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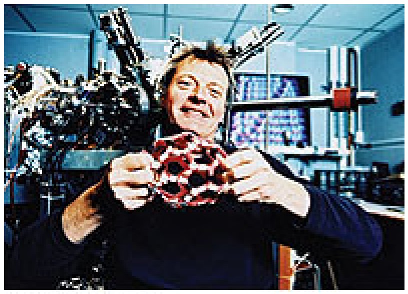
Andrew-Pelling.com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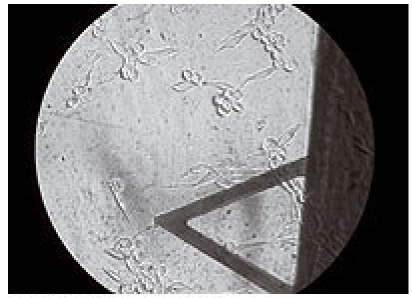
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Signal Discovery?

A Los Angeles scientist says living cells may make distinct sounds, which might someday help doctors "hear" diseases

Kids, lawn mowers, planes, trains, automobiles—just about everything makes noise. And if two California scientists are right, so, too, do living cells. In recent experiments using the frontier science of nanotechnology, the researchers have found evidence that yeast cells give off one kind of squeal while mammalian cells may give off another. The research, though still preliminary, is potentially "revolutionary," as one scientist puts it, and a possible, admittedly far-off medical application, is already being pursued: someday, the thinking goes, listening to the sounds your cells make might tell a doctor, before symptoms occur, whether you're healthy or about to be ill.

The founder of the study of cell sounds, or "sonocytology," as he calls it, is Jim Gimzewski, a 52-year-old UCLA chemist who has contributed to an art museum's exhibit on molecular structure. The cell sounds idea came to him in 2001 after a medical researcher told him that when living heart cells are placed in a petri dish with appropriate nutrients, the cells will continue to pulsate. Gimzewski began wondering if all cells might beat, and if so, would such tiny vibrations produce a detectable sound. After all, he reasoned, sound is merely the result of a force pushing on molecules, creating a pressure wave that spreads and registers when it strikes the eardrum. He also reasoned that although a noise generated by a cell would not be audible, it might be detected by an especially sensitive instrument.

Gimzewski is well suited to tackle the question, being both an expert at instrumentation—he has built his own microscopes—and comfortably at home in the world of the infinitesimal. A leader in nanotechnology, or the science of manipulating individual atoms and molecules to build microscopic machines, Gimzewski previously worked at IBM's research laboratory in

Zurich, Switzerland, where he and his colleagues built a spinning molecular propeller 1.5 nanometers, or 0.0000015 millimeters in diameter. They also built the world's smallest abacus, which had, as beads, individual molecules with diameters less than a single nanometer. If nothing else, the feats, which garnered considerable acclaim, showed that nanotechnology's much-hyped promise had a basis in reality.

For his first foray into sonocytology, Gimzewski obtained yeast cells from biochemistry colleagues at UCLA. (He "got looks," he recalls, when he explained why he wanted the cells.) Working with graduate student Andrew Pelling, Gimzewski devised a way to test for cellular noise with a nanotechnology tool called an atomic force microscope (AFM). Usually, an AFM creates a visual image of a cell by passing its very tiny probe, itself so small its tip is microscopic, over the cell's surface, measuring every bump and hollow of its outer membrane. A computer converts the data into a picture. But the UCLA researchers held the AFM's tiny probe in a fixed position, resting it lightly on the surface of a cell membrane "like a record needle," says Pelling, to detect any sound-generating vibrations.

The pair found that the cell wall rises and falls three nanometers (about 15 carbon atoms stacked on top of each other) and vibrates an average of 1,000 times per second. The distance the cell wall moves determines the amplitude, or volume, of the sound wave, and the speed of the up-and-down movement is its frequency, or pitch. Though the volume of the yeast cell sound was far too low to be heard, Gimzewski says its frequency was theoretically within the range of human hearing. "So all we're doing is turning up the volume," he adds.

The frequency of the yeast cells the researchers tested has always been in the same high range, "about a C-sharp to D above middle C in terms of music," says Pelling. Sprinkling alcohol on a yeast cell to kill it raises the pitch, while dead cells give off a low, rumbling sound that Gimzewski says is probably the result of random atomic motions. The pair also found that yeast cells with genetic mutations make a slightly different sound than normal yeast cells; that insight has encouraged the hope that the technique might eventually be applied to diagnosing diseases such as cancer, which is believed to originate with changes in the genetic makeup of cells. The researchers have begun to test different kinds of mammalian cells, including bone cells, which have a lower pitch than yeast cells. The researchers don't know why.

Few scientists are aware of Gimzewski's and Pelling's sonocytology work, which has not been published in the scientific literature and scrutinized. (The researchers have submitted their findings to a peer-reviewed journal for publication.) Word of mouth has prompted skepticism as well as admiration. A scientist familiar with the research, Hermann Gaub, chair of applied physics at the Ludwig Maximilian University in Munich, Germany, says the sounds that Gimzewski believes are cellular vibrations may have other origins. "If the source of this vibration would be found inside the cell, this would be revolutionary, spectacular, and unbelievably important," Gaub says. "There are, however, many potential [sound] sources outside the cell that need to be excluded." Pelling agrees, and says that he and Gimzewski are doing tests to rule out the possibility that other molecules in the fluid bathing the cells, or even the tip of the microscope itself, are generating vibrations that their probe picks up.

Ratnesh Lal, a neuroscientist and biophysicist at the University of California at Santa Barbara who has studied the pulsations of heart cells kept alive in a dish, says that Gimzewski's nanotechnology expertise may be the key to establishing whether cells produce sound. "The ultimate hope is to use this in diagnostics and prevention," says Lal, adding: "If there's anybody in the world who can do it, he can."

Gimzewski acknowledges more work needs to be done. Meanwhile, the findings have caught the attention of his UCLA colleague Michael Teitell, a pathologist specializing in cancers of the lymphocyte, a type of white blood cell. He's subjecting human and mouse muscle cells and bone cells to drugs and chemicals to induce genetic and physical changes; Gimzewski will then try to "listen" to the altered cells and distinguish them by their sounds.

Teitell says the thought of detecting cancer at its earliest cellular stages is exciting, but whether the technology will work as a diagnostic tool remains to be seen (or heard). He doesn't want to oversell the idea: "It could turn out that all these signals will be such a mishmash that we won't be able to clearly identify one from the other."

Gimzewski hopes the work will have a practical application, but he's thrilled as much by the hunt as the catch. "Whatever the outcome," he says, "I'm primarily driven by curiosity and excitement at the phenomenon of cellular motion—what inspired nature to create such a mechanism and to really understand in depth what these beautiful sounds mean." The mere possibility that he's discovered a new characteristic of cells, with all the intriguing questions that raises, is, he says, "already more than enough of a gift."

By Mark Wheeler

For more information on this topic, explore the Archives of *Smithsonian* Magazine:

- Birdbrain Breakthrough (June 2002)
- Brave New World (December 2001)
- How the body defends itself from the risky business of living (December 1995)
