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Figure 1: Prototype ear simulators for neonatal hearing assessment designed against a specification derived from clinical and anatomical data.

Welcome

The project "*Metrology for a universal ear simulator and the perception of non-audible sound*" (*EARS*) of the EMRP programme arrives at its final stage and we are pleased to present the sixth newsletter to you. Another time the project work has made serious progress and results were obtained which significantly promote knowledge and technology in the addressed fields. We invite you to read about several aspects of the work which are presented within this newsletter.

Following an intensive development phase ultrasonic transducers which allowed the determination of hearing thresholds for airborne ultrasound could be produced. In parallel the investigation of perception mechanisms at infrasound frequencies continued with an fMRI study. This process was accompanied by measuring the middle ear transfer of the same test persons using otoacoustic emissions. The second version of the universal ear simulator prototype was manufactured and calibration techniques were developed and tested. Thus, all prerequisites for first clinical trials, which are under way, have been created.

The organization of the two final workshops of the project has been continued. Registration is open (see News and Facts) now and the programme and invited speakers are settled. We cordially invite you to join these events, which will bring together many persons interested in these challenging topics.

I am looking forward to seeing you in Berlin or in Teddington.

Christian Koch
Coordinator

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News and facts

- Registration for the two final workshops in Berlin and Teddington is open:
- Workshop ‘Infrasound and air-borne ultrasound: measurement, impact on humans and assessment’, Berlin: http://www.ears-project.eu/emrp/ears-workshop-berlin-reg.html.
- Workshop ‘Novel ear simulator for newborns: New steps in calibration of audiological devices’, Teddington: https://www.regonline.co.uk/Register/Checkin.aspx?EventID=1642634.
- The second prototype of the ear simulator is available and calibration methods have been developed and tested.
- The clinical test of the ear simulator at collaborating medical centres is starting.

Highlights from the work packages

Measurement of hearing thresholds at ultrasound frequencies

To investigate the perception of higher frequencies and airborne ultrasound by means of brain imaging techniques (e.g. MEG, fMRI), hearing thresholds are essential for a sufficient auditory stimulation. Hence, monaural hearing threshold measurements were performed with 26 otologically normal female and male subjects’s aged 18 to 30 years. The newly developed MEG and MRI compatible insert earphone ultrasound source based on a piezoelectric transducer was used.

Frequency (kHz)	Threshold (dB SPL) Minimum	Median	Maximum	Number of valid data
14.00	18.1	32.9	67.1	26
15.75	23.5	59.3	94.8	26
16.95	35.4	75.1	109.0	26
19.10	59.6	98.5	114.0	24
20.70	84.1	109.0	117.0	21
21.50	96.5	...	...	8
22.40	101.0	...	...	8
23.75	109.0	...	...	4
24.20	109.0	...	...	3

Table 1: Monaural insert earphone hearing threshold.

The thresholds for pure tones were determined at 9 frequencies for the right ear of each subject using a 2-alternative-unforced-choice method. The used stimuli were a tone burst with a total duration of 1400 ms with 100 ms pause between the single tones. Sound pressure levels were directly measured at the entrance into the ear tip via 1/8’’ microphone.

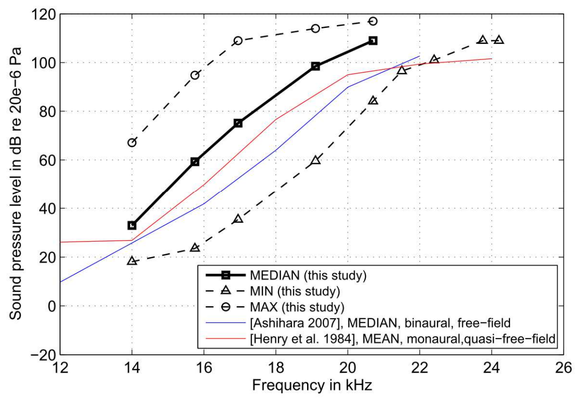

Figure 2: Median monaural insert earphone hearing thresholds (boxes) with minimum (triangle) and maximum (circles) values. Additional, binaural and monaural free-field data (blue, red) from literature [1, 2] are shown.

Figure 2 and Table 1 show the measured median with minimum and maximum threshold. 8 out of 20 subjects were able to

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hear and determine a threshold up to 22.4 kHz. The median insert earphone threshold shows a similar increase of the threshold to higher frequencies in comparison to the literature data [1, 2] despite an overall offset (6-10 dB).

[1] Ashihara, K. (2007); "Hearing threshold for pure tones above 16 kHz", J. Acoust. Soc. Am., 122(3), pp 52-57.

[2] Henry, K. R., Fast, G. A. (1984), "Ultrahigh-Frequency Auditory Thresholds in Young Adults: Reliable Responses up to 24 kHz with a Quasi-Free-Field Technique", Audiology 23, pp 477-489.

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Second prototype of ear simulator and development of calibration methods

The first sample of ear simulators specified and designed according to the universal concepts established earlier in the project, were produced in the middle of 2014 (Figure 1). The next important stage was to validate their performance against these original specifications.

The two key parameters that must be determined to enable the ear simulator to be used for traceable measurements are the microphone pressure sensitivity and the acoustic transfer impedance. The latter is the parameter the one that determines the sound pressure level generated by any given transducer, and is therefore required to be as close as possible to that of human test subjects.

The ear simulators are unlike established designs in a number of respects, and new calibration methods for both the microphone and the ear simulator have been developed ready for the validation. To increase confidence in the validation process, individual calibration facilities were established at four partner laboratories, and a round-robin calibration exercise carried out. The results can be seen in the Figure 3.

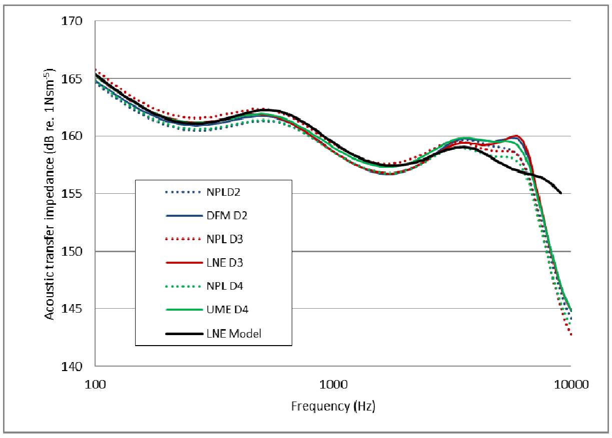

Figure 3: Results from the round-robin calibration exercise to validate the acoustic transfer impedance characteristic of the neonatal occluded ear simulator. Note that typical measurement uncertainty in each curve is around 0.5 dB.

The two striking observations that can be made are; that results from all laboratories agree very well, and they appear to follow the specification derived from numerical modelling, at least up to around 4 kHz. There is a clear departure from the model in the last octave from 5 kHz to 10 kHz, and these are the subject of further investigation. However the modelling, design and manufacturing processes are considered to be fully validated by these measurements, at least in this important part of the frequency range. Furthermore, the feasibility of appropriate calibration methods has been demonstrated, ready for the day when such devices are put into routine clinical practice.

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Measurement of middle ear transfer function using otoacoustic emissions

The transfer of low-frequency (LF) sound pressure at the ear drum into motion of the basilar membrane (BM) was measured, aiming to understand the cochlear physiology underlying psychophysically obtained equal

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loudness contours (ELCs). This so-called middle-ear transfer function (METF) was obtained by applying LF tones of various frequencies (20 – 250 Hz) to suppress the otoacoustic emission (DPOAE), a distortion product emitted by the healthy inner ear in response to two beating primary tones in the 2 KHz range [1]. The sound pressure of the LF tones was adjusted by the experimenter to achieve a constant suppression of the DPOAE by 9 dB. Assuming that his constant suppression by the LF tone indicates a constant BM biasing amplitude at the DPOAE generation site, an equal-output function (similar to ELCs) was obtained.

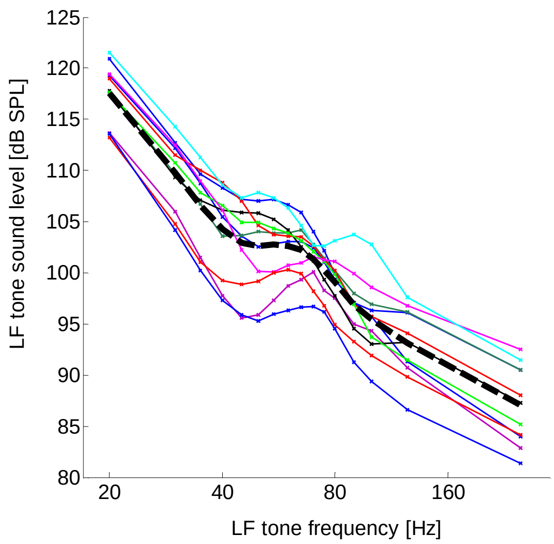

Figure 4: METF of 12 subjects (coloured lines) and their average (dashed black line). The ordinate shows the LF tone level necessary to suppress the DPOAE by 9 dB.

Figure 4 shows such METF from 12 normal hearing subjects. Almost all curves exhibit a pronounced resonance, and even with inconsistent frequency locations, this feature can still be observed in the average curve (dashed black) in form of a step. The average function was then compared to the average ELCs of the same 12 subjects (Figure 5). The later were derived from a gradient field (coloured lines show average) that was obtained by having the subject compare the loudness of a series of closely spaced tone pairs. All ELCs (shown as solid black lines) larger 20 phon reflect the step in the objectively measured METF (The black dotted average curve is the same as in Figure 4). Note that such step is not featured in the isophon curves of ISO 226:2003 (bold dashed line shows 60-phon curve). The step disappears as the loudness approaches hearing threshold. Computer simulation studies are underway to understand why this might be the case.

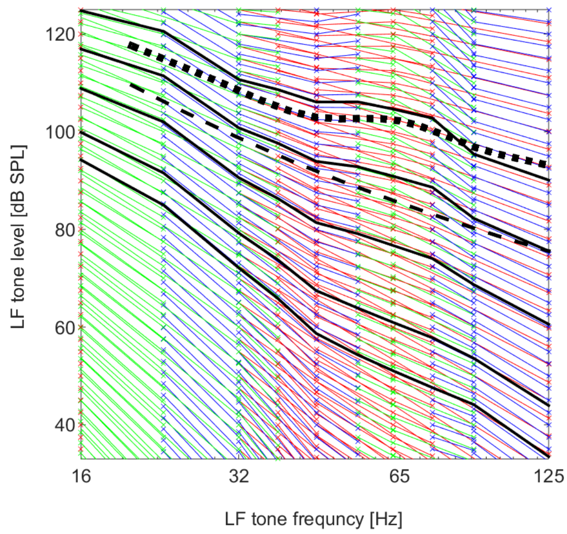

Figure 5: ELCs (thin black; 10, 20, 40 60 & 80 phon) were derived from a loudness gradient field (colored lines; average data from 12 subjects). ELCs (40 - 80 phon) show a similar step as the average METF (dotted). ISO 226:2003 does not show such step (dashed; 60-phon isophon).

[1] Marquardt, T. et al. (2007). "Low-frequency characteristics of human and guinea pig cochleae," J. Acoust. Soc. Am. 121, 3628-3638.

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Localisation of perception of infrasound in the brain using fMRI

We used functional magnetic resonance imaging (fMRI) to measure the neural response of 16 subjects to very low fundamental frequency tones covering the range from 250 Hz down to infrasound of 8 Hz.

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To perform the study we used the MEG compatible infrasound source, which was described in the Newsletter of August 2013. Subjects' individual loudness perception was tested before the measurements to provide constant subjective loudness across the frequency range. To measure brain signal we used a 3 Tesla MRI system (Siemens, Erlangen) with a sparse signal echo-planar imaging sequence, that enables us to present auditory stimuli while the scanner is silent. The stimuli were pure sine tones at frequencies of 250 Hz, 125 Hz, 63 Hz, 40 Hz, 20 Hz, 12 Hz and 8 Hz. Importantly, all subjects reported a perception down to 8 Hz.

Frequencies were presented in random order but in sync with the sparse-sampling MRI sequence. We used a general linear model approach within the SPM software module, to analyse the data.

The fMRI results indicate an involvement of auditory cortex in the processing of almost all the presented stimuli. No other brain regions were observable for the statistical threshold at $p < 0.001$ and a cluster size > 22 voxel. Interestingly, no significant activation was found for the 20 Hz stimuli. The activated regions for the different frequencies are shown in Figure 6.

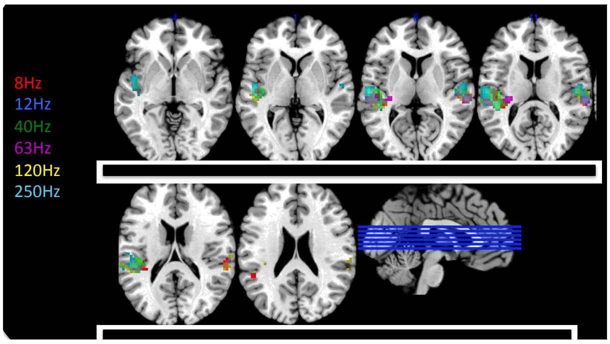

Figure 6: Results of the fMRI measurements plotted as a contrast against the baseline condition. Activation restricted to the auditory cortices is observed using $p < 0.001$ as statistical threshold and a cluster size > 22 voxel. A small shift of the activation towards central with decreasing stimulus frequency is visible.

Plotting the BOLD response in the primary auditory cortex (as defined by an Atlas provided by the SPM Anatomy toolbox, http://www.fz-juelich.de/inm/inm-1/DE/Forschung/_docs/SPMAnatomyToolbox/SPMAnatomyToolbox_node.html) as a function of frequency a U shaped curve is found having a dip at 20 Hz in primary auditory cortex (Figure 7).

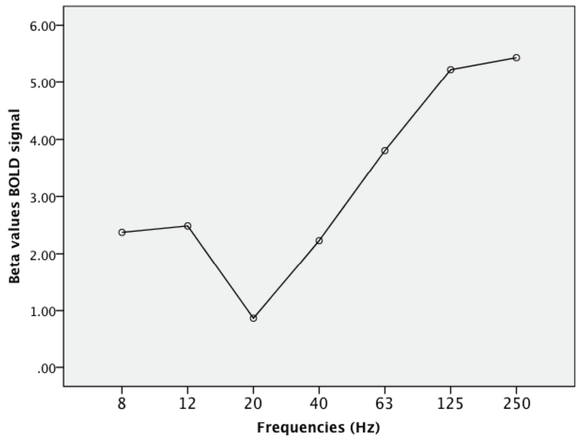

Figure 7: BOLD activity of the functionally defined primary auditory cortex showed a U shape with a dip at 20 Hz.

This behavior shown in Figure 7 may hint at two different processing pathways for auditory stimuli above and below 20 Hz. It has previously been shown that not only auditory stimulation (white noise), but also somatosensory stimulation (stimulation on the middle and index finger) can result in activation of the auditory cortex (Foxe et al., 2002). The authors find significant overlap between both types of stimulation in bilateral superior temporal gyrus. Our present hypothesis is that potentially sounds below 20 Hz are represented based on their somatosensory properties, whereas sounds above 20 Hz are represented based on their auditory properties. The observed dip at 20 Hz fits nicely to the common definition of infrasound as sounds beneath 20 Hz.

Foxe JJ, Wylie GR, Martinez A Schroeder CE, Javitt DC, Guilfoyle D, Ritter W, Murray MM (2002). Auditory-

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somatosensory multisensory processing in auditory association cortex: An fMRI study. J Neurophysiol, 88, 540-543.

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Dissemination of work

One of the cornerstones of the EMRP, is that research projects should create impact and benefits for its stakeholders. This section provides a summary of recent dissemination activities.

Workshops

The highlight of the planned dissemination activities is approaching. Two independent workshops will be held on the research outputs and impacts from the projects. The first workshop will be held at the NPL in the South-West of London, on 26 March 2015, and will cover aspects related to the universal ear simulator. The second workshop will take place at PTB in Berlin on 16-17 April 2015 on the perception of non-audible sound. There is still time to register so please visit the project website for full details.

Collaborations

Despite the project being in the final stages, it continues to attract the interest and support of people outside of the core consortium. We are extremely pleased that a host of world-leading experts have given their support to the workshops with keynote presentations and contributions to the scientific discussions.

In the UK, a desire to raise awareness that the growing prevalence of airborne ultrasound sources in society may pose possible health effects, has resulted in the formation of the UK Health Effects of Ultrasound in Air working group. The first meeting of this group will take place in March 2015. Special thanks go to Prof. Tim Leighton (Southampton University) for starting this initiative.

Presentations

Various members of the project team have been active in presenting an overview of the project and progress on specific technical aspects, at a range of scientific conferences and key metrology meetings.

Torsten Marquardt presented a paper on *Temporal integration at threshold and loudness summation of tones 4 Hz - 125 Hz* at the British Society of Audiology annual conference.

Martin Bauer presented the paper *Investigation of the auditory m100 brain response for low frequency sound stimulation* on behalf of the team working on this part of the project, at the 19th International Conference on Biomagnetism.

As the project reaches the final stages, the number of scientific papers appearing in journals is about to increase significantly. Many papers are currently undergoing peer review, so please check the project website for details as they are published.

Business card of partners:

In this column of every newsletter we will introduce one of the institutes of the consortium to you. Today: Brüel & Kjær Sound & Vibration Measurement A/S, Danish Primary Laboratory of Acoustics.

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Brüel & Kjær Sound & Vibration Measurement A/S supplies integrated solutions for the measurement and analysis of sound and vibration. As a world-leader in sound and vibration measurement and analysis, we use our core competences to help industry and governments solve their sound and vibration challenges so they can concentrate on their primary task: efficiency in commerce and administration.

Brüel & Kjær is the world's leading supplier of primary and secondary microphone and accelerometer calibration systems, laboratory standard microphones and reference accelerometers. Brüel & Kjær produces a substantial range of couplers and artificial ears together with audiometer, hearing aid and telephone testing systems.

BKSV-DPLA, the Danish Primary Laboratory of Acoustics, is responsible for development and dissemination of the Danish national measurement standards for sound pressure in confined air (pressure sensitivity) and vibration. BKSV DPLA is a Designated Institute in the decentralized Danish Metrology System, run by Brüel & Kjær, although it is kept as a separate entity to ensure independent operation. BKSV-DPLA conducts research in it fields of calibration, such as sound fields in couplers, calibration measurement techniques, and the influence of base material in vibration exciters. BKSV-DPLA co-operates with Danish Fundamental Metrology, DFM, in selected research fields and in drafting international standards for microphone calibration.

Brüel & Kjær's role in the Ears project is manufacturing of prototypes of the Universal Ear Simulator. The combination of the metrology expertise of BKSV-DPLA and the access to manufacturing abilities are important for this role.

Figure 8: Acoustic testing on a Brüel & Kjær Head–And-Torso Simulator.

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