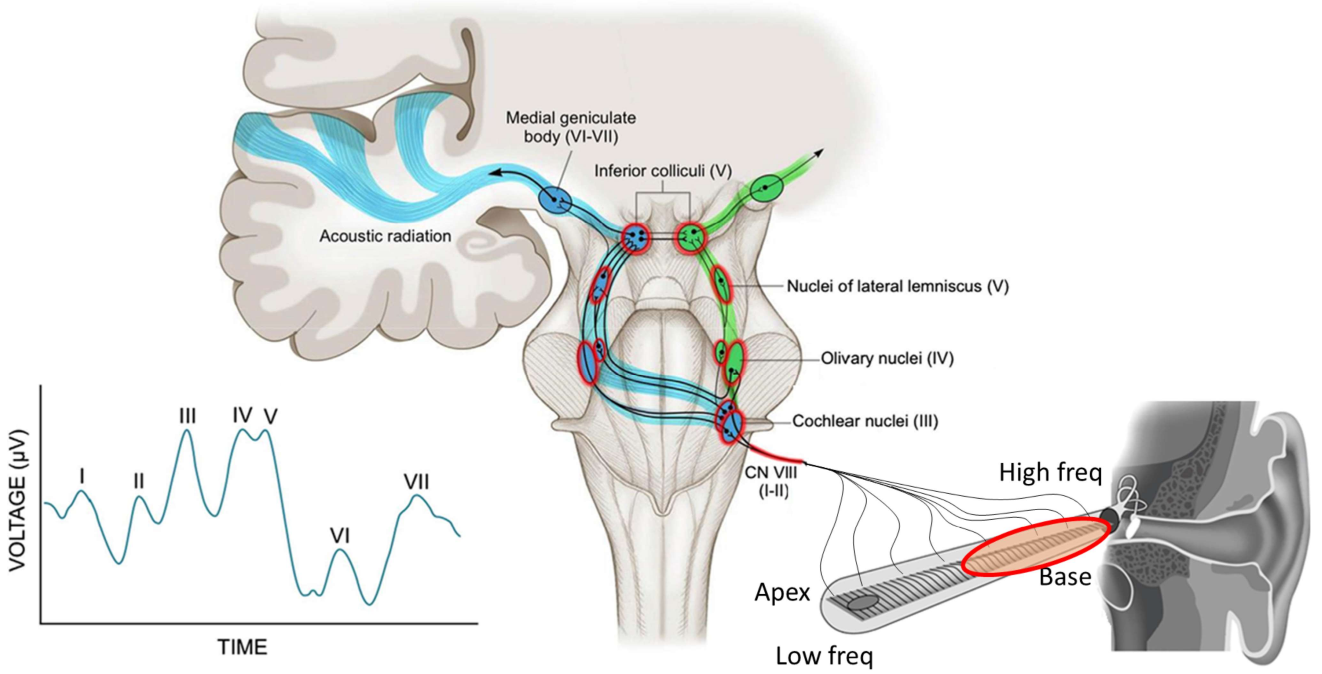
- Good morning.

- My name is Joaquin Valderrama. I am a Research Electrophysiologist with the National Acoustic Laboratories, and I am also an Honorary Research Fellow at Macquarie University.

- In this presentation, I will talk about a new stimulation strategy that enhances the brainstem response to low frequency sounds.

- Before starting, please let my acknowledge my colleagues who have also participated in this study. They are Jaime Undurraga, Lindsey Van Yper, Angel de la Torre, and David McAlpine.

The conventional auditory brainstem response



- Auditory Brainstem Responses are a number of voltage peaks that reflect the synchronous activity of the neurons in different levels of the auditory pathway.

- For example, wave I is generated in the cochlea, wave III in the superior olivary complex, and wave V in the upper midbrain.

- Thanks to the non-invasive nature of the recording of these signals, ABRs are used worldwide in many research studies to understand our neural architecture and in clinical applications like threshold estimation and intra-operative monitoring.

- Conventional ABRs are typically elicited by short duration stimuli, like clicks.

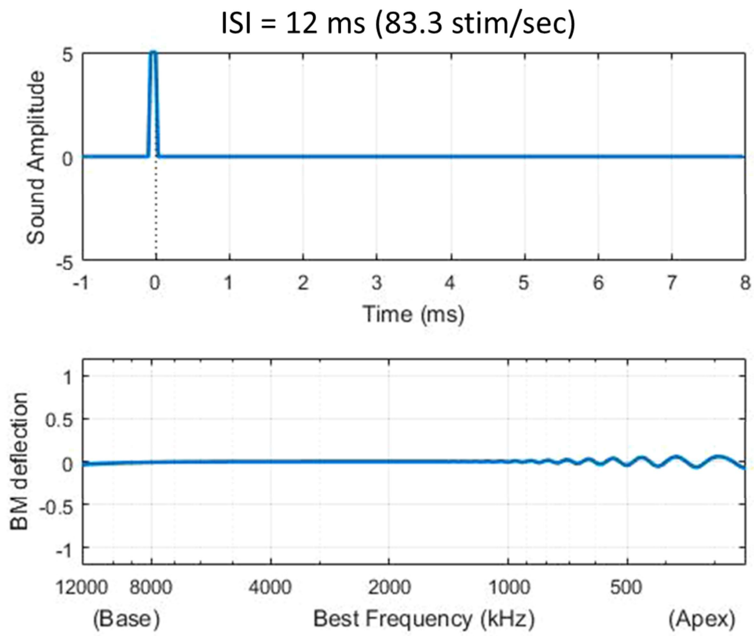
- However, it is important to note that the way we measure ABRs reflect neural activity elicited mostly from the BASAL end of the cochlea.

- This is due to 2 reasons: (1) since clicks present most of their energy in high frequency bands the contribution from apical portions (which is sensitive to low frequency sounds) is minimal, and also (2) the fact that the traveling wave is faster in the base but slows down in the apex makes that the contribution from apical portions is less synchronized with the stimulus.

- In other words, the contribution from apical portions of the cochlea is of a lower magnitude and is less synchronized with the stimulus.

- At the moment, there are not too many efficient tools to obtain ABRs evoked by low-frequency sounds.

ABRs reflect activity evoked from the base of the cochlea

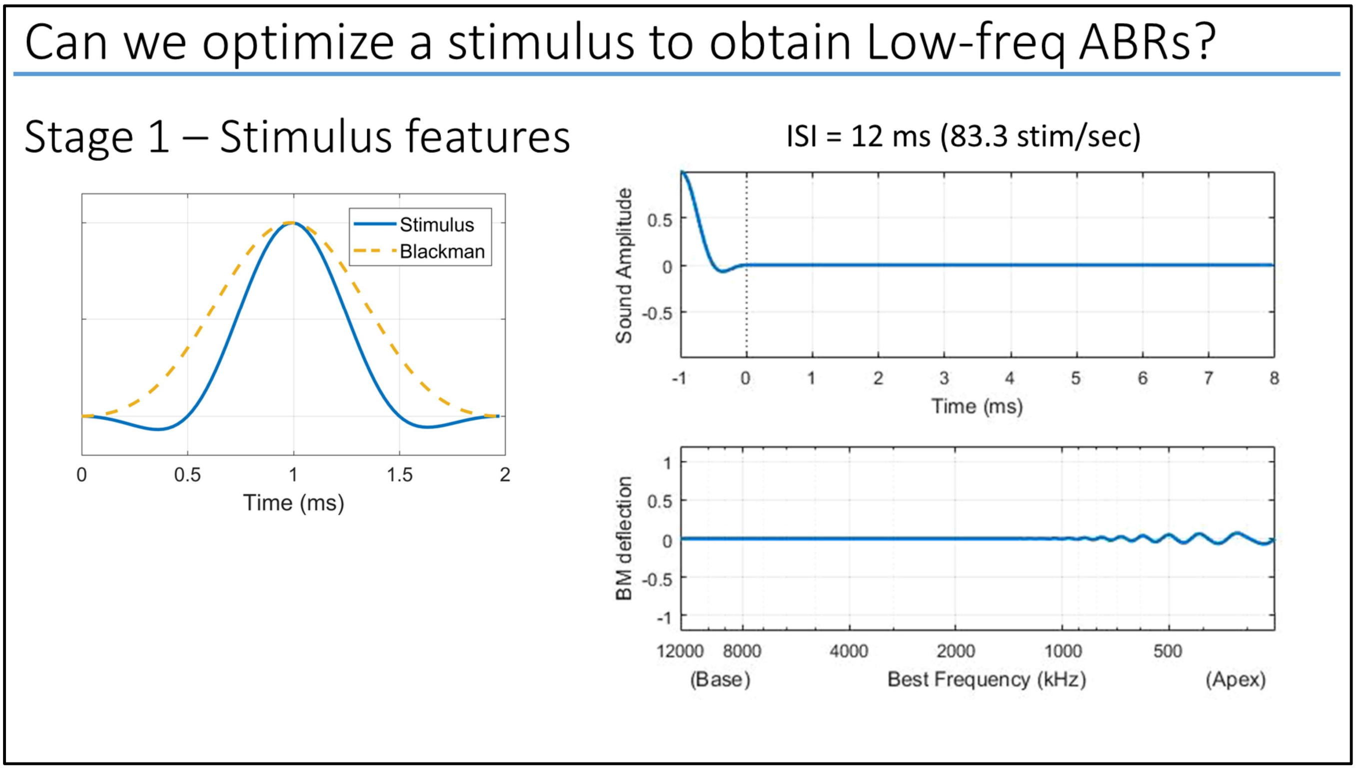


- I have created a simulation to visualize this effect.

- The top plot in this simulation shows the stimulation pattern, in this case a click presented every 12 ms. The plot at the bottom shows the BM deflection, high-frequencies in the base of the cochlea and low-frequencies in the apex.

- This simulation shows that the maximum deflection of the BM occurs at the high frequencies, and that the sections of the cochlea sensitive to low frequency sounds are of a lower magnitude and are activated many milliseconds after the stimulus onset.

- The objective of this study was to develop a stimulation strategy to optimize ABRs evoked from apical portions of the cochlea.



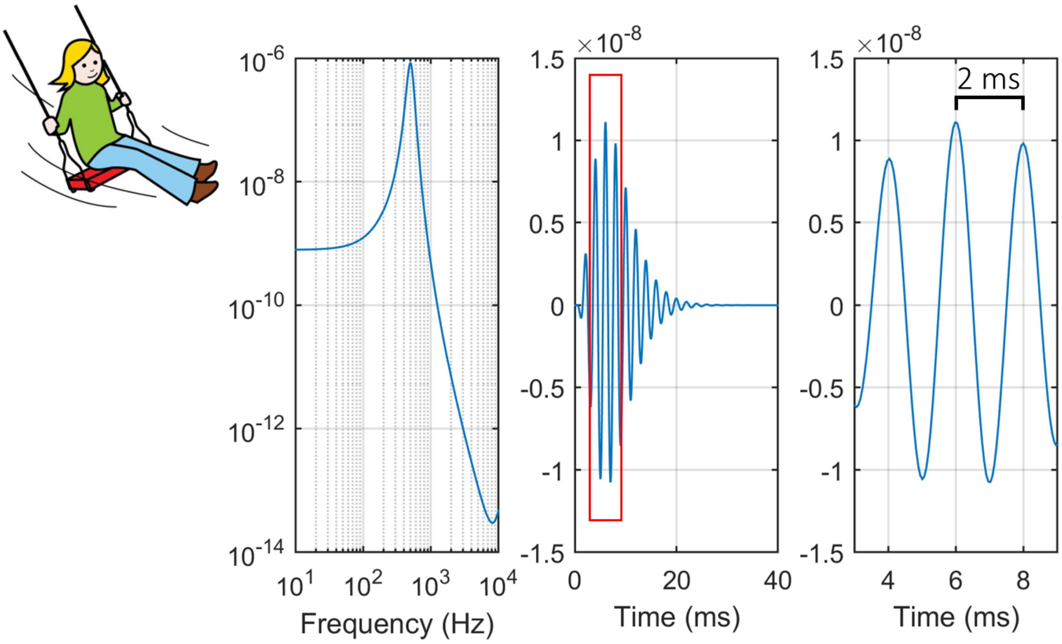
- Lets' think only for 500 Hz.

- The way we are going to do it is with this stimulus, that is a 1 period of a 500 Hz tone, windowed with a Blackman window (yellow line). Note that this stimulus has a significantly larger duration than clicks (2 ms vs 0.1 ms), but also, 2 ms is the shortest duration of a stimulus with energy in the 500 Hz frequency band.

- When this stimulus is used instead of a click, using the same presentation rate, the simulation shows that (a) the contribution from high frequencies is minimal; but note however that (b) a large range of frequencies in the apical portion of the cochlea are activated [i.e. the frequency specificity is low], and (c) the BM magnitude deflection is not very pronounced.

- This stimulus paradigm is still not optimized.

Use the ringing property of the cochlea filter (500 Hz)



- The way we are going to optimize the stimulus is based on the ringing property of the cochlear filters.

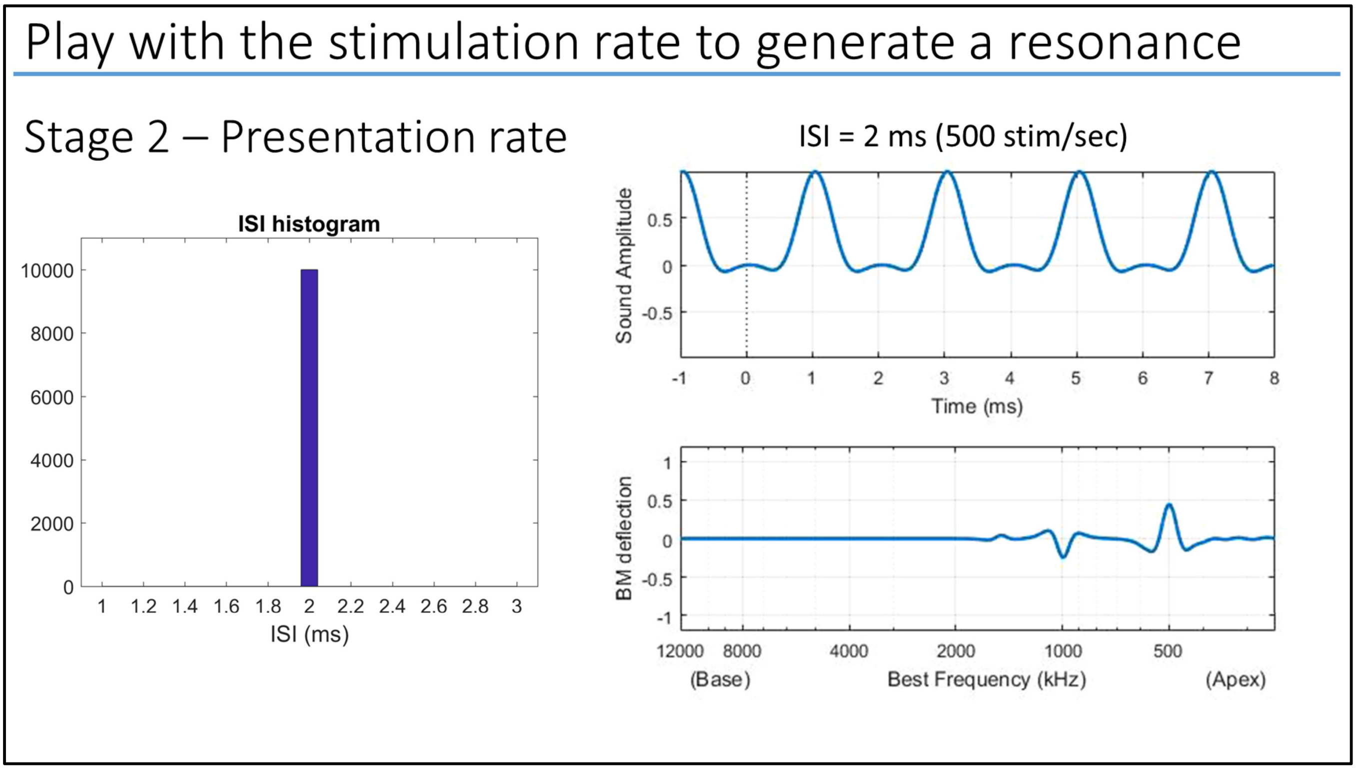
- The figure on the left shows the frequency response of a Gamma-Tone filter with characteristic frequency of 500 Hz, and the figure on the middle the impulsive response of the same filter. The figure on the right shows a detail of the section with maximum BM deflection.

- This figure shows that after the stimulus is presented, the 500 Hz filter rings during more than 20 ms with a period of 2 ms, and that the maximum deflection occurs at about 6 ms after the stimulus onset.

- Taking this into account, our stimulus paradigm aims to **present a stimulus in phase with the BM fluctuation in order to induce a resonance**.

- A similar analogy would be a swing, in which a small force applied in the correct moment can keep a swing oscillating.

- In our case, if we want to generate a resonance in the 500 Hz filter, then we would have to present stimuli every 2 ms. This is illustrated in the next slide.

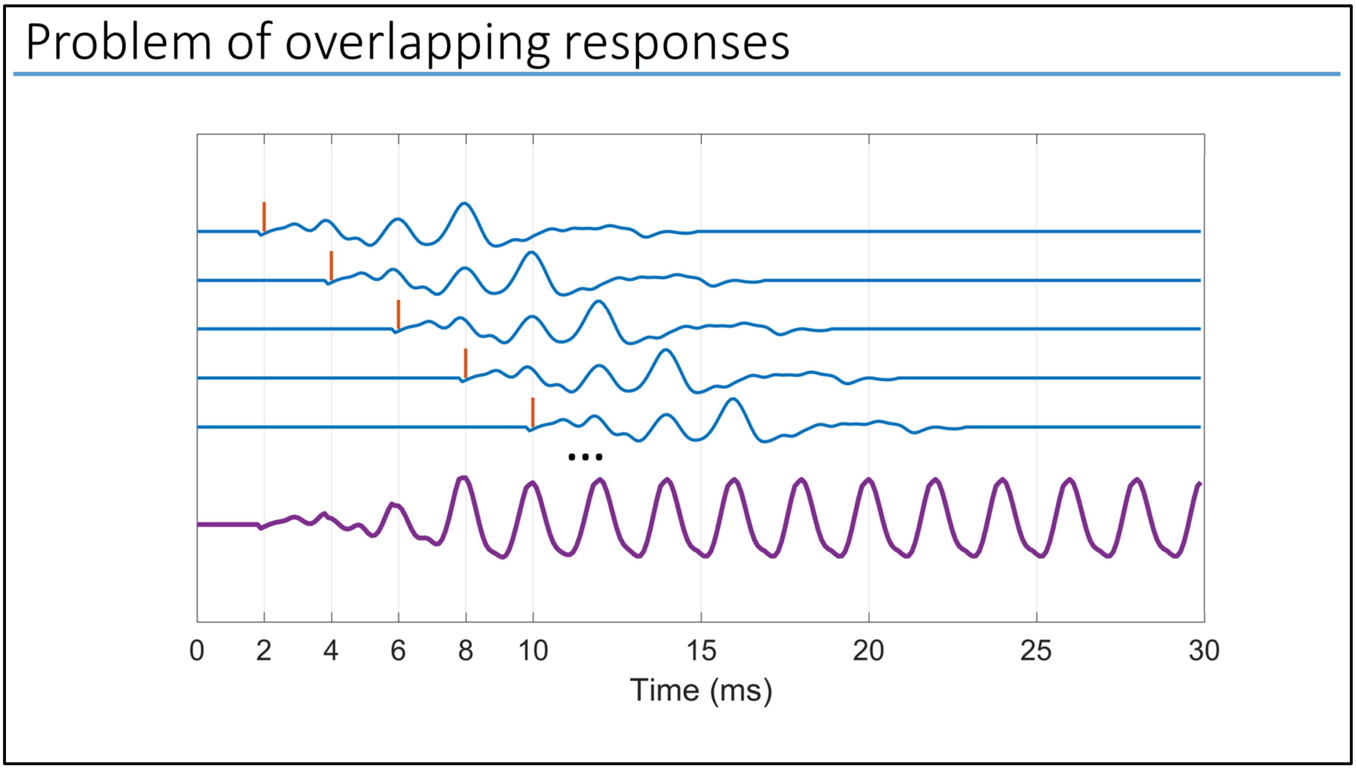


- The second optimization stage consists of presenting the stimuli with a rate of 500 stimuli per second, or an ISI of 2 ms.

- The simulation shows that this stimulus paradigm generates a BM resonance at 500 Hz and its harmonic frequencies.

- This resonance improves the frequency specificity and increases the magnitude of the deflection.

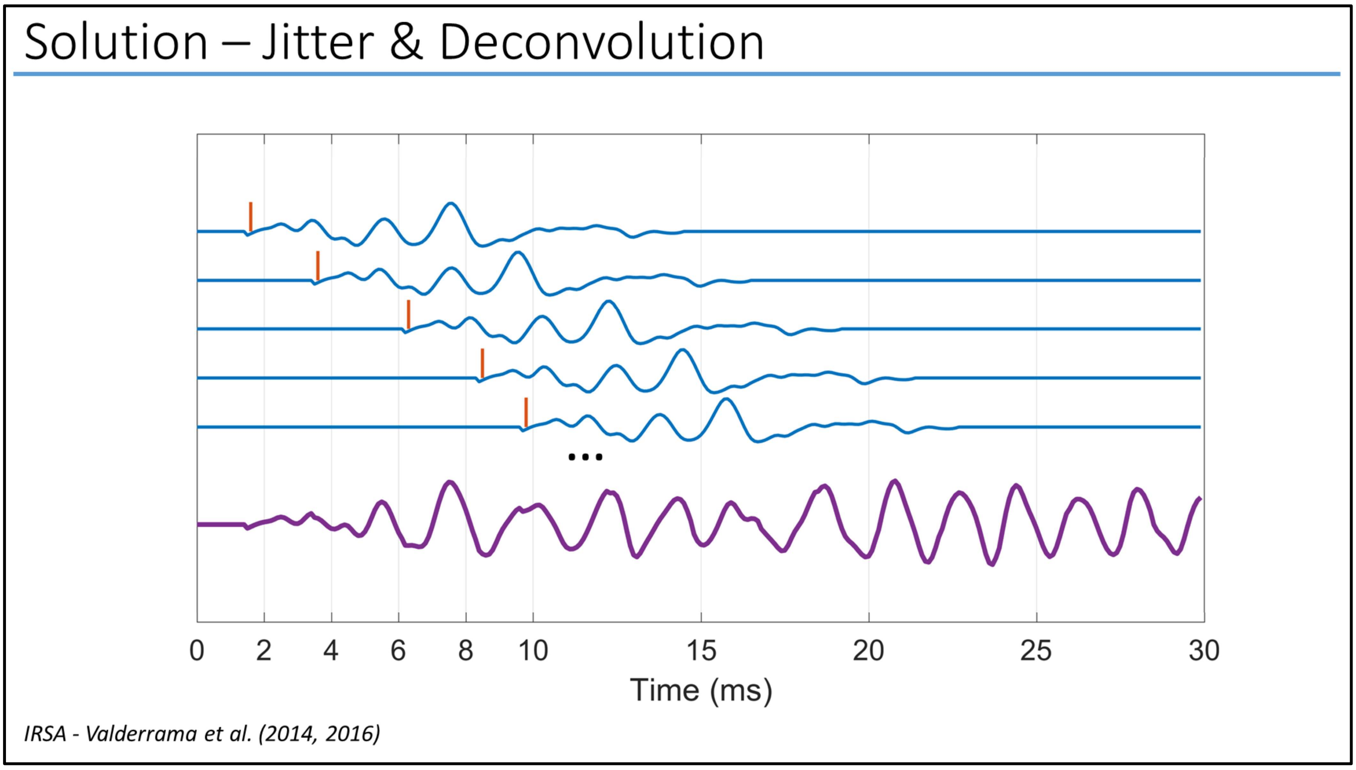
- However, presenting stimuli at a rate of 500 stimuli per second poses one important challenge. Probably many of you are guessing what this problem is.



- The problem of overlapping responses.

- Red vertical bars show the instants in which the stimuli are presented, i.e. exactly every 2 ms. The blue signals are the ABRs evoked by each of these stimuli.

- This figure shows that presenting stimuli with a fixed ISI of 2 ms leads to responses being overlapped and contaminated by adjacent responses, obtaining a steady-state response at the electrodes, from which it is widely known that it is impossible to estimate the transient ABR.



- The solution to this problem comes by jittering the presentation rate and using a deconvolution technique to disentangle the overlapping responses.

- This figure shows that the ISI in this sequence is not fixed. In some stimuli the ISI is shorter and in others the ISI is larger.

- This randomization in the ISI leads to a QUASI-steady state signal in the electrodes, from which now it is possible to estimate the transient ABR using deconvolution techniques.

- We have used the iterative randomized stimulation and averaging technique, which is described in detail in a couple of papers.

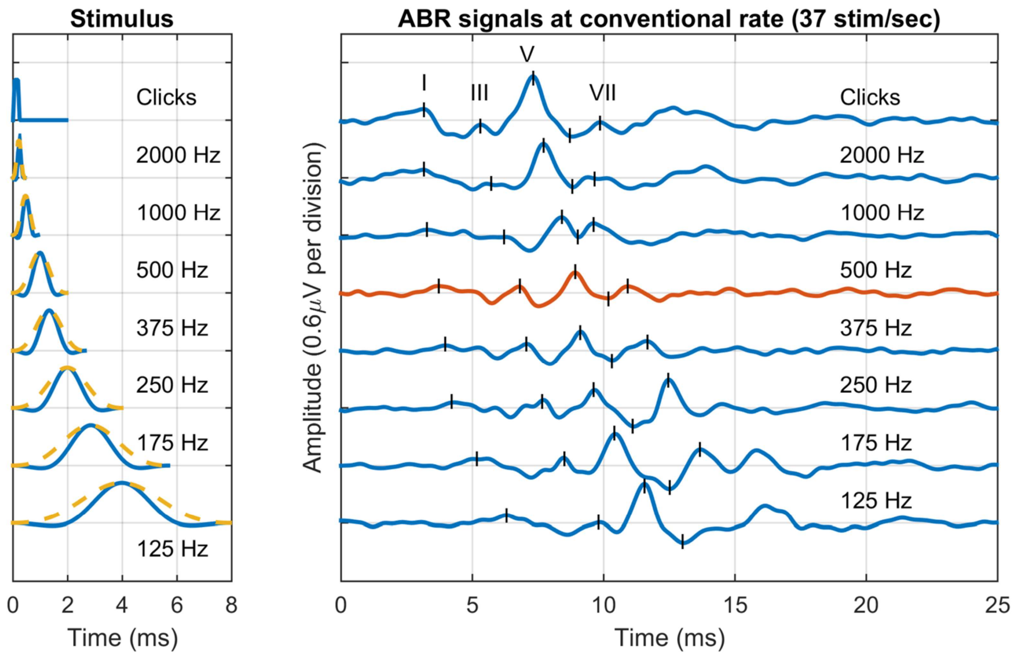
- You can probably see that this paradigm involves an important trade-off when deciding an optimal amount of jitter, or degree of dispersion of the ISI.

    - On one hand, narrow jitters, or very short differences in the ISI is optimal for the BM resonance, but complicates the deconvolution of overlapping responses.

- And on the other hand, wide jitters facilitate deconvolution but do not induce the BM resonance.

- Ok, enough theory, let's see some data. I have prepared some experiments to show the benefits of this resonance with real responses.

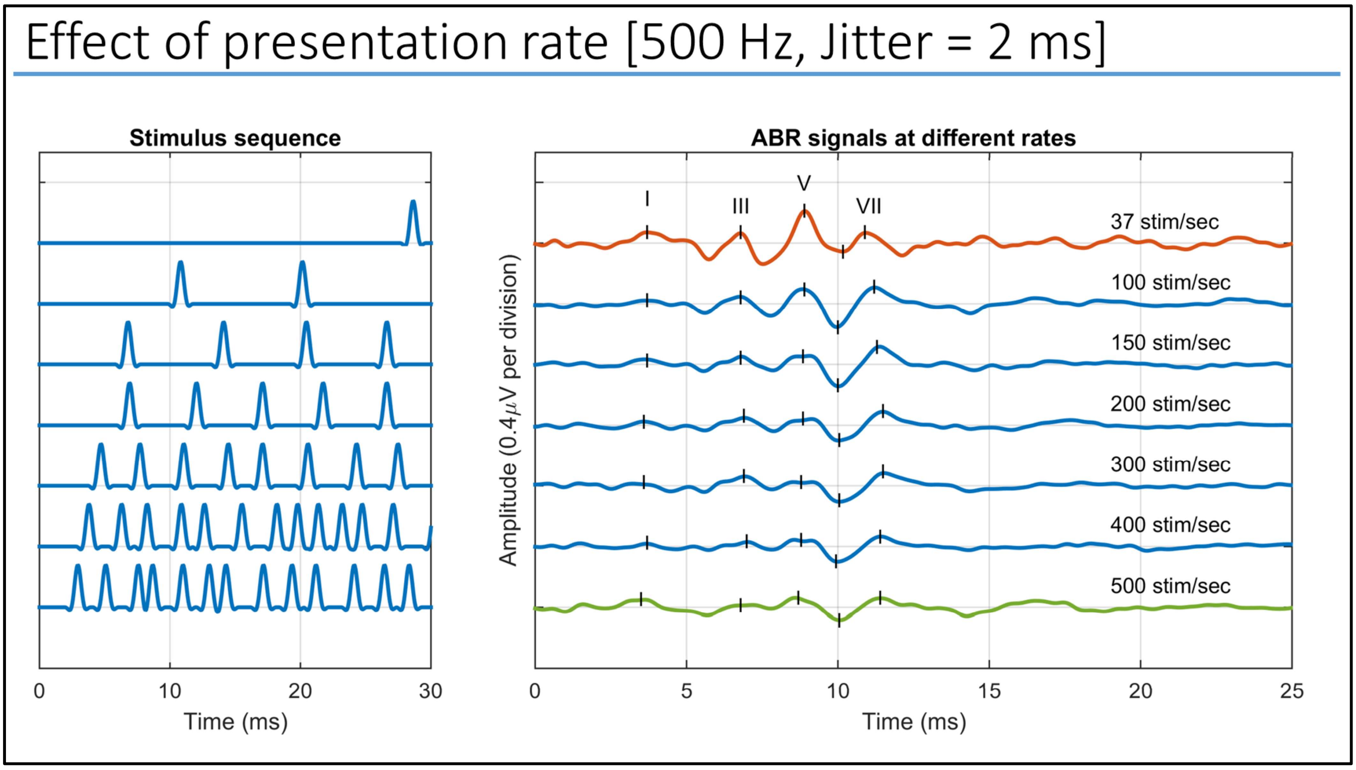
Effect of stimulus



- The first experiment shows the responses to clicks and to the stimulus defined in this study at different frequencies using a CONVENTIONAL presentation rate, without overlapping responses, so this stimulus paradigm is still not optimized.

- This experiment shows a first-order effect of the stimulus type, and is useful to track the main components from the well-established click-evoked ABR.

- Our response of interest is highlighted in red colour, corresponding to the stimulus of a frequency of 500 Hz.

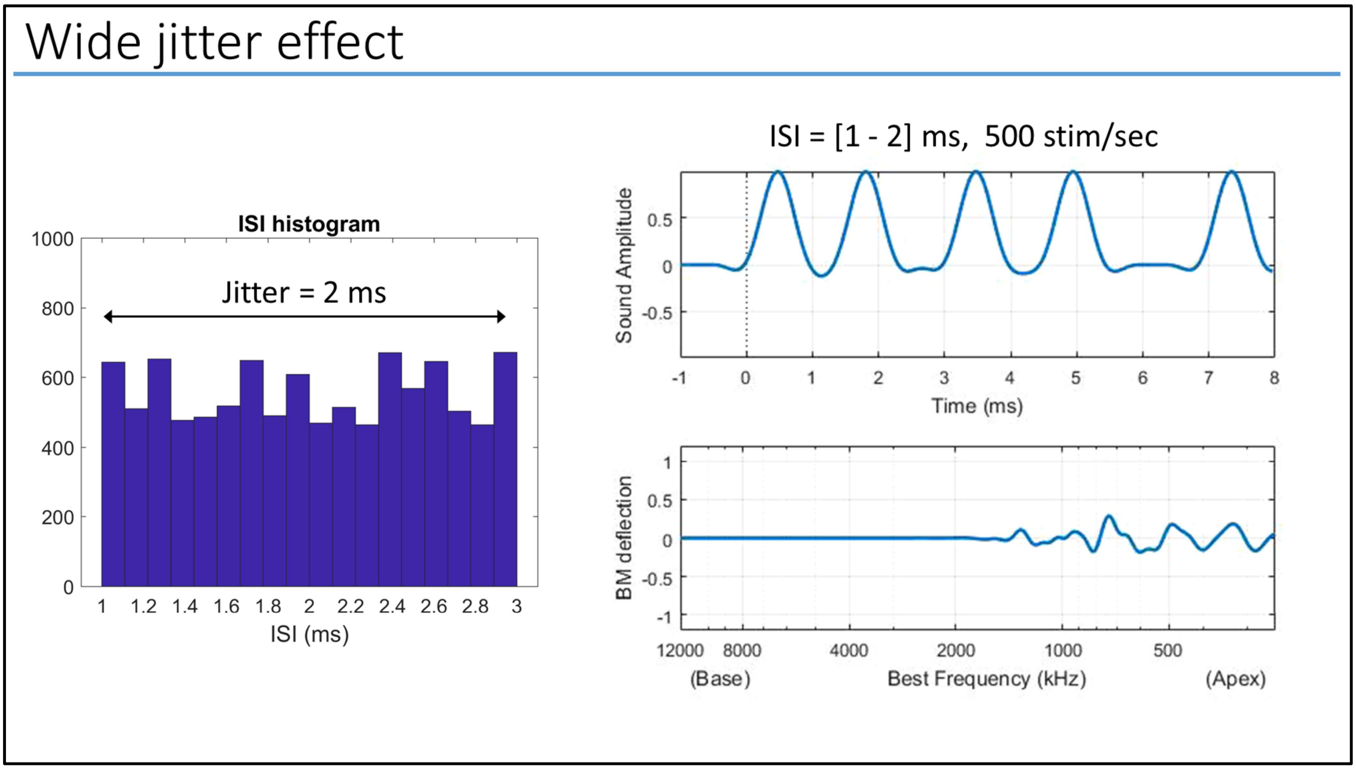


- The second experiment shows the effect of increasing the presentation rate of the 500 Hz stimulus, from a conventional rate of 37 stimuli per second, in which there are no overlapping responses, to 500 stimuli per second, in which the averaged ISI is 2 ms (signal in green).

- This figure shows that increasing the presentation rate does not have a significant effect on the latency of the main components, which can still be tracked up to 500 stimuli per second.

- Please note that in this experiment the jitter of the ISI was 2 ms.

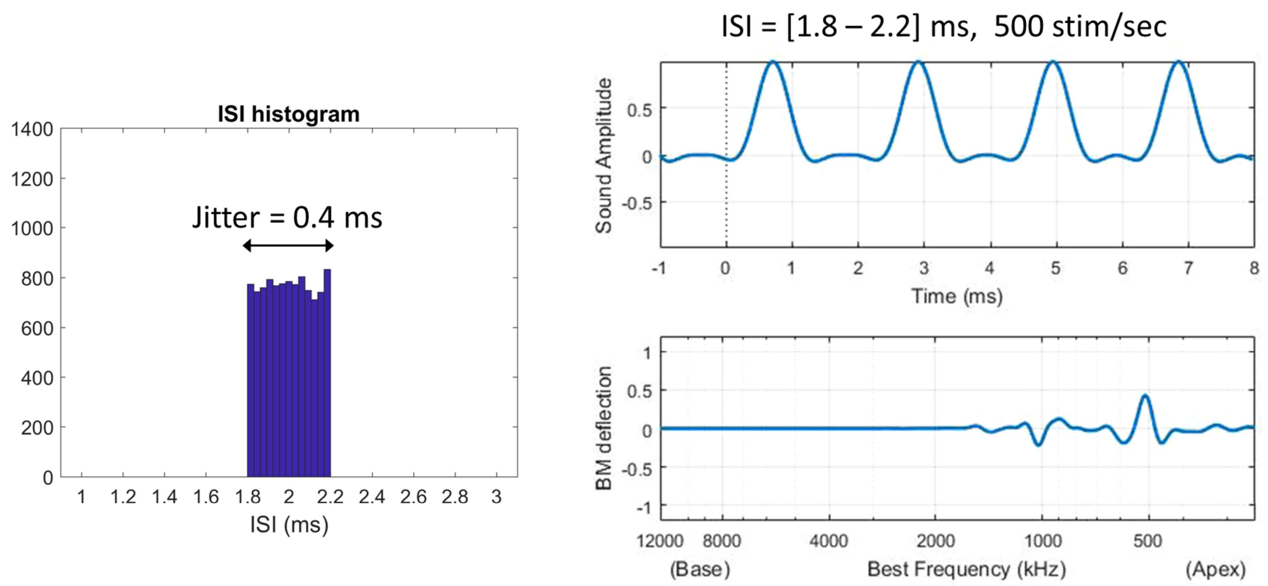
- With this wide jitter, it was expected that a basilar membrane resonance would not be induced.



- This simulation shows that when we use a wide jitter of 2 ms, no resonance is induced.

- In the analogy of the swing, we would be pushing the swing randomly without any periodical pattern.

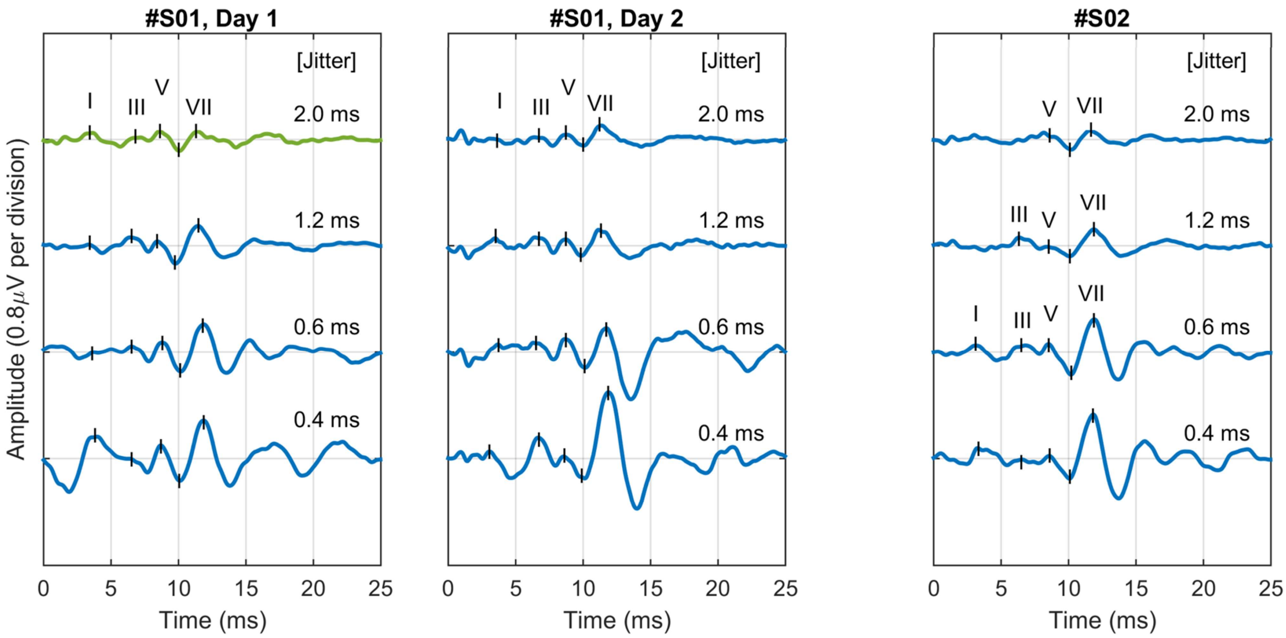
Effect of reducing the jitter



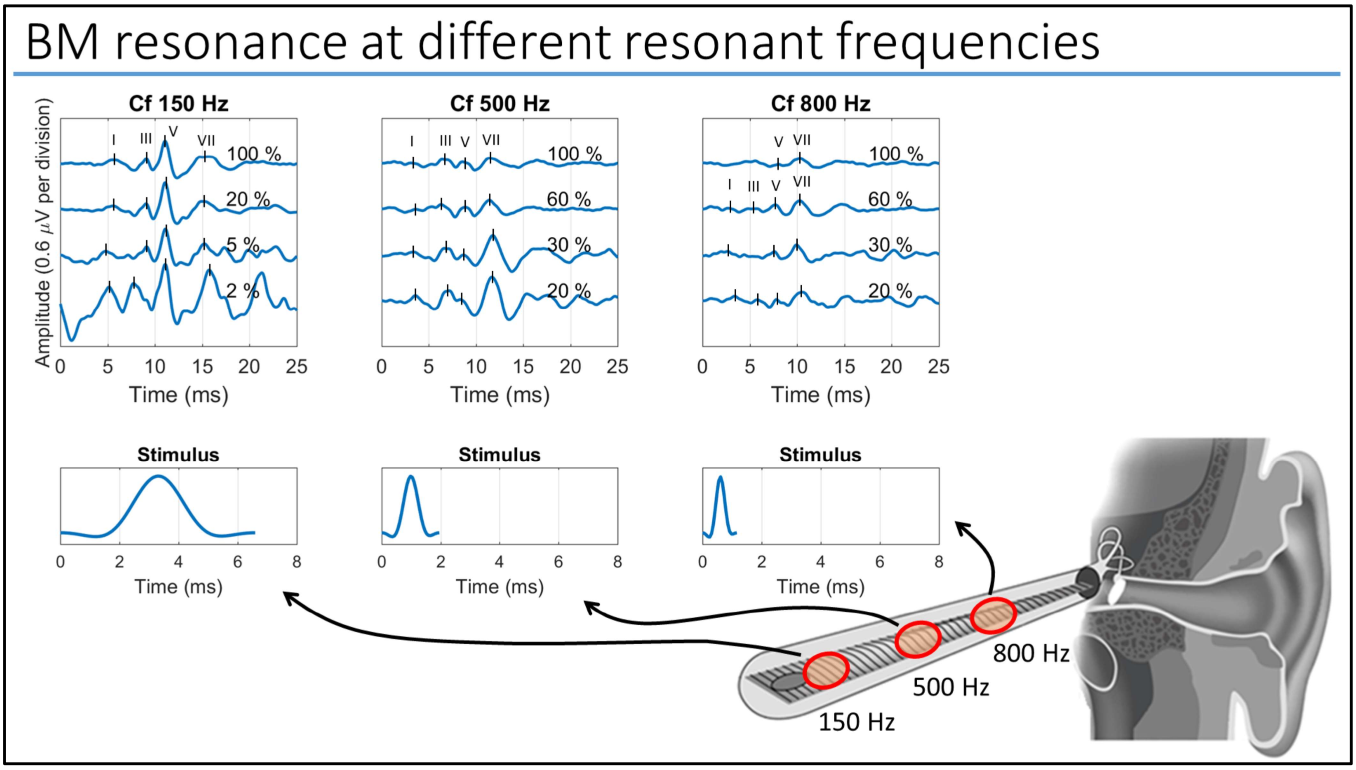
- In contrast, a BM resonance can be induced using a narrower jitter, like 0.4 ms in this example.

- Taking into account the presented theoretical framework and simulations, we hypothesized that decreasing the jitter would induce a BM resonance, which would increase the synchrony of the responses evoked from apical portions of the cochlea, and therefore, we would obtain larger ABRs.

ABRs obtained at 500 stim/sec and different jitters



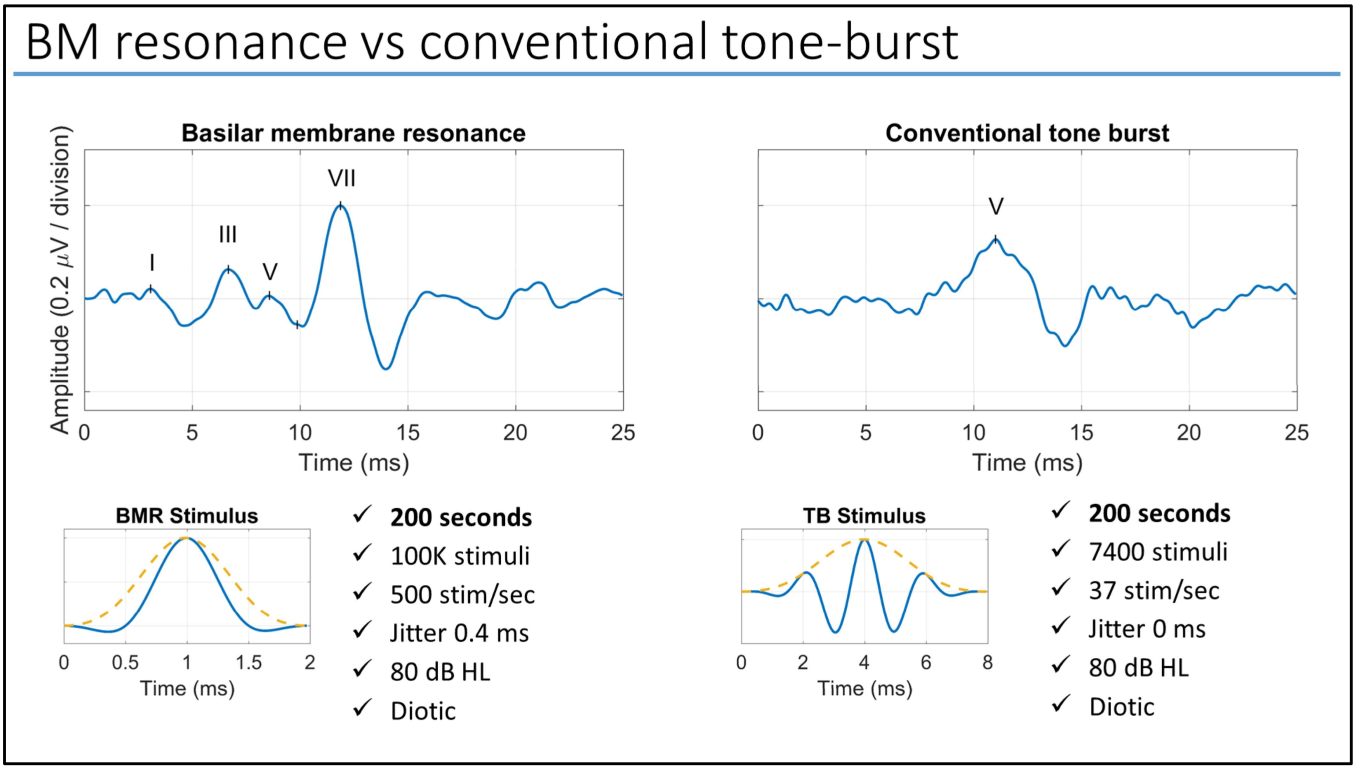
- This figure shows deconvolved ABRs from stimulus sequences presented at 500 stimuli per second and different amounts of jitters in one subject in two different days (to evaluate test-retest), and in a second subject.
- The signal in green shows the ABR obtained with a wide jitter, in which no BM resonance is expected. All components marked in this signal were labelled according to the previous experiments.
- This figure shows that **reducing the amount of jitter of the stimulus sequence enhances the magnitude of the ABR components**.
- The same effect can be observed in the same subject, with ABRs obtained in a different day.
- Wave VII seems to be the component most sensitive to the BM resonance.
- And the same effect can also be observed in a different subject.



- So far we have seen some examples of the BMR benefits at the 500 Hz frequency.

- In this figure, the jitter is expressed in terms of percentage of the duration of the stimulus. 100% indicates a jitter of 2 ms, which is the maximum jitter, and 20% indicates a jitter of 0.4 ms.

- In addition to the 500 Hz case, we have seen that



- Finally, if we compare an ABR obtained with a basilar membrane resonance using a narrow jitter and an ABR obtained with a conventional 500 Hz tone burst <u>using the same recording time</u>…

- We see clear differences between the two signals. The components in the ABR obtained with the BMR presents can be more clearly identified and are of a greater magnitude.

Take-home message

We can take advantage of the resonance properties of the cochlear filters to enhance the brainstem response elicited by selective apical portions of the cochlea

Future work

- ✓ Evaluate the feasibility of BMR-ABRs in low-frequencies threshold estimation
- ✓ Explore ITD sensitivity through BMR-ABRs elicited by binaural stimuli
- ✓ Understand the contribution from harmonic frequencies
- ✓ Expand comparison with conventional tone-bursts and narrow-band chirps.
- ✓ Improve the deconvolution algorithm

Acknowledgements

- ✓ Australian Research Council Grant *#FL160100108*
- ✓ Dr Jan Schnupp – *Auditory Neuroscience*