6 Stage 2, Signal Processing

6.1 Introduction

This chapter begins the exploration of the architecture and circuitry of the signaling function within hearing. To organize this material, it is necessary to provide some background information upon which some of the following material is based.

Stage 2 signal processing is defined as that afferent signal processing performed outside of the CNS and excluding any signal processing performed within the stage 1 sensory neurons. Stage 4 signal manipulation is defined as that signal processing performed within the CNS.

Signal summation has been discussed in the literature without regard for the physical location of that summation. As an example, the phenomenon of signal summation was introduced into a 2003 Buus & Florentine paper[1]. However, its origins were not discussed. Functionally, it appears that signal summation occurs in two domains and two forms. Summation of analog signals, as a primary task, occurs within stage 2 Signal Processing. Summation of analog signals also occurs as an incidental operation associated with feature extraction within stage 4 Signal Manipulation and stage 5 Cognition. The latter domains will be discussed in subsequent chapters. The generic term summation should be understood to include both the summing and the differencing of signals. A single neuron is capable of performing both operations, and complex combinations of these operations, simultaneously.

To understand the gross stage 2 signal processing functions of hearing, it is important to have a clear understanding of the gross architecture of the complete auditory system. This understanding suggests the character of the tasks assigned to stage 2 signal processing and allows the individual signal processing functions to be more easily isolated and interpreted. Section 1.3.1 has reviewed the gross architecture of the auditory system. A problem in defining the gross architecture of stage 2 alone is the extremely limited amount of information in the literature. What information is available is frequently contradictory at the detailed level. The caricatures available from different investigators are usually tailored to only describe a narrow part of the overall system.

6.1.1 The initial topographic subdivision of stage 2 Signal Processing

Figure 6.1.1-1 provides a top level schematic of stage 2 as defined in this work. A key observation is that the stage 2 signal processing may be divided into three sub-stages with stage 3 signal projection occurring between each pair of sub-stages. It may be expedient to speak of stage 2A processing that occurs prior to the habenula perforata, and Stage 2B processing that occurs within the spiral ganglia. Both areas involve analog signal processing but they are separated by a phasic stage 3 signal projection element. Stage 2A consists primarily of arranging connections to the spiral ganglia according to computational anatomy. This term includes the physical rearrangement of the neurites of neurons of the spiral ganglia into different spatial arrays and is better described as "anatomical computation." Stage 2B relates to the signal processing within the spiral ganglia suggested by the growth in output neurons compared to the number of input neurons. Stage 2C relates to the signal processing accomplished within the

cochlear nuclei (CN).

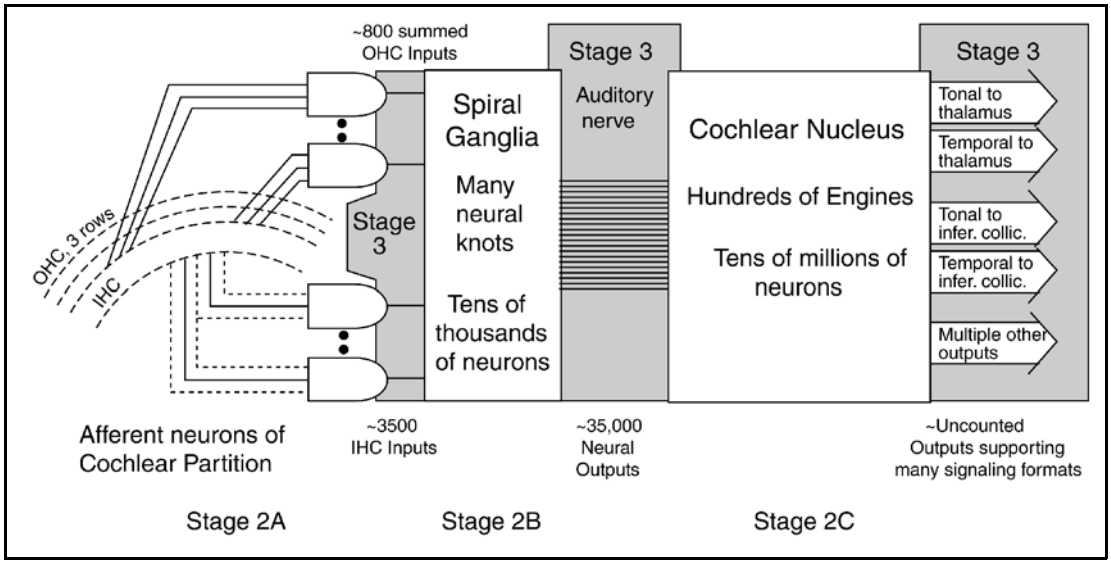

Figure 6.1.1-1 Top level signal flow diagram of stage 2 with numbers reflecting the typical human system. The detailed architecture of hearing in the peripheral nervous system is poorly resolved. See text. The fundamental summing scheme used in stage 2A has not been discovered. The processing algorithms associated with the spiral ganglia have not been explored. While some of the 35,000 neurons of the auditory nerve are clearly cochleotopic, others display very complex responses. The cochlear nucleus is considered part of stage 2 primarily because of the divergent character of its signals. It directs groups of signals to multiple engines of the CNS.

Stage 2A involves the summing of groups of OHC fibers along diagonals parallel to the direction of acoustic energy flow across the tectorial membrane of the cochlear partition. Signals from groups of three OHCs may be further combined so that one afferent stage 2 neuron conveys information from as many as 18 individual OHCs. The summation strategy applicable to the IHC is unresolved. The dashed lines in the figure suggest a degree of summation between adjacent IHCs. What is known about this strategy is discussed in Section 6.1.1.1.

As noted in Section 1.3.2, the assignment of the cochlear nucleus to a particular stage of hearing is awkward. It appears that its primary function is the merging of data, including that from several sensory modalities, before sending that data along diverging paths to multiple centers of the CNS. Feature extraction does not appear to be a major function of the CN. Morphologically, Oertel et al. described the cochlear nucleus as follows[2]. "The cochlear nuclear complex lies up against the brain stem, forming a bulge." They describe this bulge as curling around the cerebral peduncle. If the above represents a correct portrayal, the cochlear nuclei are part of the stage 2 signal processing system, both morphologically and physiologically, rather than part of the stage 4 signal manipulation system. The latter are concerned primarily with feature extraction rather than signal formatting.

It is quite likely that the detailed architecture of stage 2 in humans differs significantly from that of the lower mammals because of additional support to our larger CNS temporal lobes. On the other hand, the architecture used in humans may not support the expanded processing within the inferior colliculi associated with precise active and passive echo location as found in owls, bats and many marine species of mammals.

Finally, stage 2 is the first stage to involve both analog and pulse signaling in a very convoluted architecture. It is not sufficient to discuss only the pulse characteristics of a neuron. Nor is it adequate to discuss only the axonal characteristics on the mistaken assumption that the neuron is functionally a two-terminal device. Each neuron contains at least one three-terminal Activa along with its associated circuit elements. The Activa is fundamentally an analog device that can be easily converted to a monopulse generator of either the driven or free-running type.

The major problem with acquiring information concerning the initial stage 2A signal processing directly is the small size of many of the neurites. Most of the approximately 15,000 initial afferent neural paths in the region of interest are unmyelinated and of very small diameter. The afferent neurons remain unmyelinated until they reach the habenula. After the first Node of Ranvier, the afferent neurons of the IHC are generally larger, myelinated and much easier to trace. Farther from the sensory neurons, the state of myelination is a subject of dispute and may differ in humans compared to other species[3]. These conditions make it extremely difficult to trace individual paths faithfully. An additional problem is their confined location within a boney shroud. A similar problem applies to gaining information concerning the spiral ganglia of stage 2B, potentially the seat of considerable stage 2 signal processing.

Virtually no data has appeared describing signal flow within the spiral ganglia of stage 2B due to the complex morphology of the neurons and their very limited accessibility. The level of the activity within the spiral ganglia is indicated by the expansion ratio of three to one between the number of neurons in the auditory nerve compared to the number of sensory neurons. As suggested by the figure, the expansion ratio may even be higher if there is significant summation of signals prior to the spiral ganglia.

A second problem with acquiring information concerning Stage 2 is the functional role of the IHC. They are designed to create signatures at their axons that relate to broadband (frequently transient) stimuli at their input. The transient nature of both the stimuli and response have made their recording awkward and their analysis difficult. As a result, very few recordings of the signals associated with the broadband signal paths emanating from IHC pedicles exist. Those that do exist have usually been recorded in response to tone burst stimuli. The community is left with only conjecture as to how the output signals of Stage 1 are processed prior to their recording at the output of the spiral ganglia of Stage 2B. This situation persists with respect to the signal processing of the cochlear nuclei and the subsequent signal manipulation associated with the LOC signal path. This situation is unfortunate because up to a reported 90-95% of the Stage 2 signal paths originate with the IHC. As a result, this work cannot address the organization and performance of the broadband channels comprehensively.

Continuity is recognized between the neurons synapsing with the tonal OHC and the neurons of the MOC path to the CNS (both the thalamus and the inferior colliculus). Similar continuity is recognized between the transient channels associated with the IHC and the neurons of the LOC path to the CNS.

6.1.1.1 Stage 2A Signal Processing at the sensory neurons

Other than the work of Lorente de No in the 1930's using light microscopy, Fernandez in the 1940's using light microscopy[4] and the very early use of the electron microscope by Spoendlin in the 1960's and very early 1970's (using the cat) there is little relevant information about stage 2A. The snapshots provided in figures by these investigators should not be considered good examples of stage 2A in the human system without additional verification. Until that verification, stage 2A of humans can only be considered a black box with limited information about the signals going into and coming out of it. Kim attempted to summarize the above work in 1984 but he was firmly convinced that the OHC only functioned as actuators impacting the performance of the IHC[5]. His second and third hypotheses are not supported here.

Figure 6.1.1-2 reviews the gross signaling architecture associated with stage 2A of the auditory system. The figure is more schematic than some of the following detailed figures based on hand drawings and imaging. It is designed to capture the functional features of the system. It also provides a perspective on the number of individual signaling channels associated with different portions of the system. The figure attempts to bring a little more order to the neural architecture nearest the sensory neurons than in Lorente's early publications.

Tracing just the connections associated with one stage 2A neuron supporting a group of OHC neurons has proven almost impossible because of the small size of the unmyelinated neurites. Alternately, tracing the neurites of a single stage 2A neuron supporting one or more IHC neurons has proven exceedingly difficult because multiple neurites frequently proceed to the same IHC. As a result, only the coarsest statistics exist concerning the character of stage 2A signal processing. No statistics are available showing whether the number of sensory neurons associated with a specific stage 2A summation neuron remains constant over the length of the cochlear partition.

The signal paths associated with stage 2A involve analog signal transmission at least until they reach a structure labeled a bead (and proposed to constitute a Node of Ranvier based on this theory). These structures have not been examined in detail cytologically in the literature but phasic waveforms have been observed on their output side. These structures are very similar to the Nodes of Ranvier typically found on the orthodromic side of a stage 3 signal projection neuron. Most investigators report the neural structures prior to the habenula are unmyelinated. However, this assertion may not be sufficiently specific if some Nodes of Ranvier occur prior to the habenula. Spoendlin does

not recognize these structures morphologically except symbolically[6]. However, he calls the subsequent myelinated axon an initial segment. The term initial segment usually describes the first axonal segment following an encoding conexus. Following the first conexus, the signal paths are myelinated, as expected for the axons of stage 3 neurons. They proceed from the habenula in large groups to the spiral ganglia. The literature occasionally describes the spiral ganglia as divided into large neural masses defined as knots. Such knots are not supported in most of the literature related to humans.

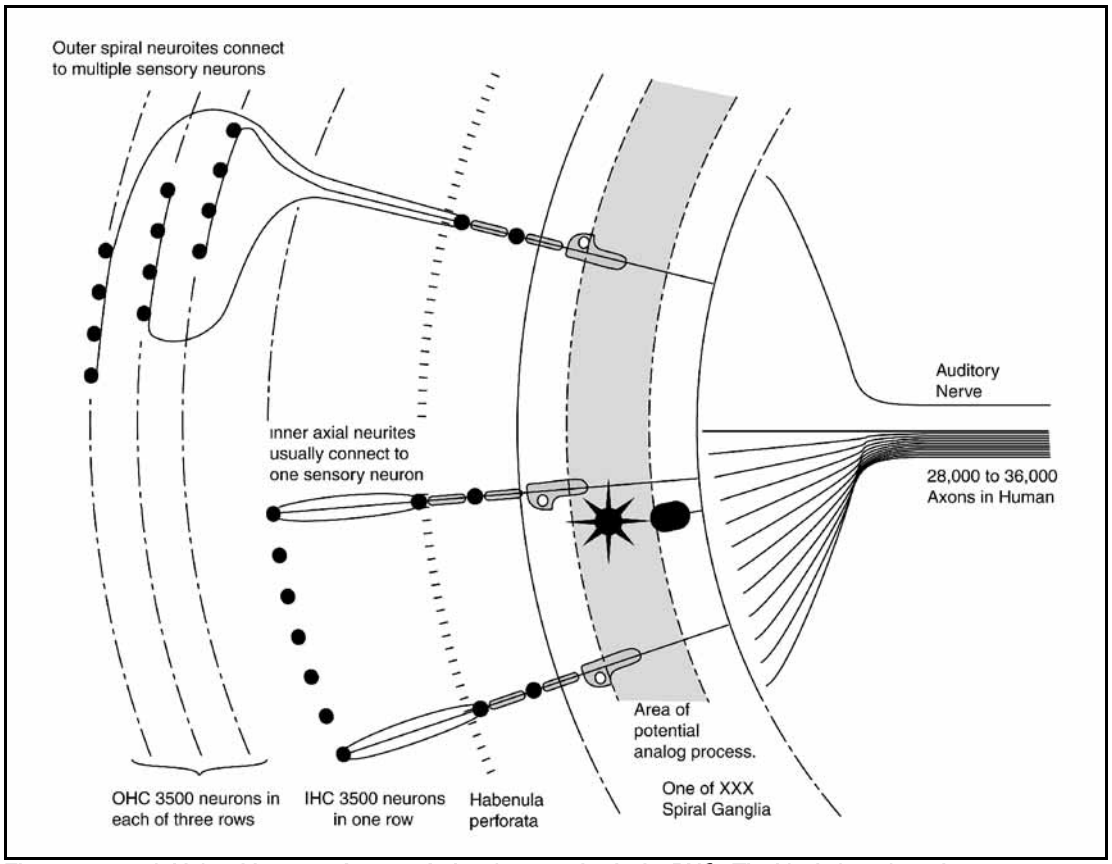

Figure 6.1.1-2 Initial architecture of stage 2A signal processing in the PNS. The black dots along the arcs represent the axonal portion of the sensory neurons. The radial displacement of the groups of OHC between rows reflects the expected direction of incident energy flow. The black dots along the radials represent unnamed functional elements ("beads") morphologically and topologically identical to Nodes of Ranvier.

In this situation, it appears a conexus has been inserted into the signal path that encodes the analog signal before the soma of the neuron is reached for more efficient phasic propagation. Depending on the length of the signal path, multiple copies of this conexus may be found prior to the soma. However, those after the first act exactly like Nodes of Ranvier (regenerating the phasic signal it receives).

Spoendlin has provided a similar figure showing some differences in the area of the afferent neurons associated with the inner hair cells (and without the above dual summation path). He associates up to 20 individual afferent neurons with one IHC. Spoendlin also associates up to 10 OHCs with one individual afferent neuron[7]. Harrison has suggested that each afferent neuron associated with the outer hair cells contacts as many as 20 of those cells[8]. On the other hand, Spoendlin estimates 2500 afferent neurons from the OHCs in cat (in Jahn & Santos-Sacchi, page 202). This value is near one afferent neuron per row of OHCs. Besides the previous references, Smolders & Klinke have provided some data on stage 2A signal summation in the caiman, *Caiman crocodilus*[9].

Spoendlin explored the morphology of a variety of species[10]. However, most of his published caricatures are based on a composite drawn from all species. Such composite views are excellent for pedagogy. However, they are not

adequate to support applied research in hearing. The literature is quite clear that different species have achieved different levels of evolutionary development with respect to hearing.

The level of sophistication documented in human hearing suggests that the afferent neuron counts of Spoendlin related to the sensory neurons in the 1960's may need to be definitized further for the human species. This was done for the guinea pig in 1975[11]. Whereas Spoendlin's global estimate was that only 5% of the afferent neurons originated at the OHC neurons, Morrison et al. found10-15% originated at the OHC neurons in the guinea pig. While their technique was immensely improved over that used 20 years earlier, they still relied upon one micron thick pieces from an ultratome to image unmyelinated fibers with sizes as small as one tenth of this dimension. They note, "The possibility of branching or *en passant* innervation cannot be excluded from the specimens studied."

Nomura asserted the method of staining is very important in investigations of the number of afferent neurons in the Cochlear partition[12]. His paper presents many aspects concerning the technique of axon counting, but his human subject was a deaf mute of advanced age at autopsy.

The 20:1 ratio related to the OHC is suggestive of how many discrete signal processing functions may be operating within the spiral ganglia. On the other hand, the ratios associated with the OHC, if taken at face value would suggest a very low degree of frequency discrimination in the hearing of these species.

6.1.1.2 Stage 2B within the spiral ganglia remains largely undocumented

Two critical features are immediately noticed about the spiral ganglia. The most important feature is that there are many more axons leaving the spiral ganglia than there are sensory neurons. The number of primary afferent neurons that connect the cochlea with the brain stem varies considerably in different species, with approximately 16,000 in the bat, 36,000 in the human, 50,000 to 60,000 in the cat and more than 200,000 in the whale[13]. A second feature is the wide variety of pulse streams found in the exiting axons based on histographic analysis. These features provide strong circumstantial evidence for additional stage 2A signal processing prior to transmission of the complete set of signals over the auditory nerve to the cochlear nucleus and the engines of the CNS. However, the literature is virtually empty regarding the morphological features, the topology, and the functional significance of the spiral ganglia. Spoendlin's 1972 paper did assert that the neurons of the spiral ganglia associated with the OHC did not interconnect with the neurons associated with the IHC[14].

The complexity of the histograms defined by Pfeiffer & Kim and widely reproduced suggest more complex signal processing within the spiral ganglia than mere coincidence detection[15]. It is very likely that some of the signals received from the sensory neurons are decoded within the spiral ganglia and processed in the analog domain. This processing would be similar to that performed by the amercine (lateral) neurons of the visual retina [PBV, 9.2.2]. This function is shown symbolically by the star (representing a multipolar neuron) and the subsequent solid box representing a secondary encoding ganglion neuron. The multipolar neuron is able to accept signals from multiple signaling channels through its neurites and perform very complex algebraic calculations. These calculations can involve time delays associated with the difference in path lengths among the input channels.

At the output plane of the spiral ganglia, all of the signals are once again encoded and delivered to the auditory nerve over myelinated axons (containing Nodes of Ranvier at regular intervals). Lorente de No has suggested, without further comment, three distinct signaling channels (groups of neurons) leave the auditory nerve[16].

As in the case of stage 1 signal generation, very few signals have been reported in the literature that reflect stage 2 signal processing prior to their encoding by stage 3 circuits. One exception is a brief comment in Ross[17]. He reports on the presence of multipolar neurons in the spiral ganglion as confirmed by Kimura et al. in their study of human material.

6.1.1.3 Stage 2C signal processing, within the cochlear nuclei

The cochlear nuclei perform a wide range of signal processing. While these bodies have been studied extensively, particularly in the cat, from a morphological and top level electrophysiological perspective, little effort has been expended on understanding the functional significance of these circuits. Because the circuits are so complex, it is frequently necessary to employ more complex analytical techniques. It is frequently necessary to determine the transfer function of a signal path of a circuit between its principal terminals while accounting for gating of that signal path by signals applied at its auxiliary terminals. As a result, the performance description of the circuit requires both a main stream transfer function and a logic-table describing temporally when the transfer function is realized. Only recently, reports have begun to document the operation of specific circuits sufficiently to allow the development of

the necessary transfer functions and logic-tables. Oertel & Young have provided a recent review that summarizes considerable data in text form[18]. Careful study of this material can lead to the description of some top level transfer functions and logic-tables. As they note, the cochlear nuclei accept signals from the auditory nerve, the vestibular system and the proprioception system. The inputs from the auditory nerve are of several types. The two primary types are those from the IHC and OHC sensory neurons. The outputs of the cochlear nuclei are passed to a variety of feature extraction engines of stage 4. These include the inferior colliculus, multiple areas of the thalamus, the precision optical servo system, etc. In accomplishing its tasks, the typical cochlear nucleus can be subdivided into three principal engines (based primarily on data from the cat) as shown in Figure 6.1.1-3.

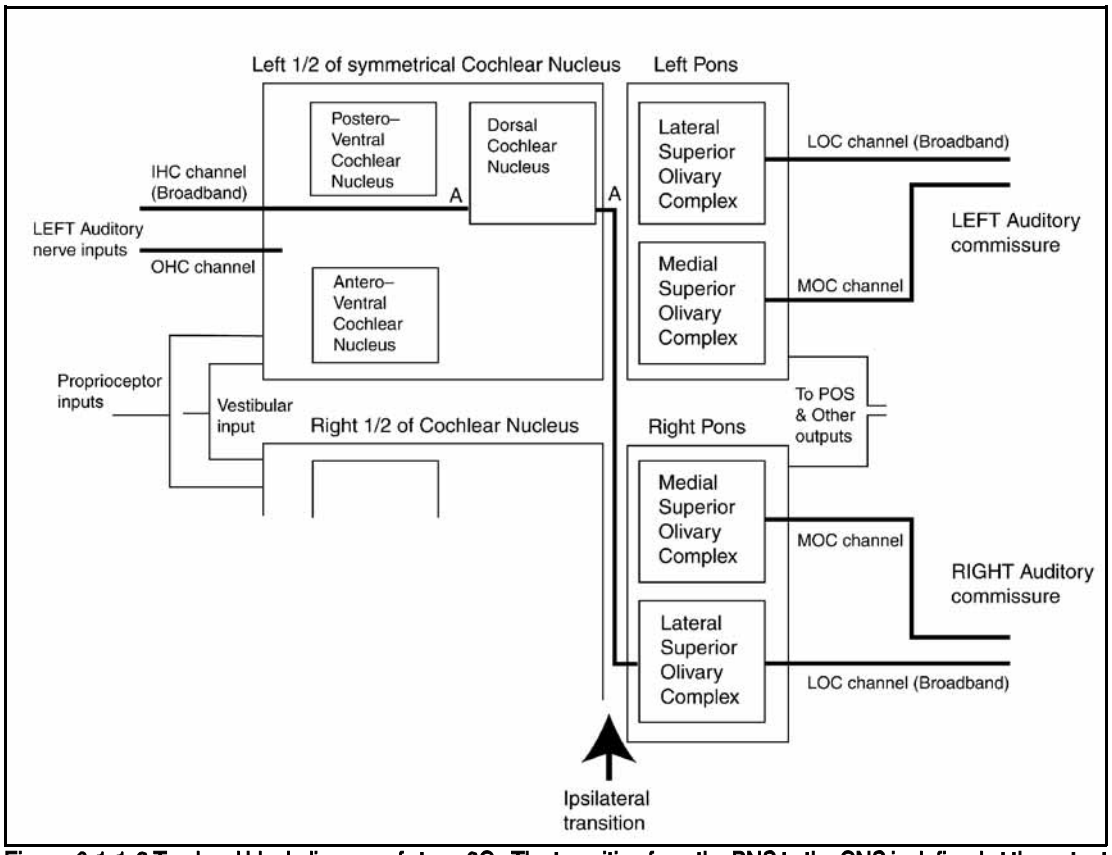

Figure 6.1.1-3 Top level block diagram of stage 2C. The transition from the PNS to the CNS is defined at the output of the cochlear nucleus. This places the ipsilateral transition before the CNS like in the visual system. The beginning of binaural processing requires showing both halves of the cochlear nucleus. The first occurrence of binaural processing is indicated by the crossing signals between these two halves. Label "A" shows the path of phasic axon signals originating in the fusiform and giant cells of the DCN en-route to the inferior colliculus as proposed by Oertel & Young in 2004.

6.1.2 Scope of signal processing within stage 2

Research into the signal processing associated with stage 2 of the hearing modality is still in an early exploratory research phase. While considerable research has been carried out within the cochlear nucleus, stage 2C, very little has been carried out with regard to the spiral nuclei, stage 2B, and little or no results are available with regard to the initial combining of the outputs of sensory neurons in stage 2A. Two classes of signal processing neurons have been encountered. Summing neurons, generally described as excitatory-excitatory based on the result of input to their dendritic inputs, are clearly present in stage 2C. Similarly, differencing neurons, described as excitatory-inhibitory based on the result of stimulating their dendritic and poditic inputs, are also present in stage 2C. However the presence of differencing neurons has not been documented in stages 2A or 2B.

Care must be taken to differentiate between;

1. the acoustic bandwidth of any stage 1 sensory neuron channel,
2. the electrical bandwidth of any stage 2 channels based on electrophysiology,
3. the pulse rate of any associated stage 3 neurons, and
4. data collected psychophysically involving the wider critical bands or equivalent rectangular bandwidths exhibited by the overall system.

The acoustic channels defined at the input to stage 1 sensory neurons tend to have Q values allowing the detection of frequency differences on the order of 0.3 percent of the center frequency. On the other hand, the psychophysical bandwidths determined based on noise masking tend to be between one-sixth (16%) and one-third (33%) of the center frequency. These wider bandwidths are associated with stage 4 correlation and will be discussed in Chapter 8. Between these two bandwidths, the bandwidths of the stage 2 and stage 3 circuits are generally unrelated to either of them. These channels have typical bandwidths on the order of 250-500 Hz regardless of these other bandwidths. The pulse rate of the action potentials within these narrower channels are typically less than 500 pps.

Smoorenburg et al. have provided extensive data extracted from the anteroventral cochlear nucleus of the cat (part of stage 2C)[19]. The data represents stage 3 action potential pulse rates resulting from earlier analog signal processing in some part of stage 2. Much of the data shows beat frequencies resulting from two simultaneous high level stimuli. The data deserves close study. It strongly suggests broad bandwidth temporal channels (as proposed in this work) or the summation of a large group of tonal channels representing a broad frequency range. However, no effort was made to determine the input spectra resulting in the output of the neurons investigated. While they strongly suspect nonlinear processes prior to the stage investigated, they are unable to predict the location of such processes or whether it is fundamentally neural or acousto-mechanical.

Rhode et al. have provided similar data to that of Smoorenburg et al. from the cochlear nuclei (stage 2C)[20,21]. Rhode & Smith then proceeded to explore the signals (unrelated to the specific neurons of the earlier studies) within the auditory nerve originating in stage 2B and leading to the cochlear nuclei[22]. The paper is worthy of considerable study. Their results strongly suggest the signals they recorded were from two different populations, one population of broadband (IHC) channels (figure 3) and a second population of narrowband (OHC) channels. Their histograms represent the P/D response of the appropriate sensory neurons as proposed by this work. The histograms clearly show the integration frequency limit of the adaptation amplifiers. They also noted two distinct populations of neurons based on their spontaneous rate of pulse generation in the absence of overt stimulation. Stimulation due to the systolic operation of the vascular system may have been present. They also measured latencies between the stimulus and the first recorded action potential. This latency varied considerably with stimulus level as predicted by the P/D equation of this work.

The delay in signal interception between the different OHC rows may be significant in the overall signal processing architecture. While it is not directly involved in the stage 2 signal processing, its impact is best manipulated with respect to this stage. The precise delay is not readily taken from the literature. Assuming the underside of the tectorial membrane is uniform in surface tension (an unlikely case at the detailed level), the delay can be calculated from the distance between the rows and the nominal phase velocity of the surface wave. Using figure 107 from Harada[23], the spacing between the rows is about 12 microns in rabbit. This would generate a delay of about four microseconds based on a 6 meters/sec acoustic propagation time. This interval is probably negligible within the stage 2A signal summing circuits. Compensation within the neural system could be provided by the routing of the dendrites of the neurons to parallel the path of the acoustic energy reaching the OHC.

6.1.3 Terminology

Terminology becomes a problem in this chapter because the relevant experimental history is all based on the concept of the neuron as a two-terminal device. In addition, the concepts of excitatory postsynaptic potentials (ESPS) and inhibitory postsynaptic potentials (ISPS) are never explicitly defined. They are generally used when discussing the potentials at the axons of a neuron prior to any synapse at that location and generally appear to relate to some earlier undefined synapse. Their conceptual definition fails when the neuron is considered a three-terminal device. In this work, the ESPS neuron will be equated to signals entering the non-inverting or summing input to an analog neuron. The ISPS neuron will be equated to signals entering the inverting or differencing input to an analog neuron. A single neuron is perfectly capable of summing signals applied to either its dendritic or poditic arborizations (separately) and subsequently forming the difference between these summations at its pedicle.

Much of the early work on the cochlear nucleus was performed by morphologists. Lacking a detailed understanding of the physiology of the neurons, they assigned them fanciful names (bushy cells, octopus cells, etc.). When the physiologist entered the picture, they gave less than functionally descriptive names to many of the waveforms observed. As a result, the terminology in this area does not contribute to the understanding of the underlying

physiological and functional relationships. As an example of the definitions used, Young et al. made the following qualitative observation related to "chopper neurons[24]."

> "The most striking difference between the response properties of primary-like and chopper units is the regularity of their discharge. . . . The primary-like units's discharge is irregular, by which is meant that the number of spikes and the pattern of discharge vary greatly from burst to burst. . . . In contrast, the response pattern of the chopper is regular in that the number and pattern of spikes are repeatable from burst to burst and the time intervals between successive action potentials are much less variable than for the primary-like units."

Young's observation will be shown to be anecdotal in Chapter 7 where changing the stimulus level alone will change the character of the output of a chopper-type neuron.

Most of the neurons of the CN that have been investigated have been stage 3 neurons. They have been either pulse-to-analog signal conversion neurons (at the entrance to the CN) or analog-to-pulse signal conversion neurons (at the exit of one of the engines of the CN). The vast majority of the neurons within the depths of the CN have not been studies or reported because their analog input and output characteristics are extremely difficult to interpret based on the current level of understanding of the circuit diagram of the CN.

Very recently, the physiologists have begun to introduce prefixes to some of the fanciful names in order to define them more clearly. T-stellate and D-stellate designations are now appearing in the literature, but not always with specific functional descriptions[25]. Additional differentiation between these morphological and physiological descriptions will be introduced in Chapter 7.

6.2 The architecture of stage 2 signal processing

Because of the great difficulty in accessing the neurological elements of hearing within the cochlea, only very limited morphological information is available. Most of the available data is based on light microscopy that is very limited at the resolution required to isolate the individual neural elements.

The empirical data on stage 2 signal processing is extensive and contradictory. Interpreting the data with precision was virtually impossible until it was shown in the previous chapter that the sensory neurons operate as integrators (not rectifiers). They operate in one mode below 600 Hz and an entirely different mode at frequencies above 600 Hz. These old empirical results must be reviewed and reinterpreted based on the operation of the sensory neurons as integrators. The compression process found in the distribution amplifiers of the sensory neurons is also important in understanding the nonlinear performance associated with much of the stage 2 data.

Describing the physiological signal processing architecture subsequent to stage 1 signal generation is particularly difficult because of the very limited amount of data from the direct measurement of signals at the pedicles of the IHC and OHC and virtually no measured data from the axons passing through the habenula perforata on the way to the spiral ganglia. Similarly, little data has been collected concerning the organization and types of signals passing down the auditory nerve to the cochlear nucleus. Lacking such data, the level of detail available concerning stage 2 processing decreases with distance from the sensory neurons.

Initially, it was assumed the stage 2 signal processing found in vision could be used as an analog for interpreting the stage 2 signal processing in the auditory system. The visual system does not provide a good analog.

As a result, the signals found at the output of the cochlear nucleus, and even the spiral ganglia are already so complex that many of them cannot be interpreted with precision or traced back to their origins.

6.2.1 Initial stage 2A architecture based on limited morphology

The early morphological work of Lorente de No and of Spoendlin is crucially important to understanding the physiology of hearing. Unfortunately, their material only provides caricatures in the form of unique individual sketches of what they strove to see through very limited instrumentation. The potential signal architectures used in even obsolete man-made communications and control systems are far more complex than those suggested by the individual views from Lorente de No and from Spoendlin. The man-made systems use overlay structures far more complex than the simple line drawings of these investigators. Fernandez has provided a series of figures showing a greater variety of signal processing strategies in the various turns of the cochlea of the guinea pig[26]. However, these remain snapshots of a very complex structure where the intent of the author is not known in detail.

The simple diagram from figure 15 of Spoendlin provides a starting point for defining the signal processing architecture[27]. Spoendlin showed that the signal from an individual IHC was provided to multiple stage 2 neurons. On the other hand, he showed that signals from multiple OHC were summed at the input of stage 2 neurons. Since there are multiple rows of OHC, it is necessary to determine how this additional architectural feature is addressed by the neural system. In the same paper, Spoendlin shows an early representation of this architecture. The suggestion is that one neurite addresses several consecutive OHCs in one row and then moves up to the next row. In that row, it interrogates another sequence of OHCs that are farther along the array than the first sequence.

The fact that sensory information at frequencies below 500-600 Hz is treated differently from that at higher frequencies within stage 1 suggests another gross architectural feature. It appears that the direction finding techniques used at low frequencies may be sensitive to the phase of the incident acoustic energy at each ear in addition to the arrival time of the energy envelope. This feature may be implemented partly within stage 2 and preserved in the encoding used in stage 3.

Lorente de No has provided a more detailed description of the neural paths associated with one knot of the spiral ganglia in the mouse[28]. It is in close agreement with an earlier schematic by Cajal (1909) except for one major feature. The Cajal graphic (reproduced in Lorente) shows "beads" along the conduits between the sensory neurons and the neurons of the spiral ganglia as well as between the spiral ganglia and the cochlear nucleus.

The research of Lorente de No offers additional details with respect to these connections. A staining regimen was used that favored afferent neural structures over efferent structures. The efferent paths, leading primarily to the IHC, are not shown. When examined closely, it is clear the numeric notation of Lorente de No was primarily in support of his discussion. Only selected fibers have been numbered (hand-drawn numbers) and only a few features have been given alphabetic labels. He makes it clear in the subsequent 1981 discussion, that the figure is a composite of a series of individual sketches made by observing a series of slices through the Organ of Corti. As he noted, the composition relied upon mental connection of fibers between individual views observed through the microscope. The image is not obtained photographically. As also noted in the 1981 discussion, the variation in efficacy of the staining process results in different levels of detail in the different slices. The staining used by him and Cajal is only applicable to very young animals. Both Lorente de No and Cajal used mice as their subjects.

Iurato has offered an alternate composite freehand drawing similar to the Lorente figure[29].

Lorente de No has provided an operating scenario between both the IHC and OHC class of sensory neurons and the spiral ganglia (without recognizing any role for the beads). It is quite plausible that the beads are Nodes of Ranvier and act as action potential pulse regenerators at intervals along the signal path. If this is the case, the first bead (counting from the sensory neurons) constitutes the signal encoding conexus of the neuron with subsequent Nodes of Ranvier (beads) acting as signal regenerators in the normal signal propagation architecture. If correct, this architecture would limit stage 2A (analog) signal processing to the region between the pedicles of the sensory neurons and the first Node of Ranvier. Wever has provided a fusion of the work of Retzius, Solovcov and Lorente de No[30].

Schwartz has provided a recent perspective and extensive bibliography on the neural connections between the spiral ganglia and the sensory neurons[31]. However, her projections of the peripheral neuron pathways do not add significantly to the previous record. She does focus on the division of the neurons of the spiral ganglia into two major classes, type I and type II. The type I neurons are significantly larger than the type II neurons and are more heavily myelinated (even including the soma area). Groups of type I neurons appear to synapse with an individual IHC while groups of OHCs synapse with a single type II neuron. No discussion ensued concerning the great expansion in the number of axons leaving the spiral ganglia compared to the number of neural paths entering it.

6.2.2 The gross topology of the PNS portion of the auditory system

There have been few attempts to model the complete neural topology of the auditory system outside of the CNS. This is understandable in the absence of a physiological model of the basic neuron. It appears that the similar topology of the visual system may provide guidance.

Figure 6.2.2-1 presents an annotated version of two figures from Kiang[32]. Frame A shows the arrival of neurons (apparently involving the OHC neurons as sources) at the cochlear nucleus in nerves associated with individual knots of the spiral ganglia. Only the paths labeled the descending branch of the nerves following this path are shown. Following Lorente, each knot receives signals from approximately 18 neurons serving possibly 24 IHCs and possibly 72 OHCs. Kiang does not address the ascending branch of the auditory nerve directly (details in Section 6.5). The

figure does show an additional bifurcation of the descending branch. It is proposed in this work that this bifurcation separates the neural signals arriving from the IHCs and from the OHCs. Kiang and other early investigators were silent on the reason for this bifurcation.

Frame B includes the notation used by Kiang. He attributed part of the notation to Osen[33]. In some cases, Kiang showed an alternate notation from Brawer et al. in parentheses[34]. While the names shown on the right are rather abstract, they are far less fanciful than the earlier names assigned by the above investigators. Neuron #1 was described as "primarylike" referring to the similarity of the response to that frequently found in the auditory nerve to a simple tone burst (as shown at left). #2 was labeled a "chopper." #3 was labeled "primarylike with notch" (next to the spike). #4 was labeled "On" referring to the fact that the pulse coincided with the initial pulse in a string of pulses. #5 was labeled a "pauser" for no obvious reason.

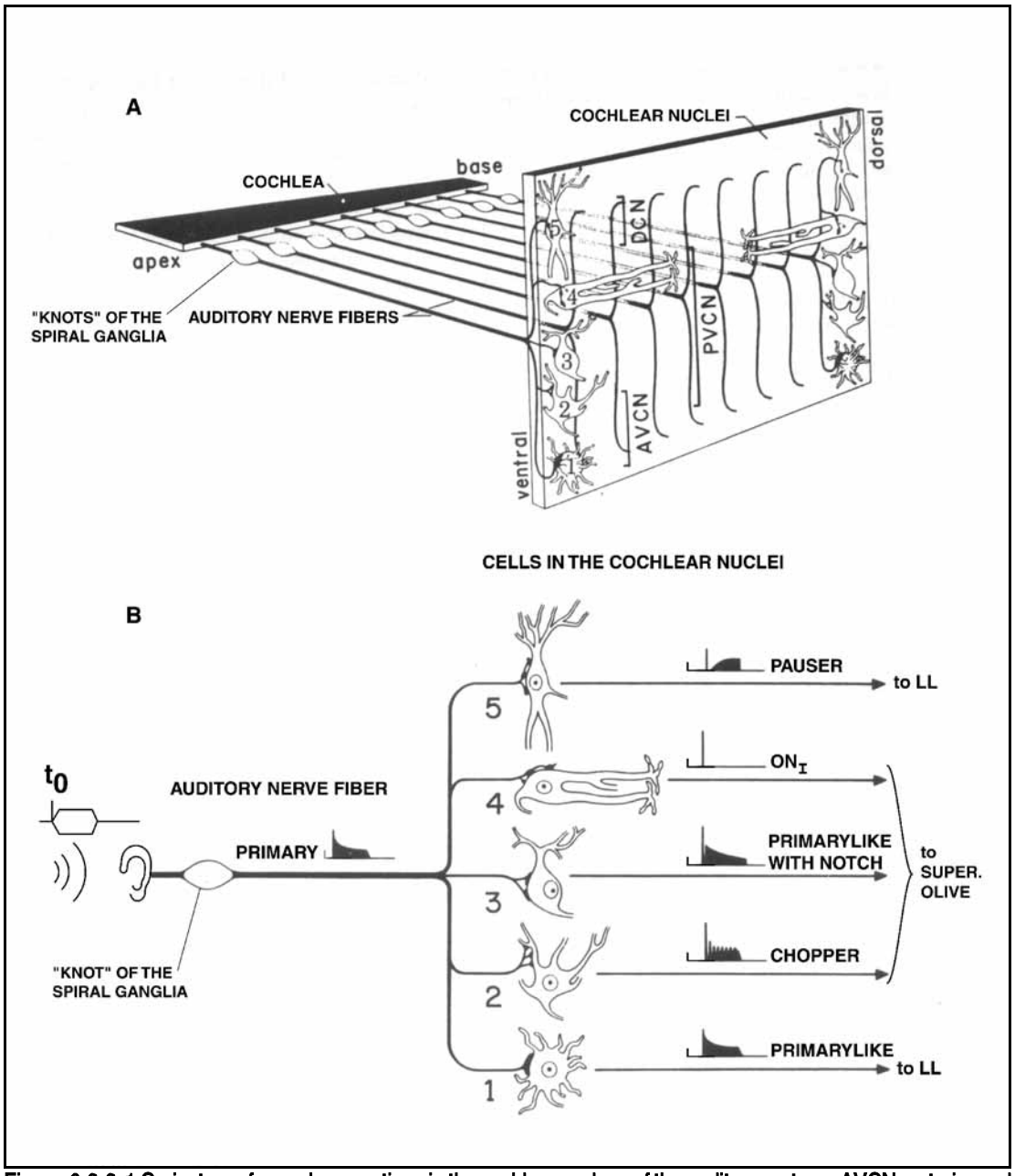

Figure 6.2.2-1 Caricature of neural connections in the cochlear nucleus of the auditory system. AVCN, anterior and PVCN, posterior ventral cochlear nuclei; DCN, dorsal cochlear nucleus. #1; spherical bushy cell in the AVCN. #2; multipolar (stellate) cell present in the posterior of the AVCN and the anterior of the PVCN. #3; globular (bushy) cell found in the interstitial nucleus and the anterior of the PVCN. #4; octopus cell occupying region in te posterior of the PVCN. #5; pyramidal (fusiform) cell found in a distinctive layer of the dorsal cochlear nucleus. See text. Expanded and annotated from Kiang, 1975.

The time delays for each of the PST histograms, with reference to t_0, was not given in the original paper. This information would be invaluable in describing the circuits both ahead of and following each neuron. The target locations in the right margin are only suggestive. The above authors give conflicting descriptions of where these neurons typically terminate. There are probably multiple terminations for most of these neurons.

Using the Electrolytic Theory of the Neuron as a framework, additional information can be extracted from Kiang's extensive discussion. It appears likely that neuron #1 is simply a relay neuron delivering its copy of the primary pulse burst to the MSO and the inferior colliculus via the trapezoid body. The type #4 (octopus) neuron is particularly interesting. Its single-pulse output corresponding to the initial pulse in a string of action potential pulses at its input. Such a circuit is ideally suited to participate in the "boxcar" circuit described in Section 6.5.5. The combination of an octopus circuit from each binaural signal path and a boxcar circuit located in the superior olive is ideal for determining the relative delay in the neural signal and therefore the direction of the original stimulus relative to the sagittal plane. The purpose of many other neural circuits can be defined based on the discussions in the above papers. However, additional timing information would be required to be explicit.

> Oertel et al. have provided the morphology of a group of octopus cells. However, their physiological descriptions must be read carefully. They were shocking, and potentially changing the bias of, their octopus cells to obtain a phasic action potential output. Their results may be pathological[35].

The recent revision of Jahn & Santo-Sacchi contains considerable new material related to the routing of the neurons via the auditory nerve to the cochlear nuclei[36]. The graphics provided by Pujol (Chapter 22) and by Brown (Chapter 23) further confirm the dual path nature of the auditory system.

6.3 Stage 2A signal processing within the cochlear partition

A cursory review of the literature suggests the signal processing in stage 2A of the auditory system is homologous with that within the neural layer of the retina closest to the sensory neurons of the visual system. The problem is our lower level of understanding of this part of the auditory system. This has been caused primarily by the great difficulty of examining the initial signal processing circuitry embedded in the bony structure protecting the cochlea. There are very few recordings of the auditory signals at the pedicles of the sensory neurons. There are essentially no analog recordings from the pedicles of stage 2A signal processing neurons in the spiral ganglia although there is evidence from stage 3 recordings of such signal processing[37]. By comparing the architecture of the auditory system to that of the visual system, and using the available psychophysical data, it is possible to establish the scope of stage 2A signal processing.

As noted in Section 6.1.1.1, the resolution of the microscopy, used to identify the neurites synapsing with the sensory neurons of hearing during the 1960s and 1970s, was inadequate. The published counts of OHC and IHC related afferent neurons are almost entirely dependent on the numbers provided by Spoendlin in the 1960's based on light microscope and very early electron microscope investigations. The numbers have been reproduced many times and criticized many times. In 1988, Spoendlin reviewed the status of this area of research and made some very important statements. After reviewing some work by Liberman, Spoendlin made the following comment. "All 56 recorded and labeled neurons from 14 cats were type I neurons associated with the inner hair cells. This strongly suggests that the activity of outer hair cell innervation has never been sampled in any of the single-unit recordings from the auditory nerve, which is possibly because the central axons of type II neurons are probably not recordable, being unmyelinated and less than 0.5 μm in diameter." This statement raises the question of what percentage of these small diameter type II neurons associated with the outer hair cells were documented during the 1960's and earlier.

Even up through the most recent investigations, it was still assumed that all neurons were two terminal devices. No papers could be found that even considered that some of the stage 2A neurons might exhibit bifurcated arborizations supporting the creation of signal differences within a single neuron. There was also no clear differentiation between the roles of the IHC and the OHC neurons. Nomuro even asked the following rhetorical statement. "There must be a functional difference between the internal and external hair cells[38]." The functional differences between, and responsibilities of, the IHC and the OHC are clear under the SAW-based Dual-Channel Electrolytic Theory of Hearing. The outer hair cells are responsible for the frequency selectivity of the auditory system and the inner hair cells are responsible for the temporal aspects of hearing.

Additional work using modern instrumentation is sorely needed in three major areas.
- The documentation of the actual number of OHC-related afferent neurons present in a single Organ of Corti.
- The documentation of the actual number of IHC-related afferent neurons present in a single Organ of Corti.
- The documentation of the interconnections between the sensory neurons and the signal processing neurons of a at least a single knot of the spiral ganglia.

This work must be based on the assumption that all neurons are three-terminal devices, and the OHC and the IHC support uniquely different purposes.

In the absence of dependable data in the above three areas, the previous speculations about the relative numbers of neural paths leading from the sensory neurons to individual neurons of the spiral ganglia, and to the neurons of the spiral ganglia as a group, cannot be supported.

The challenge is to rationalize the psychophysical performance of human hearing with the limited morphological data such as that shown in Figure 6.1.1-2. The spacing of the individual rows of OHC neurons would suggest a frequency discrimination capability on the order of 0.3% of the center frequency of each row. This is roughly the spectral selectivity achieved routinely by trained musicians. However, the summing of OHC signals from multiple rows, as suggested in that figure and by others, would suggest a much lower frequency selectivity for the subject. Either additional innervation must be present supporting individual rows of OHCs, or an additional computational capability must be present to support the measured performance using a cruder sensory array.

6.3.1 Background

Other than the material discussed above, there is no substantive literature describing the neural topography supporting stage 2A signal processing.

Kimura et al. have corroborated the presence of "multipolar neurons in the spiral ganglia of humans[39]." They introduce the potential that the spiral ganglia support a more expanded role as a significant source of stage 2 signal processing. These neurons may also lead to an understanding of the role of the efferent fibers synapsing with the sensory neurons of hearing.

Two groups of papers in the audition literature suggest a strong parallel between the stage 2 signal processing in the visual system and the auditory system. Smoorenburg et al. provide data on the intensity channels of the auditory system that are very similar to the summing circuits of the luminance channel of the visual system[40]. Brugge et al. have provided some excellent data[41]. The data suggest there are channels that are taking differences between audio signals analogous to the chrominance channels of vision.

6.3.2 Neural structures interfacing with sensory neurons

The degree of myelination of the afferent neurons interfacing with the IHC and OHC provide information concerning stage 2A signal processing. The neurons interfacing with the IHCs are found to be myelinated from a point very near the pedicles of the IHCs. The myelination begins immediately after the first Node of Ranvier (as defined in this work). This node is actually acting as the encoder transposing the analog information into the phasic domain. Physiologically, it is acting as the conexus of a ganglion neuron that is physically separated from the soma of that neuron. Neurons synapsing only with individual IHC neurons will be labeled as Type B (broadband) neurons here. Previous theories of hearing have not uniquely identified the type B broadband channels proposed to be associated with the IHC in this work.

The neurons interfacing with the OHCs are distinctly different. Each neuron has an extended dendritic structure synapsing with multiple OHCs. The myelination does not begin until after the termination of the dendritic structure at what appears to be a Node of Ranvier morphologically. Here again, this structure acts as the encoding element of the neuron even though it physically precedes the soma. If only performing signal accumulation from one or more OHC, these neurons will be described as Type N (narrowband) in consonance with the bandwidth of the information associated with these neurons. As noted earlier, the lack of myelination and the small diameter of the individual dendritic branches of the type N neurons have made their tracing extremely difficult.

Stage 2A neurons performing signal differencing will be given different labels when/if their presence is confirmed.

Both the type B and type N neurons generally exhibit dendritic branching and multiple boutons contacting each sensory neuron. This feature provides both circuit redundancy and higher total current capacity for each neural path.

6.4 Stage 2B signal processing within the spiral ganglia

Because of the limited data available relative to stage 2A topology, stages 2B and 2C must be discussed primarily from the perspective of traffic analysis, although the structure of some simple signals can be discussed based on their probable origin.

Research concerning the spiral ganglia has been restricted because of the extremely difficult problem of gaining access. As a result, most of the available literature relates to the morphology of *in-vitro* neurons and the chemical

environment of the matrix surrounding these neurons. The majority of the physiological information about the analog neurons of the spiral ganglia comes from recording the pulse streams of stage 3 neurons emanating from the spiral ganglia. These recordings are typically made by probing the auditory nerve at an unspecified distance from the encoding stage 3 neuron within the spiral ganglia.

The morphological research is not particularly useful. It leans heavily on the researchers' proclivity to divide everything into two groups, type I versus type II cells, myelinated versus unmyelinated cells, monopolar versus bipolar cells, etc. As a general rule, these properties are continua. The morphological designation monopolar versus bipolar is entirely a matter of packaging convenience and involves no functional difference. In many cases, cells described as unmyelinated are frequently "encapsulated" by material from an adjacent cell. Only an occasional investigator notes the myelination of the input neurites of some of the neurons of the spiral ganglia. Because of the complexity of the work, most of the investigations have relied upon a sampling approach, particularly at the ultrastructure level. Because of the small sample sizes, the information is usually suggestive but seldom statistically relevant.

The best available morphological information concerning the spiral ganglia appears to be in Otte et al[42]., Ota & Kimura[43], Kimura et al[44] and in Schwartz[45]. Many papers rely on Spoendlin in their introductory remarks, suggesting that type I neurons are large and originate at inner hair cells while the origin of type II neurons remains unclear. Kimura et al. back away from this position in their concluding remarks. ". . . unmyelinated large neurons which constitute the majority of the population in human ears appear to innervate inner hair cells or both inner and outer hair cells."

The limited *in-vitro* electrophysiological research has confirmed the conventional performance of the stage 3 neurons associated with the spiral ganglia based on axonal patch-clamp techniques. This research also confirms the existence of neural types other than previously reported[46]. While the work of Mo & Davis confirmed the hyperbolic relationship between the inter-spike interval and the injected current, they assumed the neurons were two terminal devices and did not determine the input/output characteristic of these neurons. While they did not provide absolute potentials for their waveforms as a function of time, some of their parametric data does. What they have not determined is whether such phasic performance is associated only with stage 3 encoding neurons at the output of the spiral ganglia or whether it is associated with relay neurons connecting directly between the stage 2A inputs and the auditory nerve.

Reid et al. make an interesting observation[47]. The one neuron they were able to trace to the neurons of stage 2A did not generate action potentials (p. 740). It was apparently a stage 3 decoding neuron providing an analog signal to multiple neurons of the spiral ganglia for further processing. If confirmed, this would suggest the neurons of the spiral ganglia perform more complex signal processing than just in-line processing.

6.4.1 The gross encoding of the afferent signals within the auditory nerve

Doucet & Relkin have reported on exploratory research regarding the signals of the auditory nerve on a global basis[48]. They have recorded signals using a capacitive probe rather than penetrate a specific neuron. They compare three waveforms in their figure 1. All were presumably collected using the bandpass filters they describe. The first appears to be a generic compound action potential (CAP) measured at the round window. Its overall duration was not shown in comparison to the stimulus duration of 16 ms. The other two signals were measured at the auditory nerve following significant signal manipulation within the spiral ganglia. They describe these waveforms as peristimulus compound action potentials (PCAP). However, these waveforms were not shown to display any of the simple features of the conventional CAP. They appear to represent a global summation of potentially a large number of stage 3 neural outputs summed by capacitive coupling. The model they used to validate their observations did not contain any adaptation mechanism or nonlinear compression.

The separation of the frequency and intensity related neurons within the auditory nerve provides the necessary cues to define the nature of these stage 3 signals. Liberman has provided extensive data on the signals emanating from the spiral ganglia, stage 2B, in cats[49,50,51]. However, he did not report on the types of signals as a function of their position within the auditory nerve.

6.4.2 The density of ganglion neurons in the spiral ganglia

Data describing the density of neurons along the spiral ganglia is quite sparse. Rasmussen & Windle have provided some data[52]. However, the data does not differentiate between neurons associated with what might be called "straight through" signal paths and those that are associated with more extensive signal processing within the spiral

ganglia. They also showed that the number of neurons within the spiral ganglia declined quite significantly with age (to about one-half at 71 years of age). They did not describe the spiral ganglia as divided into knots. Otte et al. provided a more interesting perspective when they showed the geometric arrangement of the spiral ganglia relative to the cochlear partion in humans[53]. Figure 6.4.2-1 shows their relationship between the spiral ganglia and Hensen's stripe. Liberman & Oliver have provided a generic three-dimensional caricature of the same relationship. Their caricature suggests definite knots of neurons along the length of the spiral ganglia[54].

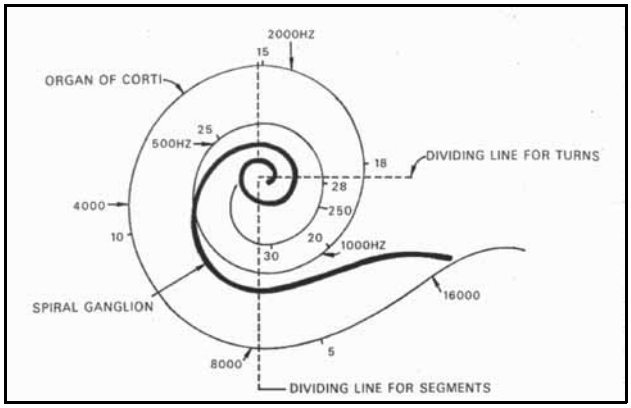

Figure 6.4.2-1 Relationship between the human spiral ganglia and Hensen's stripe. The spiral ganglia is out of plane relative to the cochlear partition. From Otte et al., 1978.

6.4.3 Representative signals at the output of stage 2B

A great amount of data has been acquired by probing the auditory nerve during carefully controlled acoustic stimulation. These phasic signals are stage 3 signals representing the output of the stage 2B signal processing. Unfortunately, little effort has been expended on determining the neurological sources and signaling paths related to, and generating these signals. By the time the signals reach the auditory nerve, it is very difficult to specify how the signals were created at a detailed level without ambiguity. As noted in Section 2.3.6, the fact that the auditory nerve twists as it progresses toward the cochlear nucleus makes documenting the relative position of the neurons inside it awkward.

Besides the work of Reid et al. and of Mo and Davis noted above, the work of Smoorenburg et al. and Brugge et al. also help define the character of the signals output by the spiral ganglia. Unfortunately, none of these groups traced their signals back to their sources. As a result, multiple explanations of how the signals were created can be presented. Smoorenburg et al. recorded sub-harmonic signals related to the sums and differences of two applied stimulus frequencies. Based on the large difference in frequency between the stimuli, the recorded signals were either from individual broadband IHC channels or they involved the summation of signals from multiple narrowband OHC channels within the spiral ganglia. In either case, the sub-harmonics could be associated with nonlinear mixing at multiple locations within the system.

Brugge et al. presented interesting data showing good phase continuity between the stimuli and the action potential pulse rates. However, they used an inappropriate ordinate in their histograms that suggests more nonlinearity in the system than appropriate (Section 7.5.1). Their data is quite consistent with what would be expected from the application of two stimuli of different frequencies to a linear system. The frequency differences used also suggest IHC channels were involved or there was significant summation of the OHC channels within the spiral ganglia.

> As an aside, Smoorenburg et al. made the following comment without further discussion (page946). "For nine neurons a purely negative spike was recorded." Such a spike within the axoplasm of a neuron is not compatible with the Electrolytic Theory of the Neuron. However, such a spike is completely compatible if measured in the podaplasm of the ganglion cell. In this case, it would generally have a negative-going amplitude of less than 20 mV. These signals could easily be confused when probing in the area of the hillock of the neuron.

Smoorenburg et al. provide considerable data regarding the threshold level for the generation of action potential by the driven ganglion cells and other characteristics of the auditory system. These data will be discussed in detail below.

6.5 Stage 2C signal processing within/adjacent to the pons

An area just below the midbrain, the pons (sometimes labeled the medulla), contains a variety of neural engines associated with hearing. These include the cochlear nuclei, the superior and inferior olives and a large group of neurons forming multiple engines but generally labeled the trapezoid body (Section 2.2.2). Various parts of the auditory nerve terminate in these engines. However, exactly how and where different parts of the nerve terminate remains unclear. Moore & Osen have provided a photograph of this region and many camera lucida images[55]. They

describe the unusual morphological orientation of the cochlear nucleus in humans. They also provide an estimate of 96,000 neurons in the human cochlear nuclei. This appears to be an estimate for the cochlear nucleus on one side of the pons. They also provide references to the fanciful names of neurons used in this area of hearing morphology. No agreed neuron counts were located in the literature for the other engines of the pons.

Figure 6.5.1-1, modified and expanded from Morest[56], provides a cutaway of the pons area viewed from an angle. This view illustrates the right hand cochlear nucleus from the external perspective and the left-hand perspective from the internal perspective. This presentation highlights the ascending branch of the auditory nerve and the AVCN on the left. It also highlights the descending branch of the auditory nerve, and the PVCN and DCN on the right. Only the neural paths seen originating from these engines are shown in the overall figure. Kiang has provided a more detailed schematic without the perspective aspects[57].

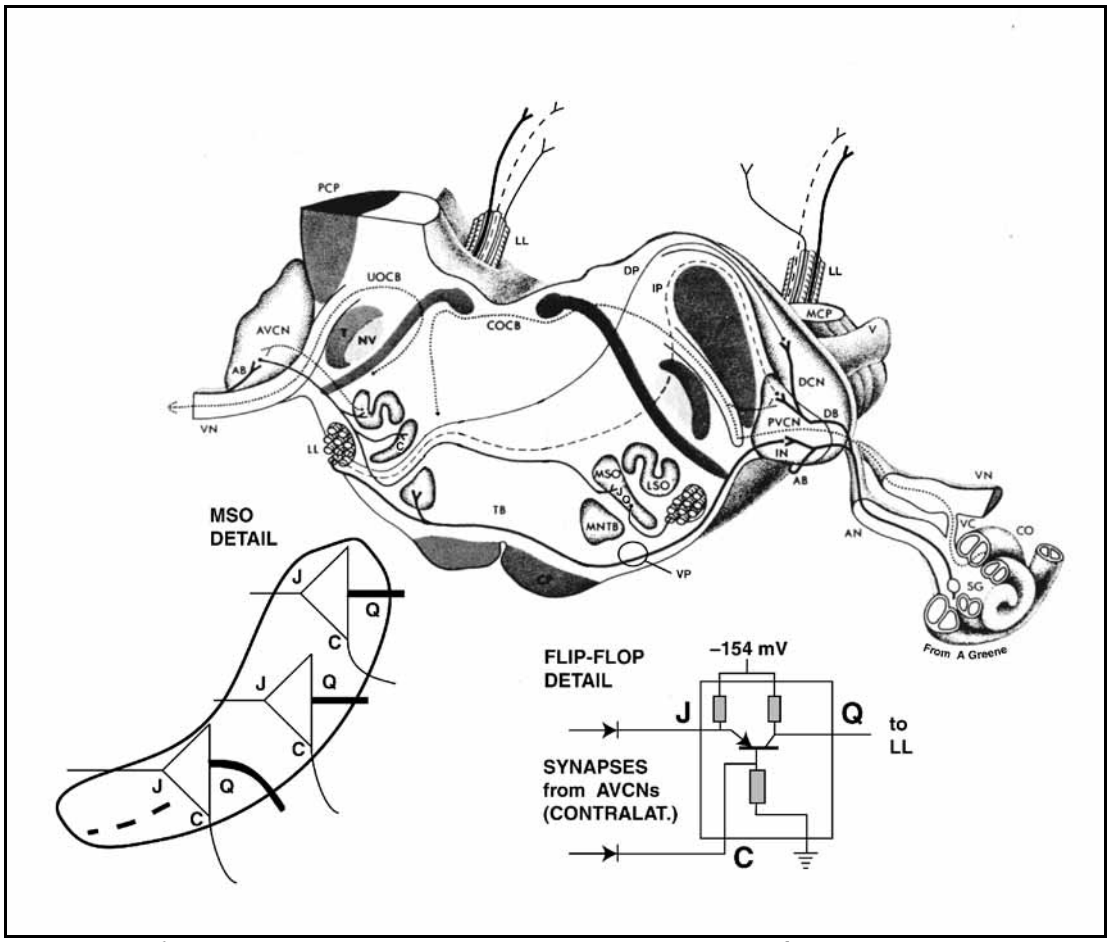

Figure 6.5.1-1 Cutaway of the pons region showing principle neural pathways. Symmetrical members of a pair of paths have been omitted. The primary neural path through the auditory nerve (AN) represents both the OHC related and the IHC related nerve bundles. This path continues through the cochlear nucleus via the interstitial nucleus (IN) and the ventral pathway (VP) to the contralateral lateral lemniscus (LL). Three major neural paths exit the pons via each lateral lemniscus; the primary neural path, the signal path from the MSO and DCN, and the signal path from the LSO and PVCN. Each MSO contains hundreds of comparator neurons (morphologically pyramid cells) functioning as flip-flops circuits. Each comparator neuron exhibits a medial dendrite (J), a lateral podite (C), and an axon (Q). The flip-flop detail shows the internal circuitry of the comparator neurons. The internal impedances associated with the dendritic (J) and poditic (C) terminals exhibit long time constants. See text. Main caricature adapted From Morest, 1975.

The physical dispersion of the engines of the pons make its comprehensive study awkward. Most of the prior work has focused on the cochlear nuclei, with a lesser volume of activity concerning the superior olivary nucleus (SON).

The great majority of the work has been morphologically oriented. The SON is divided into the lateral superior olivary nucleus (LSO) and the medial superior olivary nucleus (MSO) plus other minor engines. Three major pathways have been identified within the pons; the ventral (VP), the dorsal (DP) and the intermediate (IP) pathways.

The figure highlights the fact that the lateral lemniscus, LL, is a conduit and not a functional engine of the neural system. Three major nerves have been identified within this conduit; the fundamental auditory nerve component (heavy solid line) passing up the conduit to the thalamus, the output of the MSO (thin line) proceeding to the inferior colliculus, and the output of the LSO (dashed line).

The pons includes both ascending and descending neural paths and is the first ascending location where the major pathways change to the contralateral side. It is also the first location where the signals from both ears can be compared.

The paths labeled uncrossed olivocochlear bundle (UOCB) and crossed olivocochlear bundle (COCB) represent efferent signals originating in the pons, passing along the vestibular nerve (VN) and controlling the performance of the sensory neurons. These signals are generated in response to both local ascending signals and to signals descending from higher cognitive centers. Neither of these local ascending and descending signals are shown explicitly in the figure.

In agreement with Lorente de No, the figure shows the auditory nerve bifurcating repeatedly (on the right). Morest identifies four major neural bundles. The first bifurcation results in an ascending branch and a descending branch. The bifurcation of the descending branch results in neural groups going to the ipsilateral dorsal and posteroventral cochlear nuclei. A major portion of the ascending branch proceeds to the contralateral superior olive and lateral lemniscus by way of the ventral pathway. The references provide more details regarding these circuits.

There is a tendency in the literature to assume all the neurons of each auditory nerve terminate at their respective cochlear nuclei. This situation cannot be supported. Many neurons are seen proceeding to other engines along the ascending pathway.

In the nomenclature of this work, most of the neurons of the cochlear nucleus reported in the literature are phasic neurons of stage 3 arriving from stage 2B, not the analog stage 2C signal processing neurons of the engine. In some cases, these stage 3 neurons are decoding neurons such as the octopus cells. In other cases, they are merely relay neurons proceeding to other engines in the ascending path (as found in the interstitial nucleus, IN). The unique PST histogram of the "octopus" cell defines its role as a specialized decoding neuron (Section 7.3.5). Octopus cells are identified with the ascending branch of the auditory nerve and the AVCN. Finally, many of the neurons reported are stage 3 encoding neurons at the outputs of the stage 2C engines within the cochlear nucleus. The complexity of the PST histograms from these neurons attests to the complex signal processing carried on within stage 2C.

While the morphology of the cochlear nuclei has been studied most extensively, little has been learned about the physiology of any of these elements. Galambos et al. have provided very valuable information on the signal processing within the pons, and specifically within the medial superior olive (MSO) of the SON[58]. The MSO was identified by Galambos et al. using an earlier nomenclature, *n accessorius*. Their experiments involved both histology and electrophysiology and employed tone, click and noise stimulation in a binaural environment *in-vivo* using anesthetized cats. Although their study involved sampling, they did identify multiple neurons that belonged to each of a wide range of neuron types. Some neurons responded strongly to tones but were unresponsive to clicks and vice versa. Others responded to a mixture of tones and clicks. Galambos et al. followed an earlier protocol of identifying the stimulus level as a reduction from a high level. Thus their 75 dB was less intense than their 30 dB (fig. 7 caption). They also chose to note in their conclusions that "for several years (in 1959), it has been pointed out that the ear does not behave like a series of simple resonators, nor can the auditory brain be operating exclusively on merely a Fourier analysis of the acoustic stimulus (with references)." They also documented the shift in latency at the MSO due to stimulus intensity changes. These shifts conform to the shift predicted by the theoretical P/D response of the sensory neurons presented in Section 5.4. While this variation in latency complicates the signal processing within the pons, it is obviously accommodated.

Most of their waveforms are derived from large probes that did not penetrate a specific neuron. In one of the few figures with scales (fig 1), the voltage of 0.3 mV would indicate, and their text suggests, their signals were acquired from the interneural matrix and not from axoplasm. Their reference signal for timing was a signal collected with a bare wire near the round window. Galambos et al. encountered some signals with a duration as short as 0.3 ms. These suggest the presence of neural circuits operating at about three times the bandwidth of typical neural circuits, as might be expected in source location circuits. As discussed below, it is unfortunate that Galambos et al. did not

make any measurements relating to the absolute potentials relating to the plasmas of individually identified neurons.

As noted in many studies, the non-primates do not make good biological models of the human when studying the elements in the pons. Some sources assert the dorsal cochlear nucleus is vestigial in human. It is also asserted that within the superior olive, the medial superior olive is dominant in humans. The lateral superior olive is dominant in many species relying upon sound source location to maintain their ecological niche. This raises the question whether a given function relocates between morphological features in different species or whether previous morphological descriptions have been of limited specificity.

6.5.1 Background

Two papers by Evans & Nelson presented very valuable information on the signal processing within stage 2C[59,60]. The experiments involved more than 250 units from cats under various conditions of anaesthesia. While their experiments were largely limited to tones, they defined five distinct classes of signals. Some of the data suggests very complex summing and differencing of multiple OHC channels. The primary conclusion drawn by this author was that the signal processing of hearing has already become extremely sophisticated and complex within the cochlear nuclei of stage 2C. Only the source location task can be assigned to specific neurons within stage 2C at this time.

Keidel & Neff edited a volume containing considerable valuable material on the cochlear nucleus[61]. A paper by Goldberg discussing signals generated by both impulse and tone stimulation is very useful (pages 109-144). More recently, Hudspeth, writing in Kandel et al., has provided excellent material on the topography and some physiology of the cochlear nucleus[62].

Brown & Ledwith have provided extensive material on the paths of neurons from the spiral ganglia into the cochlear nucleus[63]. Their work was limited significantly by their reliance on light microscopy. They did not address any growth in numbers of fibers exiting the spiral ganglia compared to the number entering.

Shofner & Young attempted to place measurements of cochlear nucleus waveforms on a more stable foundation in 1985[64]. They did not describe in detail where they recorded action potentials in the cochlear nucleus. However, the waveforms are typical of those received from the auditory nerve. If they were measured at the entrance to the cochlear nucleus, they may be more representative of stage 2B processing than stage 2C processing. After organizing their recordings based on their PST characteristics and their response characteristics to tones and noise, they tried to show where some of their classifications were similar to those made earlier and assigned fanciful names. One of their observations is important: "The results of the present study show that a unit's classification in the PST histogram scheme is not uniquely related to its classification in the response map scheme. Nevertheless, systematic relationships do exist between the temporal discharge patterns and receptive-field properties of cochlear nucleus units." Their text model essentially ignored any signal processing associated with the initial afferent neurons (stage 2A) and the spiral ganglia (stage 2B). See Section 6.5.4. Their analysis was also dependent on their definition of a response map in an earlier paper by Young[65].

In 1988, Young et al. made the following revealing comment concerning the cochlear nucleus (CN)[66]. "Over the past 20 years the study of the CN has been in a 'stamp-collecting' phase, in that the important problems have been the definition of response types and correlation of those response types with morphological cell types. A detailed picture of the wiring diagram of the CN is beginning to appear, as is an understanding of the physiological mechanisms involved in generating CN responses." At that time, the neuron was still considered a two-terminal device. As a result, the discussion of wiring diagrams and physiological mechanisms remained mostly conceptual.

With most of the earlier work based on morphology, most of the recent results relate to the traffic flowing within and between the auditory nerve and the engines of the pons (with particular emphasis on the cochlear nuclei). In their studies of the efferent neural system, Warr, Guinan & White have provided a particularly clear drawing of the morphology of the pons and the cochlea of the cat[67]. The figure highlights the relationship between the spiral ganglia and the sensory neurons as well as the features of the pons body. Kiang has also offered a description of the gross signal routing within the pons[68].

Moore & Osen have provided a graphical comparison of the cochlear nucleus in the cat and the human[69]. They also provided a schematic of the major signal paths in the pons. Unfortunately, their figure contains a great many paths without any precisely defined termini.

The complexity of the signal processing within the cochlear nucleus is so complex and extensive that Lorente de No suggested it be described as a "minibrain." It is this complexity that makes it difficult to decide whether its ultimate

purpose is signal processing (a stage 2 function) or signal manipulation (a stage 4 function involving information extraction rather than intermediate signal processing).

Lorente de No (1981) has shown that the histology of the neural tissue of the cochlear nucleus is the same as that found in the cerebral cortex and most other areas of the cortex (generally excluding the thalamus). It is largely a thin sheet with several individual laminations. The extreme thinness of the complete neural layer is indicated. The fact that all neural connections are made from one side is also typical of cortical material. A great many of the smaller neurons of layer one were not shown. Describing all of the connections and individual neurons is extremely difficult because of the variety of staining techniques required to annotate those features. Harrison has reproduced (page 129) a figure from Ranson & Clark that provides a useful comparison of the results obtained by individual staining techniques[70] (Section 8.1.1).

6.5.2 The physiology of the cochlear nucleus

No concise description of the functional role of the cochlear nucleus has appeared in the literature. Its internal complexity suggests multiple functional roles. However, its location suggests its primary roles are still related to signal processing to aid the operation (information extraction) of a wide variety of later engines. IN this context, the cochlear nucleus remains defined primarily as a stage 2C element rather than a stage 4a element.

No major functional role for the lemnisci of the auditory system has been found in this work. Some texts describe the lemnisci as mere pathways. Others suggest they are functional neural engines. Brugge devotes a section to the "Extralemniscal Pathways" and discusses these alternate pathways as a lemniscal adjunct. The challenge concerning defining the role of the lemnisci clearly relates to the increasingly abstract nature of the signals. Brugge asserted the signals in these alternate paths show little cochleotopic organization, their neural elements exhibit broadband frequency responses and may be activated by other sensory modalities. When viewed in-toto, the place of the lemniscal bodies in the auditory system remains obscure and poorly documented.

Young, Robert & Shofner have compared the waveforms recorded from stage 3 neurons within the cochlear nucleus by a variety of investigators[71]. They characterize their data as from neurons with a mean latency at least one millisecond longer than the shortest auditory nerve fiber mean latencies. Based on their review, they repeat the assertion of Rouiller & Ryugo[72]: "On the basis of this apparent diversity of response types from bushy cells, the basic assumption of a close correspondence of structure and function in VCN may need to be reexamined." They also note, "Part of the uncertainty in correlating physiological response types with morphological cell types is that the techniques for characterizing physiological response types have not kept pace with morphological techniques, . . . Physiological characterizations are based primarily on PST histograms of response to short tone bursts. . . . there are situations in which ambiguities in the PST scheme become problematical." The difference here may be more than one of technique and more one of protocol (to include the investigation of analog waveforms).

A relatively large amount of data describing the waveforms of neurons within the cochlear nucleus has been gathered by the Oertel team. Their data has been collected under a variety of test protocols. Some of the best has involved current-type axonal patch-clamps. The data requires careful analysis, especially because of the low resting potentials of many of the axoplasms (in the –50 to –60 mV range). It appears that many of the neurons may have been fundamentally analog neurons that have been forced into monopulse oscillation by the addition of capacitance to the axon circuit (due to the patch probe).

Oertel & Young have recently presented a review that appears generic to all mammals[73]. While addressed from the morphological perspective, and using a variety of fanciful names, it contains considerable electrophysiological data on the interconnection of the neurons of the cochlear nucleus. In fact the text provides sufficient information to extend their basic figure, reproduced below, even farther than extended here. It is one of the first papers to report analog currents associated with many of the neurons within the DCN based on voltage-clamp measurements. Their use of the terms long-term potentiation (LTP) and the opposite, long-term depression (LTD), when speaking of polarization and depolarization also emphasizes the analog nature of many of their waveforms.

The title of the Oertel & Young paper was designed to incite thought. They note the many similarities between the neural arrangement and interconnections found in the DCN and in the cerebellum. However, they do not appear to recognize these are both neural engines of similar complexity and function composed of the same building block circuits. Unless an engine includes such specialized circuits as associative correlators, and arrays of coincidence detectors, it is necessarily similar to a wide range of other engines.

Figure 6.5.2-1 shows a schematic of part of the dorsal cochlear nucleus in the style of figure 1 of Oertel & Young.

The modifications may be considered severe. The modification is designed to emphasize the difference between the analog circuits within one engine and the phasic circuits communicating between engines.

Some of their fanciful names can be replaced by functional names, especially when they assert, "Cartwheel cells are interneurons that occupy a similar position in the DCN circuit to that occupied by Purkinje cells in the cerebellum." In other cases, the cells associated with different fanciful names cannot always be distinguished on morphological grounds. While Ortel & Young show the fusiform and giant cells separately in the figure, they choose to discuss them as one type in their text. Functionally, they are distinct in that they project signals of different information content to the inferior colliculus. They both exhibit complex input structures performing signal summation at both their dendritic and poditic terminals and differencing the resultant dendritic and poditic signals prior to encoding and projection. Oertel & Young choose to emphasize the following crucial point. "Fusiform and giant cells thus generally respond to broadband, but not to narrowband, stimuli."

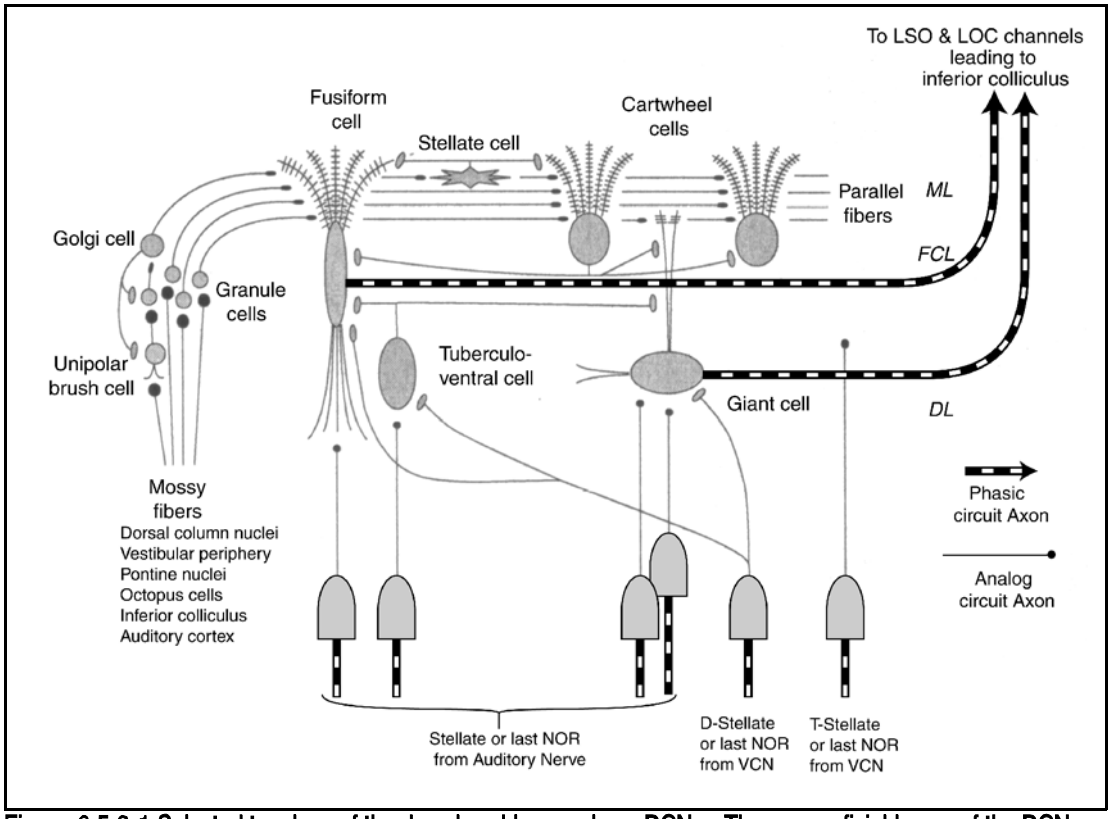

Figure 6.5.2-1 Selected topology of the dorsal cochlear nucleus, DCN. Three superficial layers of the DCN are shown; the molecular layer (ML), the fusiform cell layer (FCL), and the deep layer (DL). The following is from the original caption. "Sources of terminals in the granule cell region are listed at lower left. Not all of these have been shown to terminate as mossy fibers. Auditory nerve fibers innervate the deep layer, contacting the smooth basal dendrites of fusiform and giant cells, as well as tuberculoventral neurons. Two groups of cells from the VCN, D- and T-stellate cells, provide auditory inputs to the deep layer. The targets of T-stellate cell axons in the DCN are not known. Fusiform and giant cells, the principle cells of the DCN project to the inferior colliculus." See text. Modified from Oertel & Young, 2004.

The discussion in Oertel & Young is not explicit as to whether the D-stellate and T-stellate cells they describe are physically located within the DCN or in the VCN. The notation in the figure is designed to emphasize the signal projection axons are phasic until the signals are decoded within the terminal engine. This decoding is performed either by a complete neuron located in the terminal engine or by the last Node of Ranvier (NoR) of the neuron with its soma located within the originating engine. Chapter 7 will introduce a revised physiological nomenclature classifying morphologically labeled stellate cells more precisely.

Oertel & Young introduce plasticity into their discussion of synapses. This feature is not supported in this work. The synapses are fundamentally simple electrolytic relay circuits (Activa circuits acting as forward-biased diodes). Any plasticity is associated with the preceding or following neurons (and their more complex Activa circuits).

6.5.2.1 Gross signal routing and morphology within the cochlear nucleus

The complexity of the cochlear nucleus makes its description difficult. The literature must be studied very carefully to rationalize apparently conflicting texts. Schuknect has provided a top level topological diagram (after Sando) showing how the neurons of each cochlear turn proceed to a different area of the nucleus where they divide into two distinctly different paths[74]. On the other hand, Evans in Keidel & Neff (pages 44–45) notes that "Rose, et. al. were the first to show that there was a triple representation of the cochlea in the cat CN, namely in each of the three major subdivisions." "Within each subdivision the CFs of the cells are arranged in strict sequence from high to low frequency in the dorsal to ventral, posterior to anterior, and medial to lateral directions." The volumes edited by Keidel & Neff provide the best survey of the auditory elements in the pons as of 1975[75, 76].

Figure 6.5.2-2 reproduces one figure from a comprehensive morphological examination of the cochlear nucleus by Moore[77]. It shows the banded tonotopic structure associated with the termination of the narrowband neural paths within the cochlear nucleus. The signature representing each tone is shared with a large number of neurons within the cochlear nucleus. Note the DCN and AVCN are not arranged symmetrically with respect to frequency channels. No similar mapping associated with the broadband neural paths could be found.

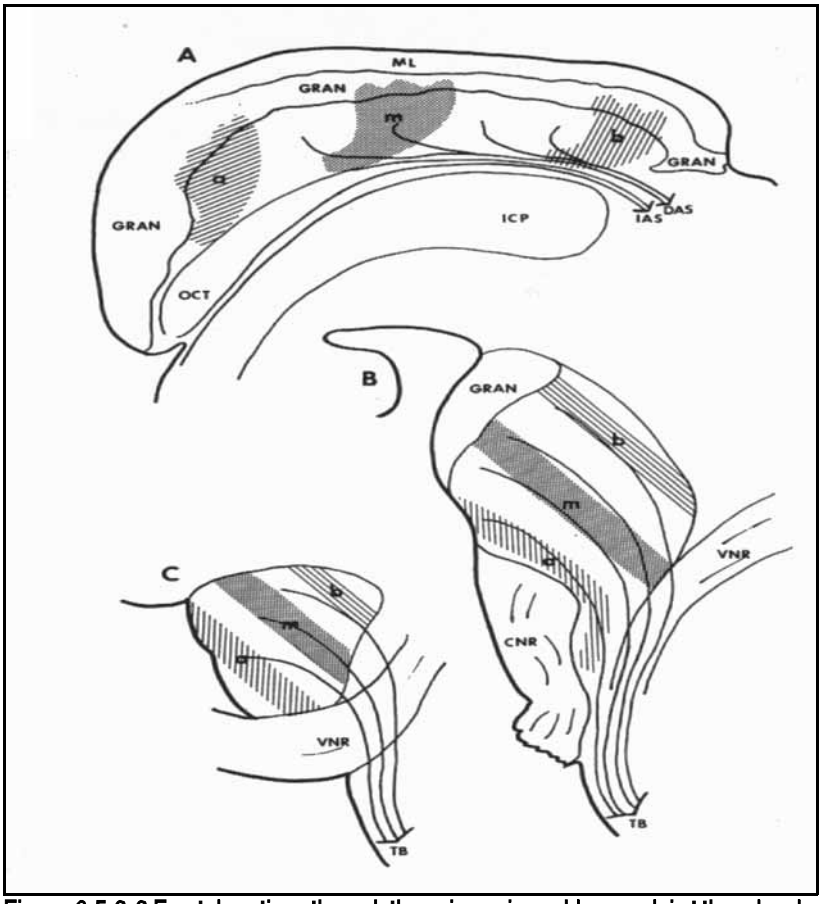

Figure 6.5.2-2 Frontal sections through the guinea pig cochlear nuclei at three levels. The locations of the sections and the nomenclature are described in other figures in the same set. In the ventral nucleus, labeled C, axons originating in the basal cochlea (b) are situated dorsomedially and those arising from the apex (a) are located ventrolateral, while axons from middle turns (m) are intermediate in position. In the dorsal nucleus labeled A, the sucession of axons represeint basal (b), middle (m), and apical (a) areas of the cochlea runs from medial to lateral in the central region of the nucleus. From Moore, 1986.

Rose has provided a broader set of figures describing the tonotopic arrangement of several individual engines within the cochlear nucleus[78]. The CF data was collected from probe penetrations parallel to the surface of the cochlear nucleus.

6.5.2.2 Measurements of cumulative signals within the cochlear nucleus

Moller has provided some good early data of an exploratory nature for the rat[79,80]. He did not trace the signal paths from the sensory neurons to the point of recording. He used AM modulated tones. The modulating frequency was very low. Unfortunately, his data is reported using the old ordinate scale of histograms using a cyclic histogram locked to his

modulating tone (see Section 7.5). The modulating tone was not a sub-harmonic of his carrier tone. As a result, his histograms are not stationary in time. The distortion parameters he computed using a Fourier Analysis appear to reflect the distortion in the ordinate of his graphs more than they do the performance of the neural path. Replotting of this or newer data appears warranted before any further analysis of this data.

6.5.3 Direct excitation characteristics of neurons found within the cochlear nucleus

This section will discuss the operational performance of neurons of the cochlear nucleus *in-vivo* and when responding to unmodified neural responses from antidromic neurons (primarily those of the auditory nerve). The next major section will discuss the observed performance of those same neurons under artificial conditions, primarily parametric tests associated with voltage or current clamp conditions applied to the axon of these same neurons. Most of the measurements in that section are made *in-vitro* for simplicity.

The following discussion will address neurons with only the dendroplasm receiving active signals unless specifically noted.

Shofner & Young have presented a broad set of analog neuron output characteristics recorded at the cochlear nuclei of decerebrate cats. They defined four distinct categories of neurons along with a variety of hybrids related to these simpler types. To avoid confusion in this work, their type designations will be preceded by a CN- prefix (ex. Type CN-III).

- Type CN-I– units give only excitatory responses to tones and noise.
- Type CN-II– units give excitatory response to noise. They give excitatory response to BF tones at levels near threshold but show inhibitory response to tones over a wide frequency range.
- Type CN-III– units also give excitatory responses to BF tones, but they have inhibitory sidebands.
- Type CN-I/III– units give excitatory responses to tones and noise, but have little or no spontaneous activity so they cannot be tested directly for inhibitory responses.
- Type CN-IV– units give excitatory responses to noise. They give excitatory response to BF tones at levels near threshold, but show inhibitory responses to tones over a wide frequency range.

The type CN-I units recorded in the VCN appear to be straightforward envelope detectors (with some possible pre-emphasis associated with the leading edge of the stimulus envelope). They successfully reproduced the signatures originating at the sensory neurons.

The response of the Type CN-I/III units would suggest they are received from a driven encoder associated with IHC channels or OHC channels. Most of the other types appear to be associated with free-running encoder neurons following differencing circuits within the spiral ganglia (circuit types they did not address in their paper).

Some of their type CN-IV units were clearly leading edge detection circuits. They only exhibited action potentials for a brief period following the start of an extended duration tone stimulus. This type of performance is closely associated with a specific form of stellate cell discussed in Section 6.5.5.

Many additional characteristics were presented that were too complex to allow easy categorization.

Shofner & Young also stimulated some of the cochlear neurons using a 100-microsecond electrical shock applied to the auditory nerve. They noted the results of these test on their Type CN-II and Type CN-IV units indicated some signal processing was carried out prior to the cochlear nucleus.

Young, Robert & Shofner presented a follow-on paper in 1988 exploring the same data in greater detail[81]. When the relationships became more obscure, a variety of statistical graphs were prepared.

6.5.4 Parametric excitation characteristics of neurons within the cochlear nucleus

As noted above, Shofner & Young carried out some experiments involving pulse excitation of the auditory nerve with data recording from the cochlear nucleus.

A group led by Oertel has obtained very useful data from various morphologically designated neurons of the cochlear nucleus of the mouse. It is important to recognize that their data relates to isolated and *in-vitro* neurons stimulated pathologically and frequently parametrically. The stimulus was not applied to the neuritic synapses or directly to the neurites of the neuron. The response was measured at the axoplasm of the neuron, frequently under current clamp

conditions. The data was collected and analyzed under the assumption the neuron was a two-terminal device. However, the data is very useful in quantifying the parameters of the circuit elements related to the output circuit of the amplifier within the neuron. Introducing a three-terminal electrolytic neuron model provides a much more detailed and quantitative interpretation of the same neurons.

Figure 6.5.4-1 shows a composite of figures from the Oertel group reproduced by Hudspeth with additional annotation based on this work[82]. The reproduction quality of the composite is not high, and Hudspeth changed the scaled ordinate axis to just the interval designation. The resting level of the waveforms tended to be between –60 mV and –70 mV. The initial transient responses (represented by the vertical arrows) did not reproduce well.

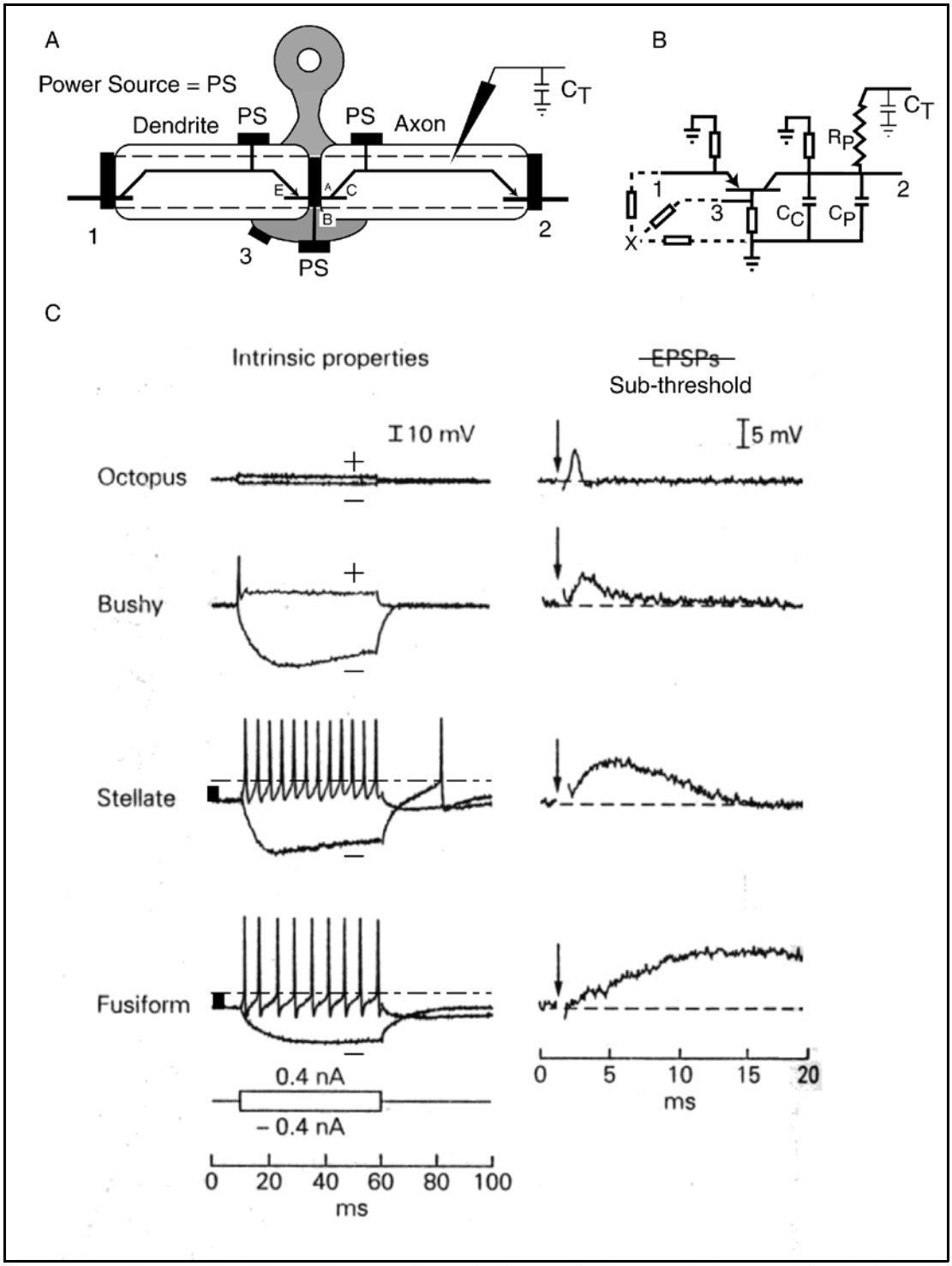

Figure 6.5.4-1 Annotated cochlear nucleus waveforms. A; diagram of a three-terminal neuron defined in this work. B; schematic of three-terminal neuron in Oertel test environment, including the undocumented location of the point of electrical shock, X. C; waveforms from a montage by Hudspeth of data from the Oertel group. See text.

Three-terminal diagrammatic and schematic representations of the neuron have been added to the figure as frames A & B. From these, it is clear that the patch-clamp technique of the Oertel group only interfaces with the axoplasm of the neuron. It does not obtain any direct information related to the dendritic or poditic structures. The technique allows the introduction of current into the axon conduit via the probe, while simultaneously recording the voltage within the conduit.

> The patch-clamp technique involves observation of the operation of a neuron when it has been excited or stabilized artificially. Such excitation is called parametric excitation because it does not involve the conventional method of cell excitation. Instead, some parameter of the circuit is varied artificially. Details regarding the concept and practical use of the patch-clamp technique are available at http://sightresearch.net/pdf/10PartII-electrophys.pdf , Sections 10.8.3 & 10.8.6.

The diagrammatic description in frame A shows the cluster of synapses associated with the dendroplasm as a single equivalent synapse labeled 1. This equivalent input and the impedance of the power supply labeled PS constitute the major passive elements of the dendritic circuit. The poditic terminal of the neuron, labeled 2, is shown as unconnected in this frame except for the presence of the poditic power supply and its internal impedance labeled PS. All of the pedicles of the axon of the neuron are represented by one equivalent pedicle, labeled 3. This pedicle and the associated axon power supply, labeled PS, constitute the major passive elements of the axon. The only active electrolytic element within the neuron, the Activa, is shown in position between the dendroplasm, podaplasm and axoplasm.

Also shown is the electrical probe penetrating the axolemma and making ohmic electrical contact with the axoplasm. In all cases, the introduction of the probe adds a very large capacitance to the total shunt capacitance associated with the axoplasm. In general, the probe also represents a series resistance on the order of 50-200 megohms by design. When discussing measured overshoots (and undershoots), it is important that these factors be taken into consideration.

The schematic description in frame B highlights the pertinent features of the typical neuron in the cochlear nucleus. The most important features of this circuit are the voltage difference between the emitter (dendrite) and the base (podite) terminals, the collector (axon) capacitance, C_C, and the collector (axon) saturation current. These features are the primary determinants of the operating mode of the overall circuit. The value of the axon capacitance relative to the output impedance of the active device, the Activa, and the load impedance associated with the axon power supply, are of major importance to the normal operation of the circuit.

It is important to note that the capacitance associated with the test probe, C_P, is frequently as large as, or larger than, the axon capacitance, C_C. As a result, the operating mode of the circuit is frequently changed by the presence of the test circuitry. This added capacitance usually results in the generation of extraneous action potentials by analog circuits, or the suppression of action potentials by phasic circuits due to the additional damping introduced.

The shunt impedance of the axoplasm with respect to the surrounding fluid matrix consists of the impedance of the load (consisting of the axoplasm power supply and the orthodromic neural circuitry at 2, if any) and the impedance of the Activa collector in parallel. When the Activa is in cutoff, the axoplasm impedance is passive and fixed. When the Activa is conducting, the axoplasm impedance is dominated by the Activa output impedance. This output impedance is nonlinear (and variable) with respect to the axoplasm potential. It is controlled by the instantaneous emitter (dendrite) to base (podite) potential.

The operation of the Activa is controlled by the voltage between the dendroplasm and the podaplasm and is largely independent of the axoplasm potential. However, whenever the Activa is conducting, the potential of the axoplasm causes a current to flow through the collector-base circuit (axon-podite circuit) of the Activa. This causes a change in the podite potential as a function of the podite impedance. The parametric injection of current into the axoplasm typically causes a change in the podite potential.

The waveforms published relating to the cochlear nucleus are generally obtained from neurons receiving signals from the auditory nerve. These signals are normally pulse type action potentials. The various neuron types typically convert these pulse signals into an analog signal through an integration process involving the input synapse, at terminal 1, and the impedance of the dendritic circuit. The output signal from the neuron may be either analog or pulse depending on the net signal applied to the emitter terminal, and the overall biasing, of the Activa.

When these neurons are surgically removed from the subject and investigated in-vitro, the input synapse is normally damaged or destroyed and the dendrite to podite potential is not controlled (or measured). Therefore, the threshold

voltage associated with the dendrite to podite potential (if present) cannot be measured directly. However, the threshold voltage as it is represented in the axon (collector) circuit is easily measured. The dash-dot lines, added to the lower left two waveforms of frame C, represent the threshold voltage as expressed by the axoplasm potential. The small boxes at the far left represent 10 mV. It can be seen that the Fusiform cell exhibits a threshold potential (expressed by the axon potential minus its resting potential) of 10 mV while the stellate (formally stellite) cell exhibits a similar threshold potential of ~13 mV. The bushy cell also exhibits a threshold of about 10 mV but reacts in a different manner.

In the experiments illustrated in the figure, the operation of the neuron is influenced by the introduction of current parametrically into the axoplasm. This action causes a change in the dendroplasm to podaplasm potential. These actions are clearly illustrated in the figure. Note the smaller signal levels involved in the waveforms on the right. These are clearly sub-threshold waveforms. The original designation EPSPs is not explicit when applied to three-terminal devices and has been discarded.

The waveforms on the left illustrate two conditions. The axons with waveforms with a plus sign (+) next to them were subjected to a depolarizing injection current. This current reduces the axon potential relative to the potential of the surrounding fluid matrix. It also increases the dendrite to podite potential. The waveforms from the same axons when subjected to a hyperpolarizing current are marked by a minus sign (–). These currents reduce the dendrite to podite potential substantially.

It should be clear that for those neurons with sufficient capacitance associated with their axon, the circuits operate as class A amplifiers at axon potentials more negative than their threshold potential. This is true whether the instantaneous axon potential is positive or negative relative to their resting potential. However, once the potential of the axoplasm becomes greater than the threshold, relative to its resting potential, the Activa goes into class C operation and generates one or more positive-going pulses. An individual pulse will be generated whenever the axon potential exceeds the threshold defined above. This is most easily seen in the case of the fusiform cell. Following each pulse, the waveform returns to the baseline. However, current continues to flow into the axoplasm thereby raising the potential above the resting potential and eventually reaching the threshold. This causes an additional monopulse to be generated. The sequence continues until the current injection stops. It should be noted that the time between pulses is determined by the level of the injection current and the nominal impedance (primarily the capacitance) of the axoplasm. Injecting charge more quickly (at higher current levels) will cause the pulses to become closer together. Figure 4 of Oertel, Wu & Hirsch show this result was obtained when the current was varied in a single cell[83]. The stellate cell waveform can be used to illustrate this process here. Either the intrinsic axon capacitance of the stellate cell was lower than that of the fusiform cell, or its shunt resistance was higher. In either case, the stellate cell axon voltage reached threshold more quickly and generated more pulses per second than did the same constant current applied to the fusiform cell.

The positive going waveform of the bushy cell shows a more complex form. The axon circuit of this cell appears to have a lower resistive impedance than for the previous two. As a result, this circuit exhibits a time constant such that the injected current cannot raise the axon potential significantly. It can only do so on a transient basis. As a result, only one action potential pulse was generated. The situation is similar for the octopus cell. The injected current was not sufficient to raise the axoplasm above threshold at any time (assuming the octopus cell was capable of monopulse generation).

The negative going currents generally hyperpolarize the neurons and drive them closer to cutoff. Note the interesting operation of the stellate cell when injected with a –0.4 nA current. It was driven into cutoff (note the straight segment of its potential waveform). This established a different operating state. When current injection stopped, the circuit relaxed by driving the dendrite-to-podite potential above threshold and resulted in an action potential generated nearly 20 ms after the injection ceased. The fusiform cell did not go into cutoff. It continues to exhibit a waveform consistent with class A operation. The relaxation of its dendrite-to-podite potential does not cause a pulse to be generated.

The waveforms on the right were generated as the result of a brief electrical shock to the INM near the neuron under evaluation, at point X, rather than by current injection. The challenge is illustrated in frame B. No information concerning the impedances between the shock location and the terminals of the neuron was provided. It is not possible to state explicitly whether the shock stimulated the dendritic or poditic terminals exclusively. However, it is possible to describe the net stimulation. The net stimulation (the change in dendrite-to-podite potential) had a polarity equivalent to that caused by a negative current injected into the axoplasm. The dendrite-to-podite potential became more positive following each shock. However, in all cases illustrated, the dendrite-to-podite potential remained below the threshold for monopulse operation. As a result, the axoplasm potential reflected the class A

amplification of the dendrite-to-podite potential as a function of time. The time constant of the driving impedance was shortest for the octopus cell and was larger for each cell below it in frame C. Similarly, the recovery time constant of the dendrite-to-podite potential was also shortest for the octopus cell and increased for each of the cells below it.

The set of waveforms selected shows an orderly difference in the axon circuits of the named neurons. However, it would be necessary to analyze a larger set of each type to justify considering these features as neuron type specific.

Oertel, Wu & Hirsch have made several comments concerning the above neuron types when observed *in-vivo*.

> "Some cells in the VCN, the bushy cells, preserve the firing patterns of inputs precisely; others, the stellate and octopus cells, preserve the precise timing only of the onset, and many cells in the dorsal cochlear nucleus (DCN) preserve little of the temporal firing patterns of the inputs."

Note, the implicit assertion that the input to these neurons are action potential pulses, not analog signals. Based on this fact, the bushy cells tend to perform as repeaters while the stellate and octopus cells tend to be initial pulse repeaters. The other cells perform fundamentally different tasks. These characteristics are suggestive of the primary role of these cells.

Unfortunately, another paragraph of the same Oertel, Wu & Hirsch paper states different views (p. 319).

> "Figure 6 shows that all cells that fired all-or-none action potentials regularly were stellate cells, and cells that fired only one or two graded action potentials and that showed strong rectification in the physiological voltage range were bushy cells."

More definitive work is obviously needed in order to reconcile the fanciful names and the actual function of the cells of the cochlear nucleus. Oertel, Wu & Hirsch recognize this need in their following paragraph.

In 1991, Oertel published an overview of the cochlear nucleus that added many additional qualitative descriptions of the neurons and their gross interrelationships[84]. However, the paper was light on specific definitions and detailed relationships. It remained focused on the parametric performance of neurons evaluated *in-vitro*. The annotated citation list is a valuable resource. The paper did note that the impedance of the axoplasm of typical neurons is between 30 and 50 megohms in the hyperpolarizing voltage range, and so small that they are difficult to measure in the physiological voltage range.

In 1996-97, Golding & Oertel[85, 86] provided additional information on the neurons of the cochlear nucleus in the mouse under current-type patch clamp conditions. Unfortunately, all of the data was collected *in-vitro* and under pathological conditions. 200-350 micron parasagittal slices were examined in a flowing bath that allowed the introduction of pharmaceuticals. Their test protocol assumed a two-terminal neuron and made no attempt to locate, isolate or control the neurites of the neurons. The capacitances of their probes were not provided although impedances of 120 to 200 megohms were indicated. They shocked (insulted) the neurons with 110 μsec pulses delivered to the INM ranging from 100 mV to 100 Volts (typical dendroplasm changes of 10 mV or less are sufficient to excite a phasic neuron). The cells were only identified by the fanciful names used by the Oertel team. A variety of currents were injected into the axoplasm while various pharmaceuticals were introduced into the INM environment.

Extensive axonal potential recordings were collected under a variety of conditions and presented. Two different digital sampling procedures were used with the slower one distorting the recorded pulses significantly. Most of the recordings showed an axon resting potential of –56 to –63 mV. The recorded pulses were typically depolarizing and extended to near a nominal zero potential (although the nature of the ground point was not defined). The axon potentials were typically depolarized by 10 mV before entering an oscillatory environment. The coarse abscissas did not allow confirmation that the pulses corresponded to action potentials. However, the pulses occurred either individually or in groups and exhibited a shape similar to that of action potentials.

Like in the Hudspeth composite, the injection of a constant current into the axoplasm caused a linear depolarization in the resting potential up to the point of oscillation.

The low resting potentials suggest the neurons were not normally stage 3 neurons or they were under pathological conditions. It is likely the capacitance of their probes created or contributed to the monopulse oscillatory capability of the cells reported.

The investigators found inconsistent and "context-dependent" results (1996, pgs 2212, 2215 & 2218). Their analysis suggests these investigators were searching for a more satisfying neuron model to aid in the explanation for their results. The three-terminal neuron defined in the Electrolytic Theory of the Neuron offers considerable insight into the results of Golding & Oertel. Merely changing the relative impedances between their (uncontrolled) point of shock and the dendritic and poditic terminals can completely reverse the operation of the neuron under test.

Future data acquisition under more detailed protocols based on a three-terminal neuron should lead to much more detailed knowledge of the cochlear nucleus and the other engines of the neural system.

6.5.5 A generic neural circuit comparing two one-shot neurons

The generic waveforms and fanciful labels of Kiang in Figure 6.2.2-1 and Oertel/Hudspeth in Figure 6.5.4-1 appear to be inconsistent. However, it is clear that some of the neurons of stage 2 generate a single pulse and this pulse is associated with the leading edge of the signature generated by a sensory neuron. Such neurons can be identified functionally as one-shot monopulse oscillators. Such neurons are useful when applied in pairs to a "latching flip-flop" circuit. The resulting circuits produce output signals that have broad application in stage 4 information extraction. One specific application is in defining the interval between stressed phonemes in the communications channels. A second application is in determining the direction of a source based on time differences between neural signals.

As a matter of convenience, the nomenclature of Figures 6.2.2-1 and 6.5.1-1 will be used here. Figure 6.5.5-1 shows the proposed implementation as it might be found in a source location circuit within the pons. It is based on the ON_I signals generated by the octopus cells of the AVCN (and possibly other cells) being processed within the medial superior olivary nucleus, the MSO. As defined in these figures, the octopus cells are "one-shot" monopulse oscillators. They generate a single pulse marking the beginning of a signature delivered to them. The actual signature may be reconstituted from a string of any number of action potentials. The timing of this first pulse exhibits a unique relationship to the beginning of the neural response in a system employing time-delay encoding. This relationship does not exist in a frequency modulation encoded system (Section 7.1.4.2).

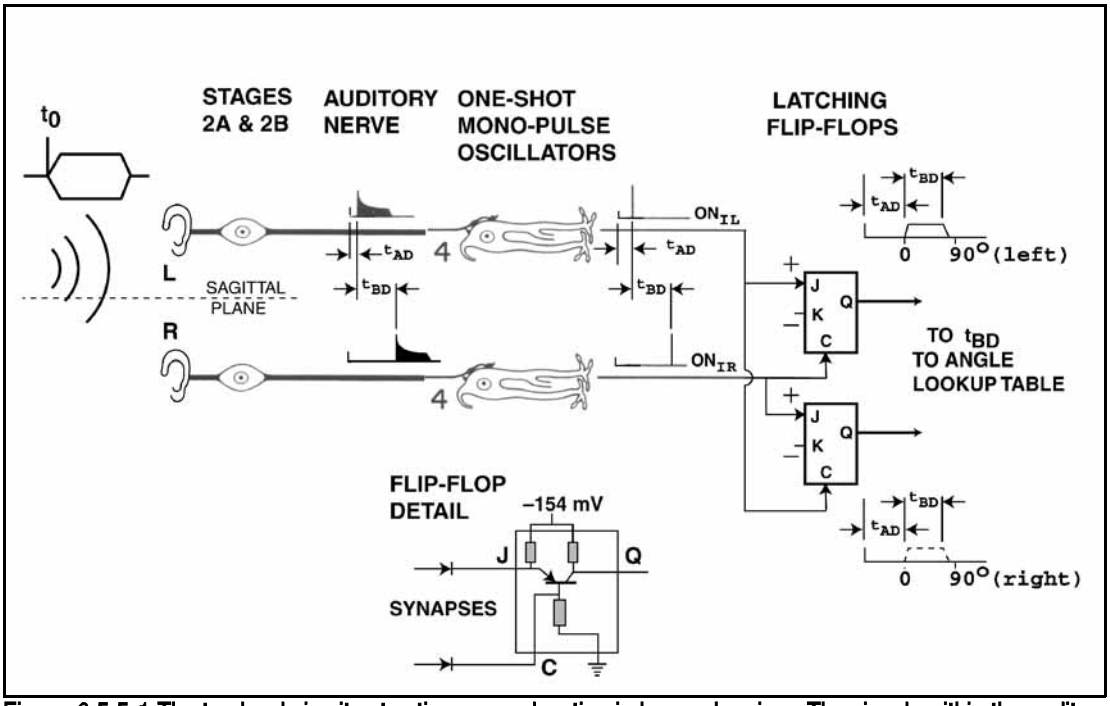

Figure 6.5.5-1 The top level circuit extracting source location in human hearing. The signals within the auditory nerves are action potentials, they are described by PST histograms. The output of the octopus cells consists of the first pulse of the action potential stream applied to that cell. The auditory delay, t_{AD}, increases monotonically as the signal moves through the system. However, the binaural delay difference, t_{BD}, remains fixed. The output waveform at upper right is an analog potential plotted versus time. The dotted output waveform at lower right only appears if the stimulus to the right ear precedes that to the left ear. In that situation, the output at upper right remains at the baseline. See text.

Note the continual increase in the aural delay (t_{AD}) associated with each channel as the signal progresses toward the brain. Note also, the binaural delay difference (t_{BD})between the pair of signals does not change once it is established by the sensory neurons. It is important to note the delay of interest here is the mathematical delay of the P/D Equation (the delay until the response departs from the quiescent signal level) and not the clinical delay ending at the peak of the first pulse.

These ON_I pulses are delivered to the two neurite terminals of specialized neurons in the MSO identified by Galambos et al (Section 6.5). Galambos used the earlier label *n. accessorius* to identify the MSO. They described the neurons as having two input structures that were special in that they emanated from the soma in distinctly different directions. This is the identifying feature of any neuron with a bifurcated arborization. The two independent input structures are a medial dendritic input and a lateral poditic input (Section 3.1.2). In this application, these special neurons are tailored to act as latching flip-flops. A man-made flip-flop has a very simple truth table. If a signal is applied to terminal J, the output at terminal Q will go "high" unless a signal is present at the clear terminal, C. If the signal at the clear terminal goes high, the output at terminal Q is forced "low" regardless of any signal at terminal J. Figure 12 of Galambos et al. show this type of performance in the in-vivo binaural circuits of the MSO of the cat.

The duration of the analog output waveform of the flip-flops defines the difference in delay between the two signals. By integrating these signals, a peak value is obtained that is equivalent to the delay duration. This value can be applied to a lookup table to find the equivalent value, encoded for use by the higher cognitive centers, corresponding to the angle of the source from the sagittal plane represented by this delay interval. The arrangement of the flip-flop pairs and the clear signals prevent both flip-flops of a pair generating output signals at the same time.

When the flip-flop output is encoded by a stage 3 neuron, the resulting pulse stream will generate a PST histogram looking exactly like the signal from an OHC encoding a tone burst. However, there is no similarity between the

underlying signals.

It is unfortunate that the measurements of Galambos et al. were limited to interneural probing. They did not report the actual potential waveforms from the plasmas of any neural chamber. As a result we have no values for the absolute potentials, or the time constants, of any of the features of the recorded waveforms.

Table of Contents

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Endnotes

1. Buus, S. & Florentine, M. (2003) Growth of loudness in listeners with cochlear hearing losses: recruitment reconsidered *J Assoc Res Otolaryngol* vol. 3, pp 120-139
2. Oertel, D. Wu, S. & Hirsch, J. (1988) Electrical characteristics of cells and neuronal circuitry in the cochlear nuclei studied with intracellular recordings from brain slices *In* Edelman, G. Gall, W. & Cowan, W. *eds.* Auditory Function: Neurobiological Bases of Hearing. NY: John Wiley & Sons Chapter 10, pg 315
3. Santi, P. (1988) Cochlear microanatomy and ultrastructure *In* Jahn, A. & Santos-Sacchi, J. *eds.* Physiology of the Ear. NY: Raven Press pp 173-197 pg 176
4. Fernandez, C. (1951) The innervation of the cochlea (guinea pig) *Laryngoscope* vol. 61, pp 1152-1172 (also pg 262 in Tobias, J. *ed.* (1970) Foundations of Modern Auditory Theory, Vol. I. NY: Academic Press
5. Kim, D. (1984) Functional roles of the inner- and outer-hair-cell subsystems in the cochlea and brainstem *In* Berlin, C. *ed.* Hearing Science: Recent Advances Chap 7
6. Spoendlin, H. (1967) The innervation of the Organ of Corti *J Laryngol & Oto* vol. 81, pp 717-738 fig. 15
7. Spoendlin, H. (1974) Neuroanatomy of the cochlea *In* Zwicker, E. & Terhardt, E. *eds.* Facts and Models in Hearing. NY: Springer-Verlag pg 28
8. Harrison, R. (1988) The physiology of the cochlear nerve *In* Jahn, A. & Santos-Sacchi, J. *eds.* Physiology of the Ear. NY: Raven Press pg 359
9. Smolders, J. Klinke, R. (1980) Phase versus frequency in caiman primary auditory fibres: is there a traveling wave? *In* Syka, J. & Aitkin, L. *eds* Neuronal Mechanisms of Hearing. NY: Plenum Press pp 43-47
10. Spoendlin, H. (1988) Neural anatomy of the inner ear *In* Jahn, A. & Santos-Sacchi, J. *eds.* Physiology of the Ear. NY: Raven Press pp 201-219
11. Morrison, D. Schindler, R. & Wersall, J. (1975) A quantitative analysis of the affrent innervation of the Organ of Corti in guinea pig *Acta Otolaryngol* vol. 79, pp 11-23
12. Nomura, Y. (1976) Nerve fibers in the human Organ of Corti *Acta Otolaryngol* vol. 82, pp 317-324
13. Spoendlin, H. (1988) Neural anatomy of the inner ear *In* Jahn, A. & Santos-Sacchi, J. *eds.* Physiology of the Ear. NY: Raven Press pp 201-215
14. Spoendlin, H. (1972) Innervation densities of the cochlea *Acta Otolaryngol* vol 73, pp 235-248
15. Pfeiffer, R. Kim, D. (1972) response patterns of single cochlear nerve fibers to click stimuli: descriptions for cat *J Acoust Soc Am* vol 52(6), pp 1669-1677
16. Lorente de No, R. (1981) The Primary Acoustic Nuclei. NY: Raven Press pg 7
17. Ross, M. (1981) Centrally originating efferent terminals on hair cells: fact or fancy *In* Gualtierotti, T. *ed.* The Vestibular System: Function and Morphology. NY: Springer-Verlag Chap 10.
18. Oertel, D. & Young, E. (2004) What's a cerebellar circuit doing in the auditory system? *TINS* vol. 27(2) pp 104-110
19. Smoorenburg, G. Gibson, M. Kitzes, L Rose, J. & Hind, J. (1976) Correlates of combination tones observed in the response of neurons in the anteroventral cochlear nucleus of the cat *J Acoust Soc Am* vol 59(4), pp 945-962
20. Rhode, W. Smith, P. & Oertel, D. (1983) Physiological response properties of cells labeled intracellularly with horseradish peroxidase in cat dorsal cochlear nucleus *J Com Neurol* vol 213, pp 426-447
21. Rhode, W. Oertel, D. & Smith, P. (1983) Physiological response properties of cells labeled intracellularly with horseradish peroxidase in cat ventral cochlear nucleus *J Com Neurol* vol 213, pp 448-463
22. Rhode, W. & Smith, P. (1985) Characteristics of tone-pipo response patterns in relationship to spontaneous rate in cat auditory nerve fibers *Hear Res* vol 18, pp 159-168
23. Harada, Y. (1983) Atlas of the Ear by Scanning Electron Microscopy. Baltimore, MD: University Park Press
24. Young, E. Shofner, W. White, J. Robert, J-M & Voigt, H. (1988) Response properties of cochlear nucleus neurons in relationship to physiological mechanisms *In* Edelman, G. Gall, W. & Cowan, W. *eds.* Auditory Function: Neurobiological Bases of Hearing. NY: John Wiley & Sons Chapter 9, pg 286
25. Oertel, D. & Young, E. (2004) What's a cerebellar circuit doing in the auditory system? *Trends in Neurosci* vol 27(2), pp 104-110, fig 1
26. Fernandez, C. (1951) The innervation of the cochlea (guinea pig) *Laryngoscope* vol. 61, pp 1152-1172
27. Spoendlin, H. (1967) The innervation of the Organ of Corti *J Laryngol Oto* vol. 81, pp 717-738
28. Lorente de No, R. (1981) The Primary Acoustic Nuclei. NY: Raven Press pp 1-7
29. Iurato, S. (1967) Submicroscopic Structure of the Inner Ear. NY: Pergamon Press pg 109
30. Wever, E. (1949) Theory of Hearing. NY: John Wiley pp 221-224
31. Schwartz, A. (1986) Auditory nerve and spiral ganglion cells: morphology and organization *In* Altschuler, R. et al. *eds.* Op. Cit. Chapter 15
32. Kiang, N. (1975) Stimulus representation in the discharge patterns of auditory neurons. *In* Tower, D. *ed.* The Nervous System, Volume 3: Human Communication and Its Disorders. NY: Raven Press.
33. Osen, K (1969) Cytoarchitecture of the cochlear nuclei in the cat *J Comp Neurol* vol 136, pp 453-483
34. Brawer, J. Morest, D. & Kane, E. (1974) The neuronal architecture of the cochlear nucleus of the cat *J Com Neurol* vol 155, pp 251-300
35. Oertel, D. Wu, S. Garb, M. & Dizack, C. (1990) Morphology and physiology of cells in slice preparations of the posteroventral cochlear nucleus of mice *J Comp Neurol* vol 295, pp 136-154
36. Jahn, A. & Santo-Sacchi, J. *eds.* (2001) Physiology of the Ear, Volume 2. San Diego, CA: Singular
37. Lewis, E. & Henry, K. (1989) Transient responses to tone bursts *Hear Res* vol 37(3), pp 219-239
38. Nomura, Y. (1976) Nerve fibers in the human Organ of Corti *Acta Otolaryngol* vol 82, pp 317-324
39. Kimura, R. Ota, C. & Takahashi, T. (1979) Nerve fiber synapses on spiral ganglion cells in the human cochlea Ann Otol vol. 88, no. 6, part 3, supplement 62, pp 1-17
40. Smoorenburg, G. Gibson, M. et al. (1976) Correlates of combination tones observed in the response of neurons in the anteroventral cochlear nucleus of the cat *J Acoust Soc* Am vol. 59, no. 4, pp 945-962
41. Brugge, J. Anderson, D. Hind, J & Rose, J. (1969) Time structure of discharges in single auditory nerve fibers of the squirrel monkey in response to complex periodic sounds *J Neurophyiol* vol. 32, pp 386-401
42. Otte, J. Schuknecht, H. & Kerr, A. (1978) Ganglion cell populations in normal and pathological human cochleae *Laryngoscope* vol 88(8), pp 1231-1246
43. Ota, C. & Kimura, R. (1980) Ultrastructural study of the human spiral ganglion *Acta Otolaryng* vol 89, pp 53-62

44. Kimura, R. Ota, C. & Takahashi, T. (1979) Nerve fiber synapses on spiral ganglion cells in the human cochlea *Ann Otol Rhino Laryng* Suppl 62, pp 1-17
45. Schwartz, A. (1986) Auditory nerve and spiral ganglion cells: morphology and organization In Altschuler, R. et al. *eds.* Op. Cit. Chapter 15
46. Mo, Z-L. & Davis, R. (1997) Endogenous firing patterns of murine spiral ganglion neurons *J Neurophysiol* vol 77, pp 1294-1305
47. Reid, M. Flores-Otera, J. & Davis, R. (2004) Firing patterns of type II spiral ganglion neurons *in vitro. J Neurosci* vol 24(3), pp 733-742
48. Doucet, J. & Relkin, E. (1997) Neural contributions to the peristimulus compound action potential: - - - *J Acoust Soc Am* vol. 101(5) pt. 1, pp 2720-2733
49. Liberman, M. (1978) Auditory-nerve response from cats raised in a low-noise chamber *J Acoust Soc Am* Vol 63(2), pp 442-455
50. Liberman, M. (1982) The cochlear frequency map for the cat: labeling auditory-nerve fibers of known characteristic frequency *J Acoust Soc Am* vol 72(5), pp 1441-1449
51. Liberman, M. & Dodds, L. (1984) Single-neuron labeling and chronic cochlear pathology. III. stereocilia damag and alterations of threshold tuning curves. *Hear Res* vol 16, pp 55-74
52. Rasmussen,G. & Windle, W. (1960) Neural Mechanisms of the Auditory and Vestibular Systems. Springfield, Il: Charles Thomas
53. Otte, J. Schuknecht, H. & Kerr, A. (1978) Op. Cit. pg 1236
54. Liberman, M. & Oliver, M. (1984) Morphometry of intracellularly labeled neurons of the auditory nerve: Correlations with functional properties *J Compar Neurol* vol 223(2), pp 163 -176
55. Moore, J. & Osen, K. (1979) the cochlear nuclei of man *Am J Anat* vol 154(3), pp 393-417
56. Morest, D. (1975) Structural organization of the auditory pathways *In* Tower, D. *ed.* The Nervous System, Volume 3: Human Communication and Its Disorders. NY: Raven Press pp 19-29
57. Kiang, N. (1975) Stimulus representation in the discharge patterns of auditory neurons In Tower, D. ed. The Nervous System, Vol. 3. pp 81-96
58. Galambos, R. Schwartzkopff, J. & Rupert, A. (1959) Am J. Physiol vol 197, pp 527-536
59. Evans, E. & Nelson, P. (1973) The response of single neurons in the cochlear nucleus of the cat as a function of their location and the anaesthetic state *Exp Brain Res* vol 17(4), pp 402-427
60. Evans, E. & Nelson, P. (1973) On the functional relationship between the dorsal and ventral divisioins of the cochlear nucleus of the cat *Exp Brain Res* vol 17(4), pp 428-442
61. Keidel, W. & Neff, W. (1975) Auditory system: Physiology of the CNS. NY: Springer-Verlag
62. Hudspeth, A. (2000) Hearing *In* Kandel, E. Schwartz, J. & Jessell, T. *eds.* Principals of Neural Science. NY: Appleton & Lange Chapter 30
63. Brown, M. & Ledwith, J. (1990) Projections of thin (type-II) and thick (type-I) auditory-nerve fibers into the cochlear nucleus of the mouse *Hear Res* vol 49, pp 105-118
64. Shofner, W. & Young, E. (1985) Excitatory/inhibitory responses typed in the cochlear nucleus: *J Neurophysiol* vol 54(4), pp 917-939
65. Young, E. (1984) Response characteristics of neurons of the cochlear nucleus *In* Berlin, C. *ed.* Hearing Science: Recent Advances Chap 7
66. Young, E. Shofner, W. White, J. Robert, J-M, & Voigt, H. (1988) Response properties of cochlear nucleus neurons in relationship to physiological mechanisms *In* Edelman, G. Gall, W. & Cowan, W. *eds.* Auditory Function: Neurobiological Bases of Hearing. NY: John Wiley & Sons Chapter 9, pg 307
67. Warr, W. Guinan, J. & White, J. (1986) Organization of the efferent fibers: the lateral and medial olivocochlear systems *In* Altschuler, R. et al. *eds.* Op. Cit. Chapter 18
68. Kiang, N. (1975) Op. Cit.
69. Moore, J. & Osen, K. (1979) The human cochlear nuclei *In* Creutzfeld, O. *ed.* Hearing Mechanisms & Speech. *Exper Brain Res Suppl II.* pp36-44
70. Ranson, S. & Clark, S. (1953) Anatomy of the Nervous System, 9th Ed. Philadelphia, Pa: Saunders
71. Young, E. Robert, J-M. & Shofner, W. (1988) Regularity and latency of units in ventral cochlear nucleus J Neurophysiol vol. 60(1), pp 1-29
72. Rouiller, E. & Ryugo, D. (1984) Intracellular marking of physiologically characterized cells in the ventral cochlear nucleus of the cat *J Comp Neurol* vol. 225, pp 167-184
73. Oertel, D. & Young, E. (2004) What's a cerebellar circuit doing in the auditory system? *TINS* vol. 27(2) pp 104-110
74. Schuknecht, H. (1974) Pathology of the Ear. Cambridge, MA: Harvard Univ. Press figs 2.67-2.70
75. Keidel, W. & Neff, W. (1975) Auditory System: Physiology (Ear), vol 5.1. NY: Springer-Verlag
76. Keidel, W. & Neff, W. (1975) Auditory System: Physiology (CNS), vol 5.2. NY: Springer-Verlag
77. Moore, J. (1986) Cochlear nuclei: relationship to the auditory nerve *In* Altschuler, R. et al. *eds.* Op Cit. Chapter 16
78. Rose, J. (1959) Organization of frequency sensitive neurons in the cochlear nuclear complex of the cat *In* Rasmussen, G. & Windle, W. *eds.* Neural Mechanisms of the Auditory and Vestibular Systems. Springfield Il: Charles C. Thomas Chap 9
79. Moller, A. (1974) Responses of units in the cochlear nucleus to sinusoidally amplitude-modulated tones *Exp Neurology* vol. 45, pp 104-117
80. Moller, A. (1975) Dynamic properties of excitation and inhibition in the cochlear nucleus Acta Physiol Scand vol 93, pp 442-454
81. Yong, E. Robert, J-M. & Shofner, W. (1988) Regularity and latency of units in ventral cochlear nucleus: *J Neurophysiol* vol. 60, no. 1, pp 1-29
82. Hudspeth, A. (2000) Hearing *In* Kandel, E. Schwartz, J. & Jessell, T. *eds.* Principles Of Neural Science. NY: Elsevier pg 606
83. Oertel, D. Wu, S. & Hirsch, J. (1988) Electrical characteristics of cells and neuronal circuitry in the cochlear nuclei studied with intracellular recordings from brain slices *In* Edelman, G. Gall, W. & Cowan, W. *eds.* Auditory Function: Neurobiological Bases of Hearing. NY: John Wiley & Sons Chapter 10, pg 319
84. Oertel, D. (1991) The role of intrinsic neuronal properties in the encoding af auditory informatioon in the cochlear nuclei *Cur Opinion Neurobiol* vol 1, pp 221-228
85. Golding, N. & Oertel, D. (1996) Context-dependent synaptic action of glycinergic and GABAergic inputs in the dorsal cochlear nucleus *J Neurosci* vol 16(7), pp 2208-2219
86. Golding, N. & Oertel, D. (1997) Physiological identification of the targets of cartwheel cells in the dorsal cochlear nucleus *J Neurophysiol* vol 78, pp 248-260