Chapter 143: Physiology of the Auditory System

Paul J. Abbas

This chapter summarizes the basic physiologic properties of the ear and the central auditory pathways. These structures provide the mechanism by which an acoustic signal in space is transduced into neural action potentials and subsequently processed within the nervous system. The incoming acoustic signal undergoes a series of transformations in a rather complex chain of events. The sound wave propagates throughout space surrounding the hear. The pressure changes in the ear canal result in vibration of the tympanic membrane. This vibration in turn causes movement of the ossicles within the middle ear cavity. The movement of the stapes within the oval window results in pressure changes within the fluids of the inner ear and consequently in vibration of the cochlear partition containing the sensory hair cells. The movement of the stereocilia of the hair cells is the effective stimulus that initiates the transduction from mechanical vibration to the flow of electrical current. The receptor potential of the hair cell results in chemical changes at the hair cell-neuron synapse, changes in the dendritic potential of the neuron, and generation of action potentials in the axons. The axons of the auditory nerve then synapse on cells within the brain stem, beginning a series of neural transformations in the central nervous system.

Different sections in the chapter describe different functional components of the auditory system. The acoustic and mechanical properties of the head, external ear, and middle ear are described in the first section. The mechanical properties of the inner ear are described in the second section, which includes a discussion of the traveling wave. The process of hair cell transduction and the related cochlear potentials are the topic of the third section. The fourth section discusses the response properties of auditory nerve fibers to different classes of acoustic stimuli. These response properties provide insight into cochlear function and also serve as a basis for understanding the responses in the central nervous system. The final section is an overview of the nuclei in the auditory pathway and the responses of each to simple acoustic stimuli, presented both monaurally and binaurally.

This chapter is meant to be an overview, not necessarily covering all topics in the detail they may warrant. Several texts in auditory physiology are currently available and are considerably more detailed in their coverage of those topics (Jahn and Santos-Sacchi, 1988; Pickles, 1988). A number of texts and review articles are listed after the references. The original articles cited throughout the chapter are, of course, an excellent source for more detailed reading on the various topics covered.

External and Middle Ear

External ear

The outer ear plays a passive role in the hearing process. Along with the head and body it can affect the propagation of sounds in space and consequently can have an effect on the acoustic signal reaching the tympanic membrane. In humans the shape of the head, pinna, and ear canal can affect the sound in a number of ways. The head acts as an obstacle in the sound field. It reflects waves off its surface and also causes diffraction of the sound waves around it. Fig. 143-1 schematically illustrates the effects of acoustic shadowing and the baffle

effect. The arrows illustrate the direction of the sound waves and their pattern of reflection and refraction around the head. *Baffle effect* refers to the fact that sound waves impinging on a surface such as the head will be reflected. The incident and reflected waves may then combine near the side of the head to create a greater sound pressure than that without the head. *Shadow effect* refers to the fact that sound waves of a relatively short wavelength (compared to the size of the head) are blocked to a certain extent and result in an area of reduced sound pressure on the opposite side. The waves bend or refract around the head, so that the shadow effect depends on sound frequency or wavelength. Higher-frequency sound results in more head shadow and consequently a greater interaural intensity difference for a sound location on either side of the head. Other parts of the body also cause reflection and shadowing, but the effects on the sound pressure in the ear canal are less pronounced.

The opening into the ear canal and the ear canal itself act as acoustic resonators and can cosequently affect the sound pressure at the tympanic membrane. Over much of the frequency range of hearing, the ear canal acts as a simple tube, open at one end. The length of such a tube to a great extent determines the resonant characteristics, typically resulting in a resonant peak of close to 3.5 kilohertz (kHz) in human ears. This resonant peak in the frequency response is broad, since the cavity is not hard walled and the vibration of the soft tissue in the canal walls tends to dissipate energy. Nevertheless, the effects of the ear canal resonance contribute substantially toward an increase in sound pressure level at the tympanum compared to what would exist in free space without the person present. Shaw (1974) has made extensive measurements of the effects of the head and external ear on the sound pressure at the tympanic membrane. Fig. 143-2 offers an example of such measurements for a sound source placed directly in front of the head. There is a substantial increase in sound pressure compared to that without the head: a range of 1 to 8 kHz.

Several characteristics of the head, body, and external ear are thought to be important in providing cues for sound localization (Blauert, 1983). The interaural intensity differences that result from the baffle and shadow effect for high-frequency stimuli are highly dependent on the position of the sound source in space. Sources on the side of the head may then result in large differences in stimulus intensity reaching the two ears. Also, the distance between the two ears results in a time difference between sound arrival at one ear and the other. This interaural time difference also depends on sound location in space and can be on the order of 60 microsec (Fedderson et al, 1957) for a sound source on one side of the head. Cells in the central nervous system are exquisitely sensitive to these small differences in interaural time and intensity. Their properties and possible role in sound localization will be discussed in a later section of this chapter.

The diffraction of sound around the head may also contribute to localization. Sound sources at different positions around a subject will result in different diffraction patterns because of the asymmetry of the head and pinna around a coronal plane. The resulting sound pressure transformations from free field to eardrum show a different frequency dependence as the angle of sound incidence is changed (Shaw, 1974). Thus the head and external ear may affect the spectrum of a broad-band signal reaching the tympanum in a different way for different positions of the source. Some animal species have voluntary control over their pinna and consequently can adjust these gain characteristics to a certain extent and further take advantage of these differences in localization of sound.

Middle ear transformer

The middle ear serves to transmit sound energy from the air space in the external auditory meatus to the fluid in the cochlea. This coupling is accomplished through the vibration of the three middle ear ossicles. The movement of the tympanic membrane in response to pressure changes in the external ear results in vibration of the ossicular chain. The vibration of the stapes in the oval window results in a differential pressure between the oval window connected to the scala vestibuli and the round window opening into the scala tympani. This pressure difference between the two scalae is critical to the vibration of the cochlear structures. Without the tympanic membrane and ossicular chain, a similar sound pressure level would be applied to both oval and round windows and little pressure differential would exist. Hence, the middle ear mechanism is important to efficiently activate the inner ear structures.

In addition, the middle ear serves as a transformer, acting to increase the sound transmission to the cochlear fluids relative to what would occur with a direct coupling. Sound generally is propagated to the tympanic membrane through air. The middle ear serves as an interface between air in the ear canal and the fluid of the inner ear. The characteristics of sound propagation in any medium depend on the properties of the material making up the medium. The specific acoustic impedance, Zs, is defined to be the ratio of sound pressure and particle velocity (how fast the particles vibrate) at a point in space. The specific acoustic impedance is characteristic of the medium. The characteristic impedance of air is much less than the impedance of the fluid in the cochlea. In air, the pressures are relatively low and the particle velocity is relatively high. The higher impedance fluid requires a higher pressure to vibrate its particles so that much of the energy is reflected from the surface of the fluid and little energy is transmitted. Consequently, direct transmission of sound from air to the cochlear fluid is inefficient. The middle ear serves to increase the efficiency of this transmission by transforming the signal from a low pressure (in air) to a high pressure (applied to the fluid). Since the middle ear serves as a transformer rather than as an active device such as an amplifier, the increase in sound pressure from the air to cochlear fluid provided by the middle ear is accompanied by a decrease in vibration velocity compatible with the impedance of cochlear fluid.

Several characteristics of the middle ear contribute to this transformer effect. One major factor is illustrated in Fig. 143-3, A. The area of the tympanic membrane (A1) is greater than the area of the stapes footplate (A2). The force on the ossicular chain depends on the effective vibrating area of the tympanic membrane (force equals pressure integrated over the area). This force applied over the relatively small area of the footplate results in a gain in pressure proportional to the area ratio. The effective area ratio has been estimated to be approximately 18:1 (Wever and Lawrence, 1954), indicating that the pressure applied to fluid would be 18 times greater than the pressure applied to fluid would be 18 times greater than the pressure applied to the tympanic membrane. A second characteristic that contributes to the transformer effect is the lever ratio of the vibrating ossicles, illustrated in Fig. 143-3, B. The vibration of the ossicular chain is such that the malleus and incus rotate as a unit in an approximately coronal plane. The movement of the long process of the incus is less than that of the handle of the malleus, so that a simple lever exists. Force is applied to the malleus through the tympanic membrane. Since the resulting displacement of the incus is less, the force on the incus is then greater, resulting in a greater pressure in the fluid. This effect may

be relatively minor in humans, in whom the lever ratio is estimated to be about 1:3 (von Bekesy, 1960). A third and final factor has been termed the *curved membrane effect* (Helmholz, 1863). Basically the curvature of the membrane, in particular the fact that certain places on the membrane are vibrating at a greater amplitude than the part connected to the malleus, provides leverage to the system in moving the ossicles. This hypothesis has been supported by experiments using time-averaged laser holography to measure the vibration pattern of the tympanic membrane (Tonndorf and Khanna, 1970).

The middle ear is a mechanical system that is effective in increasing the efficiency of sound transmission, but like most mechanical systems, it does not transmit signals of different frequencies with equal efficiency. For pure tones of the same sound pressure level, the excitation of the inner ear will vary across frequency. The transmission properties of a system are usually expressed as a transfer function, where the amplitude of the output relative to the input (usually in decibels (dB)) is pltted as a function of frequency. If a system is linear, the transfer function is unique; that is, the frequency response is the same for all input levels. A direct method of assessing the transfer function is to measure the response of the system as a function of frequency with the amplitude of the input held constant. Guinan and Peake (1967) made measurements of the middle ear transfer function in anesthetized cats. They observed linear growth of displacement with input sound level, which indicates that the system is linear, at least in anesthetized cats with middle ear muscles that are not active. They then measured the amplitude and phase of the stapes displacement as a function of frequency, holding the sound pressure at the tympanic membrane constant. The measured displacement was then proportional to the transfer function. Both they and Moller (1963) measured an essentially low pass function, the cutoff frequency being in the region of 3 kHz and the slope of the cutoff approximately 12 dB/octave. Fig. 143-4, A, is an idealized example of such a function.

The specific variables defined to be the input and the output determine the shape of the transfer function. The pressure in the cochlear fluids resulting from sound input is the effective stimulus that vibrates the inner ear structures. The velocity of the stapes is proportional to the pressure changes in the cochlear fluids. Consequently, several authors have argued that the velocity of vibration of the stapes is the relevant dependent variable (Dallos et al, 1974; Pickles, 1988). For pure tone (sinusoidal) signals, the velocity of vibration can be calculated from the displacement. Velocity increases in proportion to frequency for a constant peak-to-peak displacement sinusoid, and the transfer function for velocity can be calculated by adding a 6 dB/octave tilt to the displacement function. The resulting transfer function, if velocity is considered the output, shows essentially a bandpass characteristic with a peak near 3 kHz, as shown schematically in Fig. 143-4, B. Nedzelnitsky (1980) has made measurements of sound pressure in the cochlea scalae with acoustic stimulation. The transfer function of pressure difference between scala vestibuli and scala tympani relative to ear canal sound pressure shows a relatively broad response consistent with the velocity transfer function in Fig. 143-4, B. Therefore, if one uses pressure or stapes velocity as the relevant output of the middle ear, the transfer function can be described as bandpass with shallow cutoff slopes and a peak response near a frequency of 3 kHz.

These transmission properties are consistent with a model of the middle ear as a passive mechanical system. One way in which the mechanical properties of this system can be assessed in humans is through the measurement of acoustic impedance. If one traps a volume of air in the ear canal, then the ratio between pressure and volume velocity will depend to a greater extent on the ability to move the tympanic membrane and the structures connected to it. Thus the acoustic impedance in the external ear will reflect the mechanical properties of the middle ear. Much of our understanding of the middle ear system is based on such measurements. We can view the middle ear and cochlea as being made up of a group of discrete mechanical elements having characteristics of resistance, inertia, and mass. The schematic drawing in Fig. 143-5 illustrates a block diagram of how different elements of the system may be grouped into a circuit analog (Zwislocki, 1963, 1975).

Each of the elements in the diagram has different mechanical properties and consequently differently to the impedance measured at the tympanic membrane and also to the transfer function. The shape and size of the middle ear cavities are important in determining the vibration of the tympanic membrane. As the tympanic membrane moves in, air is compressed in the cavity, and it consequently acts as a compliant element (or a spring, in mechanical terms). Basically the compression of air makes the tympanic membrane more difficult to move. The malleus and the incus are primarily inertial components and contribute the largest mass seen in the impedance at the tympanic membrane.

The effects of the tympanic membrane on the acoustic impedance are seen primarily at high frequencies. At low frequencies the mode of vibration is such that movement of the tympanic membrane is transmitted to movement of the malleus (von Bekesy, 1960; Khanna and Tonndorf, 1972; Tonndorf and Khanna, 1970). At high frequencies the vibration mode becomes complex, and large sections of the tympanic membrane may vibrate without those vibrations being transferred to the malleus. Thus we may view the tympanic membrane as a shunt path in the model; movement is generated but not transferred to the ossicular chain and the cochlea. The cochlea itself is also a very important element in the middle ear system. The impedance of the cochlea is primarily a resistance as a result of fluid movement through the bony canal. The resistive component in the acoustic impedance at the eardrum is in large part cause by the impedance of the cochlea (Moller, 1965). Thus in very simplified terms one can view the middle ear as a system having both mass (primarily ossicles) and compliant (primarily air-filled cavity) elements and therefore having resonant properties. The very large resistance contributed by the cochlea makes the middle ear very highly damped, and the transfer function displays a correspondingly broad frequency response function. Finally, the connection between the ossicles is not rigid, and the transfer of energy through the joints is not perfect. The coupling between elements can be modeled primarily as a spring, or compliance. Consequently, at low frequencies the transmission of energy through the joint is more efficient than at high frequencies. This loss in the transmission of vibration is modeled as a shunt path in Fig. 143-5.

Middle ear muscles

The two middle ear muscles, the tensor tympani muscle and the stapedius muscle, can have an effect on the mechanical properties of the middle ear and consequently on the transmission properties of the middle ear system. Sound stimuli can activate the muscles. This reaction, termed the *acoustic reflex,* is limited in humans to activity in the stapedius muscle.

The effect of stapedius contraction on the mechanical properties of the system has been studied in a number of experiments. With the stapedius muscle contracted, the largest change in acoustic impedance is seen at frequencies below 800 Hz (Moller, 1961). This measure reflects the increased stiffness of the system because of the force of the stapedius on the ossicular chain. The impedance of a compliant element (or stiffness) is inversely proportional to frequency. The effect of muscle contraction is consequently seen primarily at low frequencies, at which the compliant elements tend to dominate impedance measures. The transmission properties of the system with middle ear muscle contraction and without muscle contraction have been compared in animal experiments. These experiments have shown the muscle contraction has the greatest attenuation at low frequencies, but they have also displayed a small range of enhanced transmission at midfrequencies (Moller, 1965; Starr, 1969; Wever and Vernon, 1955).

Middle ear muscles can be activated bilaterally by an acoustic stimulus applied to either ear. The characteristics of the stimulus necessary to elicit a reflex have been studied in several animals and fairly extensively in humans. Moller (1962) measured the sound level necessary to observe a change in impedance caused by contralateral stimulation as a function of frequency. The shape of reflex threshold versus frequency paralleled the threshold of audibility with an approximately 80 dB sensitivity difference. Reflex threshold changes with hearing loss, but not in direct proportion to threshold of audibility. The response of the middle ear muscles in time has also been studied quite extensively. Moller (1962) measured impedance changes in humans with latencies ranging from 35 to 150 msec, depending on stimulus intensity. This long latency and the slow buildup of impedance change in the acoustic reflex are important in considering the effect of the acoustic reflex on the transmission of sounds. For long-duration sounds that change slowly in intensity, the transmission to the inner ear will be suppressed at high levels. In contrast, short-duration bursts of sound energy are transmitted relatively unimpeded by middle ear muscle activity.

The role of the middle ear muscles in hearing is not completely clear. The reflex has been suggested to have a protective role, attenuating intense sounds to inner ear structures. Although the acoustic reflex can provide a protective function, the level at which the reflex is activated, the relatively long latency of the reflex, and the lack of intense sounds in nature necessitating development of such a mechanism all argue against a purely protective function. It has also been suggested that the acoustic reflex may act as a gain-control mechanism in attenuating sound transmitted to the inner ear. Wever and Vernon (1955) measured cochlear electric potentials and demonstrated a constant amplitude of cochlear response as the level of a lower-frequency stimulus was increased in a limited intensity range above reflex threshold. The contraction of the middle ear muscles thus compensated for the change in stimulus level to keep cochlear input constant. Borg (1968) used acoustic impedance changes to demonstrate a similar effect in humans, although his results simply indicated decrease in the growth of response rather than perfect regulation. Finally, a quite different role has been proposed for middle ear muscles. In addition to their response to sound, middle ear muscles are also activated in conjunction with other muscle activity, particularly chewing and vocalization. For instance, the muscles contract before onset of vocalization and remain contracted for the duration. These muscle activities are inherently noisy. One function of middle ear muscles may be to anticipate and reduce the inner ear excitation caused by this self-generated noise (Simmons, 1964).

Cochlear Mechanics

Traveling wave

Much of our understanding of the mechanical response of the cochlea is based on a series of experiments by von Bekesy (1960). In those experiments, he directly observed the vibration of the cochlear partition in response to sound and described the motion as a traveling wave moving from the base to the apex of the cochlea. Further, he developed a series of models to explain the basis for the observed excitation pattern.

Von Bekesy observed movements of the basilar membrane in guinea pigs and human cadaver ears using stroboscopic illumination. He described the response to sinusoidal excitation as a traveling wave. Each point along the cochlear partition vibrates at a frequency equal to that of the input excitation. The amplitude and phase of the response differ significantly across the length of the cochlea. The resulting pattern of vibration, when viewed along the length of the cochlea, appears as a wave traveling from the base to the apex. Further, the amplitude of the vibration changes as the wave moves the length of the cochlea. The envelope of the wave gradually builds up to a peak and then quickly decreases as the wave moves toward the apex. Fig. 143-6 shows a plot of the traveling wave. The solid lines indicate the instantaneous position of the basilar membrane at four successive instants of time. The dashed lines indicate the envelope that limits the amplitude of vibration at each place. The instantaneous waveforms show the progression of the excitation from base to apex and also show that the wavelength gradually decreases toward the apex. The long wavelength in the base of the cochlea indicates that relatively large areas are vibrating approximately in phase. More apically, the wavelength becomes shorter so that the phase changes with distance are relatively large. Said another way, the wave propagates very quickly through the base, but its speed diminishes as it moves apically. Fig. 143-6 also illustrates that the form of the envelope is not symmetric: a very gradual increase in the amplitude of vibration from base to apex is followed by a rapid decline. Because of the asymmetric form, stimuli of low frequencies are effective in stimulating the basal end of the cochlea, whereas high-frequency stimuli are relatively ineffective in stimulation of places more apical than the envelope peak. This asymmetry is reflected in neural responses that are described in later sections of this chapter.

The form of the traveling wave is similar for different frequencies except that the peak of the envelope is displaced. Fig. 143-7 illustrates the envelope of the traveling wave for different stimulus frequencies. The place at which the peak of the traveling wave occurs is approximately proportional to the logarithm of stimulus frequency.

The traveling wave envelope is essentially a plot of vibration amplitude as a function of a place for a particular stimulus frequency. One may also plot the same data as the response at a particular place as a function of stimulus frequency. Fig. 143-8 shows such a plot, with both amplitude and phase of the response as functions of frequency. The response amplitude displays a peak at a particular frequency. This "best frequency" depends on place: more basal places display higher best frequencies than more apical places do. Consistent with the asymmetric plot of traveling wave envelope, this plot is also asymmetric on a scale of log frequency. The amplitude of response tends to be larger for frequencies below the best frequency than for frequencies above it. Von Bekesy observed a rising slope below best

frequency on the order of 6 dB/octave and a falling slope above best frequency of 20 dB/octave. More recent experiments have observed much sharper tuning (Johnstone and Boyle, 1967; Khanna and Leonard, 1982; Rhode, 1971). Also consistent with the description of traveling wave is the plot of phase at a place as a function of stimulus frequency. On the basal side of the traveling wave the wavelength is long, so that for low-frequency stimuli the phase lag is short. On the apical side of the traveling wave the wavelength is short, so that as frequency is increased above the best frequency, a cumulatively greater phase lag is observed.

The basis for the development of the traveling wave is the compliance of the basilar membrane (von Bekesy, 1953, 1960). At the basal end the membrane is stiff; the stiffness decreases systemically as one moves apically. Although this gradient in stiffness results in different resonance characteristics at each place, the basis for cochlear vibration is not a simple resonance system. The form of the traveling wave and, in particular, the large phase lags in the response observed for high-frequency stimuli (Fig. 143-8) preclude such an explanation. Rather, there is an interaction between the cochlear fluids and the cochlear partition: the fluid pressure results in displacement of the partition, and displacement of the partition causes fluid flow. The gradient in compliance along the cochlear length clearly is an important factor in this interaction, in that the compliance gradient determines the direction of the traveling wave.

Nonlinear response properties

Several investigators in the past 15 to 20 years using a variety of techniques have made further measurements of basilar membrane motion. Limitations to the interpretation of von Bekesy's earlier work are centered around his use of cadaver ears for measurement and also his need to use high stimulus levels (130 dB SPL). Several investigators have used the Mossbauer technique, placing a small radioactive source on the basilar membrane to measure the velocity of vibration (Johnstone and Boyle, 1967; Rhode, 1971, 1977). Other investigators have used a capacitive probe or laser interferometer technique to measure small amplitude of basilar membrane vibration (Khanna and Leonard, 1982; Le Page, 1987; Wilson and Johnstone, 1975). The ability to measure smaller amplitudes of vibration has allowed for the use of lower levels of input signals. The general features of von Bekesy's observations are consistent with these more recent measurements; however, there are two important differences that have been observed. First, the measurements that have been made at low levels have shown a much higher degree of tuning. Second, the growth of the response with level is nonlinear; as stimulus intensity is increased, the vibration amplitude does not increase proportionally. The data replotted in Fig. 143-9 from Rhode (1971) illustrate both of these observations. The response amplitude (calculated from the velocity measure using the Mossbauer technique) is plotted for three levels of stimulus intensity. The response at low frequencies shows a linear growth in that the amplitude increases by 10 dB for each 10 dB increase in stimulus level. The response amplitude at frequencies near 7 to 8 kHz grows more slowly than linearly. The resulting frequency response function is sharper for low-level stimuli and less highly tuned for higher-level stimuli. More recently other authors have demonstrated frequency selectivity equivalent to that observed in tuning curves of auditory nerve fibers (Khanna and Leonard, 1982; Sellick et al, 1982).

The high degree of frequency selectivity and nonlinear response have been shown to be very sensitive to the state of the animal and the cochlea. Rhode (1973) observed that the frequency response after death is relatively broad and does not change in shape with stimulus level, consistent with von Bekesy's measurements on cadaver ears. Leonard and Khanna (1983) observed decreased sensitivity and decreased tuning with damage to hair cells in the cochlea. Sellick et al (1982) have shown that as the sensitivity of the ear decreases, the growth of response becomes linear and the frequency selectivity decreases. Thus the presence of sharp tuning and nonlinearity seems to be highly dependent on the physiologic state of the ear. The most recent hypotheses concerning the mechanism producing this high degree of tuning attribute these properties to the movement of outer hair cells, which is coupled to the basilar membrane. These hypotheses suggest that movement of the basilar membrane is intricately involved with the response of the hair cells, and in particular, the nonlinearity and tuning are highly dependent on the state of the hair cells. These models have as a common feature an active process that is associated with the nonlinearity and the high degree of mechanical tuning. Probably the most direct evidence of such a mechanism comes from a recent study by Ruggero and Rich (1991). They demonstrated that furosemide injections, which affect the transduction currents in hair cells, also affect the sensitivity and tuning properties of the basilar membrane movement. More details of these mechanisms will be discussed in later sections on the transduction process.

The issue of nonlinearity of the movement pattern of the basilar membrane is critical to the question of the vibration amplitude of the membrane at threshold. If one uses a linear extrapolation of von Bekesy's data (1960), the amplitude of displacement of the basilar membrane at perceptual threshold levels is on the order of 0.003 A. A linear extrapolation of Rhode's data (1971) at 7 kHz yields a vibration amplitude at threshold of 0.1 to 0.3 A. Clearly, if a linear model is not appropriate, then these values would not be valind. The nonlinearity observed by Rhode is compressive in that the growth with level is less than a linear model would predict; thus the predicted threshold value would be greater than that made under a linear assumption. More recent measurements have shown displacements for low-level signals to be relatively high; that is, responses on the order of several nm for signals as low as 20 dB SPL (Sellick et al, 1982). As measures of the basilar membrane notion have become more sensitive, the resulting estimates of threshold response amplitude have been higher.

Otoacoustic emissions

A number of studies in recent years have measured acoustic signals generated within the ear by using a small, sensitive microphone in the external auditory meatus. These signals, generally termed *otoacoustic emissions,* have been measured in response to continuous acoustic stimulation and transient stimuli and also have been observed to be present spontaneously in some ears. Several experiments have provided evidence that these signals are cochlear in origin and reflect the mechanical vibration in the cochlea. For this reason they are included in this section on cochlear mechanics.

Fig. 143-10 illustrates emissions evoked by transient signals from human ears (Kemp, 1978). The stimulus is either a click or a tone burst and is present in the canal at a much greater amplitude than the recorded signal. The latency of the emission is 5 to 10 msec after stimulus onset, with duration on the order of 10 to 20 msec. The energy spectrum of the

emission by a broadband click varies significantly among individual subjects (Kemp and Chum, 1980; Zwicker and Schloth, 1984), but the responses are quite consistent within subjects across time. The emission is very sensitive to the state of the cochlea. Kemp demonstrated a lack of emission in subjects with sensorineural hearing loss. Anderson and Kemp (1979) and Anderson (1980) demonstrated that agents such as noise exposure and diuretic poisoning can cause a decrease in the acoustic emission. The preponderance of evidence has shown that the transient-evoked emission is cochlear in origin and that its generation is very sensitive to the state of the cochlea.

A second type of emission has been measured using two continuously presented pure tones. The acoustic signal measured in the ear canal may then contain distortion products not present in the original stimulus. These "distortion product emissions" have been observed at frequencies of 2f1-f2 and f2-f1 (f1 and f2 are the low- and high-frequency components of the stimulus, respectively) (Kim et al, 1980). These distortion components are also affected by acoustic trauma (Siegel and Kim, 1982b) and by other manipulations to the cochlea, such as experimentally induced changes in the endolymphatic potential and activity of the efferent fibers synapsing on outer hair cells (Mountain, 1980; Siegel and Kim, 1982a). The data are consistent with a hypothesis that the ear canal distortion is a consequence of the presence of distortion products in the vibration of the cochlear partition (Kim, 1980). Robles et al (1990) have, in fact, observed distortion components in the vibration of the basilar membrane.

Finally, several investigators have observed acoustic signals in the ear canal with no stimulus present. These spontaneous emissions are usually narrow band, that is, tonelike, and there can be several frequencies of emission present in an individual ear. Studies have shown that only about 50% to 70% of normal hearing subjects have a measurable emission (Bright and Glattke, 1986; Strickland et al, 1985). Spontaneous emission frequencies are different across subjects although often in the range of 0.5 to 6 kHz. The frequencies of emissions are consistent across time within an individual subject, although there can be some small diurnal variations (Haggerty, 1989). Spontaneous emissions can be decreased in amplitude by the introduction of an external tone of appropriate frequency and amplitude. The level of external tone necessary to mask the spontaneous emission as a function of frequency shows frequency selectivity similar to basilar membrane tuning and other cochlear processes (Zurek, 1981). Other studies have shown a relationship between places of irregular outer hair cell arrangements in nonhuman primate cochlea with frequency of spontaneous emissions (Lonsbury-Martin et al, 1988). Several observations such as these have contributed to the hypothesis that the spontaneous emissions are cochlear in origin. Attempts to relate the spontaneous acoustic emissions to perceptual tinnitus have been unsuccessful, in that patients with perceptual tinnitus typically may not have a corresponding spontaneous emission in their ear canals.

The preponderance of evidence suggests that all types of emissions are cochlear in origin and that their generation is very sensitive to the state of the cochlea. They are produced by a nonlinear, active mechanism that probably involves the outer hair cells (see section on hair cell transduction). For these reasons and their noninvasive method of measurement, otoacoustic emissions have been developed as a clinical measure in recent years (Kemp et al, 1990; Lonsbury-Martin and Martin, 1990). Since emissions tend to be larger or more sensitive in infants and young children, these measures may be particularly useful as part of an infant screening process (Stevens et al, 1990).

Hair Cell Transduction

General features of transduction process

Roberts et al (1988) have summarized much of the recent data on hair cell function. Fig. 143-11 illustrates the elements thought to be important in the transduction process from mechanical vibration to neural excitation in the cochlea. The vibration of the basilar membrane and cochlear partition results in a shearing force on the stereocilia in a direction perpendicular to the axis of the stereocilia. The mechanical deformation of the stereocilia results in a receptor potential, measurable through intracellular recordings from hair cells and through gross electric potential recordings in the scala or at the round window. The chemical synapse at the base of the hair cell with the afferent neuron endings provides the means for stimulating the neuron. The generator potential is conducted through the afferent neuron, where it is instrumental in setting up the all-or-none action potentials. The different elements in the transduction process and the associated measures of electrical activity are discussed later.

Hair cells similar to those of the ear are found in vestibular organs and also in mechanoreceptors of the lateral line organ of fish (Flock, 1965; Flock et al, 1973). Each hair cell in these organs possesses a single long projection called a *kinocilium,* which functionally polarizes the hair cell. The bending of stereocilia toward the kinocilium acts to increase current through the cell membrane and increase the receptor potential, whereas stereocilia movement away from the kinocilium acts to decrease current. Hair cells are sensitive to a range of displacement of approximately 100 nm, which corresponds to approximately 1 degree of angular displacement (Corey and Hudspeth, 1983; Holton and Hudspeth, 1983). With the stereocilia in a resting position, there is typically a steady state current flowing through the cell (Ohmari, 1984). The movement of the stereocilia modulates the current flow around this steady state value. Bending the stereocilia toward the tallest stereocilia causes an increase in the current through the tip of the hair cell; bending the stereocilia in the opposite direction results in a decrease of the starting current (Flock et al, 1973). This variation in receptor current is the result of a change in the conductance of the cell membrane and is mainly carried through the flow of K+ ions.

Stereocilia of hair cells are typically connected to a superstructure such as the cupola, a gelatinous mass into which the tips of the stereocilia of the lateral line organ are embedded. These structures aid in the transfer of energy from a fluid movement to a shearing force that bends the stereocilia. In effect, the movement of the fluid through the action of the cupola bends the stereocilia. Hair cells in the vestibular organ in mammals have many of these same characteristics. The stereocilia of the semicircular canal organ similarly attach to a cupola. Movement of the fluid is transferred to the stereocilia through these structures. The inner and outer hair cells of the organ of Corti in mamals do not have a true kinocilium but possess a basal body. The basal body is located toward the outer edge of both the inner and outer hair cells. The tallest stereocilia of the outer hair cells are attached beneath the tectorial membrane, although those of the inner hair cells do not appear to make similar contact (Lim, 1972, 1980). The vibration of the basilar membrane results in the movement of the associated structures of the cochlear duct. Von Bekesy (1960) hypothesized that the stereocilia undegro a shearing force in the radial direction (from the modiolus to the outer edge of the cochlea) as the result of basilar membrane displacement. This radial shear is in the direction of tall to

short stereocilia and is likely the effective stimulus for excitation of the hair cell.

Hair cell potentials

Before describing the electrical response within the cochlea to sound stimuli, it is instructive to review the steady state potentials measured with no stimulus present. The potential of the perilymph compartments, the scala vestibuli, and scala tympani is approximately the same as the surrounding bone. An electrode in the scala media shows a positive potential for 80 to 90 mV, termed the *endolymphatic potential* (EP). Its source is thought to be an active metabolic process within the stria vascularis. The ionic content of the fluid spaces surrounding the hair cells in the organ of Corti is similar to that of perilymph and the potential is similarly 0 mV. Intracellular potentials for the inner hair cells are on the order of -35 mV, whereas those for the outer hair cells are somewhat greater (Dallos, 1985). The resulting electric potential across the stereociliar end of the hair cell is approximately 120 to 150 mV. This rather large electric potential can be thought of as a battery or an energy source that provides the current flow modulated by stereocilia movement.

For a number of years, investigators have used electrodes in or near the cochlea to measure electrical activity generated within the organ of Corti. These recordings are not the responses of single cells but are the result of a number of cells contributing to the potential at the electrode site. Wever and Bray (1930), in recording activity from the auditory nerve, reported that the amplified electrical signal led to a loudspeaker would result in an understandable reproduction of the acoustic input signal. This potential was later established to be cochlear in origin and is called the *cochlear microphonic* (CM). The CM refers to the AC potential measured with electrodes in or near the cochlea in response to acoustic input. In addition, a DC component, called the *summating potenital* (SP) is observed. With a sinusoidal input stimulus, the measured response has not only a sinusoidal component (CM but also a shift in the baseline or average potential while the stimulus is on. The SP can be either positive or negative, and its amplitude is the same order of magnitude as the CM (Davis et al, 1958a). The source of the SP is more complex in that these are apparently several components that contribute to this potential (Davis et al, 1958b). These include the DC potential generated by the hair cells and possibly the generator potential in the afferent dendrites.

More recently, investigators have measured the response of individual hair cells of the organ of Corti to sound stimuli. Typical responses to sinusoidal stimuli from an inner hair cell are shown in Fig. 143-12 (Russell and Sellick, 1983). Frequencies below 1 kHz evoke a substantial alternating component, which is asymmetric; that is, it is greater in the positive direction than in the negative direction. The resulting waveform can be described as having both an AC and a DC component. The capacitive properties of the cell membrane form low pass filter, resulting in the attenuation of the AC compoent at high frequencies. The traces showing responses to higher frequencies consequently show a smaller AC component with a relatively large DC component. Both components show a similar monotonic growth and reach a saturation amplitude at high stimulus levels.

The tuning properties of the hair cell are shown in Fig. 143-13, for which the stimulus level necessary to produce a criterion response amplitude is plotted as a function of frequency (Russell and Sellick, 1977). These contours show a high degree of frequency selectivity for both the AC and DC components. Both functions are similar in frequency selectivity to both the most sensitive measures of basilar membrane tuning and those of auditory nerve fibers (Khanna and Leonard, 1982; Kiang et al, 1965). Measurements from outer hair cells show a similar high degree of frequency selectivity (Dallos et al, 1982). In general, intracellular potentials of both the inner and outer hair cells reflect the high degree of frequency tuning seen in neural response.

The isoamplitude functions ni Fig. 143-13 show a change in shape for different criterion levels; that is, the functions do not simply shift up in level. These differences in shape indicate nonlinear growth of response amplitude with increasing stimulus level. The rate of growth is generally greatest for low frequencies of stimulation (below best frequency) and tends to decrease with increasing stimulus frequency above the best frequency.

The tuning properties observed in mammalian organ of Corti hair cells seem to reflect the underlying mechanical response of the basilar membrane. Nevertheless, there have been several observations that indicate that hair cells have inherent tuning properties. Work in turtles has demonstrated that hair cells can have a strong degree of electrical tuning by measuring oscillations in the response to step changes in current (Crawford and Fettiplace, 1981). Both amphibian and reptile ears have demonstrated a greater degree of frequency tuning in electrical response than the underlying mechanical vibration (Ashmore, 1983; Weiss et al, 1978). In mammals, both the stereocilia's height and their mechanical properties vary across the length of the cochlea, suggesting a contribution of the hair cell to the frequency tuning properties of the cochlea (Lim, 1980).

Models of transduction

Davis (1965) proposed a very simple but useful model of hair cell function in the cochlea (Fig. 143-14). The hair cell membrane between the scala media and the intracellular fluid acts as a variable resistance, and the resting potentials act as a DC power supply, or battery. When the basilar membrane is in vibration, the current through the hair cell membrane is modulated as the stereocilia are deflected. The modulated current flow results in the intracellular receptor potential. This current in turn produces a change in the conducting fluid media around the organ of Corti, resulting in the measured cochlear microphonic potential and the summating potential.

Several experiments have provided support for at least the basic tenets of this theory. Experimental manipulation of the endocochlear potential generally results in concurrent changes of the CM (Honrubia et al, 1976). Tasaki and Fernandez (1952) observed that positive polarization of the scala media increases the amplitude of the CM. These observations are generally consistent with Davis's model, in that changing the battery voltage changes the current flow and consequently the measured response potential. Other experiments have demonstrated resistance changes within the organ of Corti with vibration of the partition. Hubbard et al (1979) measured the resistance across the cochlear partition and showed periodic resistance changes corresponding to the periodicity of the input stimulus. Data from hair cell recordings have demonstrated that nonspecific resistance changes of the cell

membrane accompany depolarization of the hair cell (Corey and Hundspeth, 1979; Hudspeth and Corey, 1977). Measurements of flow near the tips of stereocilia have implicated the tips of the stereocilia as the place where current enters the hair cell (Hudspeth, 1982). The precise mechanism by which resistance is modulated has yet to be determined, although the cross-linked structure among the stereocilia has been suggested as a probable site for this mechanism (Pickles, 1988).

Although recent studies have shed considerable light on many of the basic properties of hair cellfunction, the purpose of the two different hair cell systems in the cochlea is not completely established. A number of morphologic differences exist between the inner and outer hair cells, particularly in the pattern of innervation, both afferent and efferent. The radial afferent fibers of the auditory nerve innervate the inner hair cells and make up the large majority of afferent fibers. There are no synaptic connections between these neurons and the outer hair cells; nevertheless, the preponderance of data on single-auditory nerve fiber responses leads one to conclude that the outer hair cells have some effect on the response of the radial afferent fibers. These two systems thus appear to interact, and this interaction adds an additional level of complexity to any model of transduction.

The outer hair cells apparently transduce mechanical deformation of the stereocilia in the same way as inner hair cells, but they also possess the ability to transduce electric potentials to mechanical movement. This motile response of the outer hair cell has been demonstrated in a number of experiments. Brownell et al (1985) observed a fast motile response in response to electrical current excitation. In addition, a slower mechanical response has been observed in response to changes in the extracellular K+ concentration (Zenner et al, 1985). A number of studies have investigated the details of these phenomena in recent years. The site of the force-generating mechanism is apparently at the plasma membrane along the sides of the hair cell body (Holley and Ashmore, 1988) and is most likely driven by the potential difference across the membrane (Santos-Sacchi and Dilger, 1988). The mechanism of force generation in hair cells is apparently quite different than that in muscle cells. For instance, the movements can occur at stimulation rates in audio frequency range (Ashmore and Brownell, 1986; Evans et al, 1989). The speed of this motile response precludes a mechanism similar to muscle cells. Also, inhibitors of ATP synthesis fail to suppress the motile response in hair cells (Holley and Ashmore, 1988). The ability of outer hair cells to generate force at these rates has led to hypotheses that they are involved in an active feedback mechanism in the cochlea. The evidence from measurements of basilar membrane response and from measurements of otoacoustic emissions indicates that there are clearly active, nonlinear processes in the cochlea that produce mechanical vibration. Several models have been developed that suggest that the outer hair cell is part of an active feedback mechanism that increases the response of the basilar membrane to certain frequency stimuli (Davis, 1983; Kim, 1984; Neely and Kim, 1983). The mechanism enhances the responses at low stimulus levels, and the effect saturate at higher stimulus levels. The result is an increase in the frequency selectivity of the traveling wave and also nonlinear growth of the vibration. The outer hair cells may function to enhance the sensitivity and frequency selectivity of the inner hair cells by positive mechanical feedback to the basilar membrane vibration. This mechanism is particularly vulnerable to various insults to the cochlea such that loss of sensitivity and frequency selectivity are sometimes linked.

Auditory Nerve

Single-neuron response properties: simple stimuli

The response of single auditory nerve fibers to both simple and complex acoustic stimuli has been measured in many experiments. Most have used an experimental approach in which a microelectrode is placed in the nerve trunk, in order to isolate activity of what is thought to be type I myelinated nerve fibers as identified by Spoendlin (1978). These afferent neurons innervate the inner hair cells and make up the majority of afferent neurons in the auditory nerve. Several early studies have outlined some basic response properties (Hind et al, 1967; Katsuki et al, 1962; Rose et al, 1967); much of what is presented in this section is taken from a monograph by Kiang et al (1965). Studies discussed here have used cats, monkeys, guinea pigs, and gerbils as experimental subjects.

With no external stimulation, auditory nerve fibers discharge action potentials in a random time sequence, called *spontaneous activity.* Some fibers discharge at very slow rates, but others have spontaneous rates up to 100 per second. Fibers have typically been placed into three groups designated high, medium, and low spontaneous rate. Fibers with high spontaneous rate (> 18 per second) tend to be more sensitive to sound stimulation. Those with low spontaneous rates have thresholds ranging up to 60 dB higher than the most sensitive fibers (Liberman, 1978).

Individual nerve fibers respond to the presence of sound with an increase in the discharge rate of action potentials. The rate of response depends on both intensity level and the frequency of pure-tone stimulus. Fig. 143-15 illustrates the pattern of action potentials in response to a pure-tone swept-in frequency; each horizontal trace corresponds to a different signal level. At low levels a relatively narrow range of frequencies is effective in eliciting a response; as the level is raised, the discharge rate increases, as does the range of effective frequencies. The threshold of response as a function of frequency is called the *tuning curve* or *frequency threshold curve* (FTC). This threshold level is determined by sweeping across the frequency at each stimulus level or by varying the stimulus level for selected stimulus frequencies (Kiang et al, 1965; Evans, 1972). Fig. 143-16 illustrates typical tuning curves from several neurons. The tip of the tuning curve, the frequency to which the fiber is most sensitive, is usually called the *characteristic frequency* (CF), or *best frequency.* The characteristic frequency of each neuron is determined by its place of innervation along the cochlear partition (Liberman, 1982). This tonotropic organization is preserved in the nerve trunk, so that fibers encountered as an electrode passed through the nerve trunk generally have a systematic progression of best frequency. As one may expect, the threshold values of the most sensitive fibers at a particular CF are close to or at the behavioral threshold for that frequency (Liberman, 1978).

The general shape of the tuning curve is similar across fiber CF; that is, relatively steep slopes on each side of the CF form a V shape. The sharpness of tuning is similar to that of the mechanical vibration and hair cell response. One way to quantify the sharpness of tuning is by the width of the tip region. Kiang et al (1965) measured the Q10 value of the tuning curve, defined as the characteristic frequency divided by the bandwidth of the tuning curve at 10 dB above threshold at the CF. The Q10 provides a measure of frequency selectivity normalized to the characteristic frequency. The values of Q10 tend to increase with

fiber CF, indicating that on a logarithmic scale the fibers with higher CF have more narrow tuning curves. The tuning curves are generally asymmetric. The increasing portion above CF tends to have a steeper slope than the decreasing portion just below the fiber's CF. Fibers with high CF also display a relatively flat low-frequency region, usually called the *low-frequency tail.* The low-frequency tail can be approximately horizontal or have a very shallow slope. The tail is typically at a level 40 to 50 dB above the CF threshold (Kiang and Moxon, 1974). Thus fibers with a high characteristic frequency generally respond to very low-frequency tones that are high enough in level. The sensitivity of such fibers changes little over a wide range of low-frequency stimuli.

The tuning curve represents essentially a threshold response of the nerve fibers. Other experiments have measured several different aspects of the suprathreshold response. The simplest of these is the measurement of discharge rates. Fig. 143-17 illustrates a plot of the discharge rate of a neuron to a pure tone as a function of stimulus level. Each curve shows the rate in response to a different stimulus frequency (Sachs and Abbas, 1974). In many cases, the discharge rate increases with stimulus level over a dynamic range of 30 to 40 dB, above which the rate saturates. Three variations to this trend are noteworthy. Instead of a saturation, some fibers displayu a distinct decrease in slope at high stimulus levels. These fibers generally display a wider dynamic range than do the fibers reaching a true saturation. Also, the rate functions for frequencies lower than the characteristic frequency have a steep slope and a small dynamic range, whereas rate functions for frequencies higher than CF have a more shallow slope and correspondingly wider dynamic range. Finally, Kiang and Moxon (1972) have observed that at a high stimulus (90 to 100 dB SPL) a dip or "notch" may occur in the rate versus level function. This dip may be evident at levels far above that at which the fiber has saturated.

The tuning curve may be derived from the set of rate versus level functions of a fiber. The sensitivity (or horizontal position) of each rate versus level function for different stimulus frequencies corresponds to the slope of the tuning curve of the fiber. Note that the concept of threshold in this situation is somewhat arbitrary, in that one really sets a criterion response rate. Since the rate versus level function do not have identical slopes across stimulus frequency, the shape of the tuning curve to some extent depends on the criterion chosen for threshold.

Another method of measuring or presenting the same response is shown in Fig. 143-18 (Geisler et al, 1974). In these experiments the discharge rate of a fiber is shown as a function of stimulus frequency, with the parameter being stimulus level. Consistent with the tuning curve data, the range of response is small for low-level stimuli. As the stimulus level is increased, there is a general increase in rate, in addition to an increase in the range of frequencies at which activity is observed. At high levels the rate is saturated at frequencies near fiber CF. Further increases in the stimulus level result in a spread of activity over a wider frequency range rather than a general increase in rate. The spread of activity with increased level tends to be toward lower frequencies, consistent with the shape of the tuning curve.

Up to this point we have discussed measures of response in which the number of action potentials is simply counted to calculate an average discharge rate. The pattern of nerve fiber discharges can also be quantified by measuring the timing of the action potentials relative to the acoustic stimulus. The poststimulus time (PST) histogram is one common method of measuring the time pattern of the response. The generation of action potentials is a probabilistic process; that is, each stimulus presentation results in a slightly different pattern of action potentials. The underlying pattern of response can be extracted by presenting the identical stimulus several times and measuring the time of each action potential relative to stimulus onset. A histogram of the number of action potentials as a function of time after stimulus onset can then be constructed.

Fig. 143-19 illustrates PST histograms in response to a click stimulus of several different nerve fibers, each with different characteristic frequencies (Kiang et al, 1965). The graph shows the number of action potentials in each bin; we may interpret the graph as being proportional to the probability of an occurrence as a function of time after stimulus. Each histogram has either one peak or a series of peaks in time, indicating that there are certain times after the click that the probability of generating an action potential is very high. The spacing between the successive peaks decreases with increasing fiber CF; at high CF only one peak is evident. Also, the latency to the first peak decreases with increasing fiber CF. These findings can be interpreted in terms of the characteristics of the mechanical traveling wave in the cochlea and the inferred characteristics of its response to impulsive stimuli. Given the filtering characteristics of the basilar membrane, each place would oscillate or "ring" at its natural frequency. Rhode and Robles (1974) have demonstrated such behavior in direct observations of the motion of the basilar membrane in response to clicks. The alternating peaks and valleys in the PST histogram then correspond to alternating excitatory and inhibitory effects of the bending of the hair cell stereocilia. The spacing between the peaks in the PST histogram for low CF fibers corresponds well to a period equal to 1/CF. For high CF fibers connected to basal portions of the cochlear partition, the vibration is at a high enough frequency and the action potential generation is imprecise enough in time that the individual peaks are not discernable. Similarly, the latency to a click stimulus depends on fiber CF or the place along the cochlear partition where the fiber synapses. The latency then indicates the time taken for the traveling wave to reach that position in the cochlea. Thus low CF fibers show a greater latency of response than do high CF fibers.

Fig. 143-20 is a composite drawing illustrating the effects of the traveling wave mechanics on the responses of individual neurons. The figure shows PST histograms of many fibers arranged according to fiber CF. For high-frequency fibers in the basal end of the cochlea, the wavelength of the traveling wave is long so that the latency is short and latency changes little with fiber CF or place. For low CF fibers in the apical end of the cochlea, the wavelenght of the traveling wave becomes shorter. The latency is longer, but also the change in latency with fiber CF or place is greater. These data are important in the discussion of far-field measures of electrical response such as the whole-nerve action potential or auditory brani stem response. Each of these measures constitutes summed neural activity across a population of neurons. The responses of high-frequency fibers tend to be well synchronized in response to a click stimulus, whereas those of more apical fibers are spread across a longer time interval. Consequently, such far-field measures tend to be dominated by high-frequency fibers whose responses occur synchronously and tend to sum with one another.

The PST histogram has also been used in measuring the response to tone-burst stimuli. Fig. 143-21 illustrates an example in which the stimulus is a 500-msec tone burst (Kiang et al, 1965). The probability of generating an action potential is very high at the onset of the tone burst, but it quickly decreases with an approximately exponential time course to a steady state response rate. After the tone offset there is a short period of reduced spontaneous activity, which recovers to the normal spontaneous rate. The rise time of a tone burst is a critical parameter in determining the relative amplitude of the onset response; faster rise-time values result in a greater onset effect (Smith and Brachman, 1980). The time course of the onset response has been measured as a three-segment function (Delgutte, 1980; Smith and Brachman, 1980). The first few milliseconds are characterized by a very fast adaptation, followed by the slower decrease seen in Fig. 143-21, before reaching steady state rate. The initial response peak at the onset of the stimulus does not grow in proportion to the steady rate with increases in stimulus level; rather, the initial peak continues to grow at levels above which the steady state response saturates. These changes in the response indicate an adaptation process that may have its source in the chemical synapse between the hair cell and the afferent dendrite (Furukawa and Ishii, 1967; Smith, 1979). Hair cell responses do not display a similar time course of adaptation (Mulroy et al, 1974; Russell and Sellick, 1978), and the excitatory generator potentials of eight nerve fibers do show these adaptation characteristics (Furukawa and Matsuura, 1978).

The width of the time bin used to plot the PST histogram determines the time resolution that can be observed. A PST histogram such as that shown in Fig. 143-21 in response to a tone burst can be measured and plotted on a much finer time scale. The example in Fig. 143-22, A, shows a PST histogram of the response to a stimulus 10 msec in duration. In this case the phase of the tone burst within the envelope was fixed so that exactly the same waveform was repeated for each stimulus. Since the width of the time bins in the PST histogram is very narrow, the histogram displays a series of peaks and valleys at a period equal to that of the tonal stimulus. These peaks and valleys are the result of the alternating excitation and inhibition of the hair cell caused by basilar membrane vibration similar to the click responses in Fig. 143-19. The high probability of eliciting an action potential at a particular phase of the input stimulus is called *phase locking.* The decreasing amplitude of each succeeding peak is a manifestation of the adaptation properties discussed relative to Fig. 143-12.

Phase-locked behavior has also been demonstrated with continuous sinusoidal stimuli using what has been called a *period histogram.* A period histogram can be generated by measuring the timing of action potentials relative to the beginning of the cycle of aperiodic stimulus waveform. Figure 143-22, B, shows a typical period histogram of the response. If the histogram were flat, that would indicate that the action potentials occur at random times relative to the input phase. The fact that there is a preferred phase, or peak, in the period histogram indicates that phase locking is occurring to the input sinusoid. It is important to understand that phase locking does not necessarily indicate an entrainment of the action potentials to the cyclic nature of the sinusoid; that is, there is not one action potential per stimulus cycle. Rather, when action potentials occur, they occur with a greater probability at a certain stimulus phase. The *vector strength* is commonly used to quantify the degree to which action potentials are phase locked to the input stimulus (Goldberg and Brown, 1969). Vector strength is the tendency of spikes to occur in a particular bin of the period histogram. A value of 1 indicates perfect phase synchronization; a value of 0 indicates a flat histogram

with no synchronization.

A final method of measuring the timing of action potentials is the use of an interval histogram. No knowledge of the input stimulus is necessary for this measure. Rather, the histogram is generated by measuring the time between successive action potentials and plotting the number of occurrences of that interval for each interval time (Rose et al, 1967). A typical response to a 1000 Hz tonal input is illustrated in Fig. 143-22, C. Each cycle does not generally elicit an action potential, but when action potentials occur, they do so at a particular stimulus phase. Consequently, most intervals between action potentials are near integer multiples of the stimulus period. As stimulus level is changed and average discharge rate is increased, the distribution of intervals also changes toward shorter intervals.

Measures of synchronization show many of the same characteristics as discharge rate (Javel, 1986). The vector strength increases with increasing stimulus level and shows a saturation at high levels. The sensitivity of the vector strength is greater than discharge rate; that is, evidence of the phase locking of action potentials appears at stimulus levels below which changes in rate occur. That is, the average discharge may be the spontaneous rate, but the timing of the action potentials is affected so that they occur preferentially at a given phase (Littlefield, 1973; Rose et al, 1967). Measures of synchronization result in tuning curves that are similar in shape to rate tuning curves but are more sensitive (Javel, 1986). At the very high stimulus levels at which discharge rate saturation occurs, the shape of the period histogram may reach a plateau (Rose et al, 1971). Finally, these phase-locking characteristics are limited to stimuli of relatively low frequency. At frequencies above 600 to 800 Hz, the maximal amount of phase locking observed decreases with stimulus frequency to approximately 4000 Hz (Johnson, 1980). At frequencies above 4000 Hz, no evidence of phase locking is observed.

Single-neuron response properties: complex stimuli

Although the responses to pure-tone stimuli have been studied in great detail, the limitations in generalizing those responses to complex stimuli have been underscored by a number of studies demonstrating nonlinear response properties. Clearly, several properties of pure-tone responses (already discussed) are nonlinear, such as the saturation of discharge rate at high levels and the different growth rate with stimulus level for different stimulus frequencies. Studies with stimuli consisting of two tones have provided additional evidence of nonlinear responses.

When two tones are presented simultaneously, the response of a nerve fiber is not simply the sum of the response to each individual tone presented separately. Several experiments have demonstrated that the discharge rate in response to a two-tone stimulus (excitor tone and suppressor tone) may be less than when just one tone (excitor tone) is presented alone (Arthur et al, 1971; Sachs and Kiang, 1968). The phenomenon has generally been referred to as two-tone suppression; that is, the second tone can suppress the response to the first tone. Fig. 143-22 schematically illustrates the stimulus parameters for which suppression is typically observed. Given that the excitor tone is at fiber CF, the level and frequency of the suppressor tone that are effective in decreasing the respnse to the excitor tone are shown by the shaded area. Suppressor-tone frequencies both above and below fiber CF can be effective suppressors. Suppressor tones that can elicit an excitatory response

presented alone can also be effective suppressors: the suppression area can overlap the area within the tuning curve. The suppression areas are not symmetric about fiber CF. The low-frequency suppression area tends to be less sensitive than the high-frequency area. At high suppressor-tone levels the low-frequency area can cover a broader range of frequencies; it is wider than the high-frequency suppression area. The growth of suppression (decrease in discharge rate) with suppressor level for a fixed suppressor frequency is a steep function for low-frequency suppressors and a progressively more shallow function for frequencies above fiber CF (Abbas and Sachs, 1976; Sachs, 1969). This is consistent with similar changes in the growth of discharge rate for single-tone stimuli across stimulus frequency.

The mechanism of two-tone suppression in single auditory nerve fibers is clearly not a neural inhibition effect as is the case with lateral inhibition in the visual system. Nevertheless, the contrast-enhancement effects observed in the visual system may have analogous effects in response patterns across frequency and place in the auditory system (Houtgas, 1974). Thus the high-level components in the frequency spectrum of a complex stimulus may suppress the response of neurons sensitive to low-level components and increase the contrast in the response across fibers. Several observations have suggested that in some cases suppression results in a quite different effect. For a fixed frequency and level of suppressor tone, the effect on threshold of response to an excitor tone is greatest at fiber CF and is less at frequencies above and below CF (Abbas, 1978; Schmiedt, 1982). Kiang and Moxon (1974) measured the tuning curve of high-frequency fibers with and without a continuous bandpass, low-frequency noise. The tuning curve measured in the presence of a low-frequency suppressor had normal sensitivity in the tai, a decreased sensitivity in the tip region, and consequently relatively little frequency selectivity. Thus, particularly for a low-frequency suppressor, the effect on high-frequency fibers may be to decrease frequency selectivity rather than enhance frequency effects.

The measurement of timing of response (as opposed to discharge rate), such as the use of period histogram, has particular advantage in the analysis of responses to complex tone stimuli. In these cases a Fourier analysis can be performed on the period or interval histogram, and, in addition to possible distortion components, the component of response at each input frequency can be extracted. An analogous measure to two-tone rate suppression, termed *synchrony suppression,* has been made in which the response component at the excitor tone frequency is measured as stimulus characteristics are varied (Arthur, 1976; Javel et al, 1978). This measure has the advantage that the response to each individual component can be separated. As a result the rate and synchrony measures differ in situations in which significant response to both component tones occurs. These differences can be illustrated by an experiment where the excitor frequency is constant at fiber CF and the suppressor frequency is varied from very high frequencies down to fiber CF. In the measurement of discharge rate as a function of suppressor frequency, the response decreases as the frequencies within the high-frequency suppressor area (Fig. 143-23) and then increases as the frequency gets close to fiber CF within the response area. In contrast, the phase-locked response to the excitor tone monotonically decreases as suppressor frequency is varied from very high frequency down to the fiber CF, even for frequencies well within the fibers' tuning curve (Javel, 1981). These differences may be interpreted to mean that the increase in discharge rate is the result of response to the suppressor tone, although the response to the excitor tone is decreased.

The origin of two-tone suppression effects has not yet been completely determined. No synaptic connections are known that would implicate a neural inhibition effect. Two-tone suppression has been recorded from fibers in the peripheral stump after the eighth nerve has been cut (Kiang et al, 1965). Two-tone suppression-like effects have been observed in hair cell response (Sellick and Russell, 1979), in cochlear microphonic potential (Dallos et al, 1974; Legouix et al, 1973), and in the vibration of the basilar membrane (Rhode, 1977). Several mathematical models that have nonlinear properties have demonstrated two-tone suppression effects, including many of the detailed properties of the phenomenon discussed above (Hall, 1977a, 1977b; Kim et al, 1973). These observations certainly implicate the mechanical vibration as at least one source of two-tone suppression effects. Javel (1981; Javel et al, 1983) has outlined several differences in the detailed properties of the neural and mechanical responses, which also suggest that hair cell processes are involved in the generation of suppression effects.

The use of period histogram has also proved to be effective in measuring the response to distortion components in the nerve fiber responses. A nonlinear system typically distorts a sinusoidal input signal in such a way that additional frequency components are produced in the output. These may be at harmonic frequencies (integer multiples of the input frequency), or for two-tone input the distortion may be at frequencies that are simple linear combinations of the two input frequencies. For two-tone stimuli, the Fourier analysis of the response can show components at various combination frequencies of the two primary input frequencies f1 and f2. The most prominent of these are the difference tone, f2-f1, and the cubic difference tone, 2f1-f2, where f2 is greater than f1.

Goldstein and Kiang (1968) performed a series of experiments in which they outlined a number of properties of the distortion product 2f1-f2. They observed fibers with substantial phase-locked response to both primaries and the combination tone. Fig. 143-24 shows data from Kim and Molnar (1975), who measured responses from a population of neurons with a wide range of CF to the same stimulus. They demonstrated not only response to the difference tone (f2-f1) in fibers sensitive to the primaries (f1 and f2), but also substantial response in fibers with CF near the frequency of the difference tone. These data are taken as evidence that at least a large part of these distortion components is generated in the cochlea and that a traveling wave is created at the distortion frequency that is propagated in the same way that externally presented tone at that frequency is. Recently, Robles et al (1990) have observed response to distortion components in direct observation of basilar membrane movement. The observation of acoustic distortion of distortion components in the ear canal is further evidence of a mechanical component of the 2f1-f2 distortion product (Kim, 1980; Kim et al, 1980).

Not only can interactions in the response occur for simultaneous presentation of two stimuli, but also very different interactions can occur for nonsimultaneous presentation of two stimuli. The term *adaptation* has been used in studies of the auditory periphery to mean changes in the responsiveness of a fiber to one stimulus (probe) caused by prior stimulation with another stimulus. One can include in this general definition of adaptation the changes in response to a single-tone burst over time as observed in the PST histogram. These perstimulatory changes not only can occur on a very fast time scale (see Fig. 143-21) but also can occur on a very long time scale. Kiang et al (1965) measured a very slow decrease in discharge rate to a continuous stimulus over the course of several hours; that is, if a stimulus

was left on for several hours, the "steady state" response was actually a very slow decrease in rate. Similarly, the recovery from adaptation as measured in the response to a probe stimulus has been demonstrated to occur over different time scales, depending on the level and duration of the adapting stimulus.

If the adapting stimulus is short (approximately 1 sec or less), then recovery is quick, usually complete within several hundred msec. The recovery function is approximately exponential in form; the magnitude of the decrease becomes greater as either discharge rate to the adapter or the duration of the adapter is increased (Harris and Dallos, 1979; Smith, 1977, 1979). Smith (1977) measured the response to a probe stimulus at a particular time after offset of the adapting stimulus (deltat); the discharge rate in response to the adapter resulted in a particular decrement (discharge rate with no adapter minus discharge rate with adapter) in response to the probe. As adapter level is increased, the increased response to the adapter results in a decrease in discharge rate to the probe. As the level of the adapting stimulus is increased so that discharge rate reaches saturation, the probe response similarly "saturates"; that is, no further decreases in discharge rate are observed. Thus the decrement in discharge rate to the probe is simply proportional to the adapter response. As the adapter stimulus parameters are varied, the decrement in probe simply reflects the changes in response to the adapter (Harris and Dallos, 1979; Smith, 1977). The source of these changes in responsiveness is probably the same as that controlling the perstimulatory changes outlined earlier (Smith, 1979).

For longer-duration adapters, particularlhy for those at high stimulus levels, longer recovery times can be observed and somewhat different response characteristics are observed with changes in stimulus variables. Whereas short-term effects "saturate" when the adapter discharge rate saturates, changes in level can produce changes in the long-term effects, even at levels where the discharge rate to the adapter is saturated (Young and Sachs, 1973). For tonal adapters the maximal effect on subsequent probe response is seen at fibers with CF above the adapter frequency rather than those at the adapter frequency (Lonsbury-Martin and Miekle, 1978). Long-term adaptation effects have been observed in the vibration pattern of basilar membrane (Patuzzi et al, 1984). Nevertheless, the source or sources of these long-term adaptation effects have not been clearly defined.

Studies of response to more complex stimuli, such as bands of noise or combinations of tones and noise, have demonstrated many effects that are consistent with those observed with similar stimuli. For instance, both suppression-like and adaptation-like effects have been demonstrated by bands of noise used as a stimulus. As the bandwidth of a noise stimulus centered at fiber CF is increased, the discharge rate may decrease, indicating the presence of a suppression band at frequencies above and below the tuning curve (Gilbert and Pickles, 1980; Ruggero, 1973). Schalk and Sachs (1980) measured the discharge rate as a function of level for band-limited noise centered either below or above fiber CF. They observed a slower growth and/or decreased saturation for the noise stimulus relative to that of pure tone, consistent with what is observed with two-tone stimuli. Discharge rate in response to a tone can be decreased by the simultaneous presentation of a background noise stimulus (Kiang et al, 1965). These changes may be observed in both the discharge rate and the phase-locked response to the tonal stimulus (Abbas, 1981; Rhode et al, 1978). A background noise can reduce the sensitivity and maximum rate of a neuron's response to a tone (Costalupes et al, 1984). Costalupes et al present evidence that noise can have not only a simultaneous effect

on the tonal responses similar to two-tone suppression, but also a nonsimultaneous effect on the responses similar to adaptation so that both adaptation and suppression may contribute toward a decreased response to a complex stimulus.

Single-neuron response properties: speechlike stimuli

The responses of auditory nerve fibers to speechlike stimuli have received much attention in the past few years. The presence of nonlinear characteristics in the response to simple stimuli, such as saturation, suppression, and adaptation, has made it necessary to determine the extent to which responses to simple stimuli can determine the characteristics of the response to complex stimuli. The research discussed below has focused on the question of how certain features of the speech stimulus, which are apparently important in the perception of speech, are encoded in the discharge patterns of auditory nerve fibers.

An important fist step in this approach has been the study of responses to vowel-like, steady state signals (Delgutte and Kiang, 1984a; Sachs and Young, 1979; Young and Sachs, 1979). Stimuli for these experiments were synthesized vowel-like sounds having a fixed fundamental frequency but different formant frequencies and consequently different areas of maximal energy in the frequency spectrum. The responses of many neurons with different CFs were measured gto the same set of stimuli, so that the response across fiber or the place in the cochlea could be determined. Fig. 143-25 illustrates the discharge rate, normalized to the saturation rate for each fiber, in response to a synthesized /e/ as a function of fiber characteristic frequency. Each curve represents the response fo a particular stimulus level. For low stimulus levels, peaks in the response occur at fiber CFs corresponding to the first two formant frequencies (Fig. 143-25, arrows). Synthesized vowels with different formant frequencies result in a different pattern of peaks in the rate versus fiber CF plot. At higher stimulus levels, no clear peaks occur in the response. The suppression of the response in regions of low energy by regions of high energy is not evident as a contrast-enhancement effect might suggest. The lack of clear peaks in the response is partially caused by the saturation of nerve fiber discharge rate; fibers less sensitive to the formant frequencies eventually reach the same discharge rate as those at the formant frequency. Also note that at high levels, a range of high CF fibers never reaches saturation rate where CF is greater than 2 kHz (see Fig. 143-25), apparently because of the suppressive effect of the low-frequency energy on the high-frequency fibers. Thus at low stimulus levels, the profile of rate across fiber CF carries information concerning formant frequencies of synthesized vowels, but at higher levels, still in the range of conversational speech, the effects are unclear. These observations led Young and Sachs (1979) to examine the response to the same stimuli in a different way, measuring the period histogram of response and calculating its Fourier transform. The vowel stimulus contains energy at the fundamental frequency of vibration of the larynx in addition to energy at each harmonic frequency. The amplitudes of the harmonic frequencies are large near the formant frequencies, the resonant frequencies of the vocal tract. The frequency analysis of the period histogram then can demonstrate the response of each fiber to the different frequency components present in the complex stimulus. Young and Sachs (1979) found that the responses of fibers tended to be phase locked to one of the formant frequencies or to a harmonic component near to the fiber's CF. They proposed a measure of averaged localized synchronized response (ALSR): in short, a measure of phase-locked activity at frequencies near fiber CF. Thus the response of each fiber was limited to the assessment of the amplitude of phase-locked response at the stimulus component closest to

its CF. When this phase-locked measure is used, the response versus fiber CF functions (Fig. 143-26) shows a peak for fibers near the formant frequencies. This response pattern is consistent across stimulus level and has been shown to be consistent under different levels of background masking noise (Voigt et al, 1981). Delgutte (1984) presented other local filtering schemes similar to ALSR but has also presented an alternative scheme for analyzing the phase-locked data in which the dominant component of the response of each nerve fiber is determined. He plotted results showing the dominant component as a function of fiber CF, which demonstrates a unique pattern for each vowel stimulus independent of stimulus level.

Although on the surface these data indicate that the phase-locked response carries vowel information in the auditory nerve, several details of the experiments make such a conclusion premature. The experiments were done with experimental animals under anesthesia, so that the efferent fibers of the auditory nerve may not have been normally responsive. The inhibitory effects (see below) of the efferent fibers may play a role in extending the dynamic range. Also there are fibers whose thresholds (low-spontaneous rate) are relatively high that are not saturated at high stimulus levels. If the response of only these fibers is plotted as a function of CF, then a pattern of response similar to the low stimulus levels is seen. Sachs and Young (1979) summarize these and a number of other possibilities for the use of rate information in vowel responses.

Responses to consonant-like stimuli have also been examined in a similar way, measuring both discharge rate and phase-locked response. Miller and Sachs (1983) observed responses to the frequency transitions characteristic of stop consonants. The average localized synchronized response was calculated at different time windows throughout the formant frequency transition. The frequencies at which the peak response occurred followed the formant frequencies in time. For voiceless fricative consonants, the profile of discharge rate across fiber CF corresponds well with the spectrum of the stimulus (Delgutte and Kiang, 1984b). For these stimuli the discharge rate provides different spectral information, even at high stimulus levels. An analysis of phase-locked activity similar to that successful in representing vowel stimuli could not distinguish fricative consonant responses. Thus an analysis of synchronized response seems appropriate for certain phonemes, whereas a discharge rate analysis seems more appropriate for others.

The dynamic properties, particularly adaptation, are also important in determining the response to speechlike stimuli (Delgutte, 1980; Delgutte and Kiang, 1984c). For instance, the acoustic difference between the /sh/ and /ch/ phoneme can be the difference in rise time of the noise burst. The response to a /c/ displays a larger onset effect in the PST histogram; the /s/ has a slower rise time and a very small onset response. The onset effect for a particular phoneme can also be affected by its acoustic environment. Delgutte (1980) measured responses to synthetic /ma/ and /ba/ stimuli. Each stimulus had the same acoustic waveform within the last 100 msec. The differences in previous stimulation, caused by the voiced /m/, resulted in a smaller transient response for the /ma/ stimulus. The role that these cues may actually play in the perception of speech is not definite, but we may at least use these data to understand how the speech information is encoded for transmission to the central nervous system.

Compound whole-nerve action potential

The compound whole-nerve action potential (AP) is the activity of auditory nerve fibers as measured by far-field recording technique. It is typically measured from an electrode placed on or near the round window, although it can be measured directly from the nerve trunk (Derbyshire and Davis, 1935). Despite its name, compound whole-nerve action potential is a composite of potentials produced by individual fibers and is not a true action potential. Although the AP does not tap activity in individual neural elements, it is of particular interest because it can be recorded in human subjects as well as in experimental animals. Recordings in humans, in a process called *electrocochleography,* are usually made by placing electrodes through the tympanic membrane onto the promontory or in the external auditory meatus (Aran, 1971; Montandon et al, 1975; Yoshie, 1968). Measurements of the whole-nerve AP have beem useful in demonstrating correlations between response properties in animal species and those in humans (Harrison, 1981; Harrison et al, 1981).

The source of the AP has been fairly well documented through a number of experiments. Kiang et al (1976) measured the voltage waveform produced by an action potential in an auditory nerve fiber at an electrode placed at the round window; each action potential produced a very small-amplitude bipolar pulse. Each action potential on each individual fiber had a similar effect on the recording electrode, which consequently summed activity across the population. Continuous stimulation of the cochlea produces a random sequence of action potentials from many fibers, the effects of each tending to cancel one another and resulting in essentially no change in the round window potential. In contrast, transient stimuli produce a synchronized response of action potentials in a number of fibers. The effects of the action potentials then tend to sum with one another, and the whole-nerve AP is evident (Dolan et al, 1983; Goldstein and Kiang, 1958).

In recording the AP, responses to several stimuli are typically averaged in time to enhance the consistent response potential relative to the random background noise. Fig. 143-27 shows AP responses measured in response to a click stimulus at different levels. The response takes the form of a series of one to three negative peaks. The first peak (termed N1) is caused by the synchronous discharge of auditory nerve fibers. The amplitude of the N1 peak increases monotonically with stimulus level, and the latency decreases monotonically with level. Fig. 143-28 illustrates this relationship. Teas et al (1962) measured the response to click stimuli in bandpass-masking noise to eliminate the contribution of specific regions of the cochlea to the AP. They demonstrated that the response to a click stimulus is primarily mediated through the discharge of high-frequency basal-turn fibers. This observation is consistent with the data on traveling wave properties and the latency of response of single-nerve fibers, discussed previously. The long wave-length in the basal turn of the cochlea results in approximately the same latency for all high-frequency fibers, and consequently that population provides a synchronous response.

Although much of the work with AP has been done with click stimuli, a tone burst with a relatively fast rise time (~1 msec) also evokes an AP response. The resulting averaged potential has a waveform similar to that in the response to clicks. The primary advantage in using tone-burst stimuli is that they are more frequency specific and therefore hold more promise as a tool for assessing functioning of different parts of the cochlea. Single-fiber tuning curves are narrow at low stimulus levels. A low-level tone burst excites only the fibers

with CF near stimulus frequency; consequently, only those fibers may contribute to the whole-nerve AP. The threshold for detecting an N1 response for tone bursts of different frequency is approximately 10 to 20 dB less sensitive than behavioral threshold-measured techniques in the same animal (Dallos et al, 1977; Price, 1978). Thus, although the thresholds are somewhat higher than behavioral measures, the shape of AP threshold versus frequency function is similar.

Chimento and Schreiner (1990) have described a technique measuring the whole-nerve activity with a bipolar electrode directly on the nerve. The auditory nerve neurophonic potential is an ensemble response of auditory nerve fibers that is not simply a transient response. Consequently, they have used the technique to measure the perstimulatory adaptation properties of the nerve and shown results comparable to single-nerve fibers.

The poststimulatory adaptive and masking properties have been measured using the standard AP paradigm. The amplitude of the AP response to a tone burst or click can be decreased by simultaneous presentation of a noise or other masking stimulus. Previous stimulation or adaptation effects may also be effective in reducing the amplitude of response to a tone burst or click; effects of both short- and long-term adaptation are evident (Abbas, 1984; Abbas and Gorga, 1981). This adaptation effect has been the basis for a number of experiments involving the AP. Since in short-term adaptation the response to a probe stimulus depends on the discharge rate in response to the adapting stimulus (Smith, 1977), the AP in response to a tone-burst probe also changes in amplitude as the response to the adapter changes. The low-level tone burst elicits response from a small population of fibers with relatively uniform CF. The effects of the adapter on the response amplitude to the probe are therefore an indication of the response to the adapter in those fibers. By choosing different probe frequencies one may assess the activity of the adapter in different populations of fibers with different CF. This adaptation paradigm has been used as an indirect measure of a number of neural response properties. For instance, an AP tuning curve is analogous to the single fiber tuning curve discussed previously. One determines the masker level necessary to decrease the amplitude of response to the probe tone to a criterion value. A plot of this level as a functin of masker frequency is the AP tuning curve, and it has properties similar to single fiber tuning curves (Dallos and Cheatham, 1976). A plot of decrease in probe response amplitude as a function of masker level has characteristics analogous to the discharge rate of a single fiber as a function of masker level (Abbas and Gorga, 1981; Harrison, 1981). Harris (1979) demonstrated two-tone suppression effects using the AP masking paradigm. The AP as an indirect measure of single nerve fiber responses has been used not only in animal experiments but also in experiments with human subjects.

Efferent system

A small percentage of neurons in the auditory nerve are efferent. The cell bodies of these neurons are located in the superior olivary complex in the brain stem, and they synapse on hair cells in the cochlea. Cells from both sides of the brain stem synapse on hair cells of both ears so that there are both crossed and uncrossed fibers in the efferent bundle going to each ear. Most of the neurons that synapse near inner hair cells have cell bodies located in the lateral part of the superior olivary complex of both sides and are called the *lateral bundle.* The efferent fibers that synapse at the base of the outer layer cells are primarily from the region around the medial superior olive and are called the *medial bundle* (Warr, 1978; Warr

and Guinan, 1979).

These efferent neurons can be responsive to sound in one or both ears. They have a wide range of spontaneous activity, they display tuning properties in response to tonal stimuli, and they have a relatively long latency, 5 to 50 msec. The innervation pattern of efferent neurons follows approximately the same frequency map as that of the afferent fibers (Fex, 1962, 1965; Liberman and Brown, 1986; Robertson, 1984; Robertson and Gummer, 1985; Rupert et al, 1968).

In several studies the efferent neurons have been electrically stimulated to assess their effect on afferent neuron response and other related cochlear potentials. Several early studies showed a decrease in the whole-nerve AP response when the efferent fibers were activated electrically (Desmedt, 1962; Galambos, 1956). Efferent activity similarly decreases the response rate of single neurons (Wiederhold, 1970; Wiederhold and Kiang, 1970). The latency of this effect on the afferent neurons after electrical stimulation of the efferents is on the order of 15 to 20 msec. After repeated electrical stimulation of the efferents, the decrease in afferent response may last up to several seconds. The greatest effects are observed in afferent fibers with CF in the range of 3 to 10 kHz. Widerhold (1970) measured rate versus level functions for acoustic stimulation with pure tone stimuli. Fig. 143-29 shows an example of a rate versus level function with and without stimulation of efferent neurons. Efferent activity results in a shift in sensitivity, so that the greatest decrease in rate occurs in the afferent fiber's dynamic range with little or no change in the region of saturation. Further, the greatest shift in sensitivity was observed when the acoustic stimulus frequency was near fiber CF, with little or no change for stimulus frequency well above or below CF. Consequently, a tuning curve measured during efferent activity would have a higher threshold in the tip region but also would have wider tuning than normal.

The experiments described above were all conducted with electrical stimulation of the efferent fibers, a somewhat artificial stimulus. Nevertheless, similar effects have been observed with acoustic stimulation of the contralateral ear, which also can activate the efferent nerve bundle (Liberman, 1989; Warren and Liberman, 1989).

Stimulation of efferent fibers may also affect other events in the cochlea. Hair cells in the lateral line organ of fish have both afferent and efferent synapses and have served as a model for understanding cochlear potentials. Efferent stimulation in these organs also results in a decrease in afferent neuron discharge, but in addition the hair cell receptor potential is increased (Flock et al, 1973). Flock et al (1973) presented a variation on Davis's transducer model to account for these observations, a change in membrane resistance caused by efferent discharge. Basically they hypothesized that efferent activity results in a decrease in membrane resistance at the efferent synapse so that current would be shunted through the efferent synapse. Less current would then flow through the afferent synapse and consequently a smaller generator potential would result in the afferent neuron. Since the total resistance through the membrane would be decreased, the total current would increase and the microphonic potential measured in the vicinity of the hair cell would also increase.

The situation in the mammalian cochlea is somewhat different, however, because of the two populations of hair cells. Efferent fibers in the outer hair cells synapse directly on the base of the hair cell and are the likely source for the change in CM with efferent stimulation.

The majority of efferent fibers synapse in the inner hair cells. At least part of the effect that efferent activity has on the afferent responses to sound is likely radiated through the outer hair cell mechanical feedback system described previously. Data on cochlear emissions have demonstrated that stimulation of the crossed olivocochlear bundle (COCB) can affect the acoustic distortion product measured in the ear canal (Mountain, 1980). Also, Mott et al (1989) have observed changes in spontaneous otoacoustic emissions with acoustic stimulation of the contralateral ear, presumably caused by activation of the cochlear efferent fibers. These observations are consistent with a hypothesis that efferent activity to the outer hair cells may have an effect in the basilar membrane motion through the motile response of the hair cells. The data further underscore the complex nature of the interaction among the mechanical, electrical, and chemical events in the cochlea.

Although efferent activity clearly can decrease the response of afferent fibers to sound stimuli, the role of the efferent system in the normal functioning of the auditory system has not been established. The differences in efferent effects on responses to high- and low-level acoustic stimuli led Dawson (1967) to hypothesize that efferent activity may decrease the response to a noise background while leaving the response to a signal intact - in effect, measuring the signal to noise ratio. Studies using the whole-nerve action potential have demonstrated such effects (Dolan and Nuttal, 1988; Nieder and Nieder, 1979). Winslow and Sachs (1987) have observed a similar effect in single-nerve fiber responses in that reduced dynamic range that is observed with a simultaneous noise masker can be restored by electrical stimulation of the cochlear efferents. Several recent studies have demonstrated that efferent activity may be important to decreasing the effects of adaptation and long-term threshold shifts caused by intense stimulation (Cody and Johnstone, 1982; Handrock and Zeisberg, 1982; Rajan and Johnstone, 1988). These studies suggest that the cochlear efferent neurons may play a role in reducing the desnsitization of the nerve fiber response under certain conditions. However, Liberman (1990) has recently reported experiments in which he measured the effects on sound-evoked efferent activity (acoustic stimulation of the contralateral ear). These data, which used a more "normal" means of activating the efferent fibers, showed that contralateral sound-evoked efferent activity was not a major determinant of threshold shift in the ipsilateral ear.

Single-neuron response properties: impaired ears

The response properties of single auditory nerve fibers have been studied in a number of animals with experimentally induced sensorineural hearing loss. In most work the changes have been induced through administration of aminoglycoside antibiotics or noise trauma. Most ototoxic agents tend to affect the outer hair cells to a greater degree than the inner hair cells. In some cases, regions of the cochlea can be left devoid of outer hair cells, with the inner hair cells left intact. Nevertheless, the changes in outer hair cells apparently have pronounced effects on the responses of the radial afferent fibers that innervate on the inner hair cells.

In certain situations the rate of spontaneous activity of auditory nerve fiber can be affected by hair cell damage. Liberman and Dodds (1984) noted a low distribution of spontaneous rate in fibers from noise-traumatized ears, particularly those fibers where the stereocilia of inner hair cells were damaged. In a situation where only outer hair cells are damaged (Robertson and Wilson, 1991), a normal distribution of spontaneous activity levels is observed.

Responses of auditory nerve fibers with experimentally induced sensorineural hearing impairment show several changes in tuning properties. The most consistent observation has been that the threshold in the sharply tuned tip of the tuning curve is higher than normal, making the fiber less sensitive to sound. In many cases the thresholds in the tail of the tuning curve are not affected. The result may be a tuning curve distorted in shape with decreased frequency selectivity. Fig. 143-30 presents several examples. Some tuning curves are very wide or bowl shaped, with very poor frequency selectivity (Kiang et al, 1970; Liberman and Kiang, 1978). In other cases there appears to be a narrow tip with relatively sharp tuning but clearly reduced sensitivity (Dallos et al, 1977). Changes in the tip of the tuning curve can also occur with acute trauma of several types, such as anoxia (Evans, 1974), and can be reversible. Cody and Johnstone (1980) observed a shift in the tip of the tuning to lower frequency with acute acoustic trauma. Liberman and Kiang (1978) also observed neurons in hearing-impaired ears with increased sensitivity in the tail region of the tuning curve. In some cases a hypersensitive tail was observed in a fiber whose tip region was relatively sensitive. The tuning curve in these cases was multipeaked or W shaped.

These changes in tuning properties are generally associated with other changes in the single-fiber response properties. The rate versus level functions tend to have a steeper slope in hearing-impaired regions (Harrison, 1981). The change in slope across stimulus frequency that is evident in normal fibers is not evident in impaired fibers, which show a uniformly steep slope at each stimulus frequency. Nonlinear effects, such as two-tone suppression, are typically reduced or absent in impaired fibers (Schmiedt and Zwislocki, 1980; Schmiedt et al, 1980). The amplitude of combination-tone response is also reduced in regions of hearing impairment (Dallos et al, 1980; Siegel and Kim, 1982b). In general, the responses of impaired auditory nerve fibers are still nonlinear in nature; that is, they demonstrate a threshold effect and clear saturation, resuling in a limited dynamic range. However, they do lose many of the nonlinear properties, particularly the properties that have been associated with similar effects in basilar membrane mechanics.

The changes in the slope of growth functions, two-tone suppression effects, and combination tones are observed both mechanically and in the neuron response. These observations are then consistent with a view that the vibration characteristics of the basilar membrane are changed in hearing-impaired cochleas relative to those in normal ears. Also consistent with this view are direct observations of basilar membrane displacement, showing that intense sounds can affect the subsequent vibration characteristics (Patuzzi et al, 1984; Sellick et al, 1982). The changes in the cochlear emissions with hearing impairment (Kemp, 1978; Siegel and Kim, 1982b) are also consistent with a hypothesis that a more linear basilar membrane response occurs with hearing impairment. Several models of hair cell transduction have led to hypotheses that an active mechanism is narrowly tuned and contributes to the sharp tuning seen in the mechanical response. Although still certainly within the realm of hypothesis, this mechanism may be responsible for the sharp tuning and high sensitivity of normal fibers in addition to many of the nonlinear response properties. The data on hearing-impaired ears would suggest that this mechanism is particularly vulnerable to insult, both temporary and permanent.

Central Nervous System

Cochlear nuclear complex

The secondary neurons in the auditory pathway are located in the cochlear nucleus. The cochlear nucleus can be subdivided both anatomically and physiologically into a number of subnuclei, including the anteroventral (AVCN), posteroventral (PVCN), and dorsal cochlear nucleus (DCN). Each of these has different anatomic cell types with different response characteristics. Whereas most of the auditory nerve fibers display relatively uniform response characteristics, at the level of the cochlear nucleus there is considerable divergence into parallel groups of cells with different response patterns.

Two different methods of classifying cells by their response characteristics have been used in the literature. The first is based on the appearance of the PST histogram in response to a tone burst (Kiang et al, 1973; Pfeiffer, 1966). Several of these classifications of neurons are illustrated in Fig. 143-31. They include the "primary-like" cells found in the AVCN, which display a time pattern similar to that of auditory nerve fibers cells. The "primary-like cell with notch" found in the interstitial nucleus displays a similar pattern except for a period of reduced response just after stimulus onset. The "chopper" cells found in the anterior portion of the PVCN display a semiperiodic discharge near stimulus onset, which is not related to the period of the tonal stimulus. The "on" responders found in the posterior part of the PVCN elicit a response only at the onset of the tone burst. The "pauser" cells found in the DCN respond with an action potential near stimulus onset, a quiet period, and then a period of sustained activity. These response properties are not unique for each cell; that is, the response pattern may not be the same for each frequency and level of stimulus, but the response patterns as defined for a moderate-level tone at fiber CF correspond well with the existence of the different cell types in different areas of the cochlear nucleus (Godfrey et al, 1975a, 1975b; Kiang, 1975).

The threshold response characteristics or tuning curves of cochlear nucleus cells are generally similar in frequency selectivity to those of auditory nerve fibers (Kiang et al, 1973). The primary exception to this observation is the tuning curves of the "on" responding cells of the PVCN, which are very broad and do not display the characteristic V shape. Cells are typically arranged tonotopically; that is, according to their most sensitive frequency. Fibers of the auditory nerve are organized according to CF from base to apex in the cochlea. This organization is preserved within the auditory nerve: fibers from each area of the cochlea are grouped together within the nerve trunk. This organization is preserved within several subnuclei of the cochlear nucleus complex, so that a map of the cochlea is reproduced within different areas. A similar organization is found within all the nuclei of the auditory pathway and at the level of the primary auditory cortex.

The response of neurons in the cochlear nucleus can show nonlinear suppression effects similar to those of the auditory nerve but, in addition, can show effects of neural inhibition. These inhibitory effects are most commonly seen with unanesthetized animals. Single-tone stimuli can produce both an excitatory and an inhibitory effect, so that tuning curves may display not only thresholds for excitation but also thresholds for inhibition (Evans and Nelson, 1973; Young and Brownell, 1976). Cells may have multiple-peaked inhibitory or excitatory response areas. These inhibitory effects may result in nonmonotonic rate versus

level functions; that is, the response may be excitatory at low levels but show a decrease or inhibition at high stimulus levels. The specific neural networks that produce such inhibitory effects have not been demonstrated, but Voigt and Young (1980) presented evidence that such inhibitory effects in the dorsal cochlear nucleus can be the result of interneurons located within the DCN itself.

The threshold responses and presence of these inhibitory effects have served as a basis for a second classification scheme for cochlear nucleus cells (Young et al, 1988). Fig. 143-32 illustrates schematic excitatory and inhibitory response areas for the different cell types. Type I cells have tuning curves similar to auditory nerve fibers and show no inhibitory response areas. Type III cells have similar excitatory response areas but also show significant inhibitory response areas above and below the characteristic frequency. Type IV cells have excitatory response for CF tones at low levels, but at higher stimulus levels they display large inhibitory areas. The growth of response may be nonmonotonic over a range of frequencies. Type II cells have no spontaneous activity and a primary-like tuning curve. They typically show no response to wide-band stimuli, which is indicative of strong inhibitory effects, however.

Types I to IV cells classified on this basis do not correspond to specific PST histogram response types. Nevertheless, type I cells show primary-like or chopper histograms and are found in the VCN. Type III cells are found throughout the CN and display a chopper or pauser histogram pattern. Type IV cells are primarily in DCN and usually show an onset or offset response in the PST histogram. Type II cells occur only in the DCN, many of which show a chopper pattern.

Many of the sounds in our environment are relatively complex in their frequency content and also change very quickly in both amplitude and frequency. It is of interest then to understand the coding of these more complex sounds as we move up in the central auditory system. The inhibitory effects on wide-band noise stimuli may be similar to those of auditory nerve fibers; that is, the response decreases as bandwidth increases, but the effects may be more pronounced (Greenwood and Goldberg, 1970). Certain cells (type II) may not respond at all to wide-band stimulation. Some cells may display an asymmetry in their response to an upward or downward sweep of a frequency-modulated tone (Britt and Starr, 1976). Moller (1976, 1978) observed cells displaying a greater response to a stimulus that was changing in frequency than to one that was constant in frequency. The response of different cell types may vary in response to amplitude-modulated signals. Primary-like or primary-like with notch PST histograms generally will result in amplitude-modulated response patterns that reflect the pattern of the stimulus. Cells that show only an onset response to a tone burst will not generally follow the details of an amplitude-modulated stimulus.

Superior olivary complex

The superior olivary complex (SOC) is made up of the lateral superior olive (LSO), the medial superior olive (MSO), and a number of periolivary nuclei. The discussion centers on the response properties of the two large nuclei, the MSO and LSO. Both receive input primarily from the cells in the ventral cochlear nucleus of both sides (ipsilateral and contralateral), either directly or through interneurons. Thus the cells of the SOC are the lowest level in the auditory pathway at which binaural processing takes place. The time pattern of discharge observed in most cells of the superior olive are similar to the response types

observed in the cochlear nucleus (Guinan et al, 1972; Tsuchitani, 1977).

Cells of the LSO form an S-shaped structure, with cells arranged tonotopically along the curvature of the S. Cells generally respond to input from each ear, with ipsilateral input excitatory and contralateral input, via the medial nucleus of the trapezoid body, inhibitory. Tuning properties are similar to those of auditory nerve fibers for both contralateral and ipsilateral input. In unanaesthetized animals ipsilateral input may demonstrate strong inhibitory effects for frequencies greater or less than those in the region of excitatory response (Brownell et al, 1979). Since each cell has a best frequency closely matched for both ipsilateral and contralateral input, the cells are sensitive to both interaural spectral differences and interaural intensity differences (Boudreau and Tsuchitani, 1970).

A large subgroup of cells in the MSO receives direct input from the AVCN of both sides of the brain stem and respond to stimuli from either ear. Goldberg and Brown (1969) described responses of cells in the MSO of dogs. They demonstrated cells receiving excitatory input from both ears (EE cells) and others displaying excitatory input from one ear and inhibitory input from the opposite (EI cells). The EE cells generally showed an increase in discharge rate with binaural stimulation, as compared to monaural stimulation. The slope of the rate versus level function with binaural stimulation was steep, making these cells particularly sensitive to changes to stimulus intensity. In contrast, the EI cells showed less response to binaural stimulation than that to the excitatory ear alone. Since stimulation of each ear had the opposite effect on the response, these cells were particularly sensitive to interaural intensity differences between the two ears.

They also measured the time pattern of responses to low-frequency tonal stimuli by using the period histogram and observed phase locking similar to that observed in auditory nerve fiber responses. Also, the average firing rate in these cells with binaural stimulation was particularly sensitive to variations in interaural time difference. Fig. 143-33 shows the cyclic variation of discharge rate as a function of interaural time difference. As the time delay is varied the discharge rate varies in a cyclic manner, with a period equal to that of the stimulus. A similar effect is observed in cells of the inferior colliculus (Rose et al, 1966). The response is probably an interaction of the phase-locked input from the cochlear nucleus of each side. As relative phases of the input stimuli are changed, the excitatory and inhibitory peaks overlap to a greater or lesser extent and produce the variation in discharge rate with ineraural time delay. The smallest time delay necessary to reach a peak in discharge rate has been termed the *characteristic delay* (Moushegian et al, 1975; Rose et al, 1966). This peak in response is generally at the same time delay for different frequencies of stimulation and is consequently somewhat unvarying for a particular cell. However, different cells within the nucleus display different characteristic delays, possibly caused by slight differences in transmission time to the SOC from each ear.

Sounds located at different points in space around an observer result in corresponding differences in intensity and time of arrival between the two ears. The cells within the superior olivary complex have shown exquisite sensitivity to both intensity differences and time of arrival differences between the two ears. These data support the notion that the superior olive is an important nucleus in the processing of information used for localization of sound.

Other nuclei of auditory pathway

Several other nuclei within the auditory pathway have been studied electrophysiologically to varying degrees. The medial nucleus of the trapezoid body accepts input from the AVCN and displays similar discharge characteristics (Goldberg et al, 1964). The nucleus of the lateral lemniscus receives input from the contralateral cochlear nucleus (primary DCN) and from the SOC. The responses of cells in this region show characteristics similar to cells of these input regions (Aitkin et al, 1970; Guinan et al, 1972).

Responses of cells in the inferior colliculus have been measured in the central nucleus, the pericentral zone, and the external nucleus (Aitkin et al, 1975). The cells within the central nucleus are arranged in a laminar structure in which the responses show a high degree of tonotopic organization; that is, the cells within each lamina have similar characteristic frequency. Although tuning curves can show a wide range of bandwidth, some show Q10 values as high as 40, much sharper than those of auditory nerve fibers. The time pattern of the response as revealed with PST histograms can show a variety of response patterns, including on-effects, sustained discharges, paused patterns, off-effects, and inhibition (Bock et al, 1972; Keidel, 1974; Rose et al, 1963). Inhibitory effects can result in complex frequency interactions and nonmonotic discharge rate versus level functions (Ryan and Miller, 1978). Like cells in the SOC, inferior colliculus cells can show synchronization of discharges to stimulus phase and demonstrate a sensitivity to interaural time delay and characteristic delay with low-frequency binaural input (Rose et al, 1966). Inferior colliculus cells may also display a strong dependence on interaural intensity differences (Benevento and Coleman, 1970; Rose et al, 1966). The inferior colliculus cells thus display many of the same binaural response characteristics of cells of the superior olivary complex.

The last auditory nucleus below the cerebral cortex is the medial geniculate body of the thalamus. Only cells of the ventral nucleus of the medial geniculate and the medial nucleus respond consistently to sound stimuli. Studies of cells in the ventral nucleus have shown quite complex time patterns of response. Some show long latency of response; others show long period of sustained response or periods of inhibition in response to a transient stimulus. Most cells are binaurally sensitive and are sensitive to interaural time and intensity differences between the two ears (Aitkin and Dunlop, 1968; Aitkin et al, 1966; Altman et al, 1970).

Tuning curves may have multiple peaks and cells may display complex patterns of inhibition (Aitken and Prain, 1974; Dunlop et al, 1969; Whitfield and Pursar, 1972). In general, the responses to dynamically changing stimuli are larger than those to steady state tonal stimulation. Cells that response to complex stimuli, such as frequency modulation, may not respond to individual components of the stimulus separately (Keidel et al, 1983). Studies that have examined responses to speechlike stimuli have demonstrated cells that are apparently sensitive to certain features of the stimulus such as consonant transitions (Keidel, 1974).

Auditory cortex

Most studies of cell responses in the auditory cortex have made recordings in the AI area, or primary auditory cortex. The responsiveness of cells in the auditory cortex is particularly sensitive to variables, such as anesthetic state and (in unanesthetized animals) the state of wakefulness and attention. As a result, many of the studies on auditory cortex have been done with unanesthetized animals, either paralyzed or with subjects performing a prescribed task. Most studies have used either cats or monkeys as experimental subjects. Generally the response in anesthetized animals is depressed when compared to unanesthetized animals (Erulker et al, 1956). A similar comparison may be made between the responses of sleeping versus awake animals (Brugge and Merzenich, 1973). Attention to a task generally increases both response amplitude and the stability of the response patterns (Beaton and Miller, 1975; Benson and Heinz, 1978).

Early studies of gross evoked potentials on the surface of the auditory cortical areas demonstrated a tonotopic representation of the cochlea in each area of the auditory cortex. Several subsequent studies have demonstrated a similar tonotopic organization in the primary cortical area at the single-neuron response level (Brugge et al, 1969; Merzenich et al, 1975; Reale and Imig, 1980). Cells arranged in columns perpendicular to the surface of the cortex tend to have similar best frequencies. A plot of best frequency across the surface of the cortex shows a series of isofrequency contours, organized according to a progression of best frequency. Most neurons in the auditory cortex show relatively sharp tuning characteristics similar to those in the auditory periphery. The sharp tuning and tonotopic organization suggest that the auditory cortex is important in a place or frequency coding mechanism.

The suprathreshold responses of cells within the auditory cortex are related to their tuning properties. Phillips et al (1985) have demonstrated that cells with monotonic rate versus level functions generally show V-shaped tuning curves. Cells with nonmonotonic growth functions generally show tuning curves that are more circumscribed; that is, they respond only over a narrow range of level and frequency. Different cells may respond over different ranges of intensity, thereby creating a "place" representation for intensity as well as frequency.

The temporal response patterns of cells in the auditory cortex are generally complex, showing "on" or "off" response patterns, sustained discharge, inhibition effects, and combinations of these effects. The discharge patterns are extremely labile and may show habituation effects with repeated stimulation. De Ribaupierre et al (1972) used periodic stimuli (clicks or noise bursts) and observed a population of cells whose discharge was precisely locked to the stimulus. They suggested that such cells may be important to the perception of periodicity pitch in such stimuli. There have been a number of other studies that have examined the ability of cells to follow temporal changes in the stimulus. Many studies have used either amplitude- or frequency-modulated stimuli to assess these temporal response properties. In general, throughout the auditory system the degree of response modulation decreases with increasing frequency of stimulus modulation. In addition, the ability of neurons to respond to a higher frequency-modulating stimulus generally decreases at higher levels of the auditory pathway; that is, neurons in the auditory cortex show poorer phase-locked responses than at lower levels (Creutzfeld et al, 1980; Moller, 1972; Rees and Moller, 1983). Nevertheless, Phillips and Hall (1990) have observed that variability in latency to the first

spike for tone- or noise-burst stimuli is similar in auditory cortex to that in the auditory nerve. They make the distinction between the precision with which the cortex encodes the transient response and the temporal responses to steady state amplitude-modulated signals. The former is preserved up to levels of the auditory cortex, whereas the steady state temporal responses are decreased.

Certain cells in the auditory cortex show response to very specific stimuli. Several investigations have measured response to signals of animal vocalizations (Funkenstein et al, 1971; Newman and Wollberg, 1973; Sovijari, 1975). Most cells responded to one or more of the selected animal cells. However, as with the FM stimuli, the response of a cell to the complex stimulus was not necessarily predictable from the response of the cell to pure tones. Glass and Wollberg (1983) observed that the response to such animal vocalizations reversed in time was equally effective as that presented naturally. The responses of cortical neurons do not necessarily correspond to a specific vocalization with a particular ecological significance. Rather, the responses apparently are determined by specific time-varying components of the vocalization to which the cell is responsive.

Cells in the primary auditory cortex are generally responsive to binaural input. Like other nuclei of the auditory pathway, they can be classified as excitatory to both ears (EE) or excitatory to one and inhibitory to the othern (EI). In addition, Kitzes et al (1980) observed cells that they termed *predominantly binaural* (PB). These cells responded only to binaural stimulation and not monaural stimulation to either ear. Cells in an electrode penetration perpendicular to the surface of the cortex tend to have similar binaural response characteristics (Abeles and Goldstein, 1970; Imig and Adrian, 1977). Middlebrooks et al (1980) further demonstrated that different binaural cell types were arranged in bands across the surface of the primary auditory cortex. The organization of these bands across the surface of the cortex was such that they were orthogonal to the lines formed by the isofrequency contours.

The very fine resolution cells in the superior olive and inferior colliculus to interaural time differences is also seen at the level of auditory cortex. EE, EI, and PB neurons all show different responses to variations in interaural intensity. The PB cells (Kitzes et al, 1980) tend to respond only for interaural time and intensity differences near zero. Cells in the auditory cortex show functions similar to the superior olive and inferior colliculus with changes in interaural time differences. The discharge rate of such cells are particularly sensitive to interaural time differences and also show a characteristic delay independent of level and frequency (Brugge and Merzenich, 1973).

The binaural responses of cortical neurons to interaural time and intensity differences indicate that they may be important in coding information concerning the sound source in space. Investigators have measured what are termed *spatial receptive fields* at several levels of the auditory pathway. Middlebrooks and Pettigrew (1981) have observed different cell types in the auditory cortex that may be omnidirectional (not sensitive), respond to a hemifield, or respond axially (that is, to a specific direction). The receptive fields of the aural cells were sensitive to the position of the pinna.

In summary, the cells of the auditory pathway, including the auditory cortex, respond to sounds but not simply on the basis of frequency content and intensity. Dynamic properties, spectral contrasts, state of the animal, and environmental relevancy may all play a part in determining response of cells. The specific parameters critical to the response and organization of these cell characteristics within the cortex or other nuclei of the auditory pathway have not been clearly demonstrated.