WEEK TWO: HOW DO WE SENSE? | ESSAY THREE

Hearing and Deafness

By Dylan K. Chan

As a clinician-scientist in otolaryngology, I treat children, from newborn babies to adolescents, with hearing loss. One such baby – let's call her HC – was identified as hearing-impaired through the Universal Newborn Hearing Screening program, which screens all babies born in hospitals prior to discharge. Her parents were looking for answers: Why can't my child hear? What can you do to fix it? Answers require an understanding of how our ears hear.

All of our peripheral sensory organs translate physical perturbations (the language of the physical world) into neuronal impulses (the language of the brain). This happens in the ear as sound waves are **conducted, amplified, transduced** (converted from mechanical to electrical impulses), and **interpreted**. When any of these four steps is disrupted, we can't hear normally, and each requires different treatments.

The most basic test of hearing is a behavioral audiogram. Increasingly louder tones are played through earphones, and the listener indicates when she hears the sound. This establishes her **threshold** of sound detection. HC didn't respond even to very loud tones, so we turned to more specific tests that allow us to distinguish between the three major kinds of hearing loss—**conductive hearing loss, sensorineural hearing loss, and auditory neuropathy**—in order to pinpoint the source of her problem along the auditory pathway. This involves understanding the nature of sound itself, so we can see how the ear transforms it, step-by-step, into signals that our brain can work with.

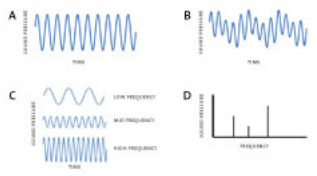

Figure 1. Sound pressure waves

A. Variation in sound pressure with time gives a sound at a single pitch (frequency). This sound pressure wave looks like a simple sine wave. B. A more complex sound pressure wave. C. This complex sound pressure wave is made up of three simple sound-pressure sine waves at different frequencies, all added together. D. Instead of representing the three individual simple sound-pressure waves separately, they can be represented as sound pressures (y axis) occurring at each of the component frequencies (x axis). ©Dylan Chan

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The nature of sound waves

Sound waves are tiny fluctuations in pressure that cause air molecules to vibrate. These vibrations have amplitude (loudness) and frequency (pitch). The simplest sound (a "pure tone") has vibrations at only one frequency – if you look at the variation in pressure with time, it looks like a simple sine wave ***(Figure 1A)***.

When multiple pure tones are mixed together, the wave looks more complicated (***Figure 1B***). However, any sound can be broken down into individual pure-tone components, which is critical to understanding how the ear hears. This particular sound is made up of three frequencies - three sine waves represented as pressure changes vs. time (***Figure 1C***). Another way of looking at this complex sound is to make a graph of the intensity of each frequency component versus the frequency itself. In this case, you can clearly see that there are three frequency components, each with its own intensity (***Figure 1D***).

Sound conduction

Sound waves in the air carry mechanical energy. Once the sound waves enter the ear canal, the energy is transferred into vibration of the eardrum. It is then conducted through the three tiny bones of the middle ear (the malleus, incus, and stapes) to the inner ear and the cochlea itself (***Figure 2***). This transfers mechanical energy from pressure changes in the air into mechanical motion of the stapes. The base of the stapes fits onto a bony oval window on the fluid-filled cochlea. If any of these structures that conduct sound are scarred or damaged – by wax in the ear canal, a hole in the eardrum, fluid in the space surrounding the middle-ear bones, or fixation or disconnection of the bones themselves – conductive hearing loss results; that is, sound is not conducted efficiently from the air to the cochlea. Hearing aids are excellent in such conditions because the deficit is purely a failure of mechanical transmission. Simply boosting the volume of sound coming into the ear overcomes the hearing loss.

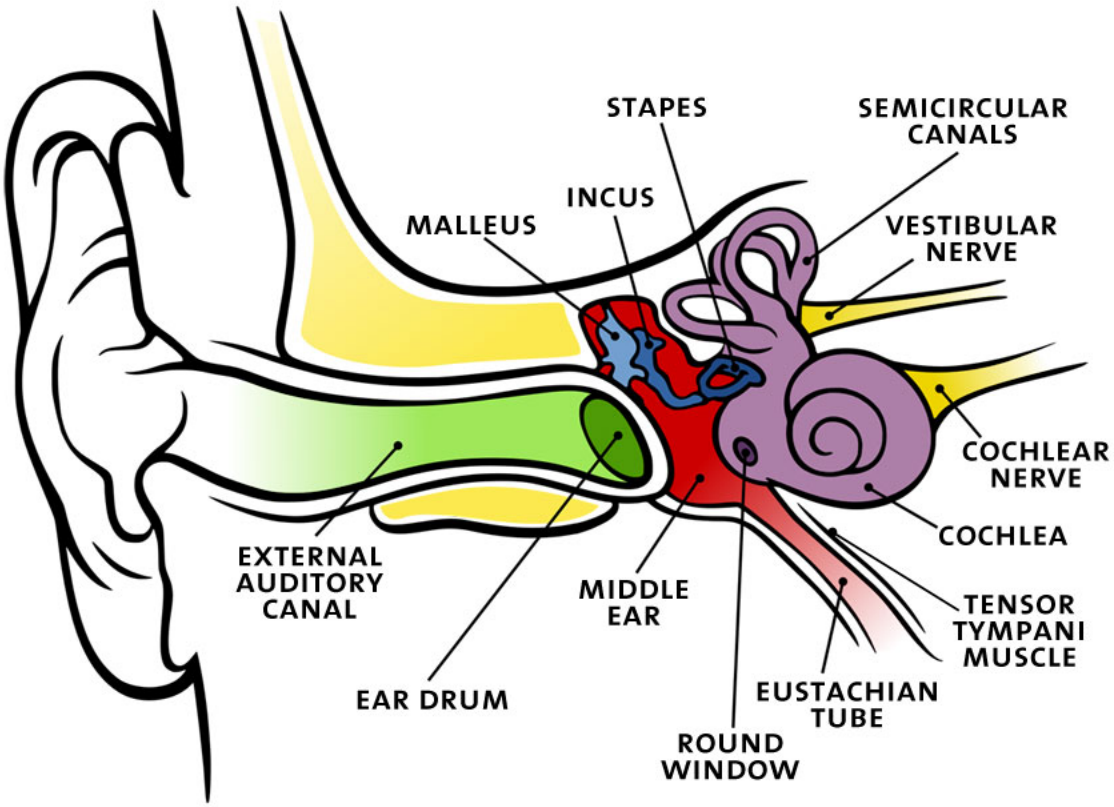

Figure 2. Anatomy of the human ear.
Sound waves are collected by the auricle and transmitted down the external auditory canal to the ear drum. Vibration of the ear drum is transmitted through the malleus, incus, and stapes to the cochlea. ©AMNH

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We were able to do a simple test on HC, by playing a sound via an oscillator pressed against her forehead,. Called bone-conduction audiometry, this delivers sound directly to the cochlea through vibrations transmitted through the skull. If her hearing loss were purely conductive, she would have heard the sound normally, and surgery could have repaired the sound conduction mechanism in the ear. But HC still heard nothing, indicating that her problem lay in the cochlea or auditory nerve – she had a sensorineural hearing

loss. About 1 in 500 babies are born with sensorineural hearing loss, making it the most common congenital sensory deficit. Those who receive appropriate interventions by 6 months typically develop normal speech and language.

Sound amplification

Vibration of the stapes at the oval window of the cochlea exerts pressure changes in the fluid-filled cochlea. This is a tube rolled up into the shape of a snail, with a "base" near the oval window and an "apex" at the opposite end of the tube (***Figure 3***). These pressure changes are felt as vibrations in the **basilar membrane**, which runs along the length of the tube and changes in stiffness. Each point along the membrane has a pitch, or characteristic frequency, at which it wants most to vibrate – higher near the taut base, and lower near the floppy apex. When a complex sound sets the entire basilar membrane into motion, the membrane breaks it down into all its component frequencies (the process described in ***Figure 1***).

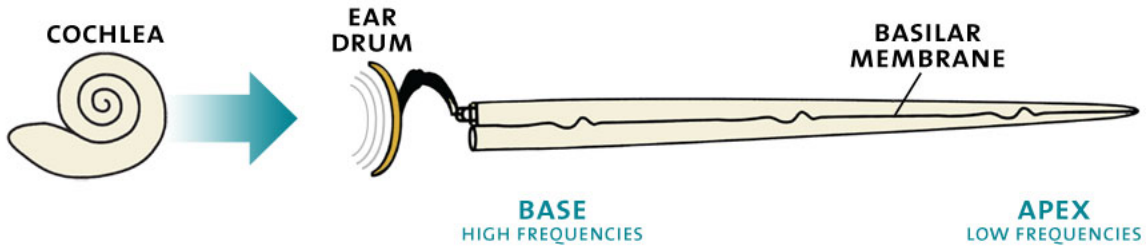

Figure 3. The cochlea

The cochlea looks like a coiled-up snail shell. When unrolled, it looks like a tube divided by the basilar membrane. Vibrations at the ear drum are transmitted to the cochlea, and cause the basilar membrane to vibrate. The basilar membrane is most sensitive to high frequencies at its base, and to low frequencies at its apex. ©A.J. Hudspeth

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A second process, known as the **cochlear amplifier**, greatly assists this process. The cochlea contains both fluid and tiny, sensitive, hair cells. Specialized **outer hair cells** on the basilar membrane tune the basilar membrane even more sharply. This mechanism preferentially amplifies quieter sounds, while a separate mechanism also based in the outer hair cells suppresses the response to very loud noises. This allows us to hear a wide range of sound intensities, from the quietest whisper to a jet engine. This sharp tuning is required for us to detect subtle differences in sounds; when it is compromised, we specifically lose our ability to hear in challenging circumstances. This is what happens in the most common forms of hearing loss related to age and noise, in which the specialized outer hair cells die. Hair cells are very fragile and do not regenerate, and simple hearing aids cannot overcome this loss. Newer hearing aids with complex digital signal processing can help, but the only way to truly fix this problem is to replace the outer hair cells, which is not yet possible.

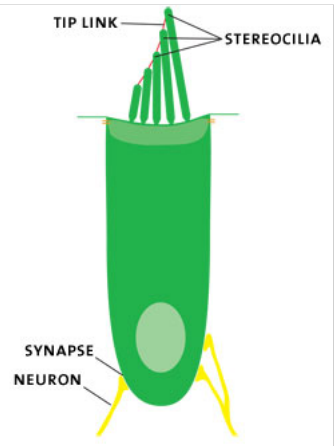

Figure 4. Hair cell

Stereocilia sitting on the surface of a hair cell are connected by tip links. Movement of the basilar membrane causes deflection of the stereociliary hair bundle. If this hair bundle is pushed to the right, the tip links will be pulled

We can test the function of the outer hair cells and cochlear amplifier by measuring **otoacoustic emissions**. These sounds are distortions produced by the ear itself due to the activity of the cochlear amplifier; they are equivalent to the distortion that can be heard when a stereo amplifier is turned up too loud. When HC was tested, she had no measurable otoacoustic emissions, suggesting that her cochlear amplifier – and likely the outer hair cells that drive it – was not functioning properly. This confirmed that the cause of her hearing loss lies at least in part in dysfunction of the outer hair cells of the cochlea,

though it didn't rule out the possibility of damage to other parts of the cochlea or the auditory nerve. This kind of sensorineural loss is typically irreversible, as the hair cells that underlie sound amplification and transduction do not regenerate when lost.

Sound transduction

A different population of hair cells – **inner hair cells** – actually convert mechanical signals into electrical impulses that are sent to the brain via the auditory nerve ***(Figure 4)***. The brain then interprets these electrical signals as sound. Tiny "hairs," or stereocilia, protrude from the top surface of the hair cells and move back and forth as the basilar membrane vibrates. When stereocilia move back and forth, ion channels open and alter the electric potential inside the hair cell. This causes neurotransmitter release at synapses onto neurons at the other end of the inner hair cells.

Because the basilar membrane is arranged tonotopically – it vibrates most strongly at its base in response to high frequencies, and at its apex in response to low frequencies - everything else in the sound transduction cascade is arranged in a **tonotopic map**. Inner and outer hair cells at a specific spot on the basilar membrane are tuned to respond to the characteristic frequency of that spot, and the neurons that connect onto that spot are also tuned for that frequency. How well we can distinguish between different frequencies depends on the density of the detection units, much like the pixels on a digital camera. There are about 4000 inner hair cells, distributed along the length of the basilar membrane, which can detect sounds from 20 Hz to 20,000 Hz. We can only detect a difference between adjacent frequencies if the difference is great enough to stimulate a different population of inner hair cells; for humans, this difference is about 0.5%.

When the cochlea is damaged, whether by noise, age, drugs, or trauma, the outer hair cells typically die first, and then the inner hair cells. While loss of outer hair cells reduces the ability to hear in noisy places and at high frequencies, loss of inner hair cells leads to profound deafness. Hearing aids that boost the sound coming in are useless, because the sound cannot be transduced into neuronal signals.

In humans with profound hearing loss, this process – converting sound into electrical signals – can be accomplished artificially with a **cochlear implant** ***(Figure 5)***. This device consists of an external microphone that functions like the basilar membrane, detecting and separating sound into its component frequencies. It then sends signals to an array of 22 electrodes, each of which gives out an electrical pulse that corresponds to a specific frequency. This array is implanted into the cochlea, where the electrodes sit along the basilar membrane and simulate the activity of the inner hair cells. The cochlear implant processor coordinates the firing of the electrodes: when an electrode fires, it stimulates neurons in the segment of the basilar membrane that would have received the electrical output of the inner hair cell tuned to that particular frequency.

Sound interpretation

The previous steps describe how the ear turns pressure waves into electrical signals. How are those electrical signals encoded in the neurons? Sound waves vibrate at up to 20,000 times a second, which is much faster than a neuron can fire. So this kind of **temporal coding** – where the firing of a neuron is synchronized to the frequency of the sounds it is meant to encode – is not practical for most frequencies.

However the tonotopic map of the cochlea lends itself very well to **spatial coding**. The basilar membrane vibrates most strongly at its base in response to high frequencies, and at its apex in response to low frequencies, and neurons are tuned to the specific frequency of the spot to which they are connected. The firing rate of that neuron, then, will be

upon. This pulls open ion channels at the tips of the stereocilia, letting in potassium ions. The resulting electrical signal inside the hair cell causes neurotransmitter release at synapses and subsequent neuron activation. ©Dylan Chan

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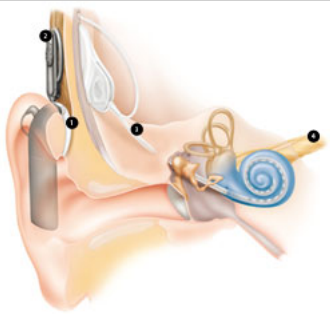

Figure 5. Cochlear implant

In a cochlear implant, a sound processor (1) converts sounds into frequency-specific electrical

proportional to the intensity of the vibration at that spot, and as long as that neuron maintains its frequency identity as it moves centrally towards the brain, the information about frequency and intensity will be preserved.

In individuals with damage to the auditory nerve, which carries signals from the ear to the brain, this information is compromised. This damage can occur as a result of tumor, trauma, or infection, and is referred to as **auditory neuropathy**. In these relatively rare cases, individuals can perceive pure tones perfectly well but can have a great deal of trouble processing more complex tones and sound patterns, especially speech, which sounds garbled. Auditory brainstem implants bypass the auditory nerve and stimulate the brainstem directly, taking some advantage of the tonotopicity of this area. But they are much less successful than cochlear implants at restoring normal and functional hearing and are very rarely performed.

We can place electrodes on the head to measure the **auditory brainstem response**. Looking at the timing between characteristic electrical responses of the cochlea, the auditory nerve, and the brain can tell us whether transmission is intact. In HC's case, the timing was normal. This suggested that her auditory nerve was functioning well even though the output from the cochlea was attenuated.

A plan for HC

The cochlea has devised an ingenious way of converting a physical phenomenon in our environment into trains of action potentials. The basilar membrane, by virtue of its intrinsic physical properties, separates out frequency components along its length; the outer hair cells further refine and amplify these frequency-specific vibrations; the inner hair cells turns these mechanical vibrations into electrical impulses; and the neurons turn these electrical impulses into temporally-coded firing patterns that are also spatially coded because of the neurons' position along the tonotopic basilar membrane.

HC's test findings were consistent with a sensorineural hearing loss, with the deficit localized to the cochlea itself. The most common causes are prenatal infections, anatomic cochlear anomalies, and mutations in one of about 70 genes. HC was found to be homozygous for the 35delG mutation in the gene encoding Connexin 26, a protein necessary for cochlear development and function. Because of her profound hearing impairment, she received a cochlear implant at one year of age, which bypassed the function of her cochlea and stimulated her intact auditory nerve. Because HC was so young, her brain was able to easily integrate the neuronal impulses stimulated by her implant and she developed age-appropriate speech and language. Her hearing, however, will never be perfect; her perception of music is different and less enjoyable, and she still has trouble hearing in noise.

As a physician, it is gratifying to localize an infant's hearing loss and be able to compensate with a mechanical device that works remarkably well. As a scientist, however, I hope to learn specifically what cells and pathways in the cochlea are affected by Connexin 26 dysfunction, and to devise treatments that actually fix the root problem and restore the cochlea to full, normal function. If HC's children or grandchildren were to inherit the same genetic mutations, their treatment might involve gene therapy to restore normal cochlear function.

Dr. Dylan K. Chan is Assistant Professor in the Department of Otolaryngology - Head and Neck Surgery at the University of California, San Francisco

signals similarly to a microphone. An electrical coil (2) transmits this electrical signal to the surgically placed implant (3). The implant conveys the frequency-specific electrical signals to frequency-specific locations along the basilar membrane. At each of these locations, the implant stimulates activation of neurons. The maintenance of this frequency coding enables the auditory nerve (4) to carry information to the brain that is interpreted similarly to natural acoustic stimuli. ©Cochlear

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RELATED LINKS

National Institute on Deafness and other Communication Disorders »

Information, resources and tips about many diseases and hearing disorders, including a section with classroom resources

Centers for Disease Control and Prevention: Hearing Loss in Children »

In-depth information from the CDC about the basics of hearing loss, diagnosis and treatment, and the latest research in hearing loss in children.

The National Organization for Hearing Research Foundation »

Current biomedical research into the preventions, treatments, causes, and cures of hearing loss and deafness.

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