BIOPHYSICS

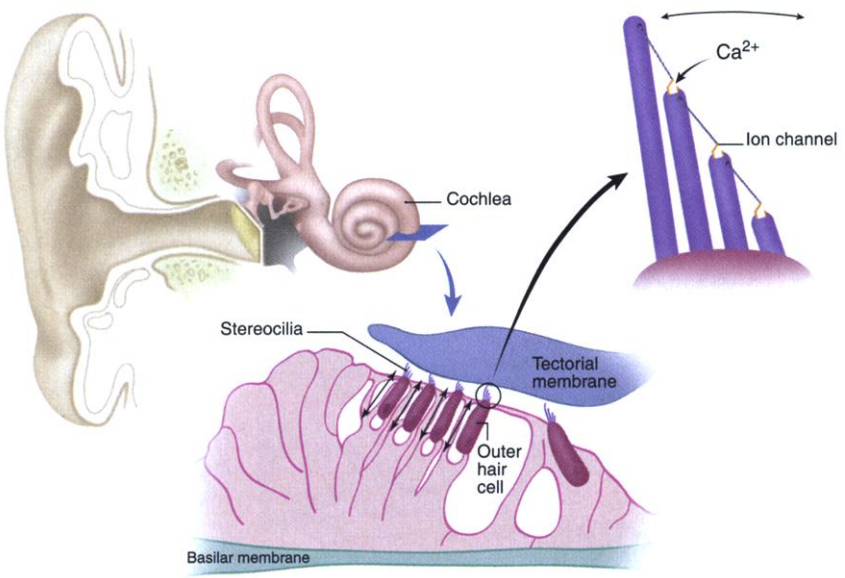
What's Shakin' In the Ear?

Auditory researchers agree that hair cells are the ear's miniature amplifiers. They just don't agree about how the curious devices work

Jimi Hendrix may have deafened many a fan with feedback, but they would have struggled to hear him in the first place without the feedback that powers the ear. The cochlea, the coiled heart of the mammalian ear, not only vibrates in response to sound, but it also pumps energy into its own vibrations to beef them up. Such "active feedback" gives the mammalian ear its exquisite sensitivity and its ability to distinguish pitch. Take it away and the ear becomes an almost useless hole in the head. But no one is sure just how the inner ear pumps up the volume.

"The notion that the cochlea has a biological amplifier, and that this is essential to normal hearing, has been an imponderable that has excited people for 20 years," says Paul Fuchs, a neuroscientist at The John Hopkins University School of Medicine in Baltimore. Auditory researchers have known for decades that peculiar cells known as hair cells turn vibrations into electrical signals, and recent advances raise the prospect of countering hearing loss by replacing dead or damaged hair cells. But the cells also appear to amplify the vibrations, and researchers have two distinct ideas about how they do it. Last month, both rival models got a boost from new findings.

Roughly speaking, it's a question of pistons versus trapdoors. Inside a mammal's ear, a long, narrow membrane called the basilar membrane vibrates in response to sounds. Low tones elicit ripples closer to one end of the membrane, while high tones raise a ruckus nearer the other. The membrane is carpeted by hair cells, and some of these, known as outer hair cells, contract and elongate when zapped with electricity, a behavior known as somatic electromotility. Some researchers believe this pistonlike pumping amplifies the motion of the membrane. The piston picture got a big boost last month. In the 11 May issue of *Nature*, neurobiologists Peter Dallos, Jing Zheng, and their team at Northwestern University in Evanston, Illinois, reported that they had isolated the protein, which they dubbed prestin, that gives the outer hair cells their unique ability to contract. Score one for electromotility.



Hear here? Outer hair cells might pump like pistons, or trapdoors in stereocilia might snap shut, to amplify vibrations in the ear.

Every hair cell, however, also wears a crown of stiff fibers called stereocilia, which tip to one side as vibrations in the basilar membrane push it up against the overriding tectorial membrane. In response, trapdoorlike ion channels open in the stereocilia and let in potassium and calcium ions. This is the mechanism that converts vibrations into the chemical signals that fire nerves. Some researchers think it also amplifies the vibrations. The calcium ions bind to the channels, snapping them shut, and some believe this pulls the stereocilia in the opposite direction, causing them to push the tectorial membrane and amplify the motion of the basilar membrane. Recently, neuroscientist Jim Hudspeth, physicist Marcelo Magnasco, and their colleagues at The Rockefeller University in New York City developed a mathematical model of such a trapdoor amplifier. In the 29 May issue of *Physical Review Letters*, they argue that a single property of the model can explain some puzzling characteristics of hearing, such as why the ear registers soft tones and pitches more effectively than loud ones.

The wrangling over how the ear amplifies sound goes back more than 50 years. At that time, scientists agreed that the cochlea could only respond passively to incoming sounds, much as the strings of a piano will ring if you shout into the guts of the instrument. But in 1948, a 28-year-old maverick astrophysicist named Tommy Gold, then at Cambridge University, pointed out that fluid in the cochlea would damp out vibrations unless the organ somehow amplifies them. Gold's idea fell on deaf ears, so to speak, because it contradicted the best data available at the time. Experiments with cochleas from cadavers led the Hungarian-born physiologist Georg von Békésy to conclude that any amplification must take place between the basilar membrane and the nervous system, not in the cochlea itself. Von Békésy's research won him the Nobel Prize in medicine in 1961.

In the 1970s, however, new experiments showed that the ear was livelier than von Békésy had reckoned. In 1971, William Rhode, a physiologist at the University of Wisconsin, Madison, discovered that in live tissue samples from squirrel monkeys, the basilar membrane bolstered small vibrations more than it would do without feedback. Other studies gave further evidence of biological amplifiers. In von Békésy's dead cochleas, it seemed, the amplifiers had simply been unplugged.

But if amplifiers existed, where were they? A possible answer emerged in 1985, when neuroscientist Bill Brownell, then at the University of Geneva in Switzerland, discovered the outer hair cells' unique ability to convert electrical energy into motion. "Nature doesn't devise a completely new mechanism for no reason," Dallos says. "So clearly outer hair cell motility does something." The discovery of prestin by Dallos's team gives a boost to the idea that that something is amplification: When the researchers genetically engineered human kidney cells to produce the protein, they found that the cells gained the ability to

ILLUSTRATION: K. SUTLIFF AND C. CAIN

contract and lengthen in response to electrical signals, just as hair cells do.

Even so, proponents of the motility amplifier still haven't explained how prestin makes cells contract or precisely how the pumping cells account for the ear's prodigious ability to distinguish between tones. "When people make models of how you should use the electromotility, they include some sort of extra [frequency] filter," says Mario Ruggero, a neuroscientist at Northwestern. "I find that somewhat dissatisfying." Researchers working with nonmammalian vertebrates have also begun to question the piston model. The hair cells of birds, amphibians, and reptiles cannot pump, they point out. Yet these animals hear nearly as well as mammals do, albeit at lower frequencies. Seeking an amplifier common to all sharp-eared animals, these researchers point to the stereocilia.

The stereocilia can explain both the ear's fine tuning and other quirks of hearing in one mechanism. Over the past 2 years, Hudspeth and colleagues have developed a mathematical model in which the stereocilia tune the ear so that it is poised between two stable states, one quiet, the other ringing like a public-address system with the volume turned up too high. That on-the-brink point is called a Hopf bifurcation. In their most recent paper, Hudspeth and his team report that it puts the ear in a nonlinear dynamical situation—one in which the output is not simply proportional to the input. That nonlinear state explains why the ear amplifies softer sounds more intensely than loud ones, and why it is better at discerning their pitch. It also accounts for the third "combination tone" people sometimes hear when two tones are played at once.

Proponents of stereocilia, however, lack a key piece of their puzzle: In spite of overwhelming circumstantial evidence, no one has ever cloned the ion channel at the heart of the model or proved that it works as researchers claim. "We truly don't know that the stereocilia mechanism exists in the outer hair cells," Ruggero says.

The biggest challenge for either theory is to explain how mammals can hear at extremely high frequencies when other animals can't. If trapdoor amplification were the only mechanism at work, then you might expect all creatures with stereocilia to have similar hearing ranges. Yet bats can perceive pitches up to 100 kilohertz, 10 times higher than stereocilia-bearing nonmammals can hear.

Because only mammals have pumping outer hair cells, it might seem obvious that electromotility accounts for the mammalian ear's startling tonal range. But that idea seems to run up against basic physics. In experiments with cell cultures, Dallos's team has shown that prestin enables cells to change shape within microseconds, fast enough to amplify vibrations at 100 kilohertz. For the protein to react that quickly, however, the voltage difference between the inside and the outside of the cell must change by roughly a millivolt within microseconds. To make that happen, a hefty charge must flow onto and off of the cell. Yet such a charge can't shuttle back and forth fast enough to keep pace, Fuchs of Johns Hopkins says.

The debate over hair cells may turn on the ear of a mouse. By knocking out the gene for prestin, researchers could turn off the pistons in the mouse's outer hair cells. Such an experiment is the next logical step, all agree. If the ion channel of the stereocilia powers the mammalian ear, the knockout mouse should hear nearly normally. "The problem is going to be the other way around," Hudspeth says. "If the mouse doesn't have normal hearing, what does that mean?" Knocking out prestin may somehow interfere with the stereocilia, Hudspeth says, so a nearly deaf mouse won't settle the issue. In which case, you'll likely hear more about it, as long as your hair cells hold out.

–ADRIAN CHO

MATERIALS SCIENCE

New Tigers in the Fuel Cell Tank

After decades of incremental advances, a spurt of findings suggests that fuel cells that run on good old fossil fuels are almost ready for prime time

It's no wonder that miniature power plants called fuel cells are a perennial favorite in the quest for cleaner energy: They generate electricity from fossil fuels without burning them and spewing pollutants. But the technology's promise has always seemed just beyond reach. For one, most versions of fuel cells work best on pure hydrogen gas—a fuel, notorious for its role in the *Hindenberg* zeppelin's fiery demise, that's tricky to store and unwieldy to transport. And a leading alternative design—fuel cells that run on readily available fossil fuels—has lagged because these are prone to choking on their own waste.

At last, however, researchers have made critical strides in developing commercially viable fuel cells that extract electricity from natural gas, ethane, and other fossil fuels. Conventional ceramic cells, known as solid oxide fuel cells (SOFCs), work this magic by converting, or reforming, the hydrocarbons to hydrogen inside the cells. That demands ultrahigh temperatures, which in turn requires expensive heat-resistant materials. But scientists have found a way to bypass this costly reforming process: a new generation of SOFCs, including one featured on page 2031, that convert hydrocarbons directly into electricity. And even the standard reforming SOFCs are on a roll. A recent demonstration of a system large enough to light up more than 200 homes showed that it is the most efficient large-scale electrical generator ever designed.

"I think we've turned the corner," says Mark Williams, who oversees fuel cell research at the National Energy Technology Laboratory in Morgantown, West Virginia. Versions of ceramic fuel cells, experts hope, will power everything from individual homes to municipal electrical grids. The market for the devices, says Subash Singhal, who heads fuel cell research at the Pacific Northwest National Laboratory in Richland, Washington, could reach billions of dollars over the next 10 to 15 years. Says Kevin Kendall, a solid oxide fuel cell expert at Birmingham University in the United Kingdom: "Suddenly things are happening that weren't possible 10 years ago."

That's rapid progress indeed for a technology now entering its third century of development. Today's hydrogen-powered fuel cells operate on much the same principles as the first cell invented in 1839 by Sir William Grove, a Welsh judge. They're configured like a battery, with a negatively charged electrode, or cathode, and a positively charged anode separated by a membrane that allows only certain ions to pass through. When hydrogen gas is infused into the space surrounding the anode, a catalyst splits the

Model of efficiency. This new fuel cell assembly converts a higher percentage of fuel to electricity than any power plant ever built.

CREDIT: SIEMENS WESTINGHOUSE POWER CORP.