The Auditory Nerve:
Anatomy, Physiology, and Function

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2.4 kHz, 27.3 s/s

1.7 kHz, 8.6 s/s

20 μm
Sound waves from the auditory environment all combine in the ear canal to form a complex waveform. This waveform is deconstructed by the cochlea with respect to time, loudness, and frequency and neural signals representing these features are carried into the brain by the auditory nerve. It is thought that features of the sounds are processed centrally along parallel and hierarchical pathways where eventually percepts of the sounds are organized.
In mammals, the neural representation of acoustic information enters the brain by way of the auditory nerve. The auditory nerve terminates in the cochlear nucleus, and the cochlear nucleus in turn gives rise to multiple output projections that form separate but parallel limbs of the ascending auditory pathways. How the brain normally processes acoustic information will be heavily dependent upon the organization of auditory nerve input to the cochlear nucleus and on the nature of the different neural circuits that are established at this early stage.
This histology slide of a cat cochlea (right) illustrates the sensory receptors, the auditory nerve, and its target the cochlear nucleus. The orientation of the cut is illustrated by the pink line in the drawing of the cat head (left). We learned about the relationship between these structures by inserting a dye-filled micropipette into the auditory nerve and making small injections of the dye. After histological processing, stained single fibers were reconstruct back to their origin, and traced centrally to determine how they terminated in the brain. We will review the components of the nerve with respect to composition, innervation of the receptors, cell body morphology, myelination, and central terminations.
This slide illustrates side views of the brains of a human (left), cat (middle) and mouse (right). The target of the auditory nerve, the cochlear nucleus, double arrow) is found along the dorsolateral surface of the pontine-medullary junction in cats and mice but is hidden by fibers of the middle cerebellar peduncle in humans. Most of the cochlear nucleus is hidden by cerebellar cortex. The trapezoid body, the output axons of the cochlear nucleus, is visible along the ventral surface of the brain stem (arrow) as a couple of “bumps” that appear to run from one side to the other.
“Surface view” of the cochlea. On the left, the otic capsule has been peeled away and a view of the organ of Corti is shown via a scanning electron micrograph. On the right (top), we have a drawing of the innervation by the two types of spiral ganglion cells as revealed by horseradish peroxidase staining of individual neurons. On the bottom is a photomicrograph of HRP-stained representative type I and type II spiral ganglion neurons. Type I neurons are large, have a thin peripheral process, innervate only inner hair cells, and represent 90-95% of the total ganglion population. Type II neurons are smaller, have unmyelinated processes, innervate outer hair cells, and represent 5-10% of the population.
Examples of type I and type II ganglion cell bodies in cats as stained by horseradish peroxidase (HRP).
Comparisons of spiral ganglion cell features across different mammalian species. The y axis represents the ratio of the central process diameter divided by the peripheral process diameter. In the HRP Cats (upper left), the ratios were determined for neurons whose processes were traced through serial sections to the innervated hair cells. The ratios allow identification of the two types of neurons using this feature for cells and animals where reconstructions were not possible.
Electron micrographs in rats reveal that type I cell bodies are filled with ribosomes (left), whereas type II cell bodies are filled with neurofilaments (right).
The EM observations were verified using basic dyes staining RNA (ribosomes) and DNA (chromatin) where type II cell bodies are mostly clear (upper left and lower right panels). Neurofilament stains (upper right) leave the larger type I cell body cytoplasm relatively clear, whereas the small type II cell bodies are stained darkly. Signal-to-noise makes identification of the separate cell types difficult. Immunostaining, however, shows that the phosphorylated form of the 210 kD neurofilament chain uniquely stains type II neurons in the mammalian cochlea.
HRP labeled type I (thick) and type II (thin) axons in the auditory nerve of a cat.
Side view of reconstructed mouse cochlear nucleus. Labeled type I and type II axons follow the same trajectory in mammals.
Side view of the mouse cochlear nucleus. Although the general trajectory is similar, the type II axons send terminals preferentially into the granule cell domain (stippled area).
HRP labeled type II axons often expressed terminal swellings in and around capillaries.
Hypothesis that type II neurons mediate tissue damage in the inner ear by loud noise.
The activated auditory receptor cells stimulate auditory neurons of the inner ear. The output of the ear is transferred by way of auditory nerve fibers to the brain. This transfer is frequency-specific from the nerve and into the cochlear nucleus of the brain.
Type II unmyelinated axon (arrow) and type I myelinated axon in the cat auditory nerve.
Diagram of the cross section of the auditory nerve; inset illustrates individual fibers and tip of recording micropipette.
When one advances a recording microelectrode into the auditory nerve, activity can be recorded even in the absence of experimenter presented auditory stimulation. This spontaneous activity can range from near zero to over 100 spikes per second.
This histogram of spontaneous discharge rates shows a bimodal distribution of SR values. Spontaneous discharge rate is one important feature of auditory nerve fiber properties.
Another important feature is frequency selectivity. This plot is of single fiber recordings where loudness is on the y axis and frequency is on the x axis. The stimulus is a tone, swept from low-to-high frequency, and each trace along the y axis varies in loudness. Note that at the lowest levels, there is no evoked activity, although the fiber is spontaneously active. However, as the level increases, activity is first evoked around 1 kHz. As the level increases, the fiber responds to a broader and broader frequency range.
If we draw a line around the envelope of activity, we get what is called a tuning curve. Every combination of frequency and loudness inside the curve produces an evoked response, whereas every combination outside the curve does not.
Here are 2 tuning curves with 1 kHz characteristic frequency or best frequency, defined as that frequency to which the fiber is most sensitive. The tuning curve in black is from a low SR fiber and the tuning curve in blue is from a high SR fiber. Note the difference in thresholds for the two types.

And the difference in width of the tuning curves.
The sharpness of tuning can be quantified using engineering methods. Here, the width of the TC is measured 40 dB above threshold for the high SR, low threshold fiber.
We can compare this measure doing the same manipulation for the low SR, high threshold fiber.
The ratio of BF/bandwidth (BW) at 40 dB above threshold is called the Q40. The high threshold fiber is more sharply tuned compared to the low threshold fiber.
And here are some representative tuning curves collected from a cat auditory nerve. There is a tip and a tail to these tuning curves. What do you think that signifies?
Q40 = CF/bandwidth 40dB above threshold

The higher the CF, the sharper the tuning curve.
There is an important relationship between spontaneous rate and threshold. Low threshold fibers have high rates of spontaneous activity.
Low threshold auditory nerve fibers have a higher maximum discharge rate compared to low SR fibers.
The two types of fibers—high and low SR—are found across the audible frequency range. They must serve different functions.
There is a Place-Frequency Map in the Cochlea

Liberman 1982
The latency to the first sound-evoked spike is determined by the fiber’s characteristic frequency. Why might this be?
The idea that there are two types of type I auditory nerve fibers definable by their physiological properties suggested that they must have different structural properties. Charlie Liberman and I were collaborating on this work and while he looked in the inner ear, I looked in the brain. The top panel is a surface preparation view of 3 IHCs. What Charlie found was that the low threshold fibers were thicker, filled with mitochondria, and terminated on the far side of the IHC. In contrast, the high threshold fibers were thinner, lacking mitochondria, and terminated on the near side of the IHC.
And this relationship is shown in the more conventional view of the organ of Corti—low SR fibers are thinner with smaller terminal boutons, whereas high SR fibers are thicker with larger terminal boutons. The red dots on the IHC represent the synaptic ribbon, as shown in the inset electron micrograph.
This summary drawing shows that each IHC receives innervation from multiple auditory nerve fibers. They are segregated around the IHC by threshold.
red = ctBP; green = GluR2

Liberman et al. showed that the low SR fibers had larger synaptic ribbons, whereas these ribbons were opposed to smaller postsynaptic densities as revealed by GluR2 staining.
A schematic drawing of IHCs, OHCs, and auditory nerve fibers
The many auditory nerve fibers innervating a single IHC gives redundancy to the input and yields a high density, high definition representation of our auditory environment. Hearing loss “pixelates” our auditory world, causing loss of resolution and detail.
This diagram from Lorente de Nó is a classic and shows the afferent innervation of the inner ear by 3 types of auditory nerve fibers: one type innervates IHCs, one type innervates OHCs, and the third type innervates both IHCs and OHCs. This latter type is probably a developmental transitional stage of innervation.
This photograph shows a side view of the cat cochlear nucleus. The cerebellum and cerebral cortex have been removed. Abbreviations: AN, auditory nerve; DCN, dorsal cochlear nucleus; IC, inferior colliculus; LL, lateral lemniscus; MCP, middle cerebellar peduncle; VCN, ventral cochlear nucleus; VN, vestibular nerve; 5N, trigeminal nerve; 7N, facial nerve.
Lorente de Nó proposed that every auditory nerve fiber was as the next, a kind of module. The fiber (blue) represented the population of auditory nerve fibers (in spite of the 3 types of peripheral innervations patterns he described).
Single fiber recording and dye injections allowed us to produce a 2D frequency map of the cochlear nucleus.
Technology limited us to 2D frequency maps—whether by mapping the AN input (left) or recording from the cell bodies in the AVCN and DCN (right). I’ll show a 3D map of the cochlear nucleus in the lecture on the VCN.
The idea of how sound is processed revolves around how fibers innervate CN neurons, and which neurons are innervated in what patterns. What we schematize here is that a single fiber might innervate the major cell types of the CN, endowing each with the same CF but perhaps modifying their input features by varying the nature--size, distribution, etc.--of the synapse. So while each of the contacted neurons would have the same CF, they would simultaneously be extracting different features.
This figure shows 3 coronal sections through the cat cochlear nucleus, indicating the main core of the nucleus in white and the small microneuronal granule cell domain in red dots.
Different cell types implies different function and different input. Here we see the border between the microneuronal granule cells laterally and the large macroneurons, the bushy cells.
Let’s reflect back on the idea of Lorente de Nó that all ANFs were the same.
Using intracellular recording and dye injections, we could test the hypothesis that every ANF was the same. What was found was that high SR fibers differed in their termination pattern compared to low SR fibers. The low SR fibers emitted long collaterals that selectively innervated the small cells that formed a shell around the cochlear nucleus.
This diagram provides a direct comparison of a low SR fiber and a high SR fiber. Note the long collaterals (red) from the low SR fiber.
We’ve modified the diagram of Lorente de Nó. The low SR fibes (red) have collaterals to the small cells in the external shell of the nucleus.
If we plot the distribution of synaptic endings from auditory nerve fibers, we see that there is selective innervation of the small cell rind by the high threshold fibers.

Why do we care about this??
The low SR fibers selectively innervate the small cells that lie between the microneuronal granule cells and the macroneurons of the VCN core.
The small cell cap (SCC) is important here.
This is how they appear under the electron microscope.
This small cell of the cap receives labeled terminals from a low SR fiber (black with cyan asterisks). Unlabeled terminals (pink asterisks) are also found around the cell body and dendrites.
We observed that labeled terminals selectively terminated on dendrites that were relatively dark. The dark appearance is due to the presence of ribosomes in the dendrites, a rather unusual feature. Even when labeled terminals approached pale dendrites, they did not form synapses.
The small cells are of interest because a couple of Connecticut Huskies did a nice set of experiments. In Duck Kim’s lab, they recorded from cells in the external shell of the cochlear nucleus. What they found was that in the superficial region of the nucleus, cells had lower maximum discharge rates, higher thresholds for sound evoked activity, but a larger dynamic range, meaning that they responded to a wider range of sound levels. So they concluded that these superficial neurons were physiologically distinguishable from the deeper lying macroneurons of the core. Could this high threshold circuit be part of the afferent limb for the feedback projections to the cochlea?
The auditory system is special because they have neurons in the brain that send axons to the sensory receptors that seem to control the sensitivity of the ear. No other sensory system has such a circuit of feedback control of the receptors. Activation of this auditory feedback system has a high threshold. Wouldn’t it be cool if the small cells of the shell was part of the circuit.
They then injected anterograde dyes into the superficial region of the cochlear nucleus (top diagram). What they discovered was that these high threshold neurons, that received input from high threshold ANFs, projected to a special set of neurons that in turn projected back to the cochlea.

But high threshold small cells weren’t the only ones projecting to the efferents. Multipolar cells of the VCN also projected to a part of this efferent system. And we know from others, including our own Professor Malmierca, that the inferior colliculus projected to these efferents neurons.
And now, we can complete the near 80-year old diagram by Lorente de Nó on the axons in the inner ear that are not attached to cell bodies of the spiral ganglion. These turn out to be the efferent axons, that arise in the brainstem—one set called the lateral efferents that terminate on ANFs under the IHCs and the other called medial efferents that terminate directly on OHCs.

Efferent control of “gain” of the ear has one circuit that originates in the high threshold ANFs and is mediated by the small cells of the cap. But efferent control, which is hypothesized to enhance our ability to extract signals from other signals—e.g., attending to the flute in a symphonic performance and then switching to the horns—gets a lot of different inputs.
SUMMARY

There are two types of spiral ganglion neurons: 95% innervate IHCs, are myelinated, and project to the magnocellular core of the cochlear nucleus; the remaining 5% innervate OHCs, are unmyelinated, and preferentially terminate in the granule cell domain.

There are two types of myelinated auditory nerve fibers. Those with high threshold and those with low thresholds. They have different innervation patterns in the ear and the brain, suggesting separate functions in auditory processing. Low threshold fibers function best in quiet; high threshold fibers function in noise.

The high threshold fibers have a special relationship with olivocochlear efferent neurons through a circuit in the small cell cap. This function enhances our ability to extract signals from noise.

The function of the unmyelinated neurons is unknown but has been speculated to be involved in signalling damage to the sensory epithelium as a result of loud noise.