

The PATH AEP technology

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Recording AEP

Auditory evoked potentials (AEPs) are electrical responses with very small voltages that can be recorded at the scalp via electrodes. While neural potentials in synapses and nerve fibers can reach several 100 mV, the resulting AEPs at the surface of the head are about 1.000.000 times weaker, therefore in the order of nano-volts (nV). This is why they cannot be measured directly, but only are detectable with certain statistical methods, the most primitive one being “averaging”.

A good overview of AEPs in general can be found at:

https://en.wikipedia.org/wiki/Auditory_brainstem_response

This white paper aims at explaining some of the general techniques that are used in the PATH medical line of instruments to provide most reliable and robust testing.

Time domain vs. frequency domain

Since evoking and detecting AEP usually involves a periodic repetition of a stimulus, there are two general techniques to detect AEP. In “time domain”, the recorded signal is cut into frames that are in sync to the stimulus, and these frames are superimposed (=averaged) into a buffer. Since unwanted noise will not be in sync with the stimulus, it will grow less during averaging than a stimulus-triggered response.

This type of time-domain recording allows the stimulus rate to vary during testing, which can be used to improve immunity against external interference. This will be referred to as “spread spectrum” later in this text.

Alternatively, one can record the signal in a (typically) longer buffer, and then perform a Fourier transform. The resulting spectrum can then be examined at the frequencies that represent the stimulus rate and multiples. The frequency resolution of the spectrum is the direct inverse of the buffer length. A 1 s buffer will therefore result in a 1 Hz frequency resolution. The FFT analysis requires the stimulus rate to be constant. However, replacing the FFT by special techniques from telecommunications engineering, this can be overcome and spread spectrum can then also be used in frequency domain.

Analyzing AEP in frequency domain is often referred to as “Auditory Steady State Responses” or ASSR. However, the same responses could as well be recorded / detected in time domain; therefore the term is at least misleading.

Some common techniques for both ABR and ASSR will be described next, including stimulus design aspects, followed by special considerations for ABR and ASSR.

Weighted averaging

As patient state may vary a lot during testing, an artifact management needs to be employed for real-world measurements of AEP. Traditionally; an artifact threshold was used to just

discard “noisy” frames of the incoming data. However, it is much more effective to use weighted averaging. Frames are weighted with the inverse of their total amplitude, resulting in “noisy” frames having less impact on the result, and “good” frames to have more impact. It can be shown with Monte-Carlo-Simulations (see Wikipedia.org: Monte Carlo method), that this is more efficient than plain artifact rejecting schemes.

Weighted averaging can be used both for ABR and ASSR recording, with some special considerations in ASSR.

In general, when any averaging is used, asynchronous noise will accumulate with the square root of test time, while the synchronous signal will accumulate linear with time. This means: To gain a factor of two in signal-to-noise-ratio (SNR), test time needs to be four times as long, and so forth. This is common fact for all statistics, and cannot be avoided, and explains why test conditions have a large effect on performance.

Stimuli

Auditory evoked potentials (AEPs) can be evoked with any type of sound. If a subject “hears” a stimulus, an AEP is generated. This does not mean, that the AEP is in fact detectable in a given test setup (subject condition, test time, etc).

Since AEPs are extremely small voltages, hidden in the overall EEG activity, stimuli are often designed to evoke higher AEP amplitudes. A typical design goal is to align as much neural activity as possible at certain points in time.

The role of the cochlea

The cochlea acts, among other things, as a real-time spectrum analyzer. A consequence of cochlea mechanics is a frequency-dependent latency between acoustic stimulus and neural activity. The latency difference from 1 to 4 kHz is in the order of 3 ms, depending on stimulus level. Values reported in different studies also vary (see Fig. 1). This results in the known fact that AEP latencies are longer for lower frequency stimuli.

Cochlea model

A number of cochlea models have been introduced to simulate cochlea mechanics, and to help designing stimuli. In this white paper, a very primitive model is used, which is still good to illustrate the general behavior of the cochlea for various stimuli. The model is linear, passive, 1-dimensional.

The main effect of cochlea mechanics that we look at here is the frequency dependent delay of processing. Different authors report varying data on this, but the general behavior is as shown in Fig. 1.

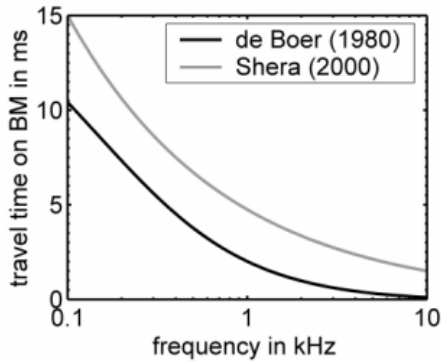


Fig. 1: Cochlea delay as a function of frequency, taken from Wegner and Dau 2002

The real cochlea would act differently at different stimulus levels, which is not reflected by the simple, passive model we are using here. Hearing impaired cochleae would also act slightly different, which means there is no optimum stimulus that fits all situations. The goal of optimized stimuli for AEP recording is to compensate this delay behavior to generate stronger AEP responses.

Dau et. al. (2000) and Wegner et.al. (2002) came up with a set of chirps, referred today as “Dau chirps” (Fig. 2). Other cochlea model based stimuli have been proposed later by Claus Elberling et al (2007), known as “CE-Chirp”, Cebulla (Cebulla et.al 2007) and other groups.

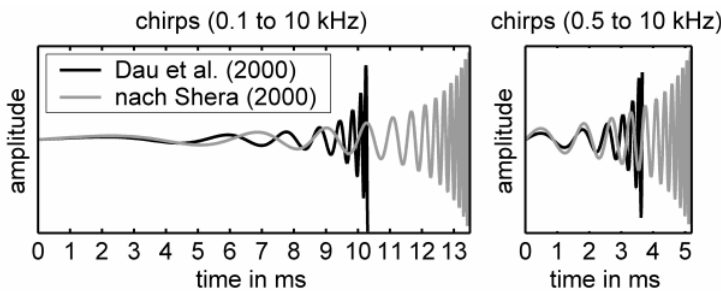


Fig. 2 Broad band chirps, from Wegner and Dau 2002

A predecessor of chirp stimuli was the so-called mixed modulation, which combined AM and FM modulation to a carrier. An example is shown in Fig. 3. Interestingly enough, the optimum phase between AM and FM was empirically found to be at values which basically result in the instantaneous frequency to rise during the amplitude maximum. This makes the resulting signal quite similar to a chirp.

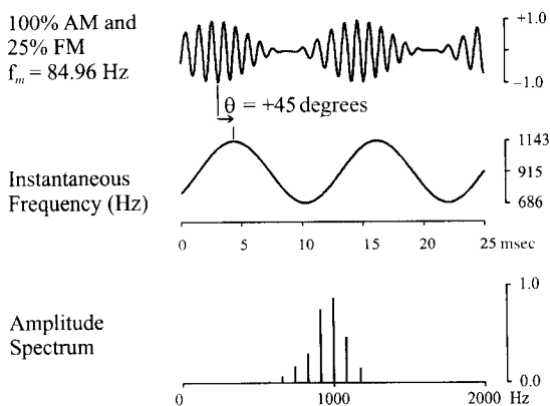


Fig. 3: „mixed modulation“, consisting of both AM and FM. Note that the AM maximum is timed to where the instantaneous frequency is rising. This results in a signal that is not far from a chirp. Image taken from Dimitrijevic et al, (2002).

In each of the cochlea model plots used herein, the top trace reflects the acoustic input signal, the next trace indicates the overall cochlea excitation over time, and the 2-dimensional color plot indicates the cochlea excitation pattern over time. The basal end of the cochlea is at the top, the apical end is at the bottom of the plot, and the four green marker lines reflect the tuning frequencies 500Hz (bottom) and 1, 2, 4 kHz. The model frequency range is about 250Hz to 8kHz.

The response of the model to a composite signal, consisting of 500 Hz, 1 kHz, 2 kHz, 4 kHz pure tones, is shown in Fig. 4. Obviously, it takes the lower frequency part of the cochlea longer to respond to the stimulus onset, and to decay after it stops. The delay effect is already represented by the simple frequency-delay plot in Fig. 1, while the attack-delay timing is not shown.

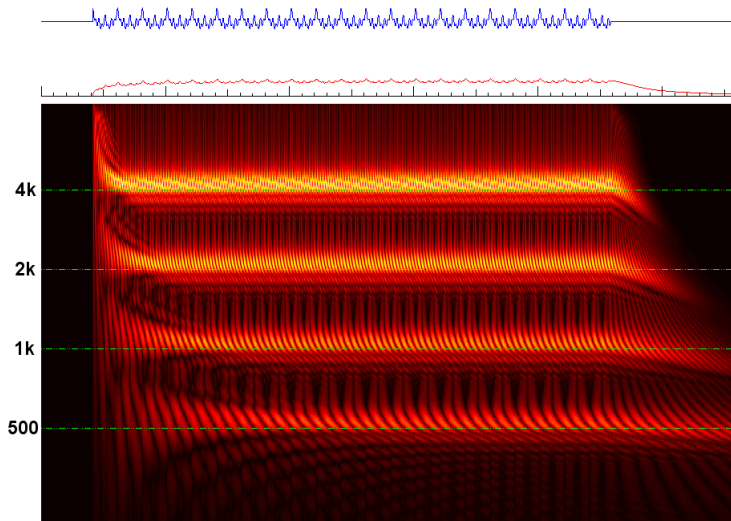


Fig. 4: Demonstration of a simple cochlea model. Top trace: Input signal, with tick marks in ms, consisting of 4 sine tones at 500Hz, 1, 2, 4 kHz. The overall cochlea activity is shown in the red trace, and the cochlea activity over time and place is shown as a colored 2D plot. Basal end is top, apical end is bottom of plot. The time scale ticks are milli-seconds.

Broad band stimuli

Broad band stimuli cover a good part of the auditory frequency range and therefore stimulate major parts of the cochlea. They are usually used to test the general function of the hearing organ, regardless of frequency response.

The most traditional broad band stimulus is a “click”, as shown in Fig. 5, which is still often used to evoke ABR in time domain. The general behavior of the cochlea for such a stimulus is shown in Fig. 6.

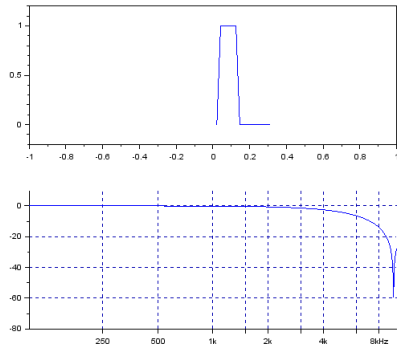


Fig. 5: 100µs “Click” stimulus and its spectrum.

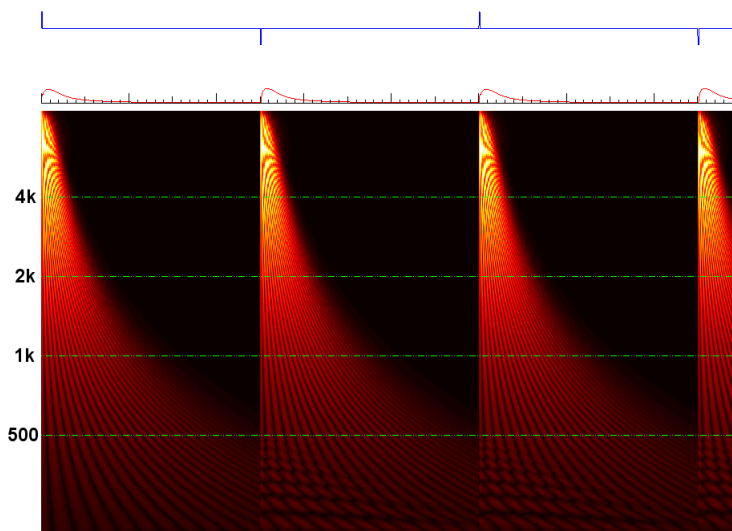


Fig. 6: cochlea response to a broad-band click (alternating polarity, repetition rate 40 Hz)

The cochlea model illustrates that the low frequency part of the cochlea responds later in time and the response is less steep.

A so-called “chirp” can compensate the delay of lower frequency response, but it cannot compensate the response steepness. A sample broad-band chirp is shown in Fig. 7. Its simulated cochlea response is illustrated in Fig. 8. The goal of the stimulus is to bundle overall cochlea activity to a single, intense peak in time domain. As the red output trace in Fig. 8 and Fig. 9 indicate, the chirp elicits a more “peak”-like response than the click.

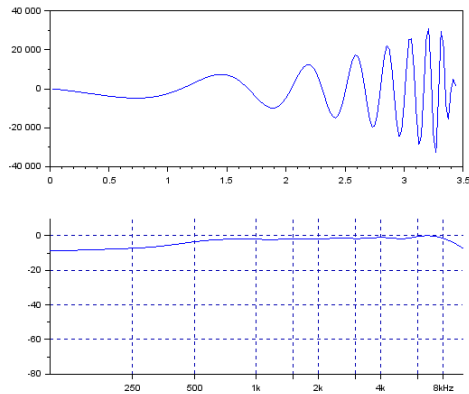


Fig. 7: Broad band chirp signal and its spectrum

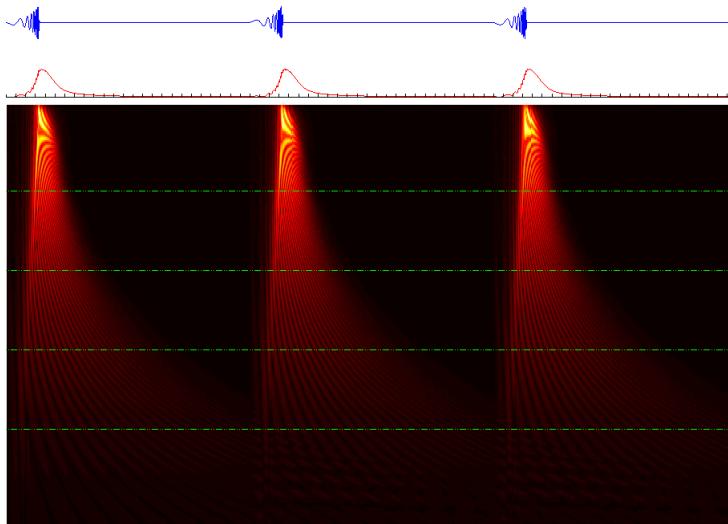


Fig. 8: Cochlea model response to a broad band chirp

Actually, modifying the chirp signal by envelope, etc, does not change the general behavior much, as long as the sweep speed (how fast does it sweep from low to high frequencies) roughly fits to the cochlea delay. A chirp that looks quite different is used in Fig. 10., generating a response that is quite similar to the one shown in Fig. 8. The spectra of all 3 broadband stimuli are almost identical.

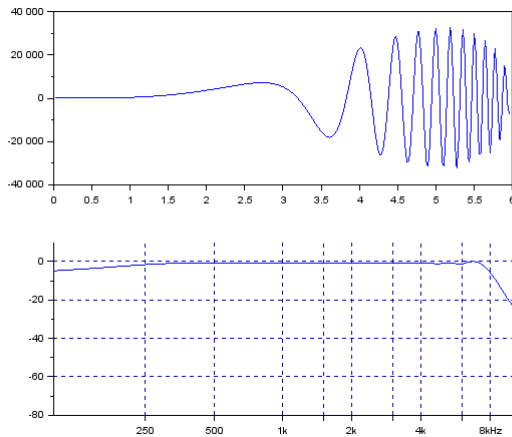


Fig. 9: Different broad band chirp time-domain and frequency range plot

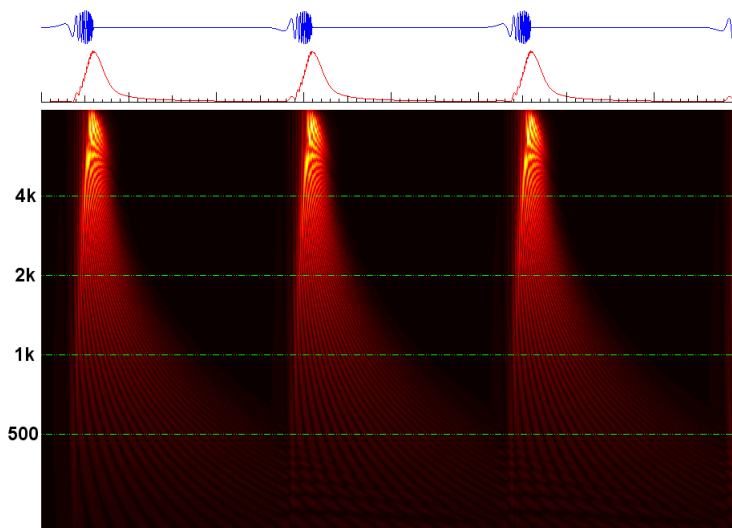


Fig. 10: Cochlea response to the chirp in Fig. 9.

Effective frequency range of broad band stimuli

A general feature of broad band, transient stimulus evoked AEP is, that most of the response originates from the basal part of the cochlea. This can be shown by just removing the lower frequency part of the cochlea model response, as shown in Fig. 11, where all activity of the cochlea below about 1.5 kHz was removed. However, the overall cochlea activity (red trace) is not much different from the full bandwidth plot in Fig. 10.

This illustrates the known fact that a low frequency hearing loss is in fact not seen in a broad band ABR response, regardless if a click or chirp is used.

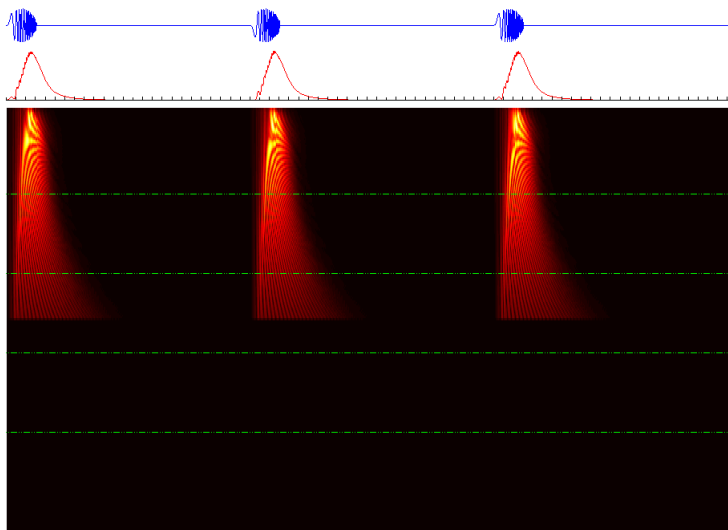


Fig. 11: Cochlea model response to a broad band chirp, with the lower frequency part disabled

Narrow band stimuli

If frequency related information on hearing is required, either narrow band stimuli are to be used, or unwanted frequency areas must be masked. The most narrow band stimulus is a sine tone, as used in audiometry. However, a constant tone does not evoke any detectable AEP signal, and is therefore not usable here.

The most primitive narrow band signal to evoke AEPs is a modulated sine tone, and its AEP response was formally referred to as Amplitude Modulation Following Response or AMFR. In time domain, quite similar stimuli are usually referred to as “tone pip”. Depending on repetition rate and envelope, tone pip and modulated sine can be just the same. An example of a 2 kHz tone, modulated 100% at a rate of 80 Hz, is shown in Fig. 12, with its cochlea response shown in Fig. 13.

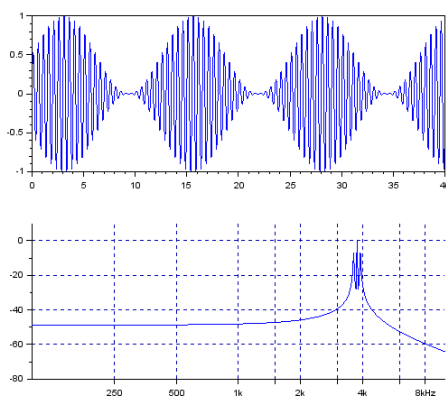


Fig. 12: Amplitude modulated sine tone and its spectrum

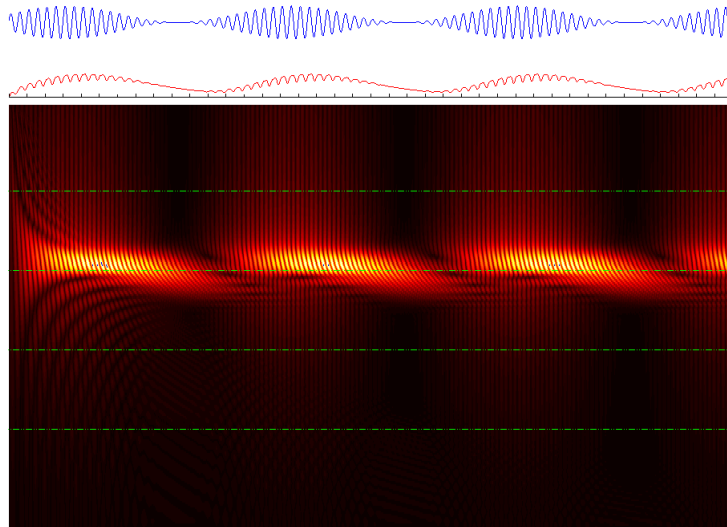


Fig. 13: Cochlea response to an AM modulated tone (2 kHz @ 80 Hz)

Narrow band stimuli, when used in AEP, have two features that drastically reduce the AEP amplitude:

- Only a small portion of the cochlea is stimulated, therefore the neural activity will be small
- The cochlea is slower when responding to narrow band signals, and the signals themselves must have a relatively soft attack and decay (otherwise they are not narrow banded). This results in responses that are less “steep” and therefore harder to detect.

Additionally, introducing the chirp concept to narrow band stimuli is less effective, because the latency range covered by a narrow-banded stimulus is much smaller (see Fig. 1) and therefore there is less delay to compensate. The effect is stronger at lower frequencies, because the cochlea tends to be slower there, and available absolute bandwidth is much smaller. The modulated sine example, when generated at 500 Hz, produces an almost constant overall cochlea activity, resulting in poor AEP response, as shown in Fig. 14.

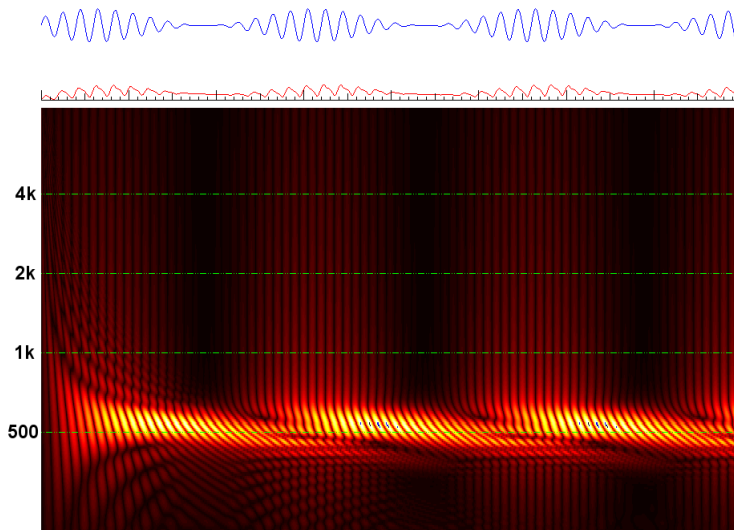


Fig. 14: Cochlea response to a 500Hz, 80Hz AM stimulus

Using a chirp signal instead of the modulated sine does not improve things significantly, as shown in Fig. 15. At a slower modulation rate, such as 40 Hz, the cochlea has more time to attack and decay, therefore the response improves. However, the effect of using chirp signals instead of modulated sine tones is still relatively moderate.

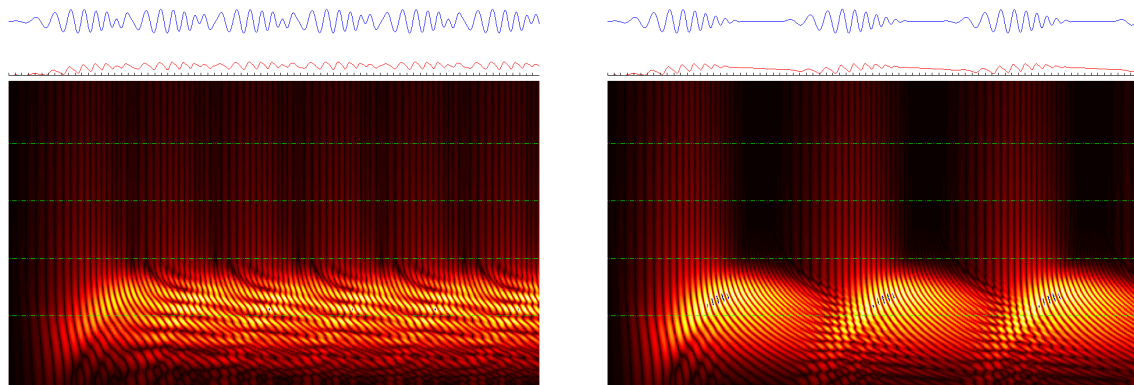


Fig. 15: Cochlea response to a 500Hz Octave-wide chirp at 80 Hz vs. 40 Hz stimulus rate.

At higher audio frequencies, the chirp concept can improve the cochlea response, as shown Fig. 17 (compared to the modulated sine from Fig. 13). The frequency range that is stimulated is broader (in this case covering about $\frac{1}{2}$ octave), but the response is steeper and higher in amplitude, making it easier to detect. The spectrum of this stimulus is shown in Fig. 16.

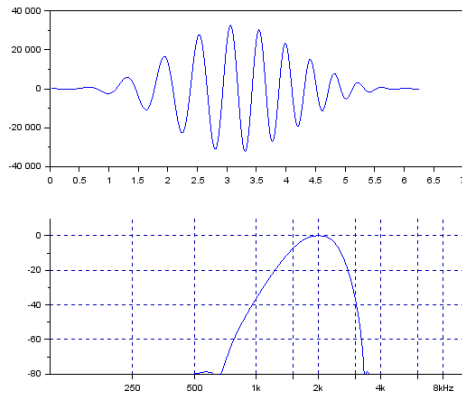


Fig. 16: Stimulus waveform and spectrum of a 2kHz chirp. The spectrum refers to a single chirp only. If repeated periodically, the spectrum would consist of lines at multiples of the repetition rate only.

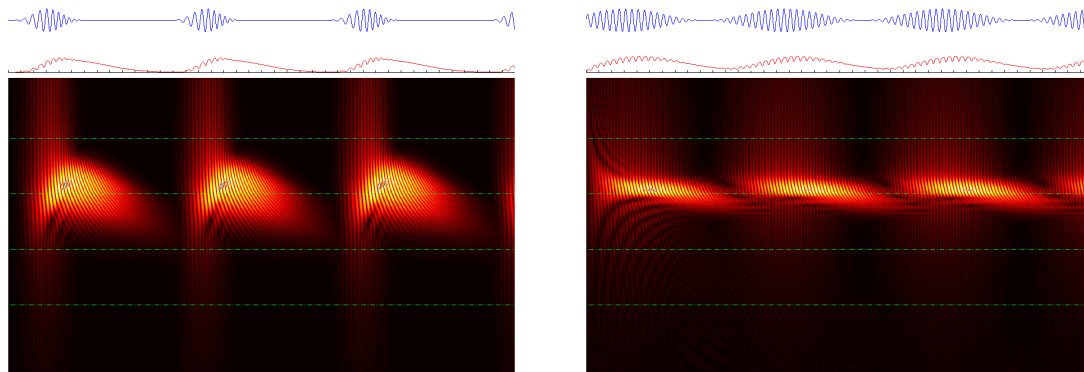


Fig. 17: 2kHz narrow band chirp at a rate of 80Hz, compared to a modulated sine stimulus. The cochlea response to the chirp is much stronger, with a slightly greater region of the cochlea stimulated.

Recording AEP in time domain: ABR

All of the above stimuli can in general be used for ABR recordings in time domain. However, as the cochlea model data suggests, low frequency stimuli will not be very effective, and broad band stimuli will mainly reflect hearing at high frequencies.

Binaural recording

AEP in general can be recorded from both ears simultaneously, as long as the stimulus rates which are presented to both ears are not correlated. A traditional recording scheme is to just apply different but constant stimulus rates to both ears, such as 37 Hz and 41 Hz. Even more preferable choices would be stimulus rates that do not have a common period (1Hz in the example above), such as 37.3816394 Hz and 41.136818273 Hz etc.

Spectrally, any neural response that is evoked by either of the stimuli contains just the stimulus rate and multiples. This means, that if averaging is done in synch to each ear's stimulus rate, responses can be recorded independently. The AEP signal that is evoked from each other ear just appears as a very small added EEG noise, since it is not correlated to the averaging.

ABR recording with spread spectrum technology

ABR recording in time domain does not necessarily require a constant stimulus rate, although this is the traditional way of doing it. Modifying the rate during testing can improve the robustness against artifacts caused by technical electric noise sources drastically. Moreover, binaural recording can be performed with equal average stimulus rates, which can be preferable over fixed different rates for both ears (such as 37 and 41 Hz).

Inter-ear latency comparison is more precise if the average stimulus rate is equal for both ears, since latency is impacted by stimulus rate. Furthermore, the number of collected frames will be close to equal for both ears.

Weighted averaging

As stated above, weighted averaging can be implemented in ABR to handle varying patient states, myogenic activity, etc. In connection with spread spectrum stimulus timing, a very robust and therefore fast ABR can be realized, often recording stable responses in a minute or less.

Template matching

ABR responses have a typical waveform, with certain peaks referred to as J1, 3, 5 etc., named after Jewett and Williston (1971). This knowledge can be used to improve automatic detection of ABR responses. The recorded signal can be cross-correlated with a template that represents a typical waveform, and the correlation signal can then be statistically analyzed instead of the unprocessed signal. This technique can also be used to estimate the latency of the response, which can get a better estimation in noisy recordings than a plain peak search would. A feasible template, along with its effective frequency response, is shown in Fig. 18. The template convolution acts as an FIR filter, therefore it also provides a frequency and phase response.

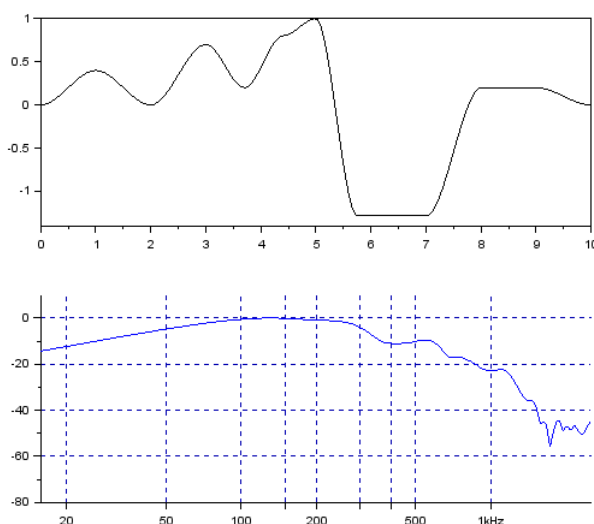


Fig. 18: ABR template for automated detection of responses. The upper panel shows the time domain data, the lower panel shows the frequency response if the template is seen as an FIR filter.

The PATH Sentiero ABR module

Using the techniques described above, the PATH medical ABR module was designed. It makes use of spread spectrum, template matching, weighted averaging and chirp

stimulation. Trace data is shown as the original recording, while all statistics, if enabled, are performed on the template convolution signal. This combines detection performance with real trace view.

The configurable options of the PATH ABR module are shown in Fig. 19. Best performance is achieved with relatively high stimulus rates of 80 or 90 Hz, broad band chirp stimulation, and binaural recording. Test times per trace of less than a minute can then be achieved.

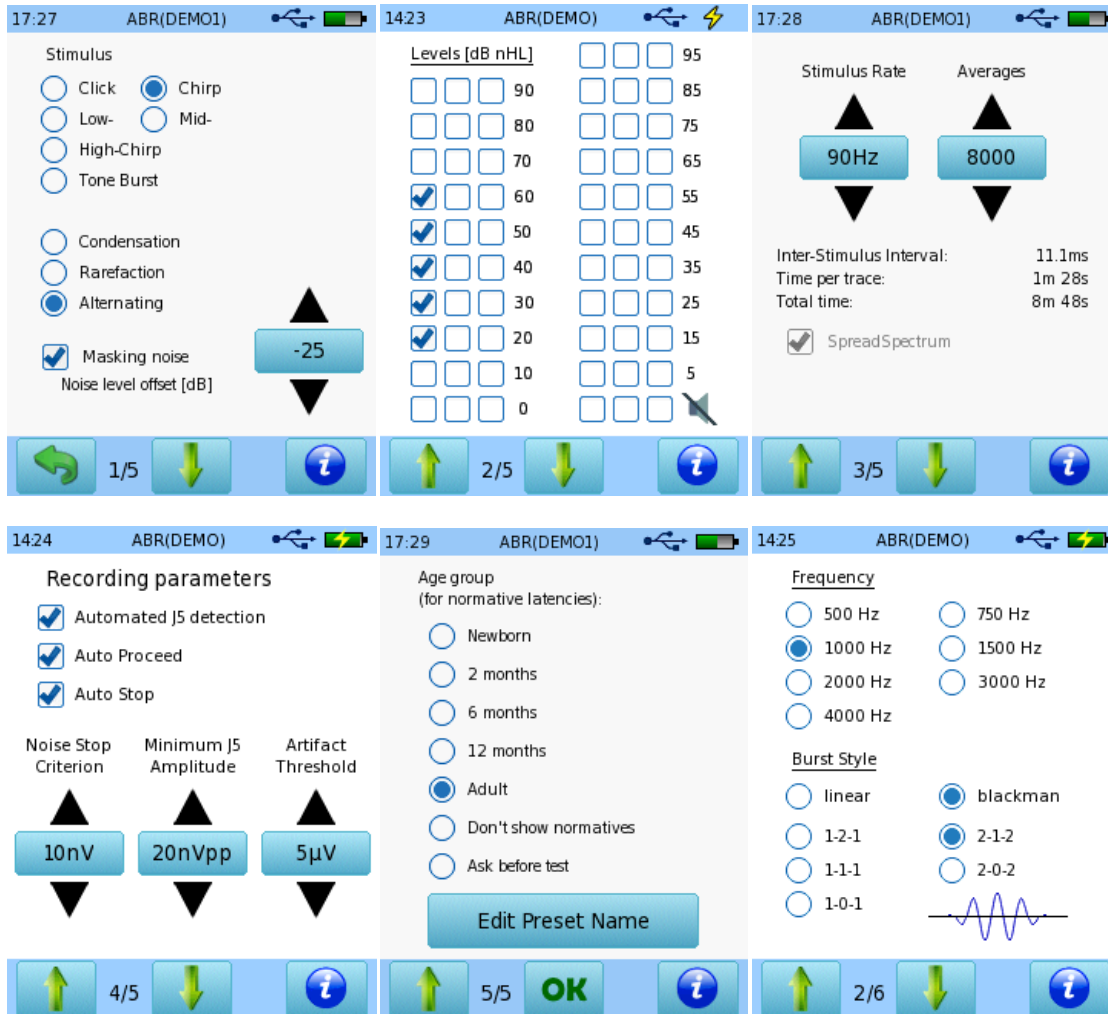


Fig. 19: Configurable options of the ABR module. From left to right: Stimulus selection, level selection, stimulus rate & averages, recording parameters, normative selection and tone burst configuration (only shown if tone burst selected as stimulus)

Recording AEP in frequency domain: ASSR

ASSR

As said above, the term ASSR is somewhat misleading, as it suggests a “steady state” of the auditory system. In contrast to this, the response is in fact reflecting how efficient the excitation of the auditory neural system is switched “on” and “off”, since the recordable response is based on the overall neural activity.

Preferable stimulus rates

In addition to the cochlea impact on stimulus effectiveness, neural aspects will also impact the selection of parameters. In particular, there are preferred stimulus rates where the neural response to the single stimuli overlaps to generate high overall activity. Typically, rates around 40 Hz and around 80-90 Hz are used. Fig. 20 illustrates the idea of ASSR as a superposition of single responses.

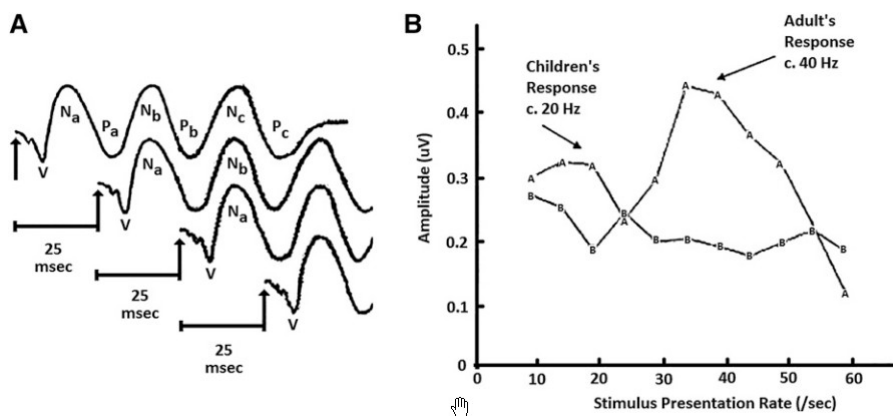


Fig. 20: 40Hz ASSR as a superposition of single responses, taken from Korczak et al (2012)

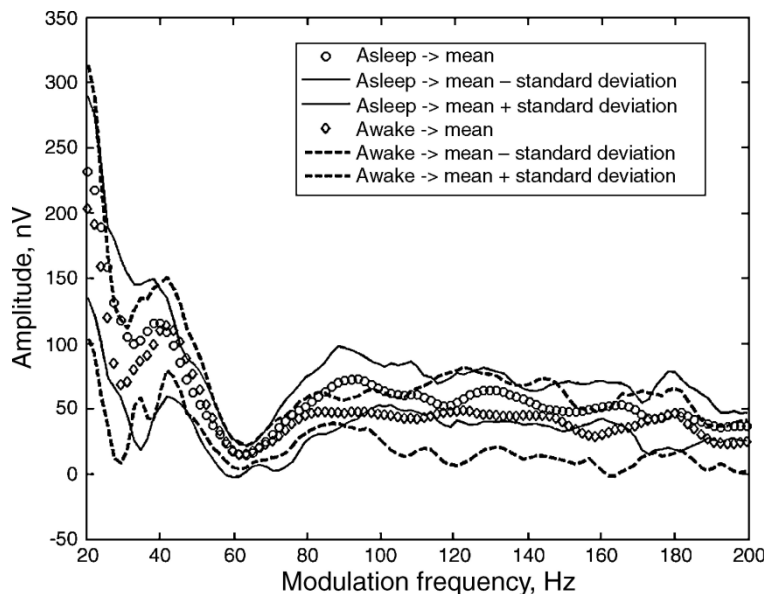


Fig. 21: Effect of the stimulus rate on AMFR amplitude (from Nodarse et. al. 2011)

Given the results from cochlea mechanics and the neural aspects, optimum stimulus rates are around 40 Hz for lower stimulation frequency ranges, and 80 Hz and above for higher frequencies (see Fig. 20 and Fig. 21). However, these observations are mainly based on analyzing the frequency component at stimulation rate only (e.g. 40Hz or 80Hz in our example), and not their harmonics.

ASSR with multi-Frequency stimulation

Using narrow-band stimuli, more than one stimulus can be applied to one ear, using differing stimulus rates. This basically allows for detecting more than one response simultaneously. The method was introduced by John et al. in 1998. If different stimuli are repeated at different rates, the rates can be found in the AEP spectrum. The idea is illustrated in Fig. 22., with rates in the range of 80 to 110 Hz. The spectra indicate that the stimulus rates of each stimulus appear in the AEP signal. Selecting different rates for the two ears also allows binaural ASSR recordings. Fig. 22. Contains responses from eight different stimulus rates, four were presented to each ear.

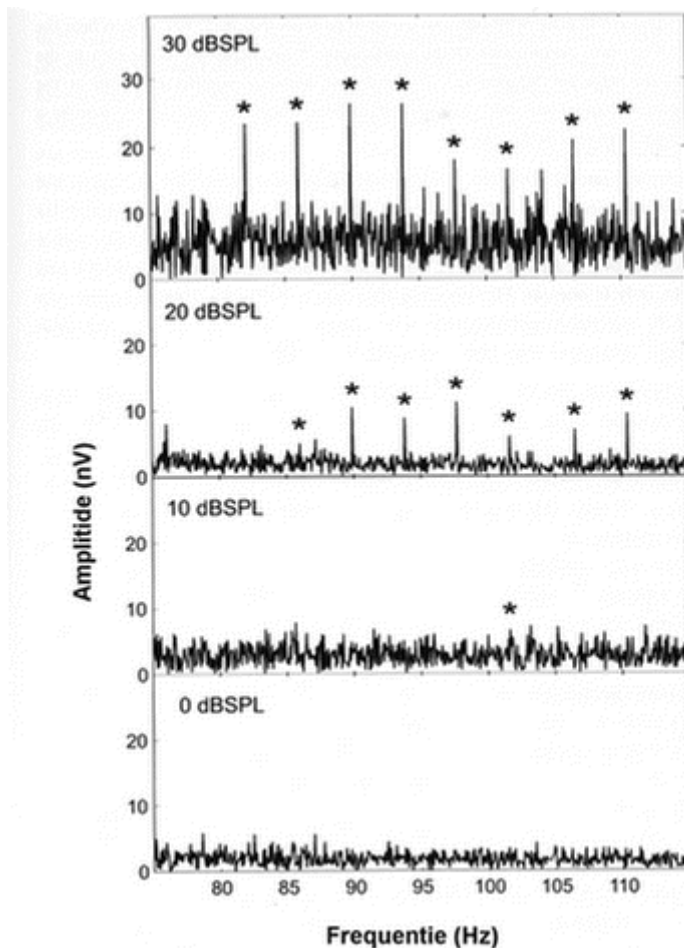


Fig. 22: The idea of multi-frequency stimulation using different modulation rates for each test frequency. Taken from Lamoré et al 2008

Traditional ASSR recording uses stimulus rates which are close to each other. Typically, all rates would be selected either in the 40 Hz or 80 Hz range. The decision on which band to use is often based on the patient status, with 40 Hz being recommended for wake adults and 80 Hz preferred for sleeping infants. Cochlea mechanics, however, suggest that selecting the rates in a wider range is more efficient and that the dynamic behavior of the cochlea plays a

greater role than patient status. This becomes even more evident if overtones are also recorded, as described later.

Fig. 23. Shows a cochlea model response to a 4-frequency stimulus, where narrow band chirps of frequencies 500Hz, 1, 2, 4kHz are presented at different rates (of about 30Hz to 90Hz). A complete set of narrow band chirp stimuli is shown in Fig. 24. If only octave-distant center frequencies are desired, the stimuli can be designed to cover more bandwidth. A set of octave-wide stimuli is shown in Fig. 25. An even coarser but faster test can be performed with 2-octave wide stimuli, as shown in Fig. 26.

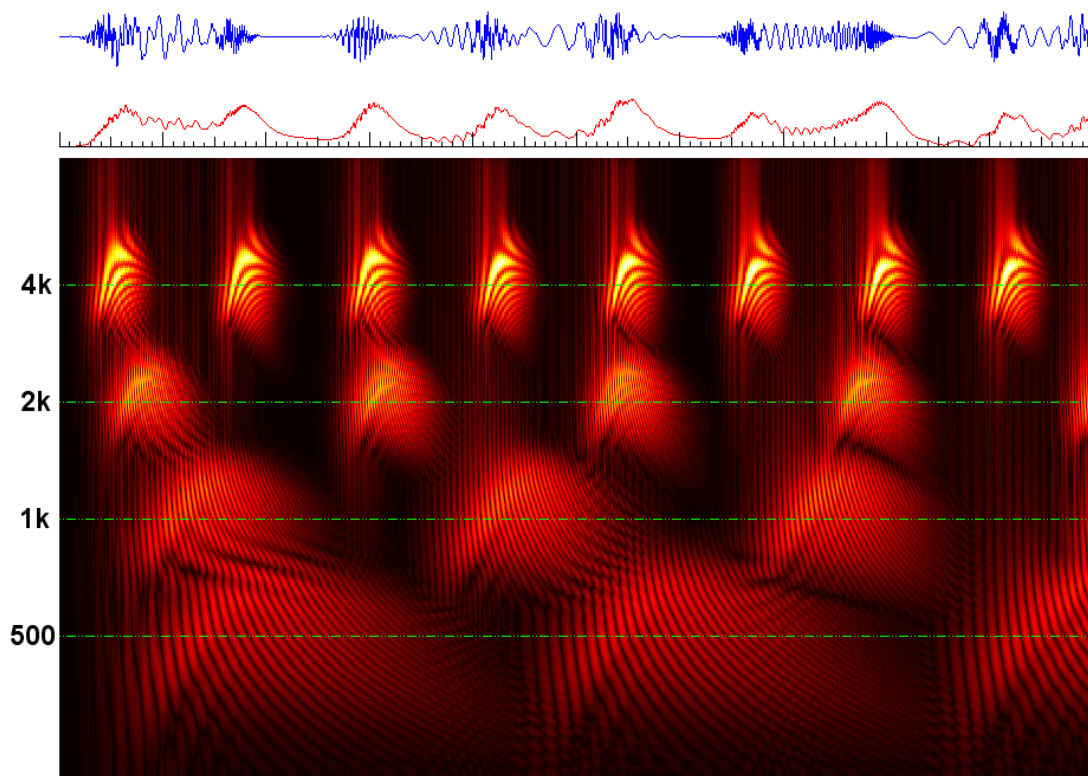


Fig. 23: Example of a multi-frequency, multi-rate stimulation. Carrier frequencies of 500Hz, 1, 2, 4kHz are stimulated at different rates from 30 to 90Hz.

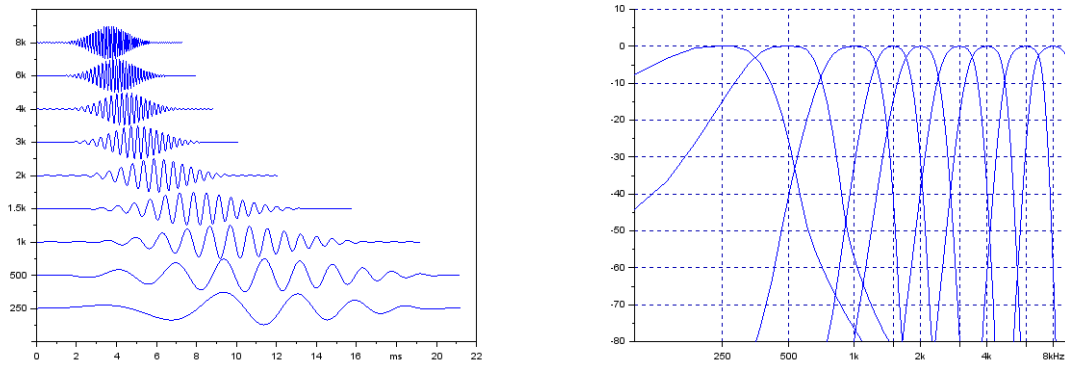


Fig. 24: Narrow band (1/2 octave) chirp stimuli for ASSR and their spectra

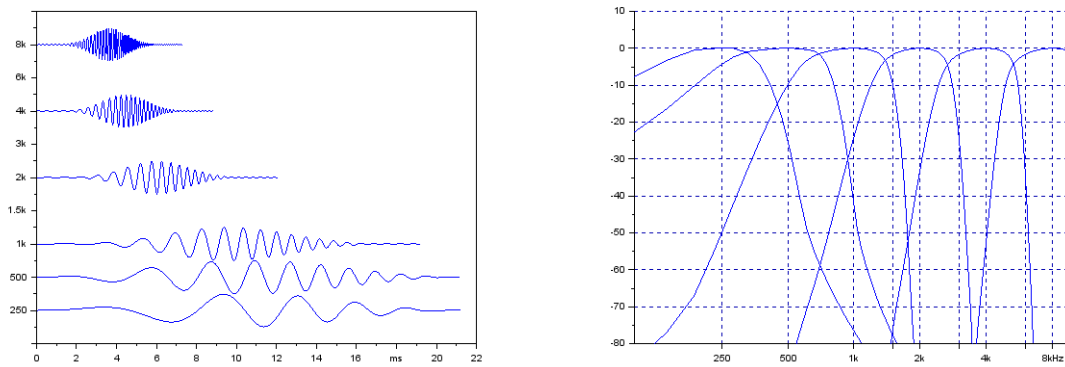


Fig. 25: Octave wide chirp stimuli for ASSR and their spectra

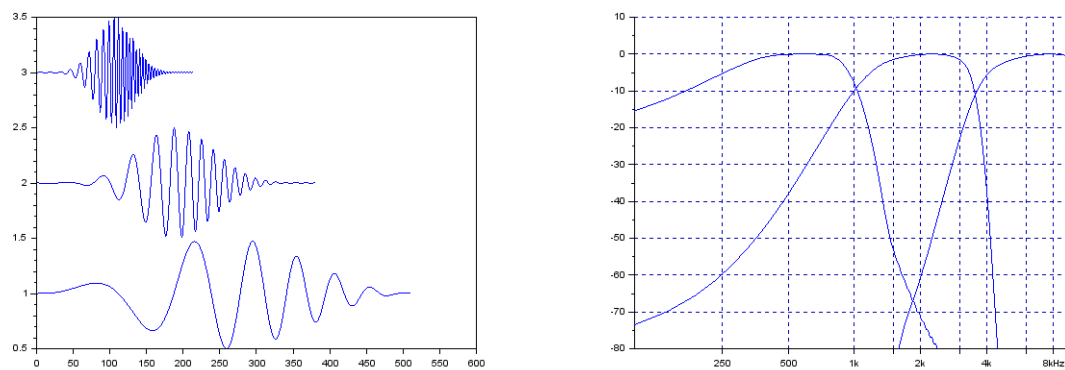


Fig. 26: 2-octave wide chirp stimuli for ASSR and their spectra

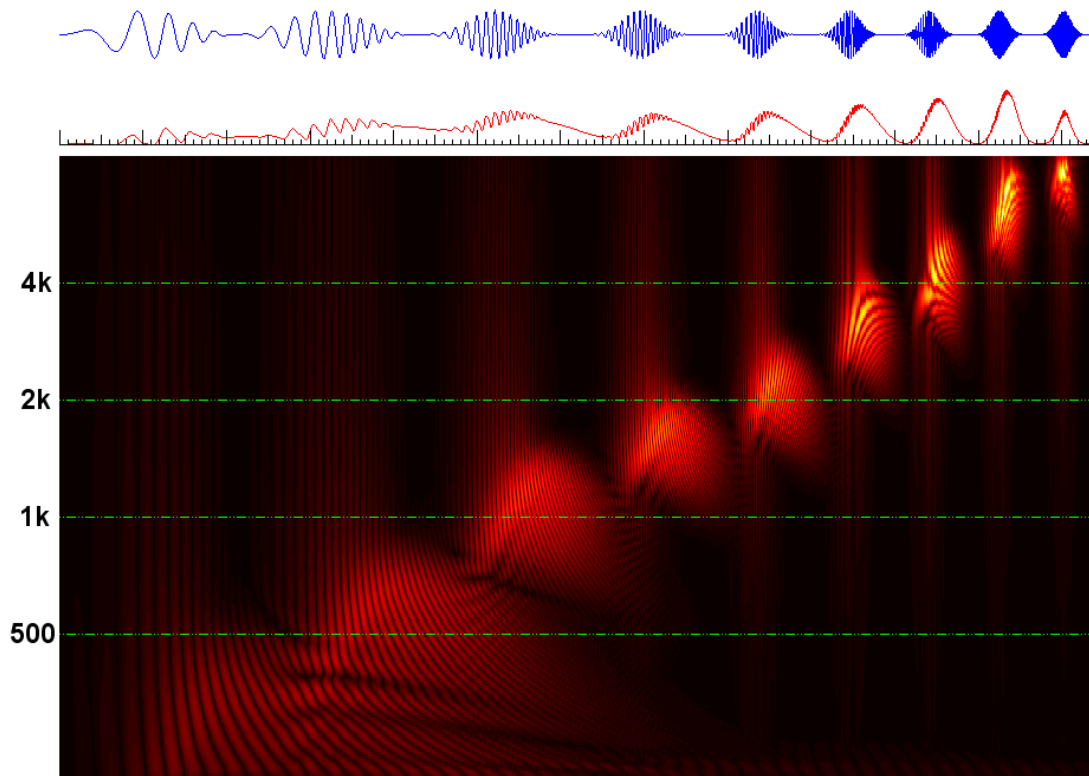


Fig. 27: Cochlea model response to the $\frac{1}{2}$ -octave narrow band ASSR chirps

AEP harmonics

An AEP response to a stimulus will typically not just be a sine wave at the repetition rate. Ideally, it would look more like an ABR response. This means, the response spectrum will also contain multiples of the repetition rate, such as 180 Hz, 270 Hz, etc. for a 90 Hz stimulation rate. Although these overtones tend to be much lower in amplitude than the fundamental, the SNR may still allow using them for statistical evaluation, as the EEG noise also decreases with frequency. Fig. 28 illustrates this idea.

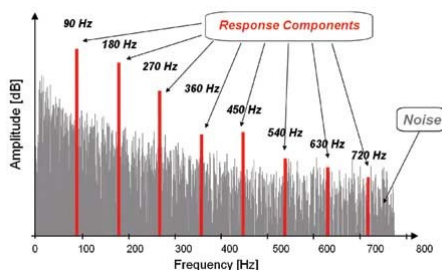


Fig. 28: Overtone detection in ASSR recording, taken from <http://www.hearingreview.com/2007/11/auditory-steady-state-response-assr-a-beginners-guide/>

The use of overtones somewhat impacts the preferable stimulus rate discussion, as, for example, a 40 Hz rate could be suboptimal in a given case if only the 40 Hz response is used, but may generate strong harmonics that could be used for detection.

Spread Spectrum ASSR

Testing AEP typically is performed at places where other electrical devices are in close proximity. Devices such as computers, monitors, telecommunication equipment, can emit electrical interference at frequencies that are related to frequencies where the AEP signal is expected. Therefore, AEP recordings are usually done at “odd” frequencies that avoid known jammers (such as 50Hz, 60Hz grid frequency and their overtones, typical refresh rates of computer monitors, etc.). However, avoiding frequencies of known sources is no guarantee that no interference takes place.

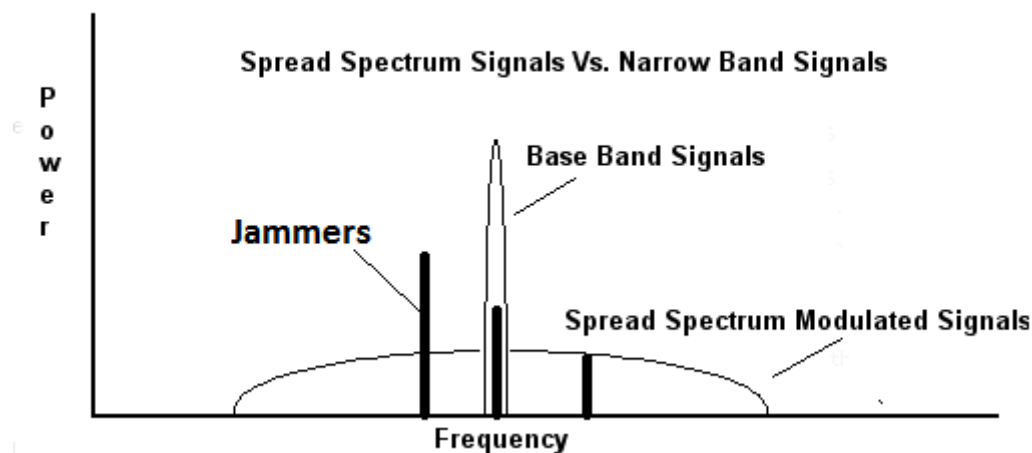


Fig. 29: General idea of spread spectrum: The signal power is distributed over a broader frequency range, which reduces the impact of narrow band “jammers” (modified image from <http://www.tutorialsworld.com/spread-spectrum/what-is-spread-spectrum.htm>)

The traditional way of detecting ASSR via a Fourier Transform needs the stimulus rates to be constant. PATHs spread spectrum ASSR overcomes this limitation and uses varying stimulus rates. This makes the ASSR much more robust against typical “jammers” that could be mistaken as a ASSR response. Spread spectrum is a technology that is widely used in radio communication from BlueTooth to Satellite radio for just the same reasons: It makes the transmission robust.

The rate variation during testing is moderate: a ± 1 Hz variation of the rate (centered at 37 to 160 Hz) does not impact AEP recording but improves robustness against interference significantly.

Artifact management

Of course, natural artifacts, such as myogenic activity, also interfere with ASSR measurements.

As said above, weighted averaging is the preferred method to implement such an artifact management. Frames are “weighted” with their inverse amplitude, resulting in “noisy” frames to have less impact on the averaging result than “silent” frames.

The effectiveness of this weighting is related to the frame size, since only complete frames of data can be weighted. Using traditional FFT-based methods to record ASSR, the frames

typically are 1 s long to achieve a 1 Hz frequency resolution. This means that one second of test time is more or less discarded if a single noise spike occurs within it. This can be of disadvantage in case of periodic muscle artifacts, such as heartbeat-related activity or eye blinks, which typically occur about once a second.

The detection method using quadrature demodulation as described above can be implemented with shorter frames, because the framing takes place in the I/Q signal domain and is independent of any FFT parameters. This allows more efficient weighting and better handling of the artifacts described above. If harmonics are used for detection, they can be independently weighted, which further improves the effectiveness of weighting.

The PATH Sentiero ASSR module

Since recording ASSR is a fully automated procedure, not too many parameters need to be configured. The main decision is to select a stimulus bandwidth, which is a trade over between test performance and frequency specificity. Wider band stimuli excite larger portions of the cochlea and therefore generate stronger evoked responses. The parameters that actually define an ASSR configuration are illustrated in Fig. 30. Spread spectrum is always enabled in the PATH ASSR module.

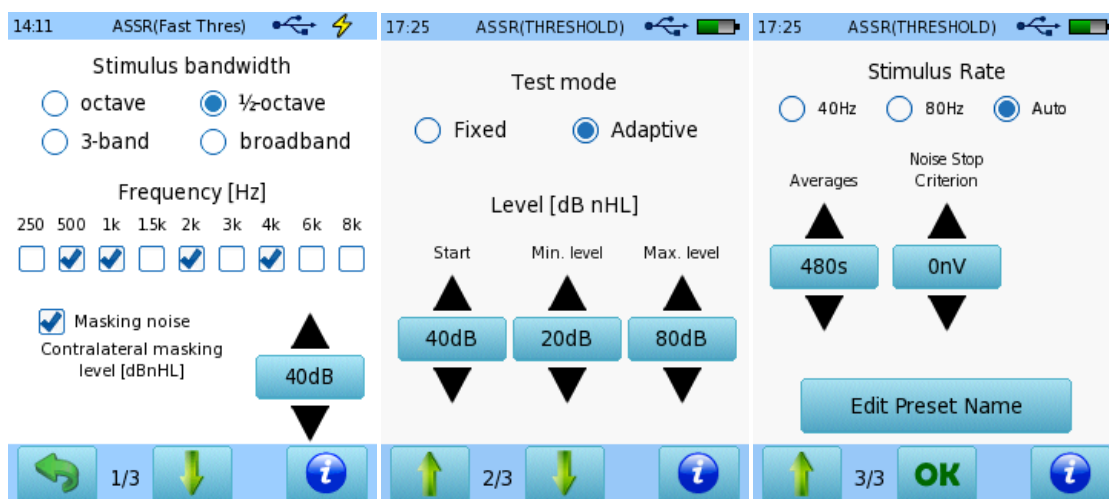


Fig. 30: Configurable options of the ASSR module

The information that is available during testing is shown in Fig. 31. Up to four frequency / level combinations can be performed on each ear simultaneously, with each of them being recorded independently. For each ear, an overview is also available which indicates which frequency / level combinations have already been tested and which are ongoing.



Fig. 31: Representation of ongoing test: Left: Default view, representing the 8 ASSR channels; mid: alternative view with raw EEG; right: status view for right ear, indicating finished and ongoing points

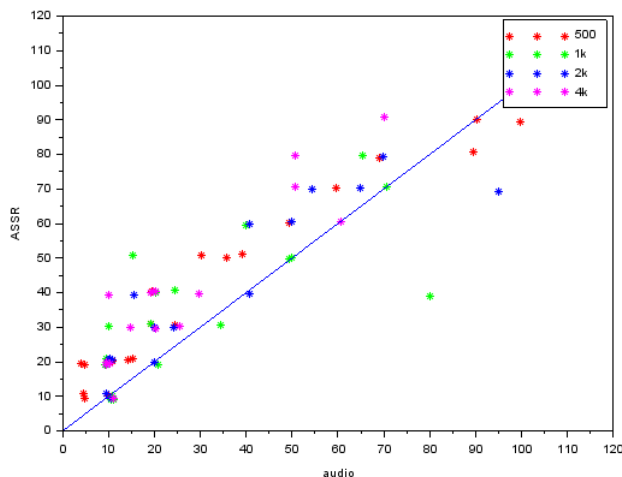


Fig. 32: Comparison of multi-rate ASSR thresholds to pure tone audiogram data for awake subjects. Test timeout per single point was 8 minutes, with up to 4 frequencies per ear stimulated. Overall average test time was approx. 15 minutes. Data is based on 12 patients, 4 frequencies per ear, resulting in 96 points. Mixed rate protocol was used, 500 1k 2k 4k tested at 37, 39, 41, 81 Hz

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