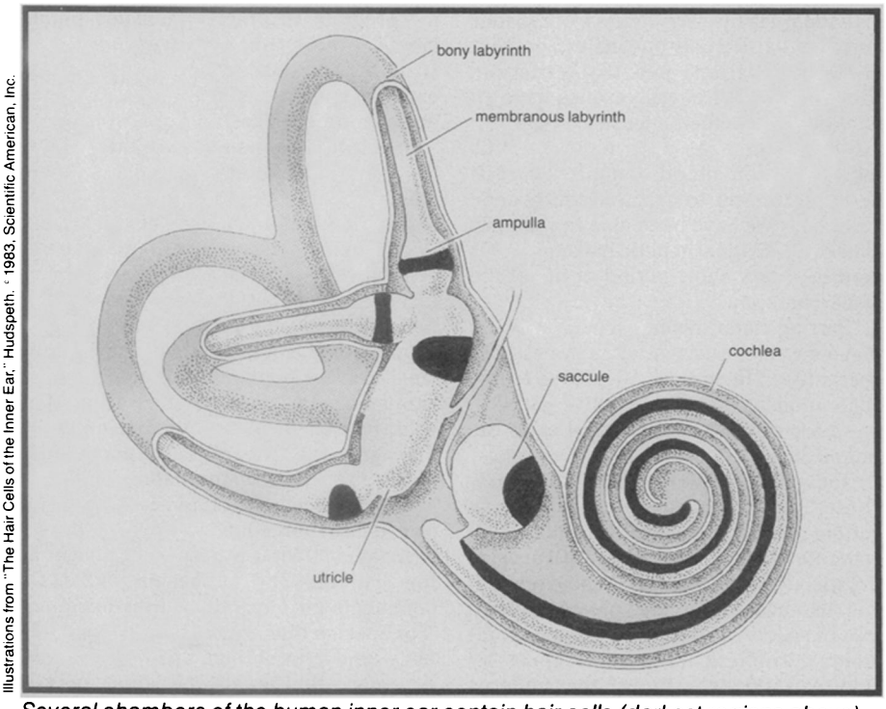
CRAFTING SOUND FROM SILENCE

Cells smaller than fleas' knees serve as key players in the sound relay from the outside world to the brain. An improved understanding of how the tiny hair cells transmit their message is already shaping scientists' views about new ways to treat hearing problems.



Illustrations from "The Hair Cells of the Inner Ear," Hudspeth, © 1983, Scientific American, Inc.

Several chambers of the human inner ear contain hair cells (darkest regions above). While some hair cells mediate balance, cochlear hair cells detect sound.

By DEBORAH FRANKLIN

Linda Jansen popped some shrimp into hot fat one night after work recently, and they started to talk. The phone's ring, too, sounded like human conversation to the 36-year-old computer operator from Sunnyvale, Calif. Far from losing her mind, Jansen, who was deafened two years ago, was reentering the world of sound with the help of an electronic device that still has some bugs to be worked out.

The device, designed and implanted by F. Blair Simmons and co-workers at Stanford University Medical Center in Palo Alto, Calif., is one of several types of "cochlear implants" now being tested and refined in research centers across the United States (SN: 11/27/82, p. 340). Without question, the new generation of hearing aids that act by directly stimulating the auditory nerve is beginning to crack the wall of silence that surrounds as many as 200,000 persons in the United States alone who are profoundly deaf because of damage to the inner ear. Many might one day be candidates for implants.

But for now, the still-experimental devices serve best as an aid to lip-reading

and in providing feedback to help deaf persons modulate their speaking voices, Simmons says. "Normal" human hearing, with its sensitivity to a relatively wide range of sounds, cannot yet be replicated electronically.

One roadblock to such replication is the still-fuzzy understanding of the mechanisms of the inner ear, the last relay station from the outside world of sounds to the brain. For many years, scientists have recognized that the key players in the relay are tiny "hair cells," named for the bundles of thin, hairlike appendages, called stereocilia, at their tips. Exactly how the hair cells turn sound waves into messages the brain can understand has been a mystery, primarily because the cells are so small, relatively few in number and inaccessible. But now, with the help of animal models and chemical tools so powerful they can detect an amino acid in a fingerprint, biochemists and physiologists are probing the inner ear and uncovering clues to sound perception that are already improving aids and might one day put some of the devices out of business.

Though most of the research is still basic, the eventual applications are obvious, says Dennis Drescher, an auditory biochemist at Wayne State University in Detroit. "We would like to draw a diagram of the workings of the business part of the inner ear, at a molecular level," he told SCIENCE NEWS, "so we can treat disorders more specifically and tell which parts need to be repaired or replaced."

The outside "parts" involved in hearing are better understood. The flap of skin and cartilage most people think of as the ear scoops up sound waves like a megaphone and bounces them down an inch-long tube to the ear drum. Vibrations in the drum are picked up by neighboring bones and converted into hydraulic pressure waves by a stirrup-shaped bone called the stapes.

A pluck of the stapes starts a chain of events in the dark chambers of the spiral-shaped cochlea, where the "business part of hearing," as Drescher calls it, begins. The cochlea can be thought of as three fluid-packed tubes sandwiched together inside a bony, coiled canal. The "basilar" membrane separating the lower two tubes contains four long rows of hair cells. When the stapes is pulled, a pressure differential is set up in the tubes that tweaks the exquisitely sensitive hairs. A movement as tiny as the width of an atom triggers a chemical change in the cell that is eventually transmitted through the auditory nerve and perceived as sound in the brain.

Three aspects of the hair cell have particularly drawn the interest of researchers in the last few years: the molecular structure of the hair bundles; the topmost tip, where mechanical tweaking starts an electrical current that spreads like a spark in a fuse to the bottom; and the base of the cell, where droplets of a still-to-be-identified chemical messenger are spewed onto the auditory nerve.

Looking at isolated hair cells, A.J. Hudspeth of the University of California at San Francisco and others have found that when the tip of a single bundle of closely knit "hairs" is nudged about 1 degree in a given direction, channels in the cell membrane open, permitting positively charged ions — mostly potassium — to rush into the cell. (A nudge in the opposite direction seems to close these channels.) A sudden change in electrical potential across the membrane then triggers a passive current along the length of the cell. Hudspeth's team is now intent on discovering exactly how the channels are opened and closed at a rate so rapid that the cell can respond to subtle stimuli that come as often as 100,000 times each second.

It has been known for some time that each hair cell responds best to sound of a given frequency: Cells at the base of the cochlea prefer sounds of high frequency, while cells in the topmost coils favor low-pitched tones. Hudspeth is currently exploring how the mechanical properties of the hair cell help to determine the preferred frequency. By videotaping the magnified motion of the hearing organ of the alligator lizard, Hudspeth's co-worker Tom Holton found last year that the length of the hair bundle determines the best frequency for each cell. The shorter bundles are stiffer, he says, and thus are more resistant to tweaking by pressure waves.

Åke Flock of the Karolinska Institute in Stockholm and David Strelioff of the University of California at Los Angeles published a report in the Aug. 16 NATURE indicating that these findings probably hold for the finely tuned frequency detection in mammalian hearing as well.

In search of the biochemical girders that determine the stiffness of the hairs, Lewis Tilney and his colleagues at the University of Pennsylvania in Philadelphia are turning electron microscopes on the fine, fibrous molecules that form a cross-linked lattice within the cilia. Some of those molecules are actin, the same protein that helps enable muscles to contract. Tilney found that exposure to high-intensity sound destroys the cross-linking. The polymers of actin molecules then break apart, and instead of waving gracefully, the hair bundles flop about like wet noodles.

The evidence in this area is quite preliminary, but it might help explain the temporary hearing loss that can occur when, for example, an unprotected factory worker is overexposed to the roar of escaping steam. Such broad spectrum or "wide band" noise is the most injurious to ears, because it contains all frequencies of sound and so can damage or kill wide swathes of hair cells in a single blast.

While the physiologists study hair cell structure, Drescher and other chemists are seeking the chemical or chemicals that transmit the sound message across a

DECIBEL RATINGS AND HAZARDOUS TIME EXPOSURES OF COMMON NOISES

Typical Level (Decibels)	Example	Dangerous Time Exposure
0	Lowest sound audible to human ear	
30	Quiet library, soft whisper	
40	Quiet office, living room, bedroom away from traffic	
50	Light traffic at a distance, refrigerator, gentle breeze	
60	Air conditioner at 20 feet, conversation, sewing machine	
70	Busy traffic, office tabulator, noisy restaurant (constant exposure)	Critical level begins
80	Subway, heavy city traffic, alarm clock at 2 feet, factory noise	More than 8 hours
90	Truck traffic, noisy home appliances, shop tools, lawnmower	Less than 8 hours
100	Chain saw, boiler shop, pneumatic drill	2 hours
120	Rock concert in front of speakers, sandblasting, thunderclap	Immediate danger
140	Gunshot blast, jet plane	Any length of exposure time is dangerous
180	Rocket launching pad	Hearing loss inevitable

American Academy of Otolaryngology—Head & Neck Surgery, Inc., Washington, D.C.

Sound levels above refer to intensity experienced at typical working distances. Intensity drops 6 decibels with every doubling of distance from noise source.

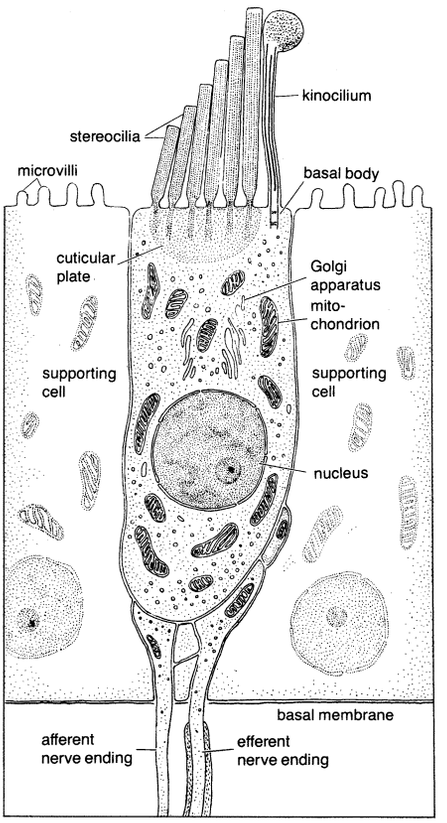
20-nanometer space between the hair cell base and the fibers of the auditory nerve. Several candidates have emerged, but the issue is far from settled. A derivative of glutamate (the "G" in the flavor enhancer MSG) may serve as a transmitter, some findings indicate, and gamma-aminobutyric acid (GABA), commonly found in the brain as a transmitter of inhibitory messages, has also been linked to the hair cells as a possible excitatory transmitter. Drescher says he has chromatographic evidence that a yet-to-be-identified "compound x," which seems to have some properties similar to GABA's, is involved in the hair cells of several animal species. It is possible, he suggests, that across species, and even within different organs of the same individual, several different transmitters are involved in hair cell function. (In man, cochlear hair cells are involved in hearing, while hair cells in the nearby loops of the semicircular canal help mediate a sense of balance. Fish and other aquatic vertebrates have similar structures along the sides of their bodies that enable them to sense mechanical movement in surrounding water.)

Positively identifying the suspect transmitter has been difficult, Drescher says, primarily because there doesn't seem to be much of the stuff, and because it is only one of many ingredients in a chemical "soup" within the cell. "Biochemists usually like to get a tissue sample containing millions or billions of cells," says Drescher, "so the 12,000 to 20,000 or so [found in each human cochlea] are just a drop in the bucket." Hence, research of the cells "depends even more on microtechniques than in the central nervous system where you have more tissue," he says.

Most of the transmitter tracking must rely on indirect evidence of its presence, says Drescher, and high-performance liquid chromatography, immunocytochemistry and other analytical tools fine tuned within the last several years have made such miniaturized sleuthing easier.

In addition to the stimulation they pick up from the outside world, hair cells in each ear are innervated by hundreds of nerve fibers that snake their way down several centimeters from the brainstem and shape the cells' response to stimuli. When these fibers are activated, the cells seem to become less sensitive to sound. The specific significance of such desensitization is not yet known, Drescher says, though when faced with tasks such as concentrating in an office din or picking out the flute section in a symphony, the brain relies on selective inhibition at several levels, including—perhaps—control of the hair cells.

Some "very exciting but preliminary" evidence hints that inhibitory input from the brain may be involved in the stiffening of the hairs, through action on the actin molecules, Drescher says. "There's a lot of evidence to suggest that the inhibitory transmitter involved here is acetylcholine."



Although closely related to nerve cells, the hair cell (shown in cross section) has no dendrites or axons. A tweak at the top sends an electrical current to the bottom, where a chemical messenger is released onto nerve endings.

Recent work by Jörgen Fex at the National Institutes of Health in Bethesda, Md., suggests that enkephalins, best known as the body's natural opiates (SN: 2/4/81, p. 101), may also serve as signal modulators in hearing, lending further texture and subtlety to the sound message perceived by the brain.

A healthy child is born with up to 20,000 hair cells in each ear, but a lifetime of loud noises, disease or drug toxicity can damage or kill the cells, usually a few at a time, taking a portion of hearing sensitivity with them. Drescher estimates that in the unlikely event that modern men and women lived to be 140 years old, they would lose all their hair cells. While a few lost cells may not be missed, when a large enough fraction disappears, the result is some degree of deafness, with symptoms that range from an inability to differentiate between similar words to a total loss of hearing. "It's no wonder we so often grow deaf as we age," Drescher says.

Research has shown that prolonged exposure to intense noise "chops, dices and otherwise hacks apart" the hair cells designed to respond to much softer sounds, Hudspeth says. Powerful antibiotics, such as gentamicin and tobramycin, when given in the especially heavy doses occasionally required to treat life-threatening infections, also damage hearing, probably by making individual hair bundles clump together into clublike appendages. High blood pressure may also cause some damage. Once hair cells are dead, they cannot be replaced.

"The promise of biochemistry, though we aren't there yet," Drescher says, "is that we may one day be able to preserve or promote the formation of hair cells. Or, possibly, we could recruit remaining hair cells to beef up the function, by giving precursors of transmitter or the transmitter itself."

In the meantime, Hudspeth suggests, the laboratory findings are already beginning to influence the way mechanical hearing aids are designed.

"The fact that cochlear implants are beginning to be used is an outgrowth of the fairly recent observation that, in most cases of what has been called 'nerve deafness,' the nerve actually survives, and it's the hair cells that die," he says. Such knowledge has prompted physicians and engineers to develop a device that bypasses the faulty hair cells and stimulates the nerve. Stimulating the brain instead—as would be necessary if the hearing loss were caused by death of the auditory nerve—would be much more complicated and dangerous, he says.

The earliest, single-channel implants have permitted recipients to distinguish a honking horn, a dog's bark and other sounds of fairly low frequency with relatively high accuracy, researchers say. The newer, multichannel models — like Linda Jansen's—that are now being tested in clinical trials should ultimately provide an improved sensitivity to sounds in the higher frequencies, such as human voices and ringing phones. Implant recipients are divided in their satisfaction with the state-of-the-art devices, but many are thrilled with the chance to hear again.

"You have to get used to it," says 68-year-old Amy Sullivan, who received one of the Stanford devices after 40 years of deafness. "It's a metallic sound. It doesn't sound like a voice, but the words come through."

Tests conducted so far indicate that hearing improves as a patient gains experience in listening with the implant, Simmons says, though the maximum benefit each wearer derives seems to vary. Patients like Jansen, who is an excellent lip-reader, might not notice as much improvement, he says, as those who lip-read poorly.

Despite feeling frustration with her less-than-perfect hearing, Jansen says she has high hopes that modifications in cochlear implants within the next few years will continue to improve sound quality.

"This may not help me," she says, "but it may benefit your grandchildren or mine." Hudspeth predicts that even sooner than that, fundamental discoveries about how the inner ear works may contribute to treatments for the estimated one in 15 persons who experience a less severe, but still significant, degree of hearing loss because of damage to the tiny hair cells. □