DORSAL COCHLEAR NUCLEUS - PHYSIOLOGY

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Presentation Number: 10

In classifying the physiological responses of neurons in the CN, two principal schemes have been employed. The one employed more frequently uses of the shapes of the excitatory and inhibitory areas within a unit's response field (Evans and Nelson 1973).

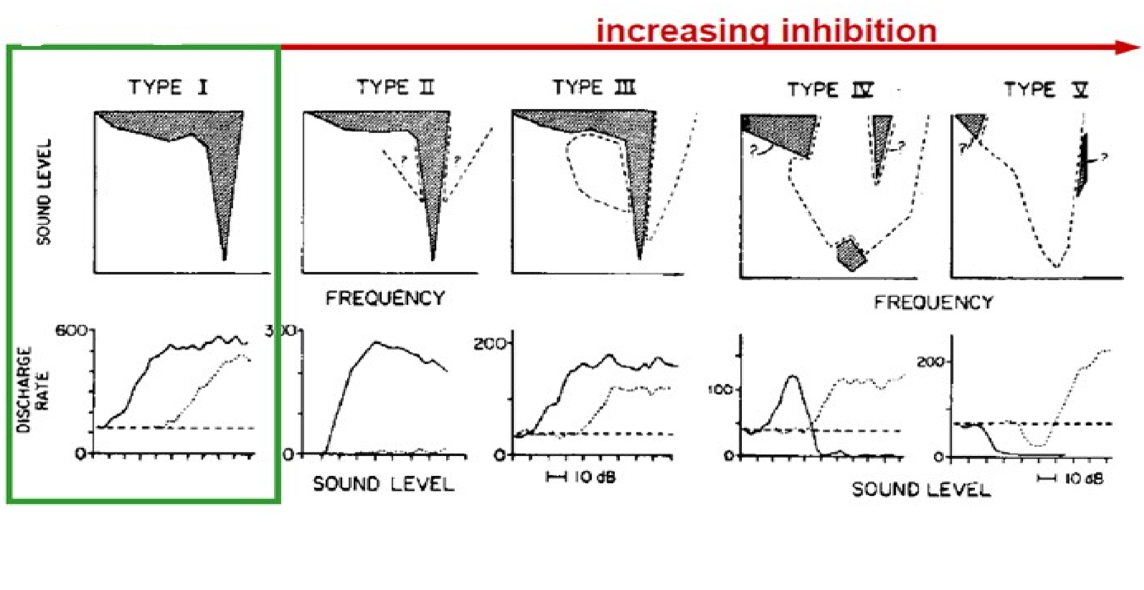
Cochlear nucleus units can be classified into 5 groups, types I to V, based on relative amount of excitation and inhibition in their response maps (Evans & Nelson 1973; Young, 1984).

The second classification scheme for physiological responses employs the shape of the post stimulus time histogram (PSTH) to categorize response patterns to tones at the best frequency (Pfeiffer 1966).

The PSTH gives the temporal distribution of action potentials over the time course of stimulus presentation.

For example, some of the self descriptive response patterns are labeled: *Primarylike, Chopper, Onset, Pauser*, and *Buildup*. These response patterns have been correlated with specific morphological cell types in the CN (e.g., Rhode et al. 1983a, b; Rouiller and Ryugo 1984).

Note that neither classification scheme is unambiguous (e.g., Davis et al. 1996; Shofner and Young 1985). In fact, in barbiturate anesthetized gerbil, the response map technique (type I–IV) was judged not useful (Gdowski and Voigt 1997).



The dotted lines delineate inhibitory areas defined by a decrease in spontaneous discharge rate if a tone is placed in those areas.

Introduction

TYPE I

These tuning curves are found only in the VCN, they have a simple V-shaped excitatory response, resembling the response of an auditory nerve fiber (Kiang et al., 1965b) Inhibitory response areas are absent. They correspond to primary like and some chopper response.

TYPE II Simple V-shaped excitatory but having inhibitory influences**.**

Found only in the DCN. The most common temporal response of this type is the chopper and OG responses arising from inhibitory interneurons. Type II units correspond to the *vertical cells* of the deep DCN.

TYPE III V-shaped excitatory area with inhibitory sidebands

Similar to type I, but they have inhibitory areas on either side of the excitatory tuning curve. Related to some chopper and pauser responses.

TYPE IV Low-level excitatory region and variable excitatory and inhibitory areas

These tuning curves have excitatory responses at characteristic frequency for sounds near threshold; at higher intensities they show extended inhibitory responses. The presence and strength of inhibition strongly depends on the depth of anesthesia. Mainly found in the DCN, and is related to onset and inhibitory responses principally of pyramidal and giant cells. A variety of temporal responses can be obtained such as pauser, buildup, chopper, and onset.

TYPE V Almost all inhibitory influences

The V^{th} type is rarely found and might be a subtype of type IV.

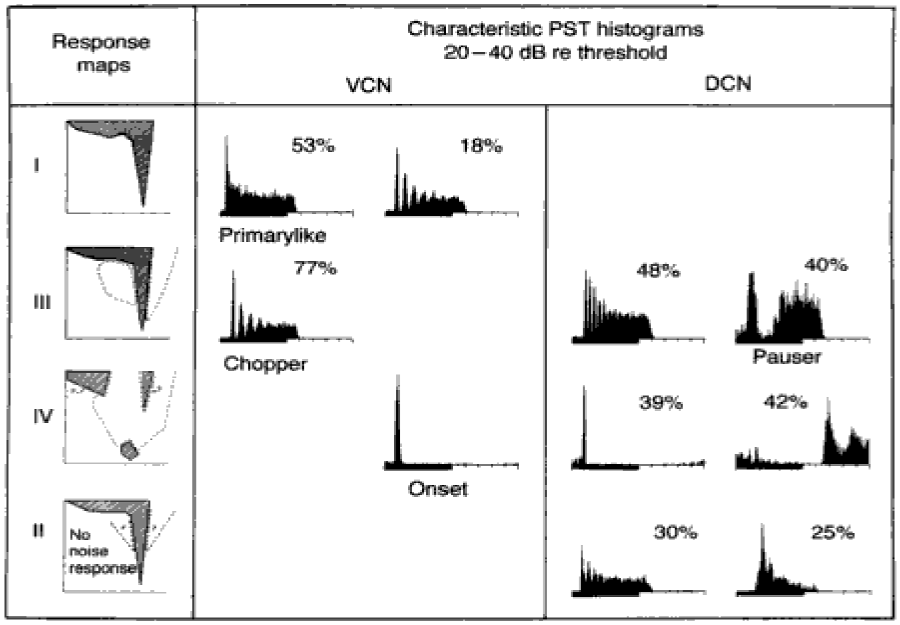
Classification based on PSTH (*only those found in the DCN*)

ONSET RESPONSE

Onset responses are present in the DCN (Rhode & Smith, 1986b)

There are various subtypes, (OI, OL, OC & OG) **O**nset responses with a **g**raded decrease in firing after the initial peak are called OG. The discharge rate reduces to zero over a 25 to 50 ms time interval after an initial burst of activity.

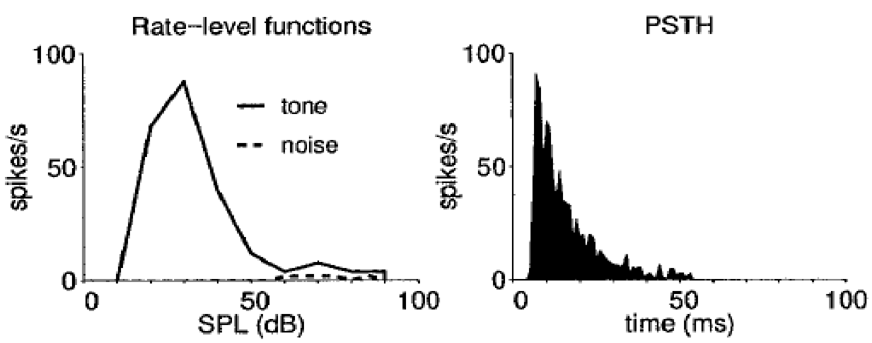
It has been shown that the response pattern termed onset-graded or On-g is associated with the vertical cells of the DCN and that they satisfy the requirements for type II units.



Response area types and PSTH in cochlear nucleus.

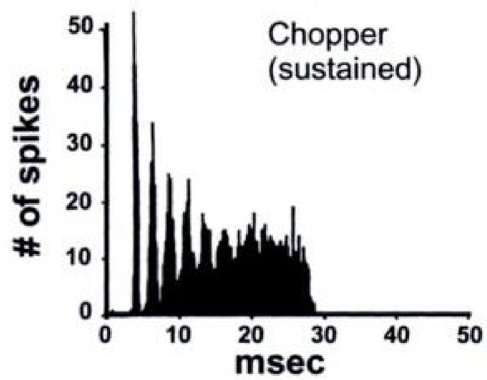
Characteristics (Rhode & Smith, 1986b)

1. No spontaneous discharge rate.
2. Long first spike latency
3. Tuning curves with a restricted frequency range
4. Non-monotonic intensity function
5. Asymmetric sweep preference to tones swept either from low-to-high or high-to-low frequencies.



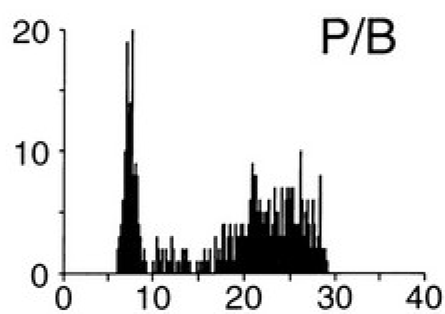
Principal features of an onset-graded (On-g) unit are illustrated. Nonmonotonic rate-level functions for tone and noise. Poststimulus time histogram (PSTH) for tones at 60 dB SPL (50 ms every 200 ms, 250 reps) at best frequency [BF = 9,500 Hz, threshold in dB SPL at BF (TH) 15 dB SPL].

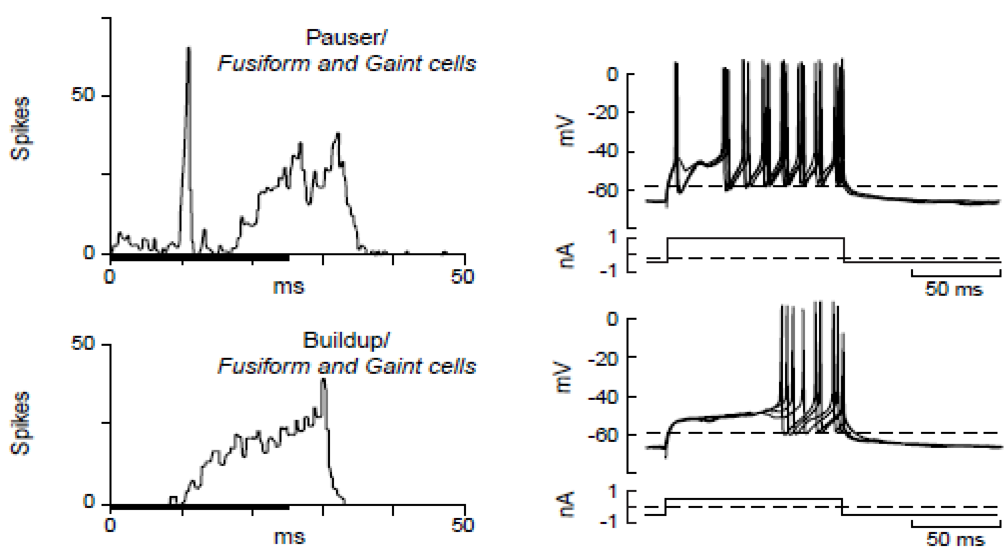
CHOPPER RESPONSES



Found in the Polymorphic cell layer of the DCN (Godfrey et al., 1975a, b)
This kind of response is derived from the PSTHs as, a multi peaked temporal pattern in which the inter peak intervals are not related to stimulus frequency (Pfeiffer, 1966a)
The chopper response found in the DCN is regular.

BUILDUP AND PAUSER RESPONSES





Pauser response shows first spike followed by 5 – 10 ms pause, and buildup spike probability increases with stimulus duration. Fusiform and giant cells exhibit either pauser or buildup response profiles, note their PSTH ordinate is in units of spikes rather than spikes per second. Pure tones were repetitively presented at each neuron's CF for 25ms to create the histograms (indicated by bar on each abscissa).

The 2 responses will be detailed together since they originate mainly from the DCN Pyramidal cells (Rhode & Smith, 1985) they have extensive inhibitory sidebands.

Characteristics

1. Latencies of the DCN cells are generally longer than in other areas of the CN, and responses to click stimulation show a latency of 2.5 – 7 ms in some cases. The longer latency may be due to multi synaptic circuits, which appear to be abundant in the DCN.

2. They show a tonic discharge which starts after a fairly long latency after the stimulus onset.

3. Short latency peak in their discharge at stimulus onset which is followed by a characteristic pause between phasic and tonic response starts.

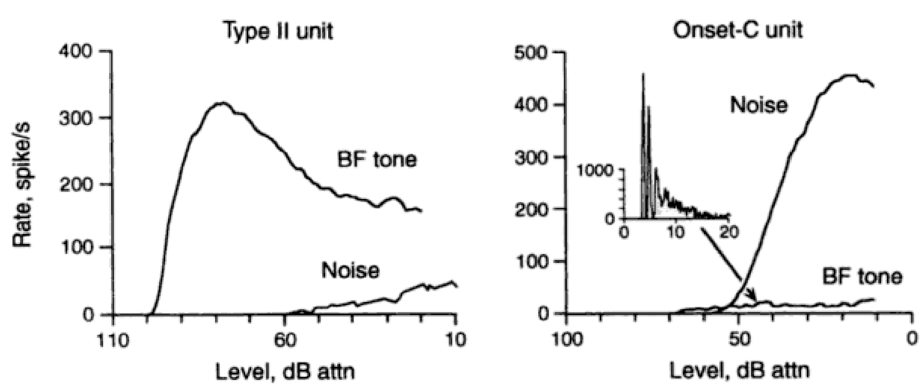
4. For any given neuron, the shape of the response may change with increasing sound intensity from a tonic activity to a pauser to eventually a buildup

5. The response complexity is even higher for the cells in the polymorphic cell region of the DCN, where a single cell can show up to 6 different types of responses, depending on the intensity and frequency of the sound stimulus (Godfrey et al., 1975b)

One of the possible factors of the shaping of the DCN response is *inhibition*, by the inhibitory interneurons (Young et al., 1985) or by intrinsic membrane properties (Kim, 1993)

INHIBITION

The 2 inhibitory interneurons 1) Vertical cells, Type II or Tuberculoventral cells → Narrow band inhibitor 2) D-stellate / Radiate neurons → Wideband inhibitor



Discharge rate versus sound level for responses of a type II (Vertical cell) unit and an Onset-C (D-stellate) unit. Rates are calculated from responses to 200ms tone or noise bursts presented once per second. The inset for Onset-C shows a PSTH of the units' responses to the first 20ms of a 50ms BF-tone bursts at 45 dB attn.

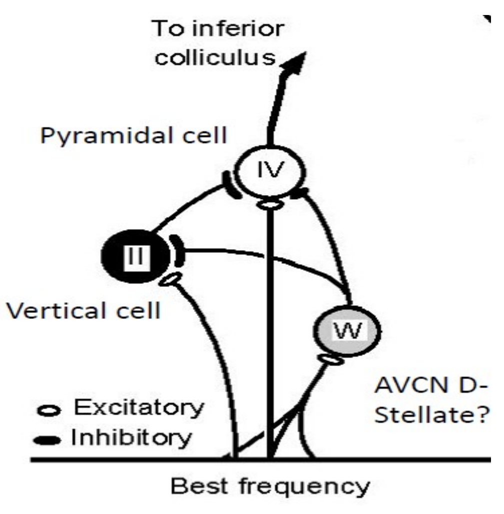
The responses of fusiform and/or giant cells are shaped by inhibition from Tuberculoventral cells of the deep layer of the DCN and D-stellate cells of the VCN.

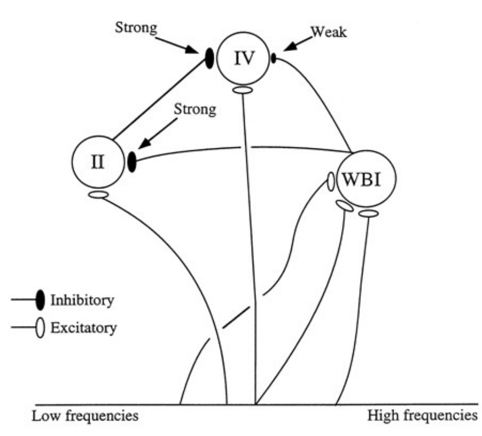
Tuberculoventral cells are also excited by a small number of auditory nerve fibers that make them sensitive to narrowband stimuli, and they inhibit fusiform and/or giant cells with similar tuning.
As a consequence of the strong inhibition from tuberculoventral cells, narrowband stimuli, such as tones that have a concentration of energy at one frequency, prevent firing in fusiform and giant cells, except when the sounds are very soft.
The inhibition from tuberculoventral cells is itself shut down by inhibition from D-stellate cells in the presence of broadband sounds, that have energy widely spread across frequency.

D-stellate cells receive input from auditory nerve fibers that are tuned to a wide range of frequencies, making them sensitive to broadband sounds; they strongly inhibit tuberculoventral cells.

Under such conditions, fusiform and/or giant cells are excited by their auditory nerve fiber inputs without also being inhibited.
Fusiform and giant cells thus generally respond to broadband, but not to narrowband stimuli.
→In the presence of spectral notches, when tuberculoventral cells tuned to notch frequencies are not excited, weak inhibition reveals a direct connection between D-stellate and Fusiform and/or Giant cells.

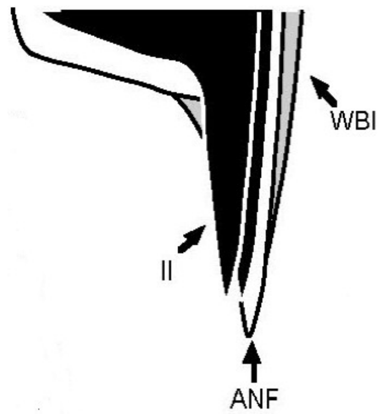
The confluence of these two inhibitory circuits on Fusiform and giant cells thus allows the principal cells to detect sounds with *peaks in their spectra* and sounds with *notches in their spectra*, both through inhibition.





Neural circuit model proposed by Spirou and Young (1991).
The bottom horizontal line represents the tonotopic array of auditory nerve fibers.
Type II neurons (II, Tuberculoventral) receive narrowband ANF input, and inhibit type IV. WBI neurons (W, D-stellate) receive wideband ANF input, and inhibit both type II and type IV neurons.
Type IV neurons receive inhibition from both interneurons, and narrowband excitation from ANF.

The size of each terminal is an indication of its postulated strength. The BF of the type IV is determined by the BF of its excitatory input, the BF of type II is slightly below that of type IV.



An outline of the overlapping excitatory areas is shown for the 3 sources of input to the type IV unit. (Frequency- abscissa, sound level- ordinate)

1) The excitatory input from the Auditory nerve fibers is shown unfilled,
2) The excitatory areas of the type II units is shown in black (2 of them)
3) The excitatory tuning curve of the wide band inhibitor is shaded. (High threshold, wide bandwidth)

The thresholds of the type II units are elevated with respect to the ANF threshold, which is consistent with the finding that type II units have higher thresholds than either low threshold (High spontaneous rate) ANF or type IV units (Davis and Young, 2000)
The type IV's excitatory area at high levels and low frequencies results from the high tail threshold of the type II units.
Notice **the threshold intensities of each input, at low sound levels; the cell only receives excitatory input from the ANF, soon followed by inhibition from type II inputs, and inhibition by WBI at even higher intensity levels. This can explain the response map of the Type IV neuron!**

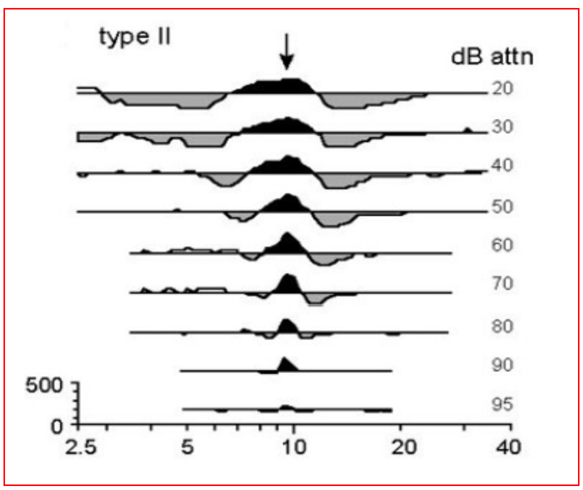
What are response maps?
They are based on response to tones of various intensities and frequencies, they show discharge rate versus frequency, at a series of fixed sound levels. Obtained by the presentation of 100 tone bursts of duration 200 ms; the tone frequencies are interpolated logarithmically over a range varying from 1-4 octaves, as shown on the abscissa.
For each plot, the attenuation was held constant at a value given by the number at the right of the curve. 0 dB attenuation corresponds to roughly 100 dB SPL.

The horizontal line is the spontaneous rate.
Arrows at the top points to the best frequency (BF).

<u>Type II</u>

<u>Response map</u>
There is a narrow V-shaped excitatory area centered on the BF and a significant inhibitory surround. Because of the lack of spontaneous activity, inhibitory responses are demonstrated by presenting a low-level BF tone of fixed attenuation and frequency (9.35 kHz, 90 dB attn.). This tone produces a low rate of background activity against which both excitatory and inhibitory responses can be seen.

The anatomic correlate of type II units is the **vertical cell interneuron**, or **tuberculoventral** cell in DCN.
Vertical cells are located in the deep DCN, in a thick band beneath the pyramidal cell layer (Oertel 1993b).
They are characterized by small somata, vertically oriented dendrites and inhibitory neurotransmitter glycine.
They are sharply tuned in frequency, and their threshold to tones, tend to be somewhat higher than type IV thresholds (Young and Brownell 1976).



Response map - TYPE II
1. It has zero spontaneous activity.
2. Narrowly tuned excitatory area.
3. Weak or no response to broadband stimuli

Although DCN structure varies considerably across species, the vertical cell system seems to be a stable feature of its organization (e.g., *cat*, Osen et al. 1990; *guinea pig*, Kolston et al. 1992; and *baboon*, Moore et al. 1996), suggesting that this inhibitory system is a fundamental part of **signal processing** in the mammalian cochlear nucleus.

Inhibition of type II by D-Stellate / Radiate neurons

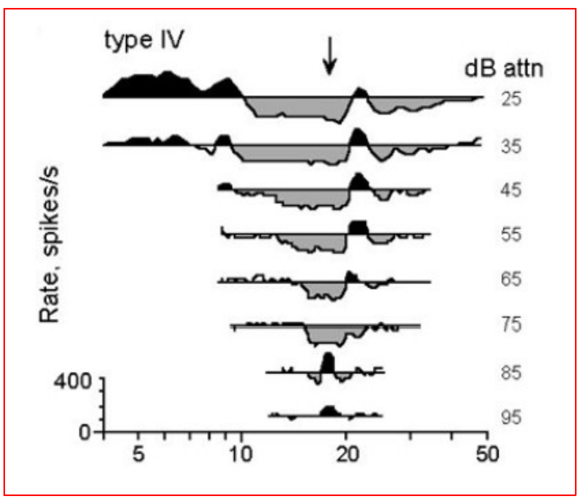
D-stellate or **radiate neurons** of the VCN project axons to DCN that terminate in regions where vertical cell dendrites are located (Oertel et al. 1990).
These neurons are glycine-immunoreactive and so could provide inhibitory inputs to vertical cells (Zhang and Oertel 1993b).
These neurons have been shown to give **onset-C response** (Smith and Rhode 1989), a prominent feature of which facilitates wideband response, which causes them to respond more strongly as the **bandwidth of the stimulus is increased** (Palmer et al. 1996).
In particular, onset-C neurons respond more strongly to noise than to tones.

On this basis, Palmer (1995) proposed that onset-C neurons form the inhibitory inputs to DCN type II units that produce weak type II noise responses in the presence of strong tone responses.

Type IV

Principal cells or **Fusiform & Giant cells** (Responses recorded from cat)

There is a small excitatory area near the threshold, centered on the neurons BF (BF, 17.5Hz).
Central Inhibitory Area (CIA) - At higher sound levels, the response near the BF is inhibitory over a V-shaped area called the CIA, centered at 16-17 Hz in this case.
There is an excitatory edge (near 22kHz here) at the upper frequency limit of the CIA which separates the CIA from an upper inhibitory sideband at higher frequencies. At low frequencies and high levels (below 10 kHz), type IV units have a large excitatory region.



Response map – TYPE IV

1. Has a **central inhibitory area (CIA)** which is usually centered below the best frequency(BF), but extends upward in frequency to include the BF. Because the CIA encroaches onto the BF, type IV units have a non-monotonic rate response to BF tone bursts; the response is excitatory over the first~ 30 dB above the threshold and then becomes inhibitory.

2. The central inhibitory area of the tone map of type IV units is thought to be the effect of type II inhibition (Spirou and Young 1991).

3. The center of the central inhibitory area tends to lie below the unit's BF, and its width is often wider than a single type II tuning curve, suggesting that more than one type II unit inhibits each type IV unit (Spirou and Young 199 1; Voigt and Young 1980, 1990).

4. Excitatory response to broad band stimuli and inhibitory response to tones.

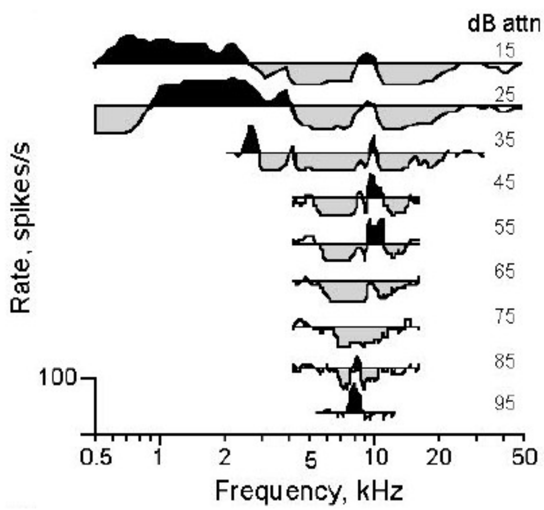


Figure 1 a

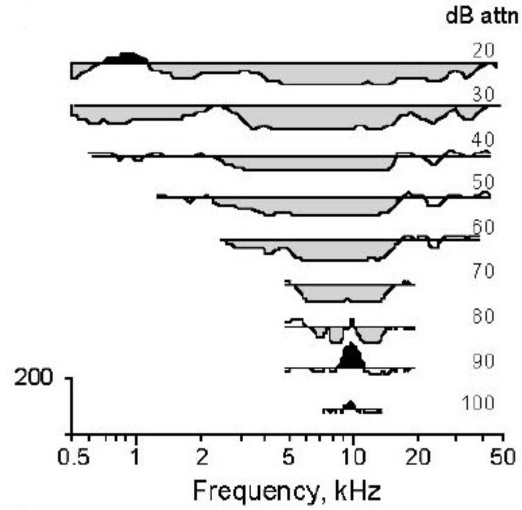


Figure 2 a

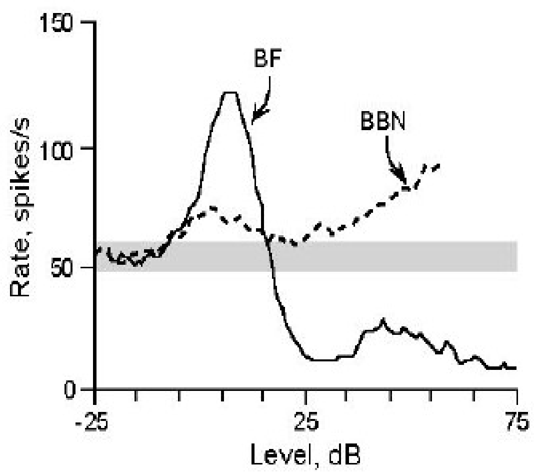


Figure 1 b

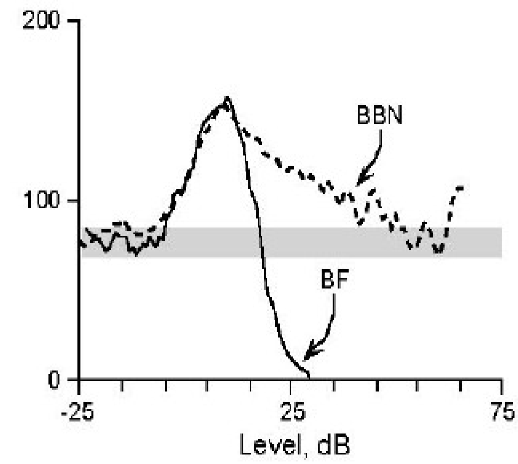
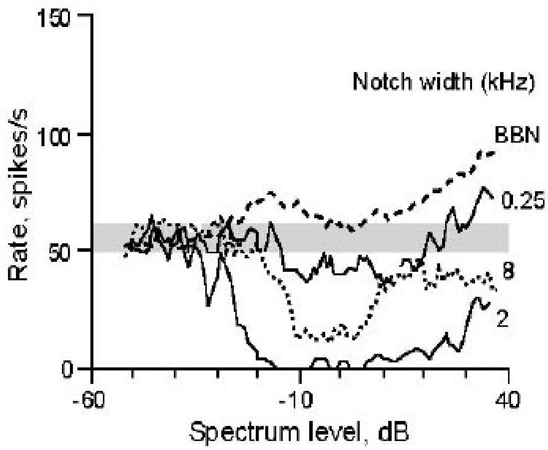


Figure 2b



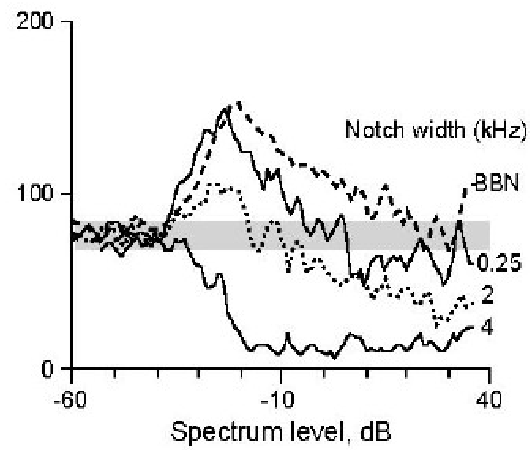


Figure 1c

Figure 2c

Response maps and responses to BBN for 2 type IV units.

Each column shows data from one unit. [Col 1(Fig 1a, b, c) & col 2(fig 2a, b, c)]

Plots of discharge rate versus sound level are shown in fig 1b & fig 2b for 200ms BF- tone burst and noise bursts. The shaded bar show the range of spontaneous rates. For both units the response to noise is excitatory at all levels, and for tones predominantly inhibitory.

Fig 1c & fig 2c show the response rate level functions for notch noise, which is BBN with a narrow notch or a broad band stop region centered arithmetically on BF. The band width of the notch is shown to the right of each curve (in kHz). The notch responses are inhibitory which is not expected from the response maps. Because responses to tone energy near the best frequency are inhibitory, in the response map, removing this energy from the BBN should produce an excitatory effect instead of the inhibitory one that is observed.

What is the function of type IV units?

1) Type IV units are extremely sensitive to low-level stimuli (Young and Brownell 1976).

2) They also have excellent masking properties: their rate level functions to BF tones shift by 1 dB for each increase of 1 dB in the level of a continuous noise masker (Gibson et al.,1985) . These properties may make them useful for detecting near-threshold stimuli, both in silence and in background noise.

3) Type IV units tend to be inhibited both by narrowband stimuli, or spectral maxima and by notch noise, or spectral minima. In other words, they are inhibited by narrow features in the

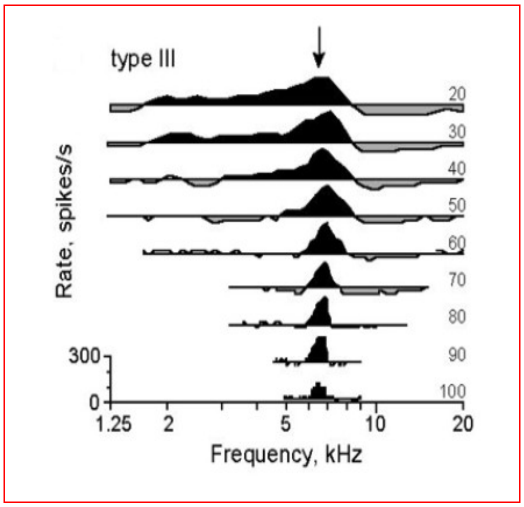
spectrum, depending on their frequency location. Therefore, we suggest that type IV units are detectors of interesting features in the stimulus spectrum, features that may carry important information about the external world.

For example, many natural sounds are defined by their spectral peaks [human speech as well as many animal communication sounds (Suga 1992)]. Spectral notches are thought to be important in sound source direction estimation (Blauert, 1983; Rice et al., 1992).

Type III

Recorded from principal cells

Response maps have a central V shaped excitatory area centered on the BF and inhibitory sidebands. They have spontaneous activity and respond to broadband noise, as strongly as they respond to tones.



Response map – TYPE III

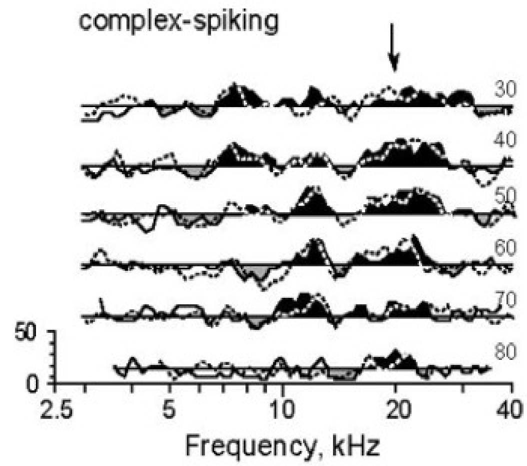
Complex Spiking Neuron

Produced by **Cartwheel cell neurons**

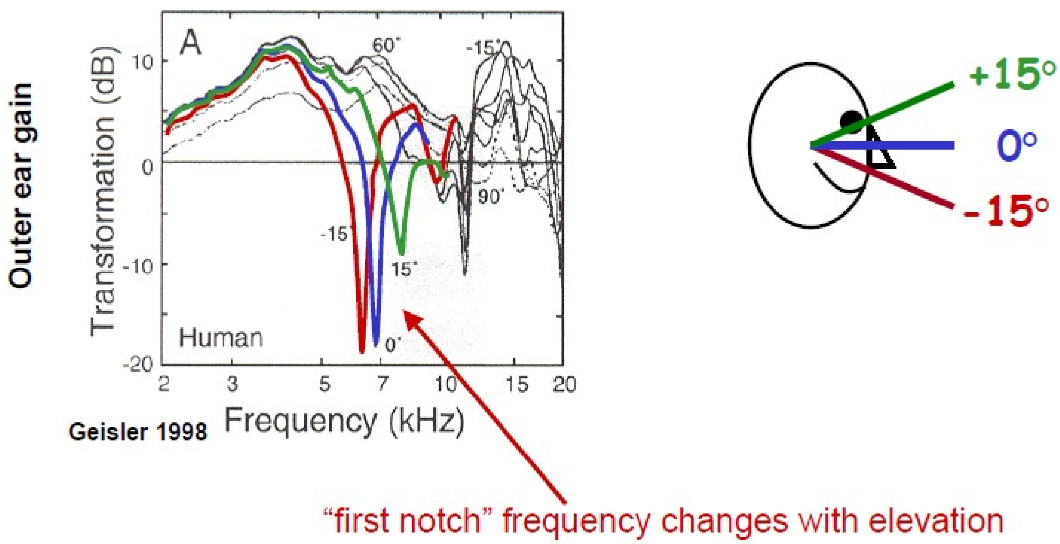
Complex spiking neurons (CSN) are whose action potentials, in extracellular recording, show short bursts of spikes. Almost all CSN respond to sound, but their responses are highly variable.

These neurons typically show fluctuations in their spontaneous rates, and it is hard to assign a BF.

Their response maps show a mixture of excitatory and inhibitory areas, but these are not organized in any typical pattern.



Spectral cues for localizing sound

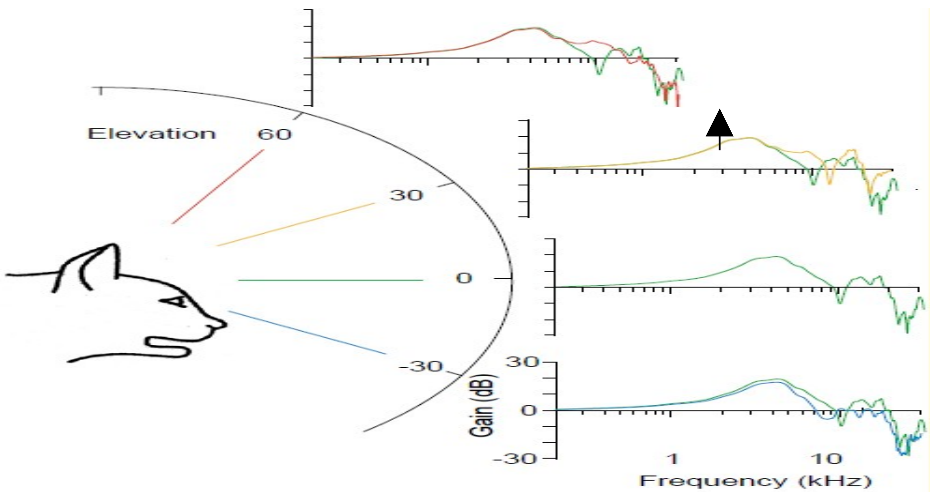


Type IV units are sensitive to HRTF first notch

When sound impinges on the external ear, it reflects off the irregular surfaces of the pinna. The reflections produce acoustic resonances in the cavities of the pinna and interference patterns at the entrance of the external ear canal. These resonances and interference patterns differ as a function of the direction of the sound source.
By placing a microphone near the eardrum of a cat, the spectra of sounds in the ear are compared with the spectra of the same sounds measured at the same place in the absence of the cat. The ratio of the two spectra is the head-related transfer function (HRTF).

For sound originating at four elevations directly in front of the cat, there are a series of peaks and valleys at frequencies >5 kHz and it varies strongly with the direction of the sound source. For reference, the 0^0 elevation curve is repeated at the other three elevations.

Note in particular the notch at frequencies between 8 and 15 kHz; this notch is a particularly strong cue for sound localization in cats. It moves from low to high frequencies as the sound source moves upward in elevation, from -30^0 to 60^0.

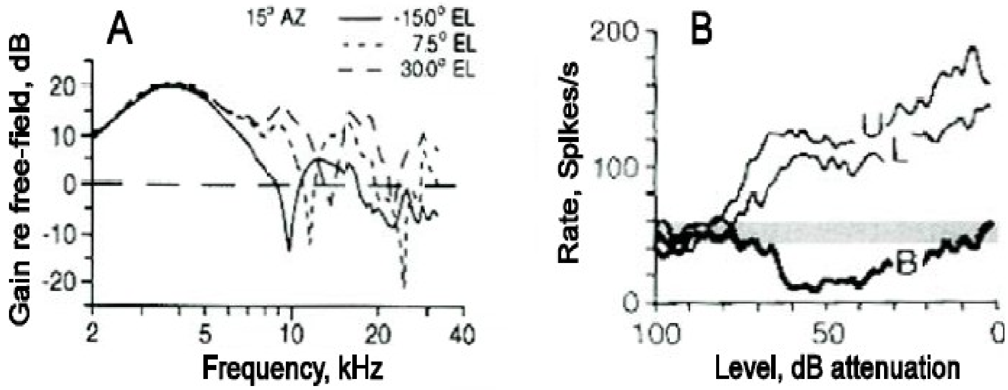


Head-related transfer functions for sounds at four elevations in the ***vertical plane.*** *Transfer functions show gain – the dB ratio of the sound at the eardrum to the free field sound – as a function of frequency.*

The acoustic effects of the external ear depend on the **size** of the ear. Resonances and interference effects occur when the dimensions of cavities and distances between reflective surfaces are larger than one-quarter of the wavelength of sounds. In the cat ear, this places these effects at frequencies >7 kHz; in the larger human ear, they are most prominent at frequencies >3 kHz.

<u>Spectral feature detection by fusiform and giant cells used for monaural sound localization</u>

(A) HTRFs from a cat for three sound source locations. White noise was emitted from a speaker held at various
locations, and the frequency response at the cat's right eardrum was measured.
Prominent notch between 8 – 18 kHz shifts to higher frequencies as sound source elevation increases. From Rice et al (1992).
(B)Rate intensity functions of a fusiform or giant cell when stimulated with HRTF-filtered noise stimuli. Stimuli are similar to those shown in a, with notch frequencies positioned at the neuron's characteristic frequency (B), and above or below it (U, L). Sound level given as attenuation, but spectrum level was the same for the three traces. Shaded bar indicates spontaneous discharge rates for this neuron. Notice a prominent inhibition (decrease in rate) when the notch is centered at best frequency, but excitation otherwise.



References

1. Ehret.G; Romand.G; The central auditory system, 1997; Oxford University Press
2. Oertal.D, Fay.R, Popper.A; Integrative functions of the mammalian auditory pathway,2002 Springer Handbook of Auditory Research
3. Oertel.D, Young.E; What's a cerebellar circuit doing in the auditory system?
4. Rhode.W; Vertical Cell Responses to Sound in Cat DCN, *J Neurophysiol* 82:1019-1032, 1999.
5. Starr.A, Britt.R; Synaptic events and discharge patterns of cochlear nucleus cells. II FM tones.
6. Joris. P; Response Classes in the Dorsal Cochlear Nucleus and Its Output Tract in the Chloralose-Anesthetized Cat