This outline summarizes major points covered in lecture. It is not intended to replace your own lecture notes.

How Sound is Heard: EAR

- Mechanical energy reaches the eardrum, moves to the middle ear, and then to the inner ear
- Energy changes from mechanical to electrochemical at nerve impulse stage in inner ear

Outer and Middle ear

- Transform energy from mechanical air pressure to motion of fluids in inner ear that leads to the generation of action potentials
- Most important function: overcome impedance mismatch between air and bone and inner ear fluids
- Sound travels through ear starting at pinnae → ear canal (external auditory canal) → ear drum (tympanic membrane)

Outer ear

- Air pressure collected by pinna (plural = pinnae)
- Major outer ear function is sound amplification
- The outer ear also has protective functions (e.g., wax captures invading foreign bodies)
- The outer ear is composed of epidermal tissue
- Going from external to ear to internal: at the centre of pinna is concha, then external auditory meatus, then ear canal (see diagrams)
- External auditory canal ~2-3 cm long
- Only mammals have pinnae, and only high frequency hearing mammals have mobile pinnae
- Resonance of concha and external auditory canal produce 5-20 dB SPL gain from 500 Hz – 9 kHz.

Sound is Altered by the Body

- Head, ear, body act as a filter that influences received signal amplitude and phase
- Impinging sound is altered in amplitude and time by head and torso
- Head Related Transfer Function (HRTF) describes how these effects vary with source location as a function of frequency (i.e. how amplitude and phase are modified by impinging on listener)

Rayleigh Head Model

- Rayleigh head model describes properties of HRTF
- Transfer Function describes the relationship between the input and output of a system (can also think of it as the transfer characteristics of a system
- Pinna and head have a large influence on received sound, depending on angle and frequency
- Amplitude changes through pressure gain (dB) depends on angle of incidence and signal frequency
- Measured SPL at ear usually increases in amplitude between 0 - 90 degrees

Function of Outer ear

- Sound frequencies vary in received sound pressure and time of arrival depending on source location
- Interaural Level Difference (ILD) – difference in signal amplitude between two ears
- Interaural Time Difference (ITD) – difference in time of arrival between the two ears
- ITD is mostly constant as a function of frequency (b/c speed of sound is also constant)
- Most amplification occurs between 1-6 kHz, and this coincides with speech spectrum
- HRTF is a nice summary of how ITD and ILD cues vary at listener's ear with position of source
- Interaural time difference (ITD) & Interaural level difference ILD – main cues to sound localization
- ILD (or IID) = interaural level difference (ILD) or interaural intensity difference (IID) — level/intensity is difference in amplitude between the two ears
- Small time delays due to high frequency diffraction around head
- Main function is amplification of sound

Middle ear

- Encased in bone
- Bound by tympanic membrane (laterally) and promontory (medially)
- Tympanum/tympanic cavity – middle ear space
- Epitympanic recess – cavity that contains most of the mass of middle ear bones
- Epitympanum connected to nasopharynx via eustachian tube

Transduction from Outer to Inner ear

- In theory, there are a number of possible ways for sound to reach middle ear:
- 1. Bone conduction – sound travels directly to inner ear (given very high amplitude signals).
- Problem: impedance mismatch between bone and air results in too much energy loss.
- 2. Middle ear cavity – sound pressure directly impinges upon oval and round windows of inner ear.
- Problem 1: impedance mismatch. Problem 2: simultaneous movement of oval and round windows is very inefficient and does not allow for release of pressure (i.e., both windows need to move in opposite directions)
- 3. Middle ear ossicles (actual solution) – small interconnected bones: mallues (hammer), incus (anvil), stapes (stirrup) whose primary function is to overcome the impedance mistmatch.

Tympanic Membrane

- Composed of layers of tissue consisting of radial and circular fibers
- Connects to malleus at manubrium (long arm)
- Maximal concavity is umbo portion

Eustachian tube

- Allows ambient pressure to reach middle ear cavity, i.e., static pressure same on both sides of tympanic membrane
- Allows efficient coupling of energy, because it is not a closed system, otherwise would have problems when air pressure was different at each side of the tympanic membrane

Middle ear Ossicles (malleus, incus, stapes)

- Bones suspended by axial ligaments
- Tympani and stapedius muscles can change tension on bones, thereby the stiffness, which leads to damping
- Footplate of stapes sits on oval window
- Stapes is smallest bone in body – connected to oval window via annular ligament
- Tension on bones can be changed via tensor tympani & stapedius muscles. Tension will cause damping, as it reduces free vibrations of ossciles.

Middle ear Functions

- Transmit vibrations of tympanic membrane into movement of middle ear bones/levers
- Vibration of tympanic membrane occurs maximally near periphery, in a ring, rather than in middle at interface with manubrium (due to impedance changes)
- Ossicles act as lever to amplify tympanic membrane movement
- Signals amplified mainly at frequency bandwidth of speech spectrum
- Provides impedance matching (coupling) between air vibrations at eardrum and bone vibrations in middle ear and fluid movement at inner ear

Middle ear Impedances

- Tympanic membrane, ossicles, and inner ear fluid contribute to impedance mismatch
- Reminder: acoustic impedance (**Z**) is complex sum of acoustic resistance and reactance

Middle ear Resistance

- Two resistive components:
  1. Inner ear fluid resistance to stapes footplate motion on oval window
  2. Friction of middle ear bones

Middle ear Reactance

- Two components:
  1. Mass reactance of middle ear bones – mass of the bones
  2. Compliant reactance of muscles and ligaments influence how freely the bones will vibrate
- Differential influence on frequencies because reactance components are dependent on frequency
- Damping from muscle contraction due to acoustic reflex
- Stiffness change is on system not the bones themselves

Overcoming the Impedance Mismatch

- Ossicles work as a lever mechanical system; gain: 1.3:1
- Due to its conical shape, the tympanic membrane buckles as it is displaced, which then causes the malleus to move with an even larger force of displacement; gain: 2:1
- Size difference between area of tympanic membrane and stapes footplate results in Force concentration. Effective area of eardrum is $55mm^2$ and the stapes footplate is $3.2mm^2$. Force is concentrated into a smaller area, so gain in pressure is 17:1 (approximately 25 dB).
- Multiplying all gains [1] x [2] x [3] reveals total system gain of 44:1 or ca. 33 dB.

Inner ear

- Transduction process in inner ear converts mechanical to neural energy.
- Stapes motion on oval window leads to motion of perilymph (fluid of inner ear)
- Stereocilia of haircells in Organ of Corti move from inner ear fluid motion
- Depolarizing hair cells lead to generation of action potentials (neural impulses) in auditory nerve
- Inner ear provides nervous system with information about stimulus frequency, amplitude and time

Inner ear anatomy

- Three temporal bone divisions:
  1. Semicircular canals – part of vestibular system, but may also influence hearing because it shares fluid with inner ear
  2. Vestibule
  3. Cochlea
- Semicircular canals open into vestibule, utricle, saccule, all involved in the sense of balance
- Cochlea – coil structure within temporal bone, is the primary auditory organ
- Central spiral axis of cochlea is modiolus
- Osseous spiral lamina – spiral bony shelf that spirals along length of cochlea
- Important to have system encased in bone for separation from other bodily sounds, and to keep entire system (from motion) so that it is sensitive to externally generations motion (sound)

Inner ear anatomy

- Helicotrema – apical tip of cochlear duct
- Consists of three chambers: scala vestibuli, scala media, scala tympani
- Scala vestibuli and scala tympani are contiguous at helicotrema
- Scala media (Coclear Duct) contains Organ of Corti
- Oval and round windows located near cochlear base
- Relative motion of fluids in scala vestibuli and scala tympani cause movement of basilar membrane and shearing motion along hair cells

Cochlear anatomy

- Cochlear duct (scala media) – contains endolymph fluid and is sandwiched between scala vestibuli and scala tympani
- Scala vestibuli and scala tympani – contain perilymph
- Scala media: bound by Reissner's membrane, basilar membrane, stria vascularis, spiral lamina
- Basilar membrane
- Tectorial membrane
- Spiral ganglion – collection of nerve cell bodies that spirals along cochlear duct
- Auditory nerve fibers – individual nerve cell axons that come from base of hair cell receptors

Organ of Corti anatomy

- Organ of Corti inside cochlear duct
- Organ of Corti contains: inner hair cells (IHC; globular), outer hair cells (OHC; elongated), tectorial membrane, basilar membrane, stereocilia, pillars of corti, tunnel of corti
- Supporting cells: Dieter (directly cup outer hair cells), Hensen's cells, Claudius cells, pillars
- Phalangeal processes of Dieter's cells create membrane to support and encase the outer hair cells, one Dieter cell for each OHC

Hair cells

- Stereocilia point up into scala media
- IHCs in one row on medial side of tunnel of Corti
- OHCs in three rows on lateral side of tunnel of Corti
- Hair cells slant toward each other
- Tallest stereocilia contact tectorial membrane
- ~ 40 stereocilia per IHC
- ~ 150 stereocilia per OHC

Cochlear dimensions

- Scalae are larger (greater volume) at base than at apex
- Basilar membrane is wider at apex than at base
- Georg von Bekesy: studied ear/cochlear mechanics; won Nobel Prize for showing ear that the ear is a frequency analyzer (like a series of mechanical bandpass filters)

Basilar Membrane Traveling Wave

- Stapes motion creates traveling wave in basilar membrane (B.M.)
- Traveling wave results in B.M. deformation from base to apex
- More displacement of membrane with greater sound pressure level (SPL)
- Membrane motion mirrors stimulus in terms of compressions and rarefactions

Basilar Membrane is Tonotopic

- Mechanical structure; wider & under less tension at apex; stiffest at base
- Vibrational mechanics; can vibrate more freely near at apex
- B.M. traveling wave start at base and travels toward apex
- Traveling wave of differential motion travels along basilar membrane
- Peak amplitude of vibration is at a particular area
- Resonate frequency varies systematically with spatial location

Basilar Membrane Displacement

- Maximum displacement of traveling wave varies with frequency
- Different frequencies maximally excite different regions of basilar membrane
- Asymmetry in envelope of traveling wave
- Low frequency stimulation: base and middle of membrane also set into motion, but peak mechanical displacement occurs toward apex of B.M.
- Mid frequency stimulation: base of membrane also set into motion, but peak mechanical displacement occurs near middle of B.M.
- High frequency stimulation: stimulates base of B.M. only,
- Compare phase of stapes motion to B.M.: larger phase shift with higher frequency
  e.g. @ 27 mm from base a 200Hz tone is 180° out of phase compared to stapes foot plate motion, resulting in a 2.5 ms travel time delay at this frequency (T = 0.005 s at 200 Hz)

Basilar Membrane motion summary

- Basal end vibrates best at high frequencies, but is also set in motion by low frequency stimulation
- Apical end vibrates only to low frequency stimulation
- Phase delay between stapes motion and peak in b.m. traveling wave vibration
- Greater motion to higher SPL sounds
- Asymmetrical traveling wave envelope: falls off gradually at basal side but is steep at apical side.

Basilar Membrane acts as a series of Mechanical Bandpass Filters

- Certain regions require less pressure to be maximally stimulated
- B.M. motion of B.M. tuned, vibrating best at characteristic frequency (CF) for that region (position)
- Because of asymmetry in envelope of B.M. traveling wave, shape of isodisplacement function (SPL to vibrate at certain amplitude) has shallow slope below B.M. CF, and a steeper slope above CF.
- Traveling wave stimulates larger region of B.M. towards base than apex
- Frequencies above CF for a given B.M. position, will cause little vibration, whereas frequencies below CF willl result in more vibrations for a single position along cochlea.
- Any point along basilar membrane acts as a mechanical bandpass filter

Motion of Basilar Membrane is Nonlinear

- Motion of B.M. is not linear with respect to SPL at characteristic frequency (CF)
- Input-output function of membrane velocity shows a compressive nonlinearity at CF.
- Change is compressive because steepness of function becomes shallower at some SPLs.
- Relationship is more linear at SPL extremes within CF
- Relationship also more linear at frequencies above and below CF for that position
- Compressive nonlinearity results in audible distortion products (e.g. harmonics and difference tones).

Inner Hair Cell (IHC) and Outer Hair Cell (OHC) Structure

- Stereocilia geometrically arranged in rows; rows have different lengths of stereocilia.
- Inner Hair Cells (IHCs) have afferent neurons connected to them and efferent neurons connected directly to the afferent neuron.
- Outer Hair Cells (OHCs) have afferent neurons connected to them and efferent neurons connected to the hair cell, not the afferent neuron as with inner hair cells.
- Stereocillia between and within rows are connected.
- Tallest stereocilia contact tectorial membrane sitting above it.
- Stereocilia within & between rows are joined by lateral cross-bridges & tip link bridges.
- Links strengthen rows and keep stereocilia moving together.
- Tip links play a crucial role in transduction process of mechanical (vibrational) to electrochemical energy. When one moves, it brings others around it with it.

Motion of Haircell Stereocilia

- Basilar membrane anchored to spiral ligament by osseous spiral lamina.
- Haircells stimulated by bending (shearing) forces acting on stereocilia.
- Tectorial membrane anchored by spiral limbus (free end)
- Stereocilia must be strong, and tip link cross bridges give strength for shearing forces.
- When tip links stretch, ion channels in haircell membrane open, causing permeability change that then depolarizes haircell; resulting in release of transmitter to afferent neuron below.
- Hair cells are receptors, not neurons.

Stereocilia Cross Bridges and Tip Links

- Depolarization based on mechanical opening of cation (K+) channels.
- Tip links synchronize K+ channel opening.
- K+ channels open when stereocilia bend toward stria vascularis.
- Haircells depolarize when K+ enters.
- Channels close *prior* to the return of stereocilia to initial position.
- Change in internal calcium concentration [Ca+2] regulates closure of K+ channels.
- Mechanism reduces time constant of channel opening, allowing cycles of mechanotransduction process to occur at high rates (frequencies) and thus follow cycle-by-cycle change in stimulus.

Innervation of Organ of Corti

- Spiral ganglion composed of ca. 35,000 bipolar neurons of two main types.
- Type I. 90% of radial afferent fibers; large and myelinated neurons synapse to base of IHC.
- Type II. 10% of spiral afferent fibers; small and unmyelinated neurons synapse to base of OHC.
- Axons of Type I and Type II afferents sends spikes to cochlear nucleus (central auditory system)

Innervation of Organ of Corti

- Type I radial afferents (to CNS) and lateral efferents (from CNS) innervate Inner Haircells (IHC).
- A radial afferent synapes on a single IHC; each IHC is innervated by multiple radial afferents.
- Type II spiral afferents (to CNS) and medial efferents (from CNS) innervate Outer Haircells (OHC).
- A spiral afferent synapses on multiple OHCs; each OHC is innervated by a single spiral afferent.

Inner Haircell (IHC) Connection to CNS

- IHC synaptically connected to Type I spiral ganglion neurons forming a radial afferent system going to Cochlear Nucleus (CN).
- Lateral efferent system arises from small neurons in ipsilateral Lateral Superior Olivary (LSO) complex; post-synaptic target is Type I radial afferent at base of IHC.

Outer Haircell (OHC) Connection to CNS

- OHC synaptically connected to one or a few small endings of Type II spiral ganglion neurons forming the spiral afferent system going to cochlear nucleus (CN).
- Medial efferent system arises from large neurons from both the ipsilateral and contralateral Medial Superior Olivary (MSO) complex.
- Both the spiral afferent system and the radial afferent system projects to the Cochlear Nucleus (CN)

Radial *versus* Spiral Auditory Nerve Fibers

- Type I (large, myleninated) spiral ganglion neurons have single synaptic ending connected to IHCs.
- Type II (small, unmyleninated) spiral ganglion neurons have multiple synaptic endings that spiral basally along cochlea; branches connect to about ten OHCs, generally in the same row.
- It takes time for the CNS to be updated with incoming sensory information and to send feedback to Organ of Corti (auditory periphery).

Electrical Potentials

- The motions and interactions of various cochlear structures generate electric potentials.
- Cochlear electric potentials tell us how the ear works.
- Electrical potential: potential energy per unit of charge associated with a static (time-invariant) electric field.
- Electric potential established whenever there is a difference in concentration of charged ions between 2 regions (e.g. across a cell membrane).
- Electric potentials present in all cells that regulate ionic content WRT extracellular environment.
- Electrical potentials measured with 2 electrodes: recording and reference electrodes.
- Recording electrode measures the electric potential difference relative to reference electrode.

Electrodes: Measuring Electrical Potentials

- Electrical potentials are measured with electrodes
    - Wire electrodes (eg. Tungsten, silver)
    - Glass electrodes (e.g. borosilicate pulled to fine tip)
- Electrodes used to measure the potential difference between two sites
- Two electrodes are necessary: recording electrode and reference electrode

Major Types of Auditory Potentials

- Electric potentials can be recorded inside various cochlear chambers (extracelluar potentials) and its cells (intracellular potentials).
- Resting potentials recorded in absence of stimulus.
- Evoked potentials recorded in response to stimulus.

1. Extracellular (Gross Cochlear) Potentials

- Scala Vestibuli Resting Potential (SVP) (minor)
- Scala Tympani Resting Potential (STP) (minor)
- Endolymphatic Resting Potential (EP)
- Summating Potential (SP)
- Cochlear Microphonic (CM)
- Compound Action Potential (CAP)

2. Intracellular Potentials

- Haircell Receptor Potential (RP)
- Action Potential (AP)

DC Resting Potentials of Cochlea

- 4 DC Resting Potentials (RP) in the intact cochlea: Scala Tympani RP (perilymph), Scala Vestibuli RP (perilymph), Scala Media RP (endolymph), Haircell RP (intracellular).
    - [1] Scala Tympani (Perilymph) 0 mV re reference electrode
    - [2] Scala Vestibuli (Perilymph) +2-5 mV re [1]
    - [3] Scala Media (endolymp) +80 mV re [1]
    - [4] Haircell Potential (intracellular) -70 mV re [1]
- Scala Tympani and Scala Vestibuli have slightly different resting potentials, suggesting that the two perilymphatic chambers are composed of different ionic compositions.
- Endolymphatic RP (+80 mV) in the Scala Media is potential of greatest significance.
- Potential difference between Scala Media and haircell receptor is: 80 mV – (–70mV) = 150 mV, resulting a huge driving force for the movement of ions.

Endolymphatic Resting Potential (EP)

- EP is a DC potential not related to auditory stimulus (i.e. it is a resting potential).
- EP is a positive resting potential (80 mV re: perilymph) located in endolymph.
- Largest resting electric potential found in body.
- Not found in endolymph of vestibular system even though fluid is contiguous with Scala Media.
- Stria Vascularis thought to be ionic source of EP.

Summating Potential (SP)

- SP is a stimulus-evoked DC potential
- Stimulus causes shift in baseline (DC shift) from endolymphatic resting potentials
- SP can be either positive or a negative
- Believed to be composed of multiple DC potentials
- Exact source of SP unknown

Cochlear Microphonic (CM)

- CM is a stimulus-evoked AC potential.
- Amplitude of CM increases with stimulus level; has wide dynamic range, but CM does saturate.
- Amplitude of CM increases in proportion to basilar membrane vibration.
- Frequency of oscillation of CM mirrors stimulus.
- CM used to measure space-time pattern of basilar membrane displacement (i.e. the cochlear traveling wave).
- Source of CM near boundary of Scala Tympani and Scala Media – thought to be the movement of OHC stereocilia.
- Remember: peak in envelope of basilar membrane traveling wave in response to low frequency stimulation occurs closer to apex, but traveling wave must still pass through base.

Compound Action Potential (CAP)

- CAP is a stimulus-evoked AC potential.
- Not a true cochlear potential (but is recorded with cochlear electrodes).
- CAP: sum of individual action potentials from auditory nerve fibers responding simultaneously.
- CAP latency varies as function of stimulus frequency due to travel time of basilar membrane traveling wave of displacement (delay = 2.5 to 4.0 ms)

Breakdown of Gross Cochlear Potentials

- Gross cochlear potentials made up of sub-components corresponding to various anatomical structures
- Sub-components can be separated and identified with filters.
- Compound Action Potential (CAP): result of synchronous activity of individual auditory nerve fibers.
- Summating Potential (SP): reflects direct current (DC) component, mainly from IHCs.
- Cochlear Microphonic (CM): resembles stimulus and reflects alternating current (AC) components; thought to originate from movement of OHC stereocilia.

Haircell Receptor Potential (Intracellular)

- In response to an acoustic stimulus, the IHCs electrical response has both a DC component (change in baseline of receptor potential) and an AC component (corresponding to structure of stimulus frequency)
- Amplitude of DC component grows with stimulus frequency; it dominates in IHCs.
- Amplitude of AC component shrinks with stimulus frequency
- AC component more important at low frequencies; it dominates in OHCs

The Action Potential Occurs in Nerve Fibers

- As haircell becomes more depolarized, neurotransmitter is released to neuron connected to haircell
- Neurotransmitter released from haircell receptor is received by specific membrane receptors on post-synaptic neuron
- Binding of neurotransmitter by the neural receptor causes ion channels to open in neural plasmalemma which in turn causes the neuron's membrane potential to become depolarized
- Eventually, the neuron's membrane potential reaches the threshold for an all-or-none action potential

Encoding Auditory Signals by Inner Hair Cells (IHCs)

- Deformation of haircell stereocilia causes ion (potassium, K^+) channels to open on IHC stereocilia.
- Flow of potassium causes depolarization of haircell receptor (graded potential), and the opening of voltage-gated calcium (Ca^{+2}) channels
- Increase in intracellular [Ca^{+2}] leads to further depolarization and release of glutamate neurotransmitter from IHC receptor, and also the active exiting mechanism for K^+
- Binding of glutamate by receptors on cell membrane of Type I radial afferents leads to depolarization and generation of all-or-none action potential (spike) in sensory neuron.
- Electrophysiologists study the number, timing and pattern of spike discharges to acoustic stimulus

Outer Haircells (OHCs)

- Function of OHCs: believed to modify incoming information and provide auditory system with high sensitivity and resolution for stimulus frequency and amplitude
- OHCs feedback energy to cochlea; thought to affect motility of tectorial membrane
- OHCs can act as a cochlear amplifier – provide gain for the system.
- Mechano- to neurotransduction mechanism probably similar as what is observed in IHC
- Acoustic stimulus causes OHC to contract (i.e. OHC have motility).
- Contraction of OHC will vary stereocilia contact with tectorial membrane
- OHC size varies along cochlear length (and thus sound frequency that they respond to)

OHC Size Changes Along Cochlea

- OHC length, not diameter, varies with position (and thus characteristic frequency)
- During acoustic stimulation, OHCs contract (length decreases) and then expand (length increases)
- Contraction cycles occur on cycle-by-cycle basis with stimulus
- Contraction affects amplitude and frequency sensitivity (stereocilia attached to tectorial membrane)

Otoacoustic Emissions (OAEs)

- Ear produces weak sounds on its own (i.e. otoacoustic emissions)
- OAEs are not echoes reflected in external auditory canal
- The amplitude of evoked otoacoustic emissions (EOAEs) increases with stimulus SPL
- Different types of OAEs
  i. SEOAE – spontaneously evoked otoacoustic emissions
  ii. TEOAE – transiently evoked otoacoustic emissions
  iii. DPOAE – distortion product otoacoustic emissions (e.g. cubic difference tone: $2f_1 – f_2$)
- DPOAE is evidence for non-linearity of auditory system

Haircells are Polarized

- Haircell stereocilia bent toward tallest stereocilium: haircells depolarized
- Haircell stereocilia bent away from tallest stereocilium: haircells hyperpolarized
- Afferent firing rate increases above spontaneous rate when stereocilia bent toward tallest stereocilium
- Firing rate decreases below spontaneous rate when stereocilia bent away from tallest stereocilium
- Haircells are therefore directionally sensitive

Auditory Nerve

- Afferent Auditory Nerve Fibers (ANFs) leave the cochlea in an ordered manner in a twisted bundle.
- ANFs from the apex of cochlea are in center of twisted bundle.
- Therefore low frequency ANFs are located on the inside of the auditory nerve.
- ANFs from the base of the cochlea are on the outside of the twisted bundle. Thus high frequency ANFs located on the outside of the auditory nerve.
- Cranial Nerve VIII is composed of auditory and vestibular nerves
- Efferent Auditory Nerve Fibers originate from the superior olivary complex in the CNS and project into the cochlea (Organ of Corti)
    - Efferents from the Laterial Superior Olive (LSO) project to Type I afferents innervating IHC
    - Efferents from the Medial Superior Olive (MSO) project to base of OHC receptor

Organization of Auditory Nerve Fibers (ANFs)

- Both afferent and efferent ANFs exit / enter Organ of Corti via habenula perforata
- Afferent ANFs enter modiolus in an ordered manner (twisted bundle)
    - Low frequency ANFs near apex of cochlea located on inside of the auditory nerve
    - High frequency ANFs near base of cochlea located on outside of the auditory nerve
- Cranial Nerve VIII is composed of both auditory and vestibular nerves

Spontaneous Activity of Auditory Nerve Fibers (ANFs)

- Spontaneous Activity: action potentials in auditory nerve fibers when no stimulus is present
- Evoked or Driven Activity: action potentials in ANFs caused by the presentation of sound stimulus
- Rate of spontaneous activity varies with threshold of Type I ANFs
    i. fibers with low rates of spontaneous activity have the highest acoustic thresholds
    ii. fibers with moderate rates of spontaneous activity have moderate acoustic thresholds
    iii. fibers with high rates of spontaneous activity have the lowest acoustic thresholds

Rate-Level Function (Input/Output or I/O function)

- Auditory Nerve Fibers (ANFs) with low spontaneous firing rates have higher evoked thresholds.
- **Rate-level functions** measure the spiking of ANFs to a variable input stimulus level (SPL).
- The dependent variable is usually spikes per second; independent variable is SPL**.**
- Sigmoid rate-level function is typical for sensory neurons.
- Rate level function systematically varies across ANFs with different rates of spontaneous activity (and thus neural threshold).
- We can use rate-level functions to generate other functions such as **Response Area Functions**, within and between ANFs.

Response Area Functions

- **Response Area Function** used to measure or derive other features about ANFs (e.g. CF).
- **Iso-level or Iso-intensity Curve** is as measure of spike rate holding SPL of signal constant.
- **Iso-rate Curve** indicates the SPL necessary to produce a constant firing rate (e.g. across frequency).
- Can make a whole family of such functions across frequency and SPL above threshold, and then plot curves for individual neurons, frequencies, etc.

Threshold Tuning Curves

- **Threshold tuning curves** display SPL of signal required to cause cell to evoke firing
- Threshold at any frequency is the SPL that evokes firing above the spontaneous rate.
- Each cell has a different **Characteristic Frequency (CF)** or **Best Excitatory Frequency (BEF).**
- The effective range of tuning curve reflects the **dynamic range** of the neuron (see I/O function).
- Effective bandwidth of tuning curve increases with CF across cells.
- Low CF fibers have a narrower bandwidth of tuning than fibers with a higher CF.
- Shape and width of **tuning curve** reflects bandpass filter properties (frequency selectivity) of **mechanical tuning** of basilar membrane.

ANF Spiking Is Phase Locked To Stimulus

- Spike (action potential) timing to frequencies < 5 kHz is non-random.
- Spikes occur at specific times (phases) of stimulus. Such spikes are said to be **phase locked.**
- ANF spikes only to positive portion of stimulus waveform (pressure condensation).
- **Rectification:** unit responds only to one direction of stimulus waveform.
- Stimulus rectification reflects directional selectivity of hair cell stereocilia.
- Phase locked discharges of ANFs important for encoding and distinguishing sound frequency.
- **Phase locked** spikes do not have to occur on every cycle of stimulus waveform.
- Upper frequency limit of phase locking (ca. 5kHz) determined by **refractory period** of neuron.
- At low frequencies, ANFs may fire multiple spikes to peak pressure of stimulus, but at higher frequencies ANFs fire fewer spikes and they may miss one or more cycles due to refractory period.
- Behaviorists and electrophysiologists graph spike timing using time domain displays re: stimulus.
- **Coefficient of synchronization** (or **Vector Strength**) is index of magnitude of cell's phase locking.
- CS = 0 represents no phase locking; CS = 1 represents perfect phase locking**.**

Graphical Displays of Neural Responses

- Used to interpret behavior and relationship between behavior and activity of nervous system
- **Period Histogram** – spiking over time, shown relative to stimulus period (or phase)
- **Post-Stimulus Time Histogram** – summary of spiking response number in bins of time
- **Interspike Interval Histogram** – summary of time between spikes in response
    - Peak height represents the most commonly observed ISIs.
    - ISI spacing of phase locked responses on PSTH decreases as frequency increases.
    - Smallest evoked ISI can't be smaller than absolute refractory period.
    - When using a click stimulus, the ISI Histogram can inform you about the CF of ANF
- **Coefficient of synchronization** (or **Vector Strength**) is index of magnitude of cell's phase locking.

Measuring Impulse Response of ANF Using a Click Stimulus

- Response of ANFs to an acoustic transient or click stimulus reveals information on transduction process.
- Periodic peaks in ISI histogram indicate that biomechanical processing of click is similar to passing the click through an electrical bandpass filter.
- **Periodic oscillations** of ANF is **ringing** of neural responses after passing through cochlear bandpass filter
- Period of temporal oscillations in ISI Histogram can be used to determine CF of ANF
- Example: ISI Histogram reveal period between spikes to click stimulus = 2.22 ms, therefore:
    - T = 1 / Frequency ; Frequency = 1 / T
    - Frequency = 1 / 2.22 $\times 10^{-3}$ s
    - Frequency = 450 Hz (i.e. the CF of the ANF = 450 Hz)
- **Time shift** in neural response (i.e. latency difference) to 180° phase reversed clicks reflects directional selectivity of hair cell stereocilia to motion of basilar membrane

Click Interspike Interval Histogram (review)

- **Periodic oscillations** of ANF is "ringing" of neural responses after passing through cochlear bandpass filter.
- **Period** of temporal oscillations ANF spiking can be used to determine the CF of ANF.
- **Time shift** in neural response (i.e. latency difference) to 180° phase reversed clicks reflects directional selectivity of hair cell stereocilia to motion of basilar membrane

Post-Stimulus Time Histogram (PSTH)

- Post-Stimulus Time Histogram displays neural responses to repeated stimulus presentations during and after the stimulus.
- Used to compare driven (evoked) activity and post-stimulus effects of stimulation.

Peri-Stimulus Histogram (PSTH)

- Peri-Stimulus Time Histogram displays neural responses to repeated stimulus presentations before, during and after the stimulus.
- Used to compare spontaneous activity to driven (evoked) activity, and post-stimulus effects

Monaural Two-Tone Suppression

- Tone 1 is presented at the CF of the ANF; Tone 2 is presented off of the CF.
- Varying the frequency and SPL of Tone 2 re Tone 1 shows suppression of the neural response
- Cause of two-tone suppression is nonlinear motion of basilar membrane vibrations to 2 tones.
- One must be cautious in trying to predict responses of a neuron to a complex sound based on its responses to simple sounds.
- Can also measure two-tone suppression effects on other spike parameters such as spike latency, coefficient of synchronization, spike rate, etc.

Binaural Two-Tone Suppression

- Function of **efferent** connections to Peripheral Auditory Nervous System (PANS) not fully understood
- **Crossed Olivocochlear Bundle (COCB) fibers** from **Medial Superior Olive (MSO)** are **inhibitory**
- **Binaural** (both ears) stimulation of an auditory neuron can result in suppressed neural response relative to **monaural** (one ear) stimulation
- In vitro experiments have shown that stimulation of COCB fibers inhibits **excitatory** responses from **ipsilateral** afferent fibers

Encoding Frequency

- **Place theory** of hearing: frequency of sound input is encoded by noting which region or **place** within the cochlea (or auditory nerve) was stimulated (or fires action potentials).
- **Temporal** or **Volley Theory** of hearing: periodicity of the volley of neural discharges (spikes) can be used to reconstruct the frequency of sound input (up to limit ca. 5 kHz; neural refractory period).

Encoding Amplitude

- **Amplitude** or **Intensity** of stimulus encoded by number of spikes and/or discharge rate of ANFs.
- **Dynamic range** of single ANF is limited to 30-50 dB (point of **saturation**), so this cannot account for the dynamic range of hearing that we measure behaviorally.
- Combining responses across population of many ANFs increases dynamic range of system.

Encoding Time

- Phase locked responses of ANFs encode timing information
- Reliable phase-locking encodes spike periods up to ca. 0.2 ms (~5 kHz).

Complex Encoding of Acoustic Information

- Combining information obtained from different cells into **population response** increases information coding ability (e.g. average normalized spike rate functions across population of ANFs).
- ALSR = Average Localized Synchronized Rate (see Fig. 9.14 in Yost 2005)
- High frequency information would reach your central auditory system first because the basilar membrane traveling wave has shorter latency of response for high frequencies, and we can record the delay between high and low stimulus frequencies.

Central Auditory Nervous System (CANS)

- We now understand the basics of how frequency, amplitude and timing information are encoded by Peripheral Auditory Nervous System (PANS).
- Now going to have brief tour of the Central Auditory Nervous System (CANS).
- Monaural and binaural neural information can be combined in the CANS.
- Emergent cellular properties and neural networks take place in the CANS.
- As we go from PANS and ascent the CANS, we see emergent cellular properties that are more removed from the neural response of primary auditory afferent fibers (cells).

Ascending Flow of Information

- Cochlear Nucleus (brainstem) ➔ Trapezoid Body ➔ Superior Olivary Complex ➔ Lateral Lemniscus ➔ Inferior Colliculus (midbrain) ➔ Medial Geniculate Body ➔ Auditory Cortex (forebrain).
- **Ascending** CANS is from cochlear nucleus toward **auditory cortex.**
- **Descending** CANS is from **auditory cortex** toward cochlear nucleus.
- Nuclei closer to the auditory cortex are the “higher” auditory centers.

Central Auditory Anatomy

- **Auditory Nucleus:** a group of cells (cell bodies) anatomically organized in certain brain region.
- **CANS** is composed of many auditory nuclei connected via nerve fibers or **tracts**.
- Some fibers send **collaterals** or **branches** to certain nuclei.
- Some nuclei receive primarily **monaural (**one ear) input from the “lower” **brainstem** centers.
- Other auditory nuclei receive primarily **binaural (**both ears) inputs.
- Still other auditory nuclei contain cells that are either monaural or binaural (i.e. mixed inputs).
- **Ipsilateral** = same side; **Contralateral** = opposite side

CANS Neural Morphology & Physiology

- Cell **morphology** reflects **physiological** specializations.
- Some cells have large dendritic trees; others have synaptic specializations to ensure faithful transmission of neural information.
- Cells can be organized in **layers** within auditory nuclei
- Morphology and orientation of cell within nucleus may help it receive inputs.
- **Cochleotopy:** neural spatial arrangement of where sound is received or transmitted; cells tuned to the same frequency are located in adjacent regions within central auditory nuclei (i.e. **tonotopy**).

Tonotopy of Cochlear Nucleus

- **Cochlear nucleus** is the first processing stage of ANF information in CANS.
- Composed of 3 divisions (nuclei):
  i. **Dorsal Cochlear Nucleus (DCN)**
  ii. **Anteroventral Cochlear Nucleus (AVCN)**
  iii. **Posteroventral Cochlear Nucleus (PVCN)**
- Spiral ganglion ANFs entering cochlear nucleus have **collateral projections** to each division.
- Each division of cochlear nucleus has a **cochleotopic** arrangement (i.e. **tonotopic** map).
- Tonotopy also exists in spatial arrangement of ANFs. High frequencies on outside of auditory nerve; lower frequencies are more toward center of the auditory nerve.

Input To Cochlear Nucleus

- Layers of neurons in each division of cochlear nucleus are tuned to different frequencies (tonotopy).
- That is, each division of the cochlear nucleus (i.e. DCN, AVCN, PVCN) is tonotopically organized.

Neural Response Properties

- Neurons in the CANS can have different responses to the same auditory stimulus.
  i. Primary-like response
  ii. Onset response
  iii. Offset response
  iv. Inhibitory response (during stimulus)
  v. Chopper response (series of peaks in PSTH)
  vi. Pauser response (pause in response of PSTH)
  vi. On-Off Response, etc.

Superior Olivary Complex (SOC)

- SOC composed of 4 divisions (nuclei):
  i. **Lateral Superior Olive (LSO)**
  ii. **Medial Superior Olive (MSO)**
  iii. **Trapezoid Body**
  iv. **Peri-Olivary Nuclei**
- LSO: binaural inputs sensitive to interaural level difference (ILD).
  - Ipsilateral input = excitatory
  - Contralateral input = inhibitory
- MSO: binaural inputs sensitive to interaural time difference (ITD).
  - Ipsilateral input = excitatory
  - Contralateral input = excitatory

Inferior Colliculus (IC)

- Composed of 3 divisions (nuclei):
  i. **Dorsal Cortex** of IC
  ii. **Central Nucleus** of IC
  iii. **Paracentral Nuclei** of IC
- IC contains both monaural and binaural neurons.
- Binaural inputs tend to be EI: Ipsilateral = inhibitory (I) and Contralateral = excitatory (E).
- Like other auditory nuclei, the IC is cochleotopic (i.e. tonotopically organized)
- Diversity of cellular response types in the physiology of IC cells (e.g. ITD coding), some of first appear at level of IC (i.e. emergent de novo response properties)

Auditory Cortex (AC)

- Human auditory cortex located in fissure of Sylvius.
- Direct inputs from Medial Geniculate Body (auditory thalamus) define primary auditory cortex (AI)
- Like other auditory nuclei, the AC is cochleotopic (i.e. tonotopically organized).
- AI is surrounded by Secondary AC (AII) and Associative AC (SII, EP) areas.
- Unique and emergent cellular response properties are seen in the physiology of AC cells.