



# A SOUND THEORY

Could two Nobel laureates and the entire biological-research community really have been wrong about the nature of nerve cells for more than 50 years? That's the controversial new claim from two physicists

**T**he nerves are the body's communications system, sending messages zipping to and from the brain along a network of 100 billion nerve cells known as neurons. Every time you move a muscle, feel a sensation, or reflexively blink in bright sunlight, it's made possible by signals that travel along and hop between neurons, which range in length from less than a millimeter to more than three feet.

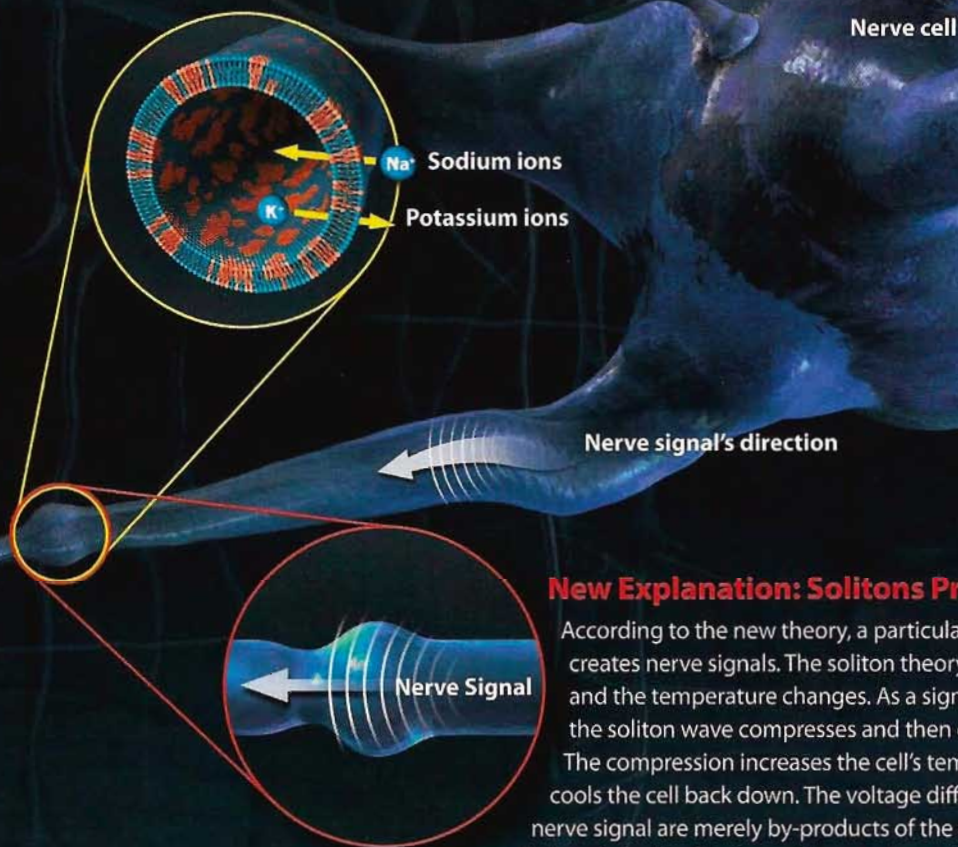
And how do the signals move along those nerve cells? Why, through elec-

tricity, of course. Open any textbook—from high school right through medical school—and you'll learn that nerves communicate via changes in electrical potential. First, sodium ions flow into the cell through open channels and potassium ions flow out. This makes the electrical charge in that area of the cell's membrane shift from negative to positive and back again, which triggers the same sequence in the next area of the cell's membrane. The process repeats over and over until, within a tiny fraction of a second, the signal courses

down the entire length of the neuron. There, either an electrical charge or a release of neurotransmitters such as serotonin or dopamine allows the signal to leap across a gap called a synapse to the next neuron. This model has been the consensus view of how nerves work for 56 years—ever since two English doctors, Alan Lloyd Hodgkin and Andrew F. Huxley, first explained it in 1952. The discovery was so important that in 1963 the researchers were awarded the Nobel Prize in Physiology or Medicine for their work.

## Classic Explanation: Voltage Differences Create the Signal

According to the Hodgkin-Huxley model, a nerve signal arises when electrically charged sodium and potassium ions stream in and out of neurons. This results in a voltage difference, or "action potential," that produces the nerve pulse. The model has not, however, been able to explain the physical bulge that develops as a signal passes through a cell. And although the model explains the rise in cell temperature that accompanies a nerve signal, it does not explain the subsequent fall in temperature.



## New Explanation: Solitons Propagate the Signal

According to the new theory, a particular type of wave called a soliton creates nerve signals. The soliton theory explains both the bulges and the temperature changes. As a signal passes down the neuron, the soliton wave compresses and then expands the cell membrane. The compression increases the cell's temperature, and the expansion cools the cell back down. The voltage differences that accompany a nerve signal are merely by-products of the soliton that are caused by the collision of electrically charged ions and proteins in the membrane.

It was an open-and-shut explanation. That is, until two scientists at the Niels Bohr Institute in Copenhagen, Denmark, declared the classical theory utterly wrong. It's not electricity that carries a signal down the length of a neuron, they say. It's sound waves.

### A Special Sort of Wave

Usually, sound waves expand in all directions, gradually weakening as they travel. It's not exactly an optimal means to send a signal along, say, the sciatic nerve from your heel to your

hip. But when a sound wave passes through a material with very particular characteristics, it is transformed into a special type of wave called a soliton, which moves in only one direction and retains its energy over a long distance until it suddenly dies out entirely. According to Niels Bohr Institute physicists Thomas Heimburg and Andrew Jackson, the lipid membranes of nerve cells have precisely the necessary characteristics to create and carry solitons when the lipids are at the transition point between their liquid and solid

states. And what is that magical melting point when the lipids are part liquid and part solid? It's right around our normal body temperature.

In this new Heimburg-Jackson model, the electrical charge that scientists observe in the neuron is merely a by-product of the actual signal. When a nerve signal in the form of a soliton travels down the length of the neuron, the cell membrane is slightly stretched at the front of the wave and then returns to its normal shape once the wave passes. The cell membrane

contains a large number of electrically charged ions, and the soliton's pressure wave alters the distances between them, producing a voltage.

This physical compression is one of several aspects of nerve function that the new theory seems to explain better than the established Hodgkin-Huxley model does. Scientists have long observed that nerves actually change in thickness as an impulse passes through them—it's reminiscent of a snake swallowing a mouse, which creates a bulge that travels down the snake's body. The Hodgkin-Huxley model doesn't explain this physical change, but it's a natural consequence of the new theory.

That's not the only previously mysterious nerve-signal phenomenon that the new theory might solve. Scientists have also known for years that nerve impulses are accompanied by a slight temperature increase in the cell

membrane, then a decrease, and finally a return to the starting temperature. The increase makes sense using the classical theory, because an electrical current heats up the channel it passes through. The decrease, however, isn't as easily explained. But if nerve signals are instead propagated as sound waves, the rise and fall in temperature can be attributed to the expansion and contraction of the cell membrane, since, according to the laws of thermodynamics, changes in volume affect temperature.

But the best argument for this controversial theory is that it may finally answer a question that has bedeviled scientists for more than a century: Why does anesthesia work?

### An Explanation for Anesthesia

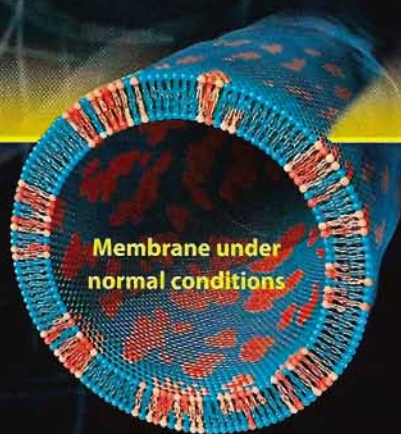
A surprisingly wide range of chemicals—from the inert gas xenon to simple inorganic compounds such as

laughing gas ( $N_2O$ ), to small organic molecules such as ether ( $C_4H_{10}O$ ) and more complex substances like isoflurane ( $C_3H_2C_1F_5O$ )—all prevent nerves from transmitting impulses. How anesthetics actually work has been a riddle ever since 1846, when ether was first used as anesthesia in a surgical procedure. The most common explanation is that the compounds bind to proteins in the neurons' cell membranes and deactivate them so they can't produce electric signals, but it's hard to imagine that such a motley assortment of substances would all bind so neatly to the proteins. Furthermore, the theory has never been proven in a lab.

Heimburg and Jackson's sound-wave theory offers a seemingly straightforward explanation for the problem. It's based on the fact that scientists have known for more than 100 years that the effectiveness of any anesthetic

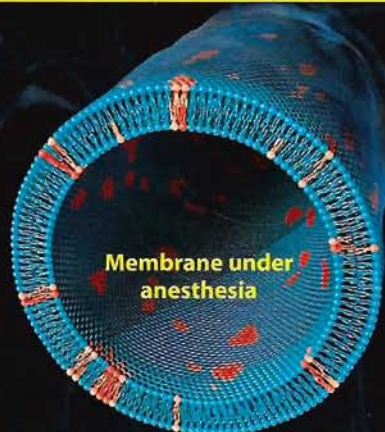
## Anesthetics Block the Sound Waves

The Heimburg-Jackson model says that the temperature of the cell membrane must be at its melting point for us to feel pain. At this temperature, sound waves (and thus nerve signals) can propagate through nerves. Anesthetics work by making the cell membranes remain liquid, which stops the progress of the sound waves.

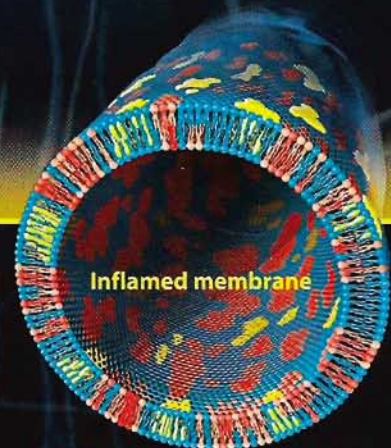


The cell membrane's melting point lies slightly below body temperature under normal conditions. Therefore, parts of the membrane are solid and parts are liquid. As a result, solitons can arise and transmit nerve signals to allow pain sensation.

## PAIN THRESHOLD



The anesthetic lowers the cell membrane's melting point so that it's almost entirely liquid. Now no solitons can be created, and nerve signals are not transmitted, so the patient is pain-free.



Inflammation increases a cell membrane's melting point, so doctors must boost anesthesia dosages to block pain. With a normal dose, the membrane will still be partially liquid and partially solid, and thus the patient can feel pain.

can be measured by how well it dissolves in olive oil. English biologist Charles Ernest Overton and German chemist Hans Meyer formulated their “lipid theory” in 1901. It suggested that any effective anesthetic simply dissolves in the neuron’s fat-containing membranes, somehow destroying the cell’s ability to create and maintain a signal. Unfortunately, the original lipid theory didn’t explain why the anesthetic should have this effect—but the Heimburg-Jackson model neatly fills this knowledge gap. When an anesthetic dissolves in the neuron’s cell membrane, the scientists say, the membrane’s melting point falls by several degrees—just as dissolving salt in water causes its freezing point to drop. And when the lipid membrane’s melting point dips, it no longer hovers in that special state between being liquid and solid at body temperature, which means it can no longer create and sustain solitons. No solitons means no nerve signals, which means no pain.

The theory may also finally explain some anomalies about how anesthesia behaves. For example, physicians know that anesthesia doesn’t work well under high pressure. Patients with serious burns, who are often treated in pressure chambers, require larger doses of anesthetics than normal. And animal experiments have shown that anesthetized animals simply wake up when subjected to increasing pressure. For

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Heimburg and Jackson, such observations are no surprise: Pressure increases the melting temperature of nerve cells’ membranes, and so there is an inverse relationship between pressure’s effects on melting point and the numbing effects of anesthetics.

Similarly, the soliton theory offers an explanation for why anesthesia doesn’t work very well when tissue is inflamed. Inflammation makes tissue

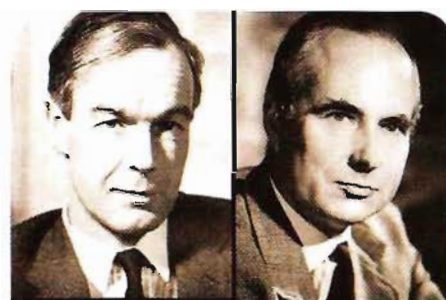
acidic, and researchers have shown that an increase in acidity causes the membrane’s melting point to rise. If the Heimburg-Jackson model is correct, this effect would explain the observed connection between inflammation and the reduced effectiveness of anesthesia.

### Nice Idea, but Can You Prove It?

No matter how neatly the theory seems to explain some previously nettlesome phenomena, it’s not likely to gain much traction against the widely accepted electrical model unless Heimburg and Jackson can produce some experimental evidence to prove it. And here’s where they run into trouble. The cell membrane is dynamic—the mix of different lipids it contains changes constantly, and the large number of proteins, salts and other molecules in it are in constant motion as well. These changes affect the membrane’s melting point and, therefore, the potential for solitons to arise. The changes are also very localized, so the melting point is never precisely the same throughout a cell’s membrane. No one has ever found a way to measure a membrane’s melting point without destroying it, and so for now it may be impossible to definitively show when a soliton propagates through a living neuron’s membrane. Currently, Heimburg and Jackson’s theory is based on observations from experiments on isolated cell membranes, not living ones.

“Replacing a well-accepted model, like the one by Hodgkin and Huxley, with a new theory without very serious experimental research would be dangerous and not very convincing,” Heimburg says. “But everything predicted by our theory has been found in real nerves: thickness changes, pressure changes, heat changes. People just haven’t called it a ‘soliton’ before we did, and we provided the mathematics first.” Some of his colleagues intend to test density and pressure changes in neurons because of the new theory. His own group is preparing to study snail and crayfish, which have large nerves that are easy to work with.

Another challenge to the theory is to explain why neurons are equipped



**Hodgkin [left] and Huxley [right] received the Nobel Prize in Physiology or Medicine in 1963.**

### Rewrite the Textbooks?

When English physicians Alan Lloyd Hodgkin and Andrew F. Huxley concluded in 1952 that nerves communicate with the help of electrical potential differences, it was a sensational discovery that finally explained one of the great mysteries of physiology. They received the Nobel Prize in Physiology or Medicine 11 years later for their groundbreaking discovery. If the new Heimburg-Jackson theory is proven and the Nobel laureates are shown to be wrong, every textbook that discusses the propagation of nerve impulses will need to be rewritten.

with an enormous number of ion channels in their membranes. These control the transfer of sodium and potassium ions—which the classical theory says are responsible for creating electrical nerve signals. In experiments with living neurons, scientists have demonstrated how these channels open and close in a neatly coordinated pattern that completely corresponds to the propagation of the nerve signal. If sound waves are carrying the signals along the neuron, what’s the point of this elaborate electrical system?

Because of these and other challenges, it could be a long time before the soliton theory has a chance to make its way into medical textbooks. But if there’s one thing the history of medicine has taught us, it’s not to dismiss a far-fetched idea just because we think we already know how something works. Always and forever, further investigation is needed. ■