elapsed time was recorded for each case.

Table 2: *Overview of the results.*

	Evaluation 1 (Voc.)	Evaluation 2 (EMD)	Evaluation 3 (switch)	Average
Percent correct answers	64.0%	60.0%	57.6%	60.5%
Confidence Interval CI95	57.7% – 69.9%	53.6% – 66.1%	51.2% – 63.8%	
Identical answers (runs 1 and 2)	74.4%	82.4%	71.2%	76.0%
Confidence	40.7	37.5	38.2	38.8
Response time	94 s	75 s	92 s	87 s

Table 3: *Contingency tables for the three evaluations and the average over all of them. Values describe % of submitted diagnoses D. R is the reference diagnosis. Correct answers (main diagonal) are highlighted.*

(a) *Evaluation 1.*

R \ D	Par	Ess	Psy
Par	**68.6**	13.8	17.5
Ess	7.8	**66.7**	25.6
Psy	27.5	16.3	**56.3**
Sum	104.0	96.7	99.3

(b) *Evaluation 2.*

R \ D	Par	Ess	Psy
Par	**70.0**	11.3	18.8
Ess	2.2	**65.6**	32.2
Psy	38.8	17.5	**43.8**
Sum	111.0	94.3	94.7

(c) *Evaluation 3.*

R \ D	Par	Ess	Psy
Par	**68.8**	10.0	21.3
Ess	8.9	**56.7**	34.4
Psy	32.5	20.0	**47.5**
Sum	110.1	86.7	103.2

(d) *Average.*

R \ D	Par	Ess	Psy
Par	**69.2**	11.7	19.2
Ess	6.3	**63.0**	30.7
Psy	32.9	17.9	**49.2**
Sum	108.4	92.5	99.1

6.1. Results

First results revealed conspicuously low hit rates for some of the patients. After a following analysis of the data by the neurologists participating in the experiment, it was noticed that four of these patients did not show any tremor during data recording. Another patient suffered from a very specific disease which does not match the typical tremor pattern. As those five data sets could not be assigned to one of the three investigated tremor categories, they were excluded from further analysis of the results.

All following results are based on the reduced data set of 25 patients (8× Par, 9× Ess, 8× Psy). Tab. 2 provides an overview of these results. On average, correct judgments reached from 58% to 64% for the individual evaluation conditions, which is far above chance (roughly 33%).

The primary test results (percent correct answers) were analyzed by using a binomial test with one variable "disease" (3 levels), assuming a constant hit rate of $1/3$ and sample size 250 (25 patients × 5 participants × 2 runs).[4] Compared to chance, the results for all evaluations were highly significantly better (assuming a significance level of 5%). The results of the individual evaluation forms were not significantly different to each other (see Tab. 2, CI95) and are therefore considered equivalent.

For further analysis of the results, contingency tables were created for the individual evaluation types (see Tab. 3a to 3c). Additionally, the average over all evaluations (Tab. 3d) gives a quick overview of the correct/wrong diagnosis of diseases.

[4]Despite the not exactly equal distribution of patients per tremor disease, calculations were done with a constant hit rate of $1/3$.

The main diagonal (percent correct diagnosis) as well as the secondary diagonals (false diagnosis) in Tab. 3d show differences between the three diseases. On the one hand, patients with parkinsonian and essential tremor were only rarely confused with each other (11.7% falsely Ess, 6.3% falsely Par); on the other hand, many of them were falsely assigned to the group of patients with psychogenic tremor (Par: 19.2%, Ess: 30.7%).

This observation is confirmed by a statistical analysis: The psychogenic tremor led to noticeably lower values of sensitivity (Par: 0.69, Ess: 0.63, Psy: 0.49), and F-measure (Par: 0.66, Ess: 0.67, Psy: 0.48), compared to both other tremors.

6.2. Discussion

When interpreting the results of the pilot study, it is important to consider several aspects concerning the design of the experiment. The system is expected to be used in real time in clinical practice. Under these circumstances, the information provided by the interactive sonification interface is supposed to be combined with other tools to form a complete diagnostic chain. Nevertheless, an isolated evaluation was necessary in order to examine its clinical benefit.

The results indicate that both sonification methods (Vocoder and EMD) provide relevant information on the observed tremor to a similar extent and can serve as a useful complement to already available diagnostic tools. Both sonifications (Vocoder and EMD) seem to deliver relevant information on the observed tremor to a similar extent. A joint usage of both sonifications, however, did not lead to an improvement in the diagnostic results.

During ensuing discussions with the participants, it came out that both sonifications were considered equivalent and test participants showed individual personal preference towards one of them. An implementation of both systems with free choice therefore seems reasonable.

Due to the similarly high percent correct diagnoses of both neurologists and audio professionals, it is assumed that the greater experience with sound, concerning the audio professionals, could be compensated by the neurologists with their greater experience with tremors. According to the neurologists, the proposed interface facilitates a detailed insight in the movement pattern of an examined tremor without visual tools. Consequently, acoustically observed characteristics can be associated directly with specific tremor diseases.

Finally, the results showed that the average percent identical answers in repeated runs was larger than the actual percent correct judgments (76.0% vs. 60.5%). It is argued here that specific tremor characteristics can be recognized robustly over several runs, even if the conclusion drawn from this observation is "incorrect". This fact lets us conjecture that discrimination performance can be further increased by training.

7. CONCLUSION AND OUTLOOK

We presented an interactive sonification interface for efficient diagnosis of tremor diseases that is intended to be used as a complementary tool in the diagnostic chain.

The evaluation of the two different sonifications showed that acoustical differentiation between tremor signals is possible and can facilitate disease classification for various tremor types. The possibility to interactively switch between the two sonifications did not improve the diagnostic performance; however, due to diverging personal preference between test participants, an optional free choice is still found reasonable.

The data analysis can be performed in the presence of the patient and possibly replaces time-consuming ex-post analysis of video and spectral data. In advantage over those methods, the sonification provides an auditory representation which is continuously following the spectral characteristics of the tremor and thus allows to keep track of the time-dependent spectral structures. Due to the high information density, the sonic result provides rather complex, but still identifiable and discriminable gestalts – especially with the EMD-based sonification. On the one hand, this leads to a holistic validation of tremori, while on the other hand, even neurologists with little aural training are able to retrieve different movement patterns in a fast and intuitive way from the sonified tremor signals. The interactive change of sonification parameters facilitates the construction of a coherent image of the observed tremor and allows informed decision making. Nevertheless, the proposed sonification interface is meant for integration into clinical practice in order to extend current diagnostic tools, which is assumed to be essential for an efficient and correct diagnosis.

For the pilot study, the EMD was performed off-line in Matlab. In case of a future application, however, aiming at fast and reliable diagnosis already during patients' examination, a real-time implementation is necessary. This causes some problems: Firstly, the EMD computation depends on future samples, which automatically introduces a delay in the output. Further, the number of necessary sifting loops to find an IMF as well as the number of IMFs contained in the signal are unknown. The consequent unknown complexity could cause some problems if a limited computing power is assumed. Based on already available solutions, e.g., [15]–[17], we are currently implementing an on-line EMD algorithm which efficiently calibrates its computation parameters to the signal's specific characteristics.

As the pilot study was based on a small number of patients (with some of them showing rare atypical tremor movement) and clinical diagnoses were not perfectly reliable, the results of the pilot study are of limited significance. Therefore, we are currently carrying out an extended study with recent data of more than 100 patients with confirmed diagnosis. We assume that aurally trained test participants can achieve better results than untrained listeners. It is further argued that neurologists can acquire these abilities providing that they obtain appropriate ear training. Accordingly, the test participants of the extended study are recruited from an expert listening panel [18], [19], a group of musicians and sound engineers with experience in listening tests. Despite the target audience being neurologists, trained listeners are chosen to ensure a best-case scenario and hence a more fair comparison of the results with the currently achieved diagnostic accuracy through visual and computer-aided ex-post analysis methods. An additional focus of the new evaluation is the interactive use of sonification parameters. First results will be presented at the ISon workshop.

References

[1] K. T. Wyne, "A comprehensive review of tremor," *JAAPA*, vol. 18, no. 12, pp. 43–50, Dec. 2005.

[2] G. Deuschl, P. Bain, and M. Brin, "Consensus statement of the Movement Disorder Society on Tremor. Ad Hoc Scientific Committee," *Mov. Disord.*, vol. 13 Suppl 3, pp. 2–23, 1998.

[3] D. Pirrò, A. Wankhammer, P. Schwingenschuh, R. Höldrich, and A. Sontacchi, "Acoustic interface for tremor analysis," in *Proc. International Conference on Auditory Display (ICAD)*, Feb. 2012.

[4] IEM. (2016). Acoustic interface for tremor analysis, Project web page, [Online]. Available: `http://tremor.iem.at`.

[5] J. Shlens, "A tutorial on principal component analysis," in *Systems Neurobiology Laboratory, Salk Institute for Biological Studies*, 2005.

[6] N. E. Huang, Z. Shen, S. R. Long, M. C. Wu, H. H. Shih, Q. Zheng, N.-C. Yen, C. C. Tung, and H. H. Liu, "The empirical mode decomposition and the hilbert spectrum for nonlinear and non-stationary time series analysis," *Proc. of the Royal Society of London A: Mathematical, Physical and Engineering Sciences*, vol. 454, no. 1971, pp. 903–995, 1998.

[7] A. Zeiler, R. Faltermeier, I. R. Keck, A. M. Tomé, C. G. Puntonet, and E. W. Lang, "Empirical mode decomposition - an introduction," in *International Joint Conference on Neural Networks (IJCNN)*, Jul. 2010, pp. 1–8.

[8] M. C. Peel, G. E. Amirthanathan, G. G. S. Pegram, T. A. Mcmahon, and F. H. S. Chiew, "Issues with the Application of Empirical Mode Decomposition Analysis," in *International Congress on Modelling and Simulation (MODSIM)*, Dec. 2005, pp. 170–176.

[9] R. T. Rato, M. D. Ortigueira, and A. G. Batista, "On the HHT, its problems, and some solutions," *Mechanical Systems and Signal Processing*, vol. 22, pp. 1374–1394, Aug. 2008.

[10] N. E. Huang and S. S. Shen, Eds., *Hilbert-Huang Transform And Its Applications*. World Scientific, 2005.

[11] S. Ayache, T. Al-ani, and J.-P. Lefaucheur, "Distinction between essential and physiological tremor using hilbert-huang transform," *Neurophysiologie Clinique/Clinical Neurophysiology*, vol. 44, no. 2, pp. 203–212, 2014.

[12] S. S. Ayache, T. Al-ani, W. H. Farhat, H. G. Zouari, A. Creange, and J. P. Lefaucheur, "Analysis of tremor in multiple sclerosis using Hilbert-Huang Transform," *Neurophysiologie Clinique/Clinical Neurophysiology*, vol. 45, no. 6, pp. 475–484, Dec. 2015.

[13] I. Carpinella, D. Cattaneo, and M. Ferrarin, "Hilbert-Huang transform based instrumental assessment of intention tremor in multiple sclerosis," *J Neural Eng*, vol. 12, no. 4, Aug. 2015.

[14] N. E. Huang, Z. Wu, S. R. Long, K. C. Arnold, X. Chen, and K. Blank, "On instantaneous frequency," *Advances in Adaptive Data Analysis*, vol. 1, no. 2, pp. 177–229, 2009.

[15] G. Rilling, P. Flandrin, P. Gonçalvés, *et al.*, "On empirical mode decomposition and its algorithms," in *IEEE-EURASIP workshop on Nonlinear Signal and Image Processing, NSIP-03, Grado (I)*, 2003.

[16] N. Chang, T. Chen, C. Chiang, and L. Chen, "On-line empirical mode decomposition biomedical microprocessor for hilbert huang transform," in *Biomedical Circuits and Systems Conference (BioCAS)*, IEEE, 2011, pp. 420–423.

[17] A. Zeiler, R. Faltermeier, A. M. Tomé, C. Puntonet, A. Brawanski, and E. W. Lang, "Sliding empirical mode decomposition for on-line analysis of biomedical time series," in *Advances in Computational Intelligence: International Work-Conference on Artificial Neural Networks (IWANN)*. Springer, 2011, pp. 299–306.

[18] R. Höldrich, H. Pomberger, and A. Sontacchi, "Recruiting and evaluation process of an expert listening panel," in *Fortschritte der Akustik (NAG/DAGA 2009)*, B. Rinus, Ed., Rotterdam (Niederlande), Mar. 2009.

[19] M. Frank and A. Sontacchi, "Performance review of an expert listening panel," in *Fortschritte der Akustik (DAGA 2012)*, H. Hanselka, Ed., Berlin (Deutschland), Sep. 2012.