Published in final edited form as:

Hear Res. 2013 April ; 298: 73–79. doi:10.1016/j.heares.2013.01.002.

Rapid measurement of auditory filter shape in mice using the auditory brainstem response and notched noise

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Abstract

The notched noise method is an effective procedure for measuring frequency resolution and auditory filter shapes in both human and animal models of hearing. Briefly, auditory filter shape and bandwidth estimates are derived from masked thresholds for tones presented in noise containing widening spectral notches. As the spectral notch widens, increasingly less of the noise falls within the auditory filter and the tone becomes more detectable until the notch width exceeds the filter bandwidth. Behavioral procedures have been used for the derivation of notched noise auditory filter shapes in mice; however, the time and effort needed to train and test animals on these tasks renders a constraint on the widespread application of this testing method. As an alternative procedure, we combined relatively non-invasive auditory brainstem response (ABR) measurements and the notched noise method to estimate auditory filters in normal-hearing mice at center frequencies of 8, 11.2, and 16 kHz. A complete set of simultaneous masked thresholds for a particular tone frequency were obtained in about an hour. ABR-derived filter bandwidths broadened with increasing frequency, consistent with previous studies. The ABR notched noise procedure provides a fast alternative to estimating frequency selectivity in mice that is well-suited to high through-put or time-sensitive screening.

1. Introduction

Mouse models have gained increasing importance for understanding the genetic and environmental contributions to the development of hearing function as well as the mechanisms underlying deafness and other hearing disorders. Basic hearing sensitivity is now routinely screened in mouse models of auditory function. However, common hearing screening protocols used in mice are often insensitive to detecting auditory dysfunction beyond elevated thresholds for sounds in quiet or reduced reactivity to loud sounds. Important information regarding auditory function may be missed when relying on these measures since animals can display significant deficits while maintaining normal pure tone thresholds (e.g., Kujawa and Liberman, 2009; Lauer and May, 2011; Allen and Ison, 2012; Satheesh et al., 2012).

Frequency resolution affects the ability to separate out components of complex sounds, detect sounds in background noise, and distinguish two sounds that are close together in frequency. Damage to the auditory system alters frequency resolution (e.g., Patterson et al., 1982; Tyler et al., 1984), contributing to common complaints of difficulty resolving sounds in the presence of competing backgrounds. Traditional behavioral measures of frequency selectivity are inefficient when considering animal models of developmental processes, early-onset hearing deficits, or models with rapidly declining hearing due to lengthy training

and testing times. Our goal is to develop efficient, behaviorally validated methods to screen complex auditory functions in mice using rapidly measured evoked potentials. To that end, we describe a procedure using auditory brainstem responses (ABRs) measured in simultaneous spectrally notched noise to estimate peripheral frequency selectivity in mice.

The notched noise procedure characterizes frequency resolution based on the presentation of a pure tone in background noise containing a spectral notch (Fig. 1). According to the power spectrum model of masking, increasing the width of the notch results in less noise interference within an auditory filter until a “critical band” is reached where further increases in notch width no longer cause a change in threshold (Patterson, 1974). These theoretical auditory filters can be approximated using a rounded exponential (roex) minimization algorithm in order to estimate the critical bandwidth as an equivalent rectangular bandwidth (ERB) value (Glasberg and Moore, 1990). In the present paper, we evaluate the effectiveness of using the ABR and notched noise procedure as a rapid method for assessing auditory filter bandwidth in mice.

The notched noise procedure is based on well-established psychoacoustic behavioral methods that have only been implemented in a small sample of animals (Marean et al., 1993; Niemiec and Shoffner, 1990; Lin et al., 1997; Finneran et al., 2002; Lemmonds et al., 2012; May et al., 2006). Similar stimuli have been used in conjunction with ABRs to rapidly estimate auditory frequency selectivity in wild birds and dolphins (Popov et al., 1997; Gall and Lucas, 2010; Henry and Lucas, 2010a, b). This paradigm yields a reasonable estimate of auditory filters at a range of frequencies within several hours rather than the months to a year required for behavioral procedures. The ABR procedure is ideal for models that may be difficult to test behaviorally, show rapid auditory system degeneration, or require testing of many animals. Moreover, these tests can be repeated at multiple time points over the course of development, aging, or treatment.

2. Material and methods

2.1. Subjects

A total of 17 CBA/CaJ mice were bred and housed in a quiet vivarium to minimize exposure to potentially damaging environmental noise (Lauer et al., 2009). Ad libitum access to food and water was provided to all subjects. Ages of tested mice ranged from 6 to 28 weeks. Hearing status remains normal in this strain throughout this age range, and normal hearing was confirmed by measuring thresholds for clicks and tones presented in quiet for each test frequency. Seven mice were tested at each probe tone frequency with 4 mice tested at multiple frequencies. All procedures were approved by the Johns Hopkins University Animal Care and Use Committee, and were consistent with the Guide for the Care and Use of Laboratory Animals.

2.2. General auditory brainstem response procedures

Auditory brainstem response procedures were based on previously published work described by members of our research group (e.g. Ngan and May, 2001; May et al., 2002; Stamatakis et al., 2006; Lauer and May, 2011; Yang et al., 2011). Mice were anesthetized with a solution of ketamine (100 mg/kg) and xylazine (20 mg/kg) in 14% ethyl alcohol such that 0.1 cc/per 20 g body weight were administered intraperitoneally. Anesthetized mice were placed on a gauze-covered heating pad and maintained at $37^{\circ}\text{C} \pm 1^{\circ}$ inside a sound-attenuating chamber lined with acoustic foam. ABRs were differentially recorded from the scalp using subcutaneous platinum needle electrodes placed over the left bulla and at the vertex of the skull. A ground electrode was inserted into the ipsilateral hind leg muscle. Heart rate, breathing, and relative movement were monitored throughout the experiment using an audio monitor and an oscilloscope. If an animal showed signs of waking at any time during

recording, supplemental doses of 1/3 to 1/2 the original anesthesia dose were administered. Stimulus generation and collection of ABR responses were controlled using custom Matlab-based software interfaced with Tucker Davis Technologies (TDT) hardware. Stimuli were amplified using a Crown amplifier and played through a Fostex dome tweeter speaker (model FT28D) or a pair of Radioshack Supertweeters located 30 cm from the vertex of the skull and aligned with the median sagittal plane of the animal. A stimulus presentation rate of 10/s was used throughout the experiment. Responses were amplified using a World Precision Instruments ISO-80 biological amplifier and filtered between 30 and 3000 Hz using a Krohn-Hite bandpass filter. Speaker calibration was performed using a 1/4-in Brüel and Kjær free field microphone, TDT hardware, and custom Matlab-based software. Periodic calibration checks were performed using a Larson-Davis LXT sound level meter fitted with a 1/2-in free field microphone throughout the experiment.

Responses were recorded for a period of 30 ms beginning with stimulus onset; ABR waves occurred within approximately 2–10 ms of stimulus onset (Fig. 2A). Thus, 0 ms indicates the time of stimulus onset in Fig. 2A. Since the presence of continuous background noise maskers often degraded the ABR signal such that it was difficult to clearly discern each wave as distinct from wavelets or merged waves at low probe tone levels, the magnitude of the ABR was determined by calculating the maximum peak-to-peak amplitude (any wave) within an 8 ms window beginning 2 ms after stimulus onset. ABR waveforms recorded in the presence of noise with spectral information near the probe frequency (small notch width) are often de-synchronized and of poor quality compared to non-masked waveforms (e.g., Van Zanten and Brocaar, 1984; Nousak and Stapells, 2005). Typically, the largest peak-to-peak magnitude occurred between the first negative and the second positive waves. Baseline response noise magnitudes were calculated by averaging the last 10 ms of each averaged 30 ms trace (no stimulus occurred during this time). If a large deflection occurred during the baseline window, the recording was discarded and repeated. This was an extremely rare occurrence. The ABR and baseline time windows are depicted in Fig. 2A.

Stimuli were first presented well above threshold to confirm the presence of a robust response and then attenuated in 10 or 20 dB steps to obtain a level series. Step size was reduced to 5 dB near threshold. Stimulus level was decreased until a response was no longer visible. Threshold was defined as the interpolated sound level at which the ABR magnitude was 2 standard deviations (SD) above the average baseline noise level calculated from the individual baseline noise levels computed for each stimulus level tested (Fig. 2B). This procedure for determining threshold is in keeping with common procedures in mice and other nonhuman species in which ABR waveforms are easily differentiated from background noise (Ngan and May, 2001; May et al., 2002; Stamatakis et al., 2006; Lauer and May, 2011; Yang et al., 2011; Walter et al., 2012). This objective criterion produced threshold estimates that were within a few dB of those obtained using a subjective visual inspection method but removed potential effects of observer bias. ABRs were averaged over 300 stimulus presentations for each condition. Pilot experiments in our lab have shown that increasing the number of repetitions does not improve the response waveform or the signal to noise ratio since the mouse ABR is a very robust response at suprathreshold stimulus levels (Fig. 2C). Animals were first tested with broadband clicks in order to demonstrate the presence of a clear ABR waveform with at least four to five peaks under standard test conditions. This ensured proper electrode placement and served as an initial screen for unexpected hearing loss. Unexpected hearing loss was not observed in any of the animals. Testing with other conditions proceeded for approximately 40–90 min as described below.

2.3. Notched noise method

Stimulus parameters, materials, and the strain of mice were chosen to mimic those used by May et al. (2006) as closely as possible. The requirements for eliciting and measuring ABRs

necessitated certain deviations from the original study with respect to tone stimulus duration, noise spectrum level, and threshold determination. The notched noise method involves masking a probe tone with a Gaussian distributed noise containing a spectral notch of varying width (Fig. 1). The notch is typically centered on the probe frequency. The power spectrum theory of peripheral auditory filtering makes the following assumptions: (i) the probe frequency is processed through a single auditory filter giving the highest possible signal-to-noise ratio and (ii) that thresholds correspond to a fixed signal-to-masker level at the output of the filter (Fletcher, 1940; Patterson, 1974; Glasberg and Moore, 1990). The filter shapes are approximated using a roex(p,r) minimization algorithm. The widths of the filters are estimated as equivalent rectangular bandwidths (ERBs; Glasberg and Moore, 1990).

ABRs were measured in response to 5 ms (0.5 ms rise/fall) 8, 11.2 or 16 kHz pure tones in quiet and in the presence of simultaneous background noise. Thresholds were first measured for the probe tones presented in quiet (ambient background noise). Continuous broadband noise (BBN) with a relatively flat spectrum between 4 and 40 kHz was presented simultaneously at an intensity level selected to raise the threshold for the probe tone by approximately 40 dB in the no notch condition as in May et al. (2006). Thus, animals in the present study were tested at sensation levels similar to those used in the behavioral study. The noise level was kept constant during the notched noise conditions. The noise spectrum level was 25.6 ± 3.4 dB. A spectral notch was introduced at 0.125, 0.25, 0.5, 1.0 and 2.0 octave widths centered at the probe tone frequency. Masked auditory thresholds were measured for probe tones for each notch width and in noise with no notch.

2.4. Derivation of auditory filter shapes

Derivation of auditory filter shapes was accomplished with the roex(p,r) filter function as described previously (e.g. Glasberg and Moore, 1990) using a Matlab analogue of the original software tools (available to the reader upon request). This involved a minimization algorithm for calculating the fitting parameters against the interpolated threshold data set by minimizing the root-mean-square error between the recorded threshold values and the filter-generated predicted values. The program differed from the original minimization fitting procedure in that it was governed by an unconstrained nonlinear optimization (Matlab's *fminsearch* function) instead of a custom programmed simplex algorithm. In this study, the roex(p,r) model for the determination of weighted filter shapes was used to maintain consistency with data collected previously by May et al. (2006). Newer filter models (Unoki et al., 2006) developed to improve upon the roex(p,r) fitting procedure have been shown to be less stable (Gall and Lucas, 2010; Henry and Lucas, 2010a, b). Other changes to the algorithm were made in order to minimize mean squared error in the data fitting procedure. This included optimization of the efficiency of the filter by shifting the power output to accurately match the data (Gall and Lucas, 2010; Henry and Lucas, 2010a, b). Filter parameters and mean squared error are summarized in Table 1.

To summarize, the power spectrum model evaluates the masked threshold of a signal (P_s) as the area defined by the power spectrum of the noise ($N(f)$) and the weighting function of the signal ($W(f)$ ranging from 0 to 1) in the frequency domain. This calculation is represented by the following equation:

$$P_s = K \int_{-\infty}^{\infty} N(f) W(f) df \quad (1)$$

The constant K is a scalar adjustment factor that is equal to the probe signal-to-masker ratio at the output of the filter that is required to achieve threshold. From this interpretation the

weighted filter function can be determined by subtracting frequency components from the power spectrum of noise with spectral notches and measuring the resulting acoustic thresholds. A common model for weighted auditory filter shapes is the rounded exponential (roex) fit:

$$W(g)=roex(p, r)=(1-r)(1+pg)e^{-pg}+r \quad (2)$$

The parameter g is used as the normalized deviation from the center of the filter ($\Delta f/f_c$). The parameter p determines the slope of the filter skirt and r places dynamic range limitation and flattens the filter at frequencies remote from the center frequency. Since $W(g)$ is the dominating term in Equation (2), it is often useful to integrate Equation (2) to yield the following equation:

$$\int W(g)dg = \frac{1-r}{p}(2+pg)e^{-pg}+rg \quad (3)$$

Typically, the power spectrum value can be treated as a scalar and removed from the integral. By assuming symmetry in the filter shape we can simplify the integral by doubling its value and evaluating over the positive frequency domain. Equations (1) and (2) can be combined to yield Equation (4) which is analogous to Equation (1) converted from the frequency domain to the power spectrum domain. By shifting the masked threshold data by the maximum threshold level (occurs with no spectral notch), Equation (4) is then used to directly compare masked auditory thresholds to the optimized filter output values.

$$Ps=K+10 * \log_{10} \left(N_f * 2 \int_g^{\infty} roex(p, r) \right) \quad (4)$$

Although the updated Matlab filter program formulates filters that match the input data well, the filter parameters and by extension the behavioral ERB measurements differed somewhat from the values reported by May et al. (2006) generated using Glasberg and Moore's (1990) Fortran program. Filters calculated based on the ABR threshold measurements were thus compared to the new behavioral filter calculations based on the updated Matlab filter program. By convention, masked thresholds and filter magnitudes were plotted against the normalized lower edge of the deviation ($(f_c - \text{lower edge})/f_c$).

2.5. Equivalent rectangular bandwidth

The equivalent rectangular bandwidth (ERB) is an estimate of the critical bandwidth of the calculated auditory filter shapes. Using the $roex(p, r)$ filter parameters, the ERB value is calculated according to the following equation (Glasberg and Moore, 1990):

$$ERB=2f_c \left\{ \frac{(1-r)}{p} [2 - (2+p)e^{-p}] + r \right\} \quad (5)$$

ERB values were calculated from the average masked thresholds at the specified probe frequencies. Values were compared against human ERB values and behaviorally-derived mouse ERBs at equivalent frequencies (Glasberg and Moore, 1990; May et al., 2006).

3. Results

3.1. Masked thresholds

ABR masked thresholds decreased with increasing notch width (Fig. 3A). As the spectral notch widened from a normalized deviation of 0.159–0.293, the ABR thresholds decreased for all three center frequencies tested. Inter-animal variability was noted to be greatest at a deviation of 0.159 for 8 and 16 kHz and 0.04 for 11.2 kHz. Quiet thresholds (not shown) were within the normal range for CBA/CaJ mice, but were approximately 15–25 dB higher than behavioral thresholds measured in the same strain (Radziwon et al., 2009).

3.2. Auditory filter shapes and equivalent rectangular bandwidths

The $\text{roex}(p,r)$ auditory filter estimates provided a good fit to the ABR masked threshold data with mean squared error values of 1.00, 2.01 and 0.73 for 8, 11.2 and 16 kHz, respectively (Fig. 3B, Table 1). ERBs calculated from ABR-derived filters are plotted in Fig. 4 along with human ERB data and behaviorally-derived ERBs measured in CBA/CaJ mice. Filter bandwidths increased with increasing frequency between 8 and 16 kHz. The ERBs for the ABR data were 980, 1284 and 1517 Hz at 8, 11.2 and 16 kHz, respectively. ABR-derived ERBs closely matched human ERB estimates reported by Glasberg and Moore (1990) but were slightly lower than behavioral ERBs.

4. Discussion

Behavioral measures used to estimate auditory filters with the notched noise paradigm are effective and sensitive for investigating auditory frequency selectivity, but these studies are limited to just a few species due to the length of time and expertise needed for animal training and testing. As an alternative, ABR procedures have been used to obtain auditory filter measurements in a matter of hours in birds and dolphins using the notched noise paradigm (Gall and Lucas, 2010; Henry and Lucas, 2010a, b; Popov et al., 1997). In the present paper, we used ABRs and the notched noise method to rapidly estimate auditory filters in normal-hearing mice.

ABR masked thresholds decreased with increasing spectral notch width in CBA/CaJ mice as expected based on previous studies. Average ABR masked thresholds were higher than behavioral thresholds reported by May et al. (2006) in the same strain of mice. It is well known that ABR thresholds are elevated by as much as 15–20 dB in mammals compared to behaviorally measured thresholds (e.g., Gorga, et al., 1984; Stapells et al., 1995; Stapells and Oates, 1997; Stapells, 2000; Borg and Engstrom, 1983; Wenstrup, 1984). The ABR represents a population of neurons that are activated simultaneously in response to the onset of a brief (~5 ms) stimulus in an anesthetized animal. In traditional behavioral psychoacoustic tests, the animal is awake and actively attending to sounds with longer durations (typically at least 200–500 ms) than optimal ABR-eliciting stimuli. Behavioral thresholds for longer sounds are lower than for short sounds due to temporal integration of neural activity in response to the longer stimulus, but the same is not true for ABR thresholds (Zwislocki, 1960; Penner, 1972; Gorga et al., 1984).

Filter bandwidths calculated from the ABR masked thresholds increased with increasing center frequency. The ABR-derived filter bandwidths were close to those estimated for humans at similar frequencies according to Glasberg and Moore (1990), although the ABR-derived ERBs for mice remained slightly lower than the human ERBs (Fig. 4). This result suggests that at higher frequencies (above 8 kHz) mouse frequency selectivity may be somewhat sharper than that of humans, although this may not be true for lower frequencies not tested in mice. Frequency resolution studies in other species have suggested enhanced tuning at specific biologically relevant frequencies (cf-bats: Suga et al., 1976; budgerigar:

Dooling and Searcy, 1985; owl: Dyson et al., 1998). However, other estimates of auditory frequency selectivity suggest that human tuning may be considerably sharper than in other mammals (Shera et al., 2002; Joris et al., 2011). Some authors have suggested that such claims overestimate the sharpness of auditory frequency tuning in humans (Ruggero and Temchin, 2005). Clearly, estimates of frequency resolution vary somewhat depending on the method of measurement.

In the present study, ABR-derived ERBs were slightly lower than behaviorally-derived ERBs reported by May et al. (2006) in the same mouse strain. Behaviorally-derived ERBs matched more closely with human ERBs estimated using a filter fitting procedure by Moore and Glasberg (1983) rather than the Glasberg and Moore (1990) human ERB estimates. Physiological and psychophysical studies of auditory frequency selectivity have shown that auditory filters broaden with increasing stimulus level (Ruggero et al., 1997; Oxenham and Simonson, 2006; Weber, 1977; Rosen and Stock, 1992; Rosen et al., 1998; Hicks and Bacon, 1999; Glasberg and Moore, 2000) or do not change (Glasberg and Moore, 1982). Higher noise levels were required to increase ABR thresholds by 40 dB compared to the levels required to raise behavioral responses by the same amount, therefore, one might predict that ABR-derived ERBs would be broader compared to behavior. However, auditory filter estimates are not always broadened with stimulus level. When off-frequency listening is controlled by introducing background noise, the effect is eliminated (Green et al., 1981; Nelson et al., 1990; Glasberg and Moore, 2000) and tuning sharpness may actually increase with increasing stimulus level (Jennings and Strickland, 2012). The effect of increasing stimulus level on notched noise-derived ERBs has not been explored in mice; therefore, discussion of the potential effect of level remains speculative. In addition, the effects of off-frequency listening and level-dependent shifts in tuning may be different for behaviorally- and ABR-derived filters. The brief probe tones with rapid onsets required to elicit robust ABRs likely produce a significant amount of spectral splatter. For narrow notch widths or no-notch conditions, this splatter is presumably masked by the background noise. At wider notch widths, the spectral splatter might become more detectable, thereby decreasing the response threshold.

An additional factor to consider is the method of calculation used to estimate auditory filters and ERBs. Though the present study and the May et al. (2006) study used the software tools distributed by Glasberg and Moore (1990), slight differences in the parameters might have affected the data. We recalculated the behaviorally-derived ERBs with our Matlab-based filter-fitting program using the average masked threshold data reported by May et al. (2006), and we still found that the ABR-derived ERBs were lower (data not shown). The older age range of the animals in the behavioral study (19–22 weeks at initial threshold, up to nearly a year for some data points) compared to the ABR animals (6–28 weeks) may have also contributed to the difference in filter band-widths. Indeed, the May et al. (2006) paper reports age-related broadening of auditory filters in animals aged over one year. It is possible that the behavioral data even at “young” ages reflect a mild age-related effect.

Activation of the olivocochlear reflex by the background noise may also account for the difference between behavioral and ABR-derived ERBs. Olivocochlear suppression of cochlear activity is stronger in awake animals (Chambers et al., 2012), and olivocochlear activation broadens cochlear frequency tuning (Cooper and Guinan, 2006). Though olivocochlear activation was not measured in the present study or by May et al. (2006), animals anesthetized for ABR recordings presumably had less activation than awake, behaving animals and less olivocochlear-mediated broadening of the auditory filters.

Despite the slight difference between ABR-derived auditory filter bandwidths reported here and behaviorally-derived auditory filter bandwidths reported previously, the notched noise

method combined with ABRs provides a useful tool to rapidly assess frequency selectivity in mice. Previous studies used a forward masking stimulus paradigm to measure frequency selectivity in mice (Song et al., 2007, 2008). Forward masking ABR procedures are also more efficient than behavior for testing animals rapidly and, in that case, at multiple developmental time points. However, forward masking procedures are not ideal for use with mouse models that have temporal processing deficits resulting from genetic and environmental manipulations (e.g., Lauer and May, 2011). Thus, the present study extends the toolbox of ABR-based tests available for comparatively rapid screening of mouse models of hearing and hearing loss. Potential applications of the ABR notched noise auditory filter estimates include developmental studies in which trained behavioral tasks cannot be implemented within the short time-course between hearing onset and adult hearing; genetic manipulations that hinder an animal's physical or cognitive abilities; conditional genetic manipulations that turn a function on or off at certain time points in development; optogenetic or other photo-stimulation manipulations targeting specific populations of cells; genetic manipulations where repeated exposure to routine daily testing and experience with stimuli may trigger compensatory mechanisms and auditory learning (for example, olivocochlear mutants) that could obscure identification of abnormal auditory processing; animals that must be tested at very specific ages or time points during the course of the study; studies in which repeated measurements are performed on a periodic basis during the course of treatment and recovery; studies of aging and loss of function; environmental manipulations in which animals are exposed to conditions during a critical period. Future studies could investigate the contribution of peripheral and central influences on auditory filtering. Measures of frequency selectivity could also be combined with other measures of complex auditory processing such as temporal resolution to describe a constellation of effects while avoiding complications that arise when switching trained tasks.

5. Summary

The ABR measurements using the notched noise method of estimating frequency resolution can be an efficient tool for researchers who wish to study more complex auditory functioning in mouse models. As to be expected, ABR-derived masked thresholds were slightly elevated compared to behavioral thresholds, but the general pattern of increased filter bandwidth (ERB) with increasing center frequency was consistent. The main advantage of using an ABR paradigm rather than a behavioral paradigm to estimate auditory frequency selectivity is that the timeframe for testing is considerably reduced, allowing for higher throughput screening, testing at multiple time points, and testing of very young or difficult to train animals.

Acknowledgments

This research was supported by the National Organization for Hearing Research and NIH grants DC005211 and DC009353. The funding sources had no role in the study design; data collection, analysis, and interpretation; writing of the report; or the decision to submit the manuscript for publication. We thank Eric Young and Bradford May for discussions regarding the project, and Judy Park and Jessica Stuyvenberg for data collection assistance.

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List of abbreviations

ABR	auditory brainstem response
dB	decibel
Hz	Hertz
ERB	equivalent rectangular bandwidth

Fig. 1.

Schematic of the notched noise method of estimating auditory filter bandwidth. Thresholds are measured for a probe tone presented in the presence of broadband noise containing a spectral notch centered on the probe tone frequency. The shaded portions of the figure represent the noise energy falling inside the filter that masks the probe tone frequency. As the notch is widened, less and less energy falls within the auditory filter rendering the tone more detectable.

Fig. 2.

(A) Representative ABR waveform in response to an 80 dB click stimulus. The ABR peaks occur approximately 2–10 ms after stimulus onset. The magnitude of the ABR was determined by calculating the maximum peak-to-peak amplitude. Baseline noise levels are sampled during the end of the recording epoch when no tone stimulus is being presented.

(B) ABR threshold calculation method. Closed circles represent the ABR magnitude at each stimulus level. The dashed line represents two standard deviations (SD) above the average baseline noise level. Open circles represent the average baseline noise level for each averaged response. Threshold is defined as the point at which the ABR magnitude exceeds the baseline noise magnitude by 2 SD. (C) Example ABR waveforms in response to a click presented at descending levels.

Fig. 3. (A) Averaged ABR masked threshold data comparing CBA/CaJ mice at 8 kHz, (B) 11.2 kHz, and 16 kHz probe frequencies. Notch widths of 0, 0.125, 0.25, 0.5, 1 and 2 octaves correspond to normalized deviations of 0, 0.04, 0.083, 0.159, 0.293 and 0.5, respectively. (B) Estimated roex filter functions plotted against the interpolated averaged masked ABR threshold functions at 8, 11.2 and 16 kHz center frequencies.

Fig. 4. Equivalent rectangular bandwidths (ERB) for both ABR-derived and behaviorally-derived filters (May et al., 2006) compared with human ERB measures as described by Moore and Glasberg (1983) and Glasberg and Moore (1990).

Table 1

Roex filter estimation parameters and mean square error.

Frequency (kHz)	p	r	K	Mean squared error
8	35.6	2.44×10^{-5}	0.63	1.00
11.2	37.2	1.45×10^{-5}	0.54	2.01
16	39.5	1.61×10^{-5}	0.56	0.73