PHYSIOLOGICAL-MORPHOLOGICAL PROPERTIES OF THE ANTEROVENTRAL COCHLEAR NUCLEUS

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✔ The cochlear nucleus complex is the first relay station of the central auditory pathway. The neuronal architecture and physiological properties of cochlear nucleus neurons almost certainly play a key role in defining the functional organization of the ascending auditory system. The structural and physiological organization of the cochlear nucleus complex is complicated by the fact that it is not a single nucleus but a complex of distinct neuronal populations. The cochlear nucleus complex is divided into three divisions; anteroventral cochlear nucleus (AVCN), posteroventral cochlear nucleus (PVCN) and dorsal cochlear nucleus (DCN) on the basis of differing cytoarchitectures. The AVCN contains two major types of neurons which are bushy and stellate cells. Bushy cells have been implicated in the signaling of precise temporal information in order to compute the location of a sound source. The role of stellate cells in acoustic processing is not well understood, although their responses to pure tones are well documented.
Key words: *Cochlear nucleus, auditory pathway, hearing system.*

✔ **Anteroventral Koklear Nukleusun Fizyolojik-Morfolojik Özellikleri**
Koklear nukleus kompleksi merkezi işitme yolunun ilk durak yeridir. Koklear nukleus nöronlarının nöronal yapısı ve fizyolojik özellikleri, çıkıcı işitme sisteminin fonksiyonel organizasyonunun belirlenmesinde önemli bir anahtar role sahiptir. Koklear nukleus kompleksinin yapısal ve fizyolojik organizasyonu tek bir nukleusun değil aynı zamanda farklı nöron populasyonlarının bir karışımıdır. Koklear nukleus kompleksi hücre yapısına göre üç gruba ayrılır; anteroventral koklear nukleus (AVCN), posteroventral koklear nukleus (PVCN) ve dorsal koklear nukleus (DCN). AVCN bushy ve stellate hücre adı verilen iki büyük nöron tipini ihtiva etmektedir. Bushy hücrelerinin bir ses kaynağının yerini tesbit etmek için tam bir temporal informasyon sinyali oluşturduğu bildirilmiştir. Pure ton seslere karşı verdikleri cevaplar hakkında çok sayıda çalışma olmasına rağmen akustik işlemde stellate hücrelerin rolü çok iyi anlaşılmamıştır.
Anahtar kelimeler: *Koklear nukleus, işitme yolu, işitme sistemi*

The cochlear nuclei (CN) are situated laterally on the brain stem at the transition of medulla oblongata and the pons. As a cytoarchitectural complex, the CN comprises several heterogeneous subdivisions and a variety of cell types. Each fiber of auditory nerve branches on entering the nucleus, sending one branch rostrally and the other caudally. The rostral branch innervates the division known as the anteroventral cochlear nucleus (AVCN), whereas the caudal branch innervates both the posteroventral division of the nucleus (PVCN) and the dorsal cochlear nucleus (DCN) (Figure 1)[1,2].

The three divisions of the cochlear nucleus (AVCN, PVCN and DCN) show broadly different response properties, and it is very likely that they have correspondingly different functions. The AVCN is the site of the first synapses along the auditory

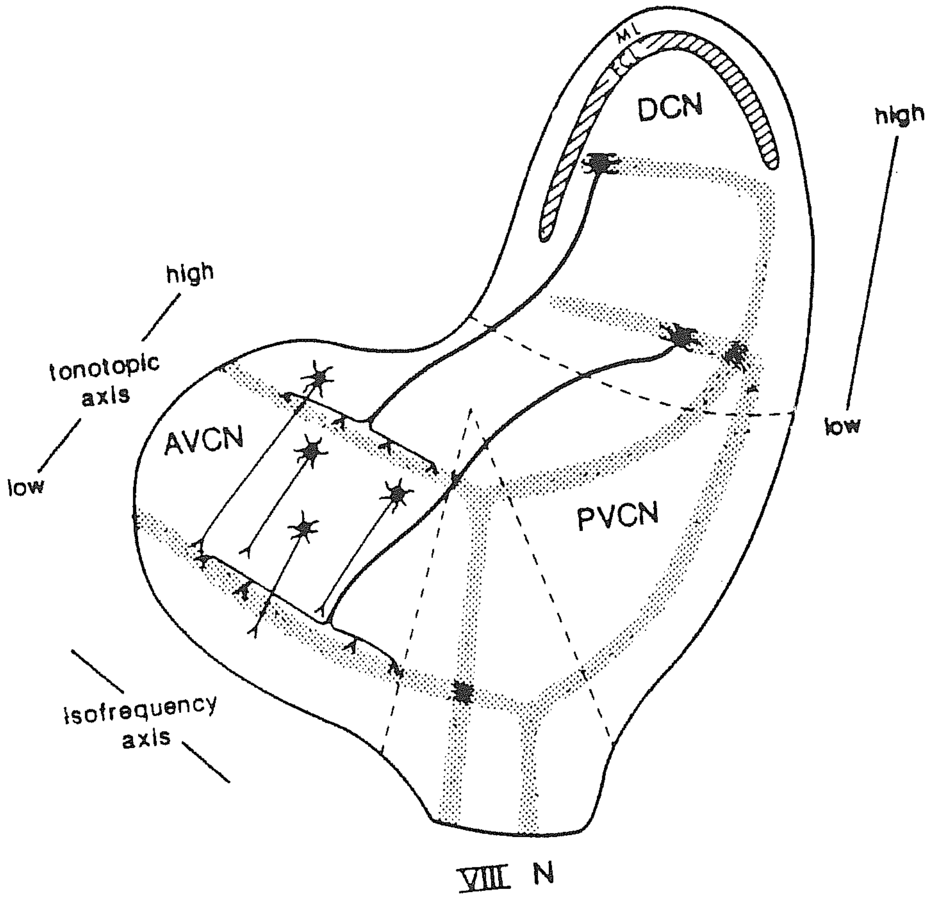

Figure 1. Schematic presentation of tonotopic projection from the dorsal to the anteroventral cochlear nucleus.
AVCN: anteroventral cochlear nucleus, PVCN: posteroventral cochlear nucleus, DCN: dorsal cochlear nucleus, ML: molecular layer, FCL: fusiform cell layer. From Wickesberg & Oertel (1988), figure 5.

pathway. In general, neurones of the AVCN have properties rather similar to those of auditory nerve fibers, and may well function much as simple relay for afferent information. In Golgi-stained material there are two distinct cell types in the AVCN which are bushy cells and stellate cells[2-4].

Anatomy of AVCN Neurones

Recent studies suggest that in the most rostral portions of the AVCN, where bushy cells predominate, direct correlation can be made between the bushy cells and the large spherical cell classification put forward by Osen[5], and these cells can be referred to as spherical bushy cells[6]. Spherical bushy cells are found near to the entire dorsal edge of the AVCN. They are regularly and densely packed in the rostral pole whilst back towards the nerve root. As their name suggests, they are frequently circular in profile, although more ovoid cells are often observed[7]. Spherical bushy cells are known to project the medial superior olive bilaterally and the lateral superior olive ipsilaterally[8,9]. A second type of bushy cell can be roughly correlated with the globular cells seen in Nissl preparation[5]. As their name suggests, these cells are an elongated ovoid in shape, approximately 28-30 µm by 15-18 µm across their longest and shortest axes respectively[7]. They have a nucleus which is frequently to be eccentrically placed, bulging out to one side[7].

The small spherical and globular cells described in Nissl preparations receive smaller end bulbs or calyceal processes from several incoming acoustic nerve fibers[6,10]. Webster and Trune[4] reported that mice do not have a large spherical cell area which, in other animals, is a low frequency area.

Stellate cells are found throughout the AVCN though they are rarer in the ventral region of AVCN. They have between 2 and 12 dendrites which can project in spherical, half moon or cylindrical configuration[4]. Webster and Trune[4] reported that the diversity of AVCN stellate cells of mouse tempts one to subclassify according to shape of dendritic field and extent of dendritic branching but it is safer to retain this as single, heterogeneous group of cells. The stellate cells receive smaller cochlear nerve endings or buttons that make contacts preferentially on their somata and on the proximal dendrites[10,11]. The diameters of stellate cell bodies vary between 10-30 µm in the AVCN in mouse[4].

Extracellular Recordings from AVCN Neurones

Neurones of AVCN have markedly different responses to sound. On the basis of extracellular recordings, bushy cells are described as primary-like[12,13] because when tested with short tone bursts, they fire in similar way to auditory nerve fibers with an initial peak at the onset, declining gradually to lower levels (Figure 2)[14,15]. There is evidence that some of the histologically defined spherical bushy cells of the AVCN form at least some of the primary-like neurones[16]. For instance, primary-like responses are obtained from the spherical cell area and further indirect evidence comes from the waveform of the extracellular action potential. Many such recordings show a positive deflection just before the usual monophasic or diphasic waveform a cell body, and Pfeiffer[14] has suggested that this corresponds to the depolarization of the large end bulbs of Held, the presynaptic endings on the auditory nerve fibers on the cells. The primary-like responses, together with the short synaptic delay on these cells, as well as the time pattern of spontaneous activity, suggests the existence of what have been called "secure" synaptic connections, in which each afferent action potential produces an action potential in the output. This suggests, that the cells act simply to relay the activity of auditory nerve fibers to higher centers.

The primary-like-notch subclass of primary-like responses are recorded from globular bushy cells[13,15-18]. The primary-like-notch units respond to tones with a well-timed first spike[16]. A comparison of spontaneous firing rate and saturation firing rate of primary-like-notch units with auditory nerve fibers suggest that primary-like-notch units receive one to four auditory nerve fiber inputs[16].

Evans and Nelson[19] developed a classification scheme based on the presence or absence of inhibitory side bands on the response to noise that has been further developed by Young and Brownell (20). At one extreme, cells are found with properties very similar to those of auditory nerve fibers, with

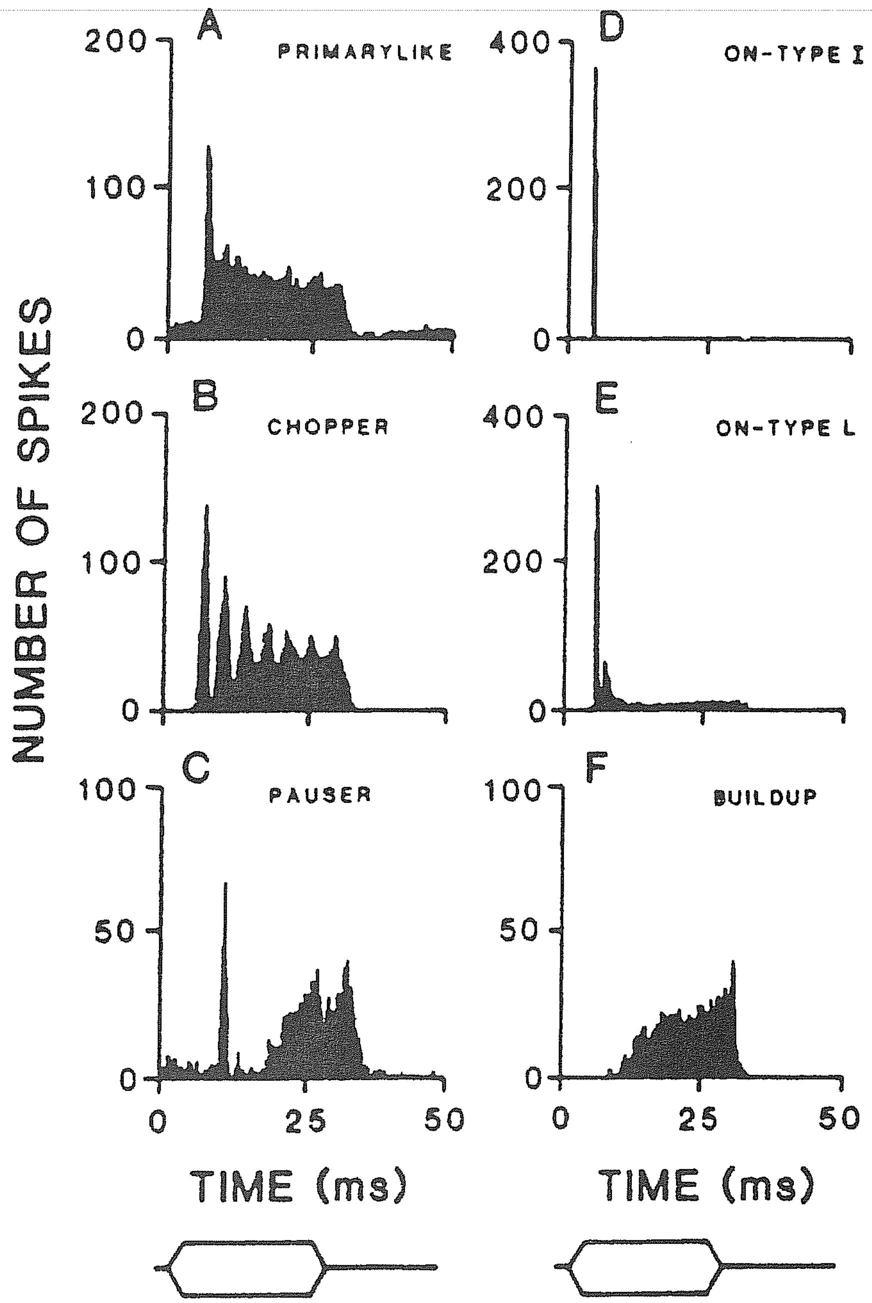

Figure 2. Peristimulus time histograms (PZTH) illustrating major response patterns of the neurons in the cochlear nucleus. The PSTH shows the number of action potentials occurring as a function of time, during and after pure tone stimulation. The tone burst of 25 ms duration, with envelope, is indicated beneath the abscissa of the lower histograms.

A: primary-like responses, B: chopper responses, C: pauser responses, D: and E: onset responses, F: buildup responses. From Irvine (1986), figure 19.

very similar response areas and no inhibitory responses beyond those arising from suppression in the auditory nerve. Young[21] classed these cells as Type I. It is assumed that they correspond most closely to the primary-like cells of Pfeiffer[14].

Stellate cells produce the characteristic "chopper" pattern of firing in response to similar stimuli[12,13,15]. Chopper units tend to fire repetitively during a sustained tone burst with timings of the action potentials unrelated to the period of the stimulus waveform. The peristimulus time histograms (PSTHs) therefore shows a series of peaks, which, because the timing of the spikes becomes variable during the latter part of tone burst declines towards the end[14,22]. Three varieties of choppers are found which are chop-S, chop-T and chop-U[17]. Chopper units are recorded from stellate cells in both AVCN and PVCN[12,13].

Intracellular Recordings from AVCN Neurones

On the basis of intracellular recordings using brain slices in vitro coupled with histological observations, bushy cells are known to produce a single spike response to sustained injection of depolarizing current (Figure 3A) and to have non-linear current-voltage relationships (Figure 3B)[23-26,28]. After the single spike, they show a small persistent depolarization (24, 26, 28). Injection of sine wave currents into bushy cells produce rapid and repetitive firing of action potentials when stimulated at a frequency of 102 Hz[28]. However, these cells fire 9 action potentials when stimulated at 99 Hz or 126 Hz[28]. These results indicate that a stimulation frequency of 102 Hz is the optimal stimulation frequency for bushy cells.

In contrast, stellate cells produce a sustained train of action potentials in response to injected current pulses (Figure 4A) and have linear or apparently purely resistive current voltage plots (Figure 4B) [23,24,27,28]. Stellate cells also have a characteristically large undershoot (hyper-polarization) after action potential, followed by a slow depolarization to threshold.

Manis and Marx[29] have investigated the role of outward conductances in these properties with voltage clamp techniques in enzymatically separated neurones and have suggested that bushy and stellate cells each have two potassium conductances.

In bushy cells, potassium currents become active at -70 mV, blocked by 4-aminopyridine (4-AP), and at -35 mV, blocked by tetraethyle ammonium chloride (TEA)[29]. The 4-AP sensitive current may account for non-linear outward rectification of the current-voltage relationship and prevent further firing because this is activated close to resting membrane potentials, whereas the TEA sensitive current probably accounts for repolarization after the action potential because it is activated closer to peak of action potential[28,29].

The potassium currents of stellate cells become active at voltages more positive than -35 mV, and blocked by TEA and 4-AP[29]. Analysis of tail current reveals two voltage depencies for channel opening. One may count for repolarization after the action potential and the other for duration of the undershoot, perhaps to control the interspike interval. Manis and Marx[29] conclude that the acoustic response properties of these neurones are partly explained by these conductances.

Coding Properties of AVCN Neurones

Both spherical and globular bushy cells are thought to participate in coding of

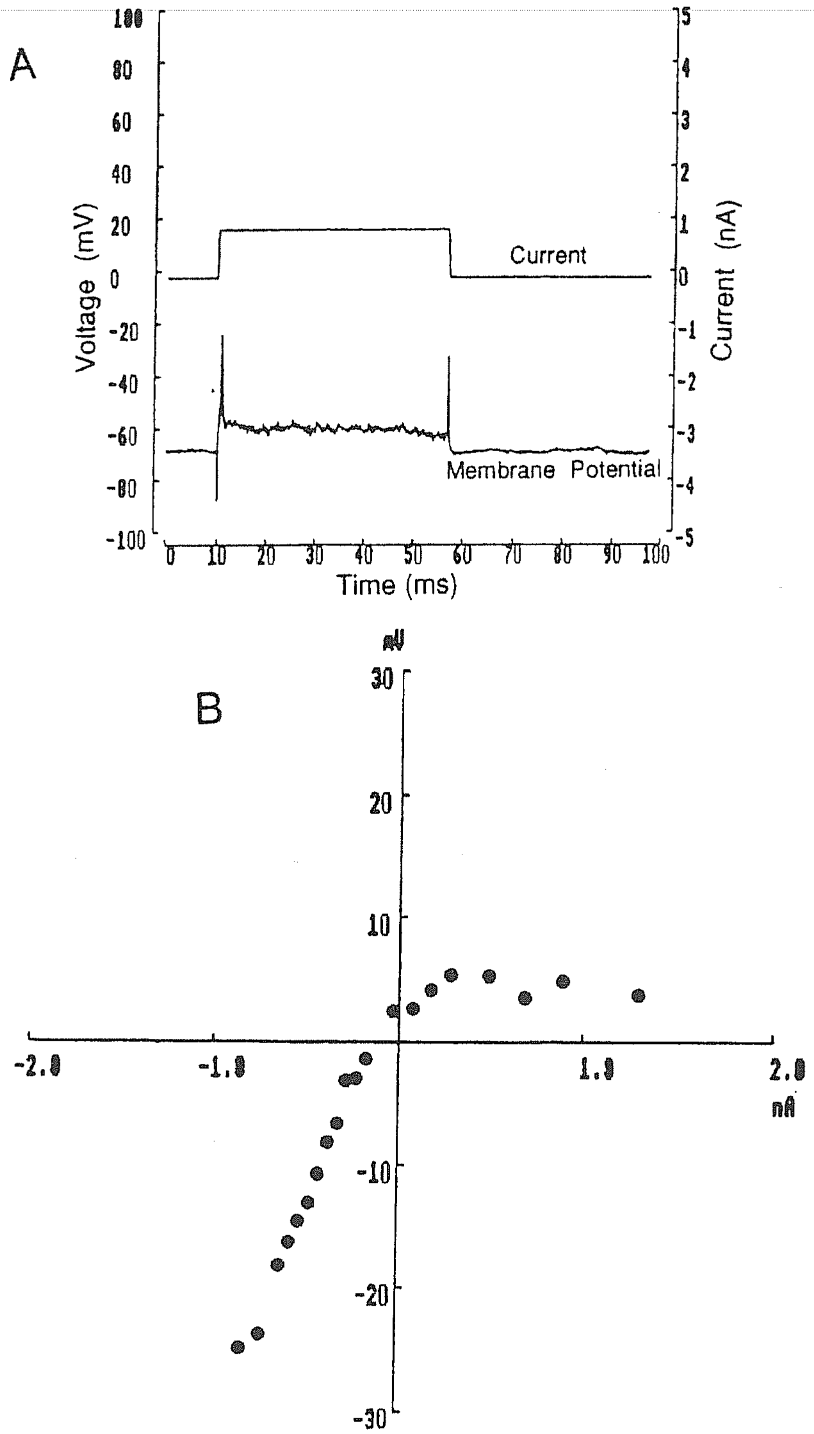

Figure 3. **A.** Bushy cells fire only a single action potential (lower trace) at the start of injected current pulse (upper trace). From Ağar et al (1996), figure 1A.
B. Bushy cells have non-linear current-voltage relationship. From Ağar et al (1996), figure 2D.

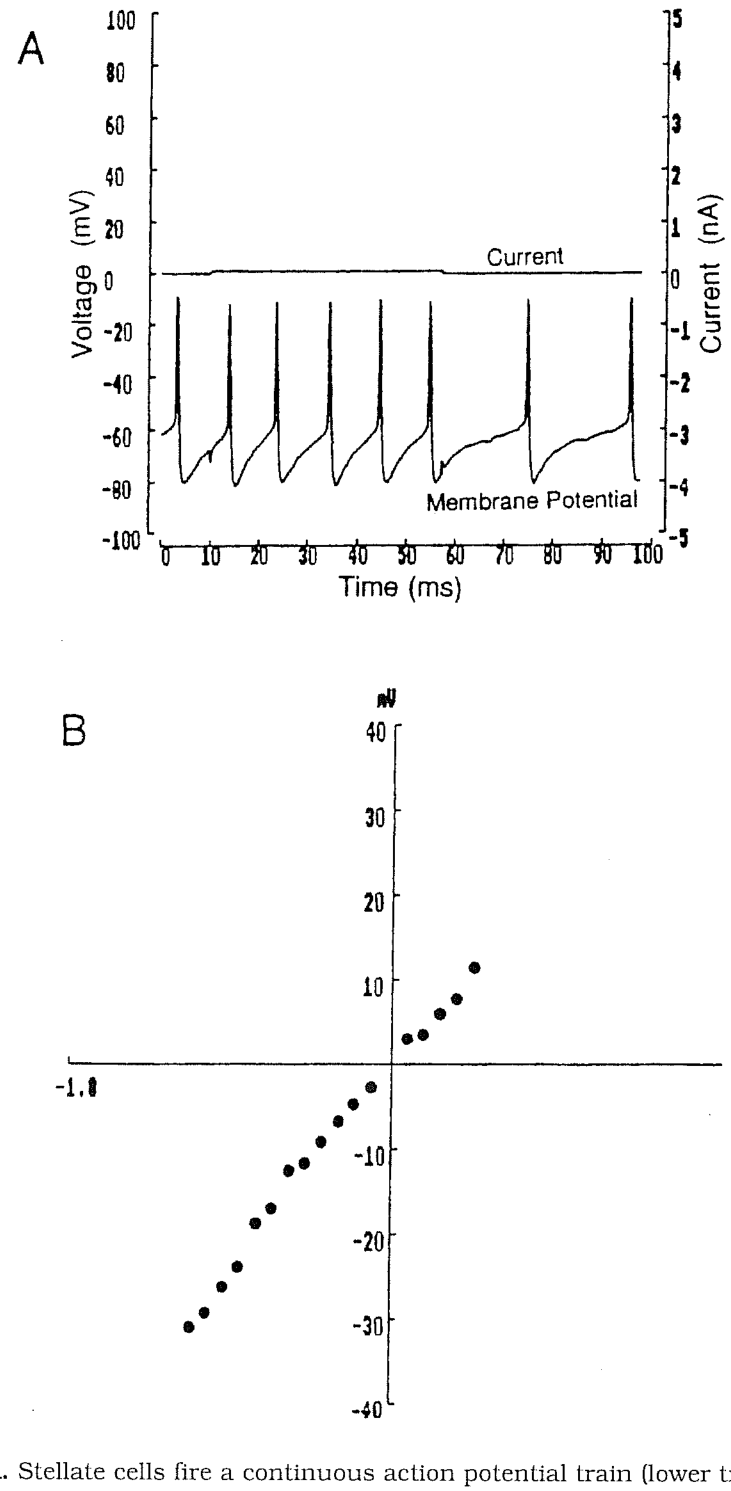

Figure 4. **A.** Stellate cells fire a continuous action potential train (lower trace) in response to injected current pulse (upper trace). From Ağar et al (1996), figure 1B.
B. Stellate cells have linear current-voltage relationship. From Ağar et al (1996), figure 5A.

temporal and intensity cues for the localization of sound[30]. The spherical bushy cells, residing in the anterior part of the AVCN, send their axons through the anteroventral acoustic stria (trapezoid body) to the contra and ipsilateral medial superior olives (MSO)[8,9,31]. The medial superior olive is a structure which receives predominantly low frequency input[32,33]. This pathway is thought to be responsible for detecting time differences in low frequency sound arriving at both ears, which are then used by the system to compute the location of the stimulus[32,34]. Spherical bushy cells may also participate in coding of interaural intensity differences[35].

Stellate cells (choppers) are the most widely recorded units in the cochlear nucleus[12,15,17], but their role in the choppers group, have been further defined [16,17]. However, the precise roles of these subgroups in sound processing are yet to be determined.

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