00:06

Can you hear me OK?

00:07

Audience: Yes.

00:09

Jim Hudspeth: OK. Well, if you can, it's really amazing, because my voice is changing the air pressure where you sit by just a few billionths of the atmospheric level, yet we take it for granted that your ears can capture that infinitesimal signal and use it to signal to the brain the full range of auditory experiences: the human voice, music, the natural world. How does your ear do that? And the answer to that is: through the cells that are the real hero of this presentation -- the ear's sensory receptors, which are called "hair cells."

00:45

Now, these hair cells are unfortunately named, because they have nothing at all to do with the kind of hair of which I have less and less. These cells were originally named that by early microscopists, who noticed that emanating from one end of the cell was a little cluster of bristles. With modern electron microscopy, we can see much better the nature of the special feature that gives the hair cell its name. That's the hair bundle. It's this cluster of 20 to several hundred fine cylindrical rods that stand upright at the top end of the cell. And this apparatus is what is responsible for your hearing me right this instant.

01:29

Now, I must say that I am somewhat in love with these cells. I've spent 45 years in their company --

01:35

(Laughter)

01:36

and part of the reason is that they're really beautiful. There's an aesthetic component to it. Here, for example, are the cells with which an ordinary chicken conducts its hearing. These are the cells that a bat uses for its sonar. We use these large hair cells from a frog for many of our experiments. Hair cells are found all the way down to the most primitive of fishes, and those of reptiles often have this really beautiful, almost crystalline, order.

02:04

But above and beyond its beauty, the hair bundle is an antenna. It's a machine for converting sound vibrations into electrical responses that the brain can then interpret. At the top of each hair bundle, as you can see in this image, there's a fine filament connecting each of the little hairs, the stereocilia. It's here marked with a little red triangle. And this filament has at its base a couple of ion channels, which are proteins that span the membrane.

02:36

And here's how it works. This rat trap represents an ion channel. It has a pore that passes potassium ions and calcium ions. It has a little molecular gate that can be open, or it can be closed. And its status is set by this elastic band which represents that protein filament. Now, imagine that this arm represents one stereocilium and this arm represents the adjacent, shorter one with the elastic band between them. When sound energy impinges upon the hair bundle, it pushes it in the direction towards its taller edge. The sliding of the stereocilia puts tension in the link until the channels open and ions rush into the cell. When the hair bundle is pushed in the opposite direction, the channels close. And, most importantly, a back-and-forth motion of the hair bundle, as ensues during the application of acoustic waves, alternately opens and closes the channel, and each opening admits millions and millions of ions into the cell. Those ions constitute an electrical current that excites the cell. The excitation is passed to a nerve fiber, and then propagates into the brain. Notice that the intensity of the sound is represented by the magnitude of this response. A louder sound pushes the hair bundle farther, opens the channel longer, lets more ions in and gives rise to a bigger response.

04:04

Now, this mode of operation has the advantage of great speed. Some of our senses, such as vision, use chemical reactions that take time. And as a consequence of that, if I show you a series of pictures at intervals of 20 or 30 per second, you get the sense of a continuous image. Because it doesn't use reactions, the hair cell is fully 1,000 times faster than our other senses. We can hear sounds at frequencies as great as 20,000 cycles per second, and some animals have ever faster ears. The ears of bats and whales, for example, can respond to their sonar pulses at 150,000 cycles a second.

04:45

But this speed doesn't entirely explain why the ear performs so well. And it turns out that our hearing benefits from an amplifier, something called the "active process." The active process enhances our hearing and makes possible all the remarkable features that I've already mentioned.

05:06

Let me tell you how it works. First of all, the active process amplifies sound, so you can hear, at threshold, sounds that move the hair bundle by a distance of only about three-tenths of a nanometer. That's the diameter of one water molecule. It's really astonishing. The system can also operate over an enormously wide dynamic range. Why do we need this amplification? The amplification, in ancient times, was useful because it was valuable for us to hear the tiger before the tiger could hear us. And these days, it's essential as a distant early warning system. It's valuable to be able to hear fire alarms or contemporary dangerous such as speeding fire engines or police cars or the like. When the amplification fails, our hearing's sensitivity plummets, and an individual may then need an electronic hearing aid to supplant the damaged biological one.

06:11

This active process also enhances our frequency selectivity. Even an untrained individual can distinguish two tones that differ by only two-tenths of a percent, which is one-thirtieth of the difference between two piano notes, and a trained musician can do even better. This fine discrimination is useful in our ability to distinguish different voices and to understand the nuances of speech. And, again, if the active process deteriorates, it becomes harder to carry out verbal communication.

06:42

Finally, the active process is valuable in setting the very broad range of sound intensities that our ears can tolerate, from the very faintest sound that you can hear, such as a dropped pen, to the loudest sound that you can stand -- say, a jackhammer or a jet plane. The amplitude of sounds spans a range of one millionfold, which is more than is encompassed by any other sense or by any man-made device of which I'm aware. And again, if this system deteriorates, an affected individual may have a hard time hearing the very faintest sounds or tolerating the very loudest ones.

07:21

Now, to understand how the hair cell does its thing, one has to situate it within its environment within the ear. We learn in school that the organ of hearing is the coiled, snail-shaped cochlea.

It's an organ about the size of a chickpea. It's embedded in the bone on either side of the skull. We also learn that an optical prism can separate white light into its constituent frequencies, which we see as distinct colors. In an analogous way, the cochlea acts as sort of an acoustic prism that splits apart complex sounds into their component frequencies. So when a piano is sounded, different notes blend together into a chord.

08:05

The cochlea undoes that process. It separates them and represents each at a different position. In this picture, you can see where three notes -- middle C and the two extreme notes on a piano -- are represented in the cochlea. The lowest frequencies go all the way up to the top of the cochlea. The highest frequencies, down to 20,000 Hz, go all the way to the bottom of the cochlea, and every other frequency is represented somewhere in between. And, as this diagram shows, successive musical tones are represented a few tens of hair cells apart along the cochlear surface.

08:40

Now, this separation of frequencies is really key in our ability to identify different sounds, because very musical instrument, every voice, emits a distinct constellation of tones. The cochlea separates those frequencies, and the 16,000 hair cells then report to the brain how much of each frequency is present. The brain can then compare all the nerve signals and decide what particular tone is being heard.

09:09

But this doesn't explain everything that I want to explain. Where's the magic? I told you already about the great things that the hair cell can do. How does it carry out the active process and do all the remarkable features that I mentioned at the outset? The answer is instability. We used to think that the hair bundle was a passive object, it just sat there, except when it was stimulated. But in fact, it's an active machine. It's constantly using internal energy to do mechanical work and enhance our hearing. So even at rest, in the absence of any input, an active hair bundle is constantly trembling. It's constantly twitching back and forth. But when even a weak sound is applied to it, it latches on to that sound and begins to move very neatly in a one-to-one way with it, and by so doing, it amplifies the signal about a thousand times.

10:02

This same instability also enhances our frequency selectivity, for a given hair cell tends to oscillate best at the frequency at which it normally trembles when it's not being stimulated. So, this apparatus not only gives us our remarkably acute hearing, but also gives us the very sharp tuning.

10:28

I want to offer you a short demonstration of something related to this. I'll ask the people who are running the sound system to turn up its sensitivity at one specific frequency. So just as a hair cell is tuned to one frequency, the amplifier will now enhance a particular frequency in my voice. Notice how specific tones emerge more clearly from the background. This is exactly what hair cells do. Each hair cell amplifies and reports one specific frequency and ignores all the others. And the whole set of hair cells, as a group, can then report to the brain exactly what frequencies are present in a given sound, and the brain can determine what melody is being heard or what speech is being intended.

11:17

Now, an amplifier such as the public address system can also cause problems. If the amplification is turned up too far, it goes unstable and begins to howl or emit sounds. And one wonders why the active process doesn't do the same thing. Why don't our ears beam out sounds? And the answer is that they do. In a suitably quiet environment, 70 percent of normal people will have one or more sounds coming out of their ears.

11:45

(Laughter)

11:46

I'll give you an example of this. You will hear two emissions at high frequencies coming from a normal human ear. You may also be able to discern background noise, like the microphone's hiss, the gurgling of a stomach, the heartbeat, the rustling of clothes.

12:06

(Hums, microphone hiss, dampened taps, clothes rustling)

12:21

This is typical. Most ears emit just a handful of tones, but some can emit as many as 30. Every ear is unique, so my right ear is different from my left, my ear is different from your ear, but unless an ear is damaged, it continues to emit the same spectrum of frequencies over a period of years or even decades.

12:40

So what's going on? It turns out that the ear can control its own sensitivity, its own amplification. So if you're in a very loud environment, like a sporting event or a musical concert, you don't need any amplification, and the system is turned down all the way. If you are in a room like this auditorium, you might have a little bit of amplification, but of course the public address system does most of the work for you. And finally, if you go into a really quiet room where you can hear a pin drop, the system is turned up almost all the way. But if you go into an ultraquiet room such as a sound chamber, the system turns itself up to 11, it goes unstable and it begins to emit sound. And these emissions constitute a really strong demonstration of just how active the hair cell can be.

13:30

So in the last minute, I want to turn to another question that might come up, which is: Where do we go from here? And I would say that there are three issues that I would really like to address in the future.

13:41

The first is: What is the molecular motor that's responsible for the hair cell's amplification? Somehow, nature has stumbled across a system that can oscillate or amplify at 20,000 cycles per second, or even more. That's much faster than any other biological oscillation, and we would like to understand where it comes from.

14:04

The second issue is how the hair cell's amplification is adjusted to deal with the acoustic circumstances. Who turns the knob to increase or decrease the amplification in a quiet or in a loud environment?

14:18

And the third issue is one that concerns all of us, which is what we can do about the deterioration of our hearing. Thirty million Americans, and more than 400 million people worldwide, have significant problems on a daily basis with understanding speech in a noisy environment or over the telephone. Many have even worse deficits. Moreover, these deficits tend to get worse with time, because when human hair cells die, they're not replaced by cell division. But we know that nonmammalian animals can replace their cells, and those creatures' cells are dying and being replaced throughout life, so the animals maintain normal hearing. Here's an example from a little zebra fish. The cell at the top will undergo a division to produce two new hair cells. They dance for a little bit, and then settle down and go to work.

15:10

So we believe that if we can decode the molecular signals that are used by these other animals to regenerate their hair cells, we'll be able to do the same thing for humans. And our group and many other groups are now engaged in research trying to resurrect these amazing hair cells.

15:27

Thank you for your attention.

15:29

(Applause)