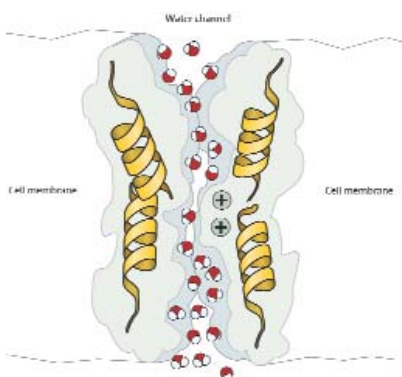


at Harvard Medical School, MacKinnon decided that to really understand the channels he was studying, he needed to see them. That meant learning to do x-ray crystallography—a monumental undertaking tantamount to changing careers. “A lot of us questioned it,” says a postdoc in MacKinnon’s lab during that era, Kenton Swartz, now at the National Institute of Neurological Disorders and Stroke in Bethesda, Maryland. Getting membrane proteins to crystallize is notoriously difficult, and ion channels are even more unwieldy than most. “It seemed like a pie-in-the-sky idea even to me,” MacKinnon concedes. But it paid off.

In 1998 MacKinnon sent a jolt through the field with the first high-resolution picture of an ion channel derived from x-ray crystallography (*Science*, 3 April 1998, pp. 69 and 106). Based on the crystal structure, his team later presented an elegant model of how ions—in this case potassium ions—pass through the core of the channel and explained the channel’s ability to let potassium ions through while excluding smaller sodium ions.

Just as a rock star moves through a crowd with a ring of bodyguards clinging to his person, a sodium or potassium ion moves through a solution with an entourage of water molecules. Passing through the potassium channel’s “selectivity filter,” however, requires leaving the escorts behind. The filter makes this easy for potassium ions by providing four conveniently located carbonyl groups. Potassium forms bonds with these just as easily as it does with water, and so it slips through the filter, leaving its waters behind. Sodium, however, is smaller. As a result, it can only bind two of the carbonyl groups at a time. This doesn’t provide the energetic incentive needed to lure sodium ions away from their waters; thus the ions retain their escorts and stay outside the filter.

Although many in the field had predicted MacKinnon would one day take home a Nobel for this work, most envisioned him getting a slice of the physiology prize. “I think the choice of chemistry is actually very



clever,” says Gary Yellen, a biophysicist at Harvard Medical School in Boston. Although the question of how ion channels achieve their selectivity is critically important for biology, Yellen says, the answer was ultimately a matter of chemistry.

Prizewinning proteins. This year’s chemistry Nobel recognizes work on potassium channels (near left) and aquaporins.

More recently, MacKinnon, now at Rockefeller University in New York City, stirred up the field with the first portrait of a voltage-gated ion channel. These channels reload neurons after they’ve fired an impulse. Based on the channel’s structure, MacKinnon’s team presented a model of its mechanism that flew in the face of the view widely held by researchers in the field, many of whom refused to accept it (*Science*, 27 June, p. 2020). But even the critics acknowledge the research as a tremendous accomplishment and say it has energized the field. “He certainly deserves this,” says Clay Armstrong of the University of Pennsylvania in Philadelphia. “He’s packed two or three careers into 10 years.”

—GREG MILLER



Cool Theories Garner Super Kudos

Three theorists have gotten a warm reception for their work on the very cold. Vitaly Ginzburg, Alexei Abrikosov, and Anthony Leggett have been awarded this year’s Nobel Prize in physics and will split the 10 million kronor (\$1.3 million) award.

Ginzburg, of the P. N. Lebedev Physical Institute in Moscow, and Abrikosov, currently at Argonne National Laboratory in Argonne, Illinois, were honored for their work on superconductors, materials that lose all electrical resistance at very low temperatures. In 1950, Ginzburg and a colleague, Lev Landau, formulated a theory that describes how superconductors behave in a magnetic field.

The Ginzburg-Landau theory implied that superconductors can respond in two different ways when exposed to ever-stronger magnetic fields.

Type I superconductors are completely impermeable to magnetism; the “field lines” can’t pass through the superconducting material at all. If the magnetic field gets too strong for the material to resist, the superconductivity disappears. Type II superconductors, which include all of the famous high-temperature ones, allow field lines to penetrate under some conditions. Abrikosov built upon the Ginzburg-Landau theory to characterize the behavior of type II superconductors; he predicted, for example, that penetrating field lines would create a regular lattice pattern in the superconductor, a phenomenon observed directly in 1967.



PHYSICS

Superheroes. Laureate Anthony Leggett (left) plunged into liquid helium; Vitaly Ginzburg (center) and Alexei Abrikosov braved the resistance-free currents of type II superconductors.



CREDITS: (TOP TO BOTTOM, LEFT TO RIGHT) ROCKEFELLER UNIVERSITY; THE NOBEL MUSEUM; BILL WIEGAND/UNIVERSITY OF ILLINOIS; ALEXANDER ZEMLIANICHENKO/AP; STEPHEN J. CARRERA/AP

He also described how ever-increasing field strengths can finally overwhelm even type II materials and rob them of their superconductivity.

Although a fuller description of superconductivity would have to await BCS theory, which three physicists (John Bardeen, Leon Cooper, and J. Robert Schrieffer) formulated in the late 1950s, “Ginzburg and Abrikosov did extremely important phenomenological work before BCS theory,” says Leggett, who hails from the University of Illinois, Urbana-Champaign. Schrieffer, currently at Florida State University, Tallahassee, says that the Russians’ equations “correctly predict where you get a high [magnetic] field coexisting with superconductivity.”

Leggett’s own contribution, however, has to do not with superconductivity, but with a related phenomenon, superfluidity. In superfluidity, a substance such as very cold liquid helium acquires outlandish properties, such as flowing without friction, for reasons similar to those that cause superconductivity. BCS theory explained helium-4’s superfluidity nicely, but it didn’t seem to work for helium-3, whose superfluid phase was discovered in 1972.

The breakdown occurred because the atoms in helium-3 pair up, making it a more complex beast than the solitary atoms in superfluid helium-4. Electrons in superconductors form similar pairs, which BCS theory describes handily. But helium-3 pairs have orbital momentum and spin that make them more difficult to understand, says Douglas Osheroff, a physicist at Stanford University.

Shortly after Osheroff and his colleagues made superfluid helium-3 for the first time, Leggett forged a theoretical framework that took the mathematical complexity of the helium-3 pairs into account to explain the puzzling and unexpected behavior of the new substance. “He was as close as you can come to an oracle when it came to helium-3,” Osheroff says. In the process, Leggett brought helium-3 superfluidity under the umbrella of existing theory. “It actually fits beautifully into the BCS pattern, but it has a much richer structure,” says Leggett.

“I was absolutely floored,” says Schrieffer of his reaction to Leggett’s analysis. “We thought that the reach of the theory would be for ordinary metal superconductors” but not for helium-3. Schrieffer says he repeatedly nominated this year’s winners for the prize.

In making the award, the Nobel committee displays a pattern of its own: Four of the last eight physics Nobels have honored work in the physics of low temperatures. Clearly, cold research means anything but a cold shoulder from the Swedish Academy.

—CHARLES SEIFE



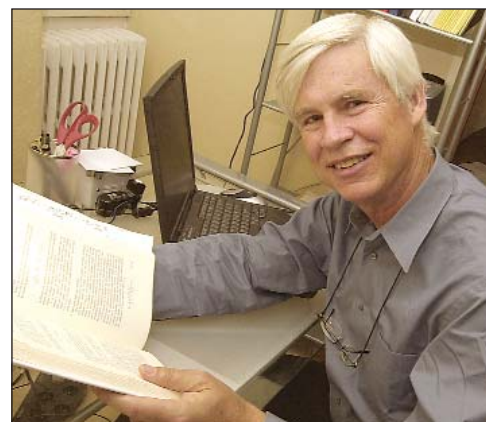
Clearer Forecasts for the Dismal Science

Time is not always on your side, at least in the volatile world of finance. The complicated mathematics of analyzing how indicators such as stock indexes fluctuate over time stumps economists, but Robert Engle and Clive Granger have helped clear up the confusion. The two have won this year’s Bank of Sweden Prize in Economic Sciences in Memory of Alfred Nobel for giving analysts tools to understand time series—data sets that show how variables change as time flows.

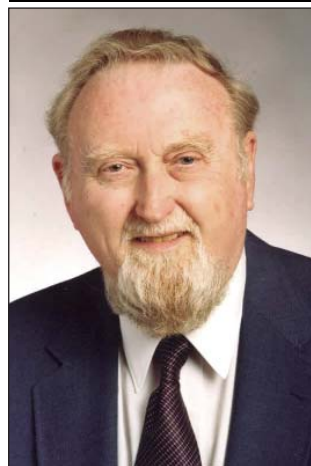
Economists Engle, of New York University, and Granger, of the University of California, San Diego, revolutionized the way the financial community dissects these unpredictable series. “It’s fair to say that their work has had a profound impact on time-series analysis,” says Princeton University economist Yacine Aït-Sahalia.

Granger showed that making simplistic assumptions about the time-dependent behavior of economic indicators can lead to ridiculous conclusions. In the 1970s, he proved that the techniques then in use could make it look as if random processes are linked even when they’re independent. He also came up with ways of measuring whether two indicators that meander in seemingly different ways have hidden relationships. In the short term, for example, a population’s wealth tends to fluctuate much more than the amount of goods and services the population consumes, even though consumption and wealth are interlinked. Also, Granger devised means of determining when one economic effect causes another—crucial inferences for economists to make. “It’s easy to fall into the trap of mistaking correlation for causality,” says Aït-Sahalia. “This has serious implications for economic policy; in understanding the Federal Reserve you want to know, for example, do changes in interest rates cause a change in employment?”

Engle is best known for developing a mathematical technique, known as ARCH, for analyzing time series in which the variance, or volatility, of an indicator can change over time. “Before [Engle], people didn’t pay attention to variances and took the variances to be constant. It was kind of a leap, conceptually,” says Tim Bollerslev, an economist at Duke University in Durham, North



ECONOMICS



Time pundits. Robert Engle (*above*) demystified time-series data with changing volatility; Clive Granger untangled economic causes and effects.

Carolina. Taking that leap is vital to financiers, says Princeton’s Christopher Sims. “In finance, you want to predict how volatility changes because you can make money off of that,” he says. “Variance is absolutely central to evaluating risk.” And the central principle of maintaining an investment portfolio, he says, is making the appropriate tradeoff between its risk and its returns.

Engle and Granger will split the \$1.3 million prize and will attend the ceremony in Stockholm in December. In the meantime, financiers will try to use the pair’s methods to make money on their own, and economists will continue to use their analyses and methods to make crucial forecasts. “I think the beauty of it is that the stuff just works,” says Aït-Sahalia.

—CHARLES SEIFE