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Research Paper

Input-output curves of low and high spontaneous rate auditory nerve fibers are exponential near threshold[☆]

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ABSTRACT

Input-output (IO) properties of cochlear transduction are frequently determined by analyzing the average discharge rates of auditory nerve fibers (ANFs) in response to relatively long tonal stimulation. The ANFs in cats have spontaneous discharge rates (SRs) that are bimodally distributed, peaking at low (<0.5 spikes/s) and high (~60 spikes/s) rates, and rate-level characteristics differ depending upon SR. In an effort to assess the instantaneous IO properties of ANFs having different SRs, static IO-curves were constructed from period histograms based on phase-locking of spikes to the stimulus waveform. These curves provide information unavailable in conventional average rate-level curves. We find that all IO curves follow an exponential trajectory. It is argued that the exponential behavior represents the transduction in the IHC and that the difference among ANFs having different SRs is predominantly a difference in gain attributed most likely to synaptic drive.

1. Introduction

Trains of spikes of primary afferent auditory nerve fibers (ANFs) encode sensory information transduced within the inner ear, and information about the acoustic stimulus is relayed with high fidelity to the central nervous system. Morphologically, ANFs can be classified into large and myelinated type I ANFs that contact the pillar side of inner hair cells (IHCs), smaller myelinated type I ANFs that contact the modiolar side of IHCs and small, unmyelinated type II ANFs that innervate the outer hair cells (OHCs) (Spoendlin, 1973; Liberman, 1980). The majority of ANFs (90–95%) are type I ANFs and each type I ANF contacts a single IHC in the domestic cat. The number of ANFs contacting each IHC peaks at approximately 30 in the vicinity of the 10 kHz region and decreases progressively to about 10 for apical hair cells (Spoendlin, 1973; Liberman et al., 1990). On physiological grounds, ANFs can be classified according to a variety of criteria, including spontaneous discharge rate (SR). SRs of ANFs in deeply anesthetized cats vary from near zero to about 100 spikes/s, with approximately 60% exhibiting high SRs (SR > 17.5 spikes/s), 25–30% exhibiting medium SRs (0.5 spikes/s ≤ SR ≤ 17.5 spikes/s) and 10–15% exhibiting low SRs (SR < 0.5 spikes/s). Each IHC is contacted by low, medium and high SR ANFs (Liberman, 1982; Wu et al., 2016).

As part of the larger effort to understand the processing of sounds by the auditory periphery, inner ear input-output (IO) relationships have been assessed traditionally by measuring average discharge rates produced by type I ANFs in response to relatively long duration periodic signals, including both tone-burst and spectrally complex acoustic stimuli (e.g. Kiang et al., 1965; Rose et al., 1967; Johnson, 1980; McGee, 1983; Horst et al., 1990). In general, average discharge rates increase sigmoidally with increasing sound stimulation level, exhibiting either a saturating or a sloping shape at high levels for ANFs with high- and low-SRs, respectively (Sachs and Abbas, 1974; Winter et al., 1990; Yates et al., 1990). Information contained in such rate-level curves is limited by the fact that response variations observed within a

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stimulus period are not represented, in contrast with information contained in period histograms. A period histogram is a graph of the instantaneous discharge rate plotted on a time scale modulo the stimulus period. As a consequence, spike occurrences within a period histogram provide information on the relation between instantaneous stimulus pressure and instantaneous discharge rate.

Numerous studies have shown differences in the responses of low- and high-SR ANFs. For example, expansive nonlinear behavior has been observed at low stimulus levels in responses of ANFs with relatively low SRs (Geisler, 1990). Kiang et al. (1965) and Geisler and Silkes (1991) found that peristimulus time histograms (PST) were more deeply modulated for low-SR ANFs than for high-SR ANFs in response to the fundamental frequency of periodic complex tones. In addition, low-SR ANFs produce higher synchronization indices in response to pure tones than do high-SR ANFs (Johnson, 1980; McGee, 1983; Joris et al., 1994; Dreyer and Delgutte, 2006; Temchin and Ruggero, 2010). Similarly, Horst et al. (1986a, 1990) found a lack of response to small peaks in the temporal waveforms of complex stimuli in ANFs with relatively low SR. Geisler (1990) has suggested fundamental differences in rate-level curves between ANFs with low SR and ANFs with high SR.

On the other hand, work by Kiang et al. (1965) and Evans (1968) has suggested that the relation between instantaneous discharge rate and instantaneous stimulus pressure for ANFs of all SRs can be represented by an exponential function. This relation has been used successfully in modeling work by Siebert (1970), Colburn (1973), Johnson (1974) and Goldstein and Srulovicz (1977). Consequently, there appears to be a disagreement between this early modeling work and later experimental findings indicating that differences in the response properties of low-SR ANFs and high-SR ANFs exist.

Directly comparing average discharge rate-level curves and instantaneous discharge rate-instantaneous pressure relationships is hampered by the fact that rate-level curves are based on averages of spike numbers regardless of variations in rate across the stimulus period. That is, they cannot reveal information, such as the exponential input-output curve, on a time scale shorter than the stimulus period. To overcome this, here we show input-output relations based on the variation in instantaneous rate measured within a stimulus period.

Average discharge rate and instantaneous discharge rate are both determined by measuring the number of spikes in certain intervals and determining the number of spikes per unit of time. The important difference lies in the choice of the sampling intervals. In the case of average rate, the relevant interval is the time during which the stimulus was present and the computation of average discharge rate involves averaging across repetitions of the tone burst, periods of the stimulus, and all phases within each period. In the case of instantaneous discharge rate, the computation of rate involves averaging across repetitions of the tone burst and cycles of the stimulus, but not across all phases within each cycle, just some range of phases depending on the bin width chosen. In this way, the variation of discharge rate can be measured within the stimulus period (instantaneous discharge rate) and examined as a function of the instantaneous stimulus pressure.

In this study, in an effort to investigate these different types of input-output relations, we compared the IO properties of ANFs in deeply anesthetized cats based on traditional average discharge rate-stimulus level curves with IO curves based on instantaneous discharge rate vs. instantaneous pressure derived from period histograms at near threshold stimulus conditions.

By using tone-burst stimuli, the effect of filtering (response attenuation) that occurs when there is a mismatch between the characteristic frequency (CF) of the auditory filter and stimulus frequency can be dismissed; the filter effect will not affect the shape of the waveform. This is in contrast to a complex stimulus whose components can be differentially attenuated depending on their frequency relative to the characteristic frequency of the filter.

2. Materials and methods

2.1. Surgical preparation

Data were acquired from four adult, healthy domestic cats and experiments were performed in an electrically shielded, double-walled sound attenuating chamber specially designed for acoustic isolation (Industrial Acoustics Corp.). Animals were anesthetized with sodium pentobarbital (40 mg/kg) administered intraperitoneally and supplemental doses were administered as needed throughout the experiment; i.e., when a pedal reflex was observed. Body temperature was thermostatically regulated and maintained at approximately 38 °C. The pinna of the right ear was resected to the level of the tympanic annulus, and the skin and musculature overlying the posterior aspect of the skull were reflected and the skull overlying the cerebellum was trephined, the dura mater was opened, and the cerebellum overlying the cochlear nucleus complex was aspirated. The auditory nerve was exposed by wedging small pieces of cotton between the brainstem and the internal auditory canal. A plastic Davies-type chamber was placed over the nerve, cemented into place and filled with warm mineral oil to minimize brain pulsations and prevent tissue desiccation.

The experiments were approved by the Institutional Animal Care and Use Committee at the Boys Town National Research Hospital.

2.2. Sound delivery and data acquisition

Stimuli were delivered via a Beyer DT48 dynamic earphone that was connected through a short piece of plastic tubing to an ear piece that was inserted into the external auditory meatus and sealed in place, forming a closed acoustic system. Glass electrodes filled with 3M KCl and having an AC impedance of 20–30 MΩ at 1 kHz were used to isolate and record the extracellular activity of single ANFs.

The experimental paradigm started with the determination of spontaneous rate (SR) by measuring spike activity during a 10 s "quiet" data collection window. A tuning curve was then acquired using a modification of the algorithm described by Liberman (1978). This provided estimates of the ANF's characteristic frequency (CF) and threshold determined using a criterion of 20 spikes/s above baseline rates. Average discharge rate based IO curves, usually called rate-level curves, were constructed at CF from responses to tone-burst stimuli presented at levels spanning the ANF's dynamic range, i.e. the level range over which the average rate increases from the spontaneous rate to saturation, in 5 dB increments. Tone-burst duration was one second with 5 ms rise/fall times and stimuli were presented at a rate of one per 1.5 s. Stimuli were repeated until at least 500 spikes were obtained. Levels were incremented from low to high to minimize adaptation concerns.

Period histograms were generated by plotting discharge activity modulo stimulus period. The discharge activity was represented as instantaneous rate (the number of spikes collected in a bin divided by the total time spent in that bin). Spike times were recorded at levels near discharge rate thresholds based on values obtained from tuning curves, although data were collected near synchronization threshold (based on visual inspection) when possible. A minimum of 500 spikes was acquired to permit the construction of well-defined period histograms, a process that generally required a collection time of 500/(spontaneous rate) s. Consequently, no more than 28 s of data collection time were required to obtain requisite data for high-SR ANFs, while several minutes of data collection time