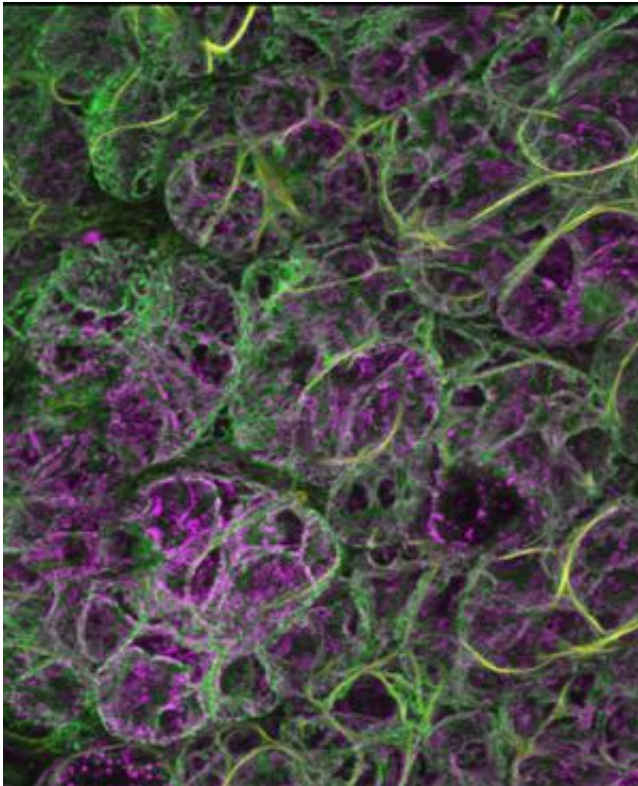


Shaking up cell biology: Researchers focus in on decades-old mitochondrial mystery

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A volume rendering of mitochondria

Elvis did it, Michael Jackson did it, and so do the mitochondria in our cells. They shake. While Elvis and Michael shook for decades before loud and appreciative audiences, mitochondrial oscillations have quietly bewildered scientists for more than 40 years.

Now, a team of scientists at National Institutes of Health's National Institute of Dental and Craniofacial Research (NIDCR) has imaged [mitochondria](#) for the first time oscillating in a live animal, in this case, the salivary glands of laboratory rats. The report, published online today in the journal *Cell Reports*, shows the oscillations occur spontaneously and often in the rodent cells, which leads the researchers to believe the oscillations almost surely also occur in human cells.

"The movements could last from tens of seconds to minutes, which was far longer and frequently at a faster tempo than observed previously in cell culture," said Roberto Weigert, Ph.D., an NIDCR scientist and senior author on the study. The mitochondria also appear to synchronize their movements not only in an individual cell but, quite unexpectedly, into a linked network of oscillators vibrating throughout the tissue.

"You look through the microscope, and it almost looks like a synchronized dance," said Weigert. "The synchronization, to borrow an old cliché, tells us that we need to differentiate the forest from the trees—and vice versa—when studying mitochondria. It may be that the forest holds the key to understanding how [mitochondria function](#) in human health and disease."

The mitochondrion (the singular of mitochondria) is one of several distinct compartments, or organelles, in the cell cytoplasm. Although mitochondria are jacks of many biochemical trades, they are best known as the power plants of the cell. They generate a continuous supply of the molecule ATP that, like bits of coal, serve as the cell's main source of energy to power the heart to beat, muscles to stretch, and virtually every movement that the body makes.

To keep cells fully charged, mitochondria operate four biochemical production lines that coalesce with oxygen molecules from normal respiration to produce ATP. One of these production lines starts with

processing the molecule nicotinamide adenine dinucleotide, or NADH. Weigert and colleagues recognized that they could use their high-magnification microscope to visualize NADH as it naturally emits electrons as part of the ATP production process.

The key was their choice of microscopy. Weigert and colleagues are masters of intravital microscopy, an extremely high-resolution technique that dates back to the 19th century. It had been too powerful to use in live animals until recently.

"Animals breathe, their hearts beat, and their appendages twitch," said Weigert. "The combined effect under very high magnification is like watching a 6.0 earthquake. Everything shakes and blurs out of focus. We have developed approaches to better stabilize our organ of interest and minimize the motion artifacts. At this point, it is just a matter of generating more powerful optics to visualize the chemistry of life that really unfolds in the body, not under artificial laboratory conditions that stress cells and likely modify their behavior."

The powerful optics allowed the scientists to visualize the oscillations in their native milieu and to puzzle over their cause. Based on a series of subsequent experiments and observations, the researchers discovered that the oscillations are linked to the production of reactive oxygen species, a chemically interactive byproduct of making ATP. This finding suggests that the oscillations likely are not inherent to mitochondria but a response to conditions in their environment.

"These findings emphasize how important it is scientifically to study biology on its own terms, not under artificial laboratory conditions," said Natalie Porat-Shliom, an NIDCR scientist and lead author on the paper. "We saw things in live animals that you don't see in cell culture. The reasons, in this case, very well may be that the mitochondria continue to receive an influx of signals from the blood vessels, the nervous system,

and their surrounding environment. The entire system can't be reassembled in cell culture."

Porat-Shliom noted that these findings should be of broad interest scientifically in framing studies of mitochondria, and may have future clinical implications. An estimated 2 million Americans have mitochondrial disease, an energy-depleting failure of mitochondria to function properly, which can have disabling effects on the brain, heart, kidneys, and other body systems. Many scientists also suspect that as mitochondria become better understood, they likely will be understood to play a more prominent role in [human health](#) and disease.

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