through to the colder surfaces. Two Cn atoms were detected, both at the warm end; the researchers concluded that Cn was more like Hg than like Rn.

Elemental

The future of the ^{48}Ca technique depends on the stability and ease of making the target materials. Synthesis of element 119 using a ^{48}Ca beam would require an einsteinium target, probably ^{254}Es, with a half-life of 276 days. But ^{254}Es has been produced only in microgram quantities; synthesis of the required milligram amounts would be a multimillion-dollar effort. Fermium, the next actinide in line, has a shorter lifetime still, and only picograms of it have been made. It's likely, therefore, that future element discoveries will be made using a higher-Z beam. That doesn't mean that ^{48}Ca is finished. Heavier isotopes of Cf, for example, could be used to make heavier atoms of element 118 and its decay products.

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Yoking real and virtual cells confirms theory of cochlear amplification

Elastic coupling between cells in the inner ear enhances the hearing of amphibians, reptiles, birds, and mammals.

To detect a clap of thunder, the ears of a frog, mouse, or other terrestrial vertebrate convert mechanical vibrations into electrical impulses. The transduction takes place in the cochlea and is mediated by micron-scale hairs that sprout from specialized hair cells.

To the tiny hairs, the watery liquid that surrounds them is viscous, just as honey would be to a tuning fork. If the hairs are to do their job, they need a source of energy—an amplifier—that sustains their vibrations, especially from the faintest sounds.

Experiments on live animals and extracted hair cells have revealed that hair cells themselves act as amplifiers. Each one is tuned to a narrow range of frequencies. The cochlear amplifier delivers resonant kicks to the hairs: firm ones for faint sounds, light ones for loud sounds. And in the absence of sound, the kicks persist as spontaneous vibrations whose faint, "otoacoustic" emission serves in humans as a medical diagnostic.

In the hair cells of birds, reptiles, and amphibians, the amplifying kicks are delivered within the hairs by a system of active molecular pulleys controlled by the flow of calcium ions in and out of the cell. Mammals have a more complex apparatus, but it makes use of the same mechanism.

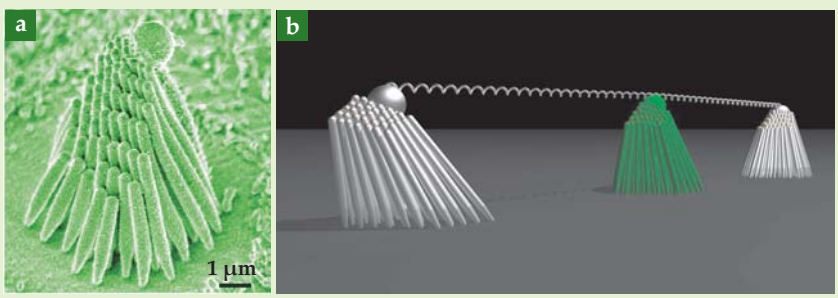

Figure 1. The hairs that sprout from hair cells convert sound vibrations to nerve signals. **(a)** As this electron micrograph shows, the hairs are arranged in a pyramidal bundle topped by a structure called the kinociliary bulb. **(b)** To investigate the role of intercell coupling, the Paris–Dresden team extracted a hair cell and applied a time-dependent force to it with a flexible whisker. By using a model of how hair cells behave mechanically, the team could control the whisker in a way that mimics the situation shown here: a live cell (green) yoked elastically (white springs) to two virtual cells (white).

In 1999 James Hudspeth of the Rockefeller University in New York and his postdoc Pascal Martin measured the performance of single hair cells extracted from a bullfrog. However, it turned out that the cells' sensitivity—that is, their deflection per unit force—is barely one hundredth of the value deduced from live animals.[1]

An explanation for the discrepancy came two years ago from Frank Jülicher, Kai Dierkes, and Benjamin Lindner of the Max Planck Institute for the Physics of Complex Systems in Dresden, Germany.[2] In the cochleae of nearly all terrestrial vertebrates, the sound-sensing hairs poke into an elastic membrane or other kind of elastic structure. The structure helps convey vibrations to the hair cells. It also, the theorists argued, lowers the detection threshold by coupling the hairs' vibrations and averaging out their stochastic fluctuations.

The coupling hypothesis has now been confirmed in the lab by a team composed of Martin, who left Hudspeth's lab for the Curie Institute in Paris; Jülicher; and their respective students.[3] Achieving the proof was technically demanding. Once extracted, hair cells function for barely an hour before they die. Keeping several of them alive while measuring their performance and retaining and measuring their coupling proved impracticable. Instead, Martin's graduate student Jérémie Barral and Dierkes came up with a different approach: They coupled a live hair cell to two virtual cells.

Cyber clones

In the cochleae of terrestrial vertebrates, each hair cell can be said to experience intercell coupling as a time-dependent force. Barral and Dierkes realized that a flexible whisker, if brought into contact with a single extracted hair cell, could in principle impart the same net force as one, two, or any number of elastically coupled cells—provided the whisker accurately mimicked the cells' coupling and mechanical behavior. The real cell would therefore be coupled through the whisker to virtual cells—"cyber clones," as Barral and Dierkes called them.

Figure 1 shows an electron micrograph of a hair cell and a schematic representation of the cyber-clone concept. According to the Dresden group's theory, the greater the number of coupled cells, the bigger the boost to performance. Martin and his collaborators chose to couple a live cell to just two clones to avoid having the clones dominate the system's dynamics.

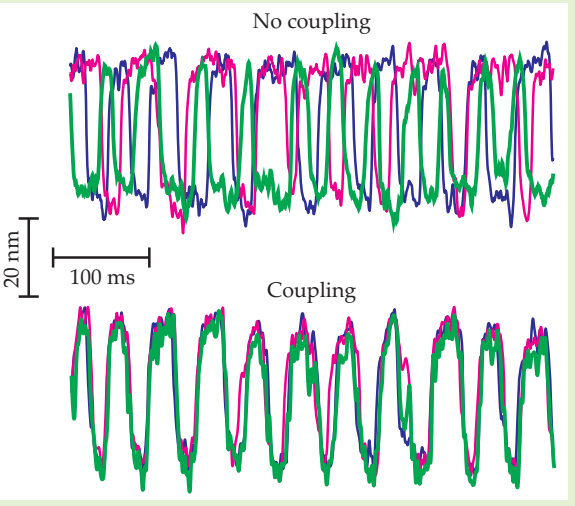

Figure 2. Hair cells amplify signals by driving their hairs to oscillate in resonance with incident sound. When no sound is present, the hairs oscillate spontaneously. By coupling a live cell (green) to two cyber clones (pink and purple), the Paris–Dresden team demonstrated that coupling brings spontaneous oscillations into phase, thereby mitigating the effects of stochastic fluctuations and lowering the detection threshold. (Adapted from ref. 3.)

The cyber-clone approach builds on the experience that Martin and his collaborators had gained from measuring the properties of hair cells. Another key ingredient is a model of hair cell behavior that he, Jülicher, and Jean-Yves Tinevez developed. The model gives a hair's deflection as a function of applied force in terms of both the physical properties of the hair, such as stiffness, and a parameterization of the molecular pulleys. Crucially for its realism, the model also includes stochastic fluctuations.

For their live hair cells, Martin and his collaborators took cells from a bullfrog's saccule, an organ in the ear that senses surface vibrations and low-frequency sound. The saccule is convenient for experimenters because its hair cells are large and sit on a flat cartilaginous substrate. The substrate makes it easier not only to mount the cells for microscopy but also to keep them alive. Although the cell body is immersed in a sodium-rich solution, the hairs require a potassium-rich solution. Martin and his collaborators had to bathe the cells in a two-compartment container.

A further experimental complication concerns the cells' frequency selectivity. It's difficult to identify an extracted cell's resonant frequency in advance. Martin and his collaborators therefore had to use up some of the cell's precious lifetime to measure its resonant frequency. But once they'd determined it, they could select a pair of matching cyber clones from a preprogrammed set that spanned the saccule's spectrum.

At the start of an experimental run, a thin borosilicate glass whisker is brought into contact with the knoblike structure, the kinociliary bulb, at the top of the bundled hairs (see figure 1). The force imparted on the cell by the whisker is varied by changing the position of the clamp that holds the whisker's other end. The key to the experiment lies in successively calculating the clamp's position. The calculation proceeds as follows.

At each time step, the deflection of the live cell is measured through an optical microscope and uploaded to the control computer. Based on that value and on the cyber clones' calculated deflections in the previous time step, the computer applies Hooke's law to determine the elastic force each clone imparts on the live cell. To the elastic force, the computer adds the instantaneous force due to a resonant sine wave. The clamp's position is then shifted by an amount that corresponds to the total force. In the same time step, the computer applies the hair cell model to update the cyber clones' deflections in time for the next iteration.

The experiment found that the coupling does indeed boost the hair cell's performance. People who study hair cells define gain as the ratio of the cell's sensitivity to faint sound (at the threshold of detection) to its sensitivity to loud sound (where sensitivity saturates at a low value). A single, uncoupled hair cell has a gain of 10. Coupling it to two cyber clones raised the gain to 20, a value predicted by the Dresden model. Another of the model's predictions was also confirmed: Coupling is most effective when the stiffness of the virtual springs matches that of the hairs.

Martin and his collaborators could also verify the underlying cause of the coupling's effectiveness. When no sound is present, the live cell and the

cyber clones oscillate spontaneously and with considerable stochastic fluctuation. As figure 2 shows, turning on the coupling brings the spontaneous oscillations into phase and mitigates the stochastic fluctuations.

In principle, coupling can account for the cochlear amplifier in mammals, whose ears are more complex than those of the bullfrog and other lower vertebrates. Mammals have two kinds of hair cell, inner and outer. The outer cells are elastically coupled to each other but not to the inner cells, which convey the auditory signal to the brain. It's likely that the outer cells deliver their amplification signal to the inner cells through the intervening fluid via viscous coupling.

But something else happens in the outer hair cells. Embedded in the membrane of each cell at a density of around 4500 molecules/μm^2 is a rod-shaped protein called prestin. Depending on the voltage across the membrane, the prestin molecules either lie parallel to the membrane surface or bunch together perpendicular to it.

That piezoelectric bunching shortens the cell and provides a second mechanism for converting mechanical energy into electrical energy. At around 1 ms, the membrane's discharge or *RC* time is too long for the voltage-dependent bunching to play a role in amplifying high-frequency hearing, but it could supplement elastic coupling at lower frequencies.

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Focus on improving transmission electron microscopes starts to pay off

The latest advance is the chemical identification of closely spaced, lightweight atoms.

Since their invention in the 1930s, transmission electron microscopes (TEMs) have been an invaluable tool, providing highly magnified images of objects that range from biological specimens to electronic materials. Now, researchers are seeking greater performance from those instruments, especially the capability to determine three-dimensional structures with atomic resolution, to chemically identify individual atoms, or to follow the dynamic behavior of atoms within a sample. Of particular interest are materials with low atomic number *Z*. Some researchers are keen to explore materials such as carbon nanotubes, graphene, and boron nitride for novel electronic applications. Others are interested in determining the structures of biological molecules, especially ones that aren't amenable to being crystallized and hence aren't candidates for crystallography.

A worldwide 60-year effort to correct spherical and chromatic aberrations has brought about, in the past decade, TEMs with much better resolution.[1,2] Spherical aberration results when electrons traveling at different distances from the axis of an electron beam are focused differently by magnetic-field "lenses." Chromatic aberration stems from the different focusing of electrons of different energies. Uncorrected TEMs have operated for many years with electron energies of 200 keV and above because the effect of aberrations grows worse for lower-energy electrons.

TEM designers can compensate for spherical aberration by adding magnetic multipoles along the electron-beam path. It sounds simple in principle but is difficult in practice because the correction for one aberration can unleash a horde of parasitic aberrations. Chromatic aberration can be mitigated by reducing the energy spread of the electron source, typically to a few tenths of an eV. But reduction in energy width can decrease the beam intensity and hence degrade the image quality. Another way is to build a corrector that focuses electrons to the same point regardless of energy.

With aberration correction, TEM resolution has been improved by a factor of two to three. The improvement has been greatest at the electron energies below about 80 keV that are required to avoid radiation damage to materials containing low-*Z* atoms. The knock-on damage threshold is set by the energy an electron