sue in the 1960s but hadn't been cultured.

When researchers have no clues about what kind of organism is responsible, they sometimes turn to another powerful PCR technique called representational difference analysis (RDA). In this method, both healthy and diseased tissues are subjected to a variant of PCR that "subtracts" sequences common to both specimens, leaving only the genome of the infectious agent. Using RDA, in 1994 molecular biologists Patrick Moore and Yuan Chang at Columbia University in New York City isolated small bits of DNA from a skin lesion in an AIDS patient afflicted with Kaposi's sarcoma, a cancer that often affects HIV-infected people. From these genetic segments the pair was able to sequence the complete genome of a new virus called KSHV, now thought responsible for the cancer.

Powerful as they are, these techniques are laborious and time-consuming—and not always successful. So researchers are working to improve their methods. For example, Relman, working with Stanford biochemist Patrick Brown, has begun exploring the use of "pathogen detection chips," using the DNA chip technology developed by Brown and others (*Science*, 24 October 1997, p. 680). The idea is to put DNA strands from known pathogens on the chip and then see whether labeled DNA from an unknown microbe binds to any of the fixed pathogen DNA.

Relman and Brown have also begun using this DNA microarray technique as "cellular scouts" to detect changes in gene expression in the host, for example in immune system cells. Their goal is to create profiles of the gene expression changes triggered by specific kinds of invaders. Thus they would use the body's own response to identify pathogens, an approach Perkins calls "totally revolutionary." Preliminary results are promising: Brown's lab has shown that white blood cells express different genes when exposed to different combinations of immune signaling proteins called cytokines, which are produced in response to infection. If related microbes provoke similar cytokine responses, Moore says, the scout approach might quickly narrow the hunt to certain groups of organisms.

Meanwhile, the search for new methodologies continues. And researchers say that the molecular identifications thus far suggest that combining heightened surveillance with state-of-the-art techniques is bound to pay off sooner or later. Says Moore of the working group: "I think they have a really good chance of making some great discoveries."

–MICHAEL BALTER

PHYSICS

# How Matter Can Melt at Absolute Zero

**New tools are revealing the crowd behavior of electrons at close to absolute zero, where freezing and melting are governed by quantum mechanics**

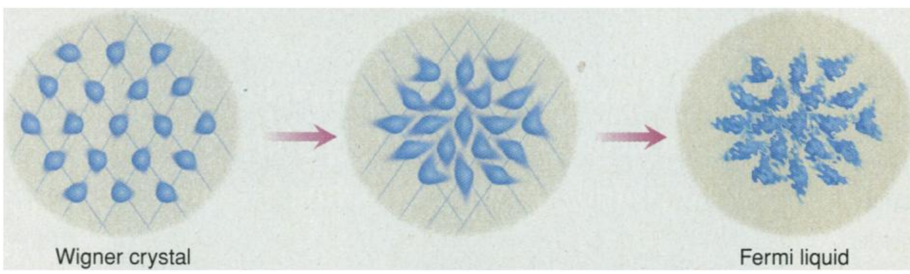
If you cool a piece of ice to the very lowest temperatures possible, about the last thing you would expect it to do is melt. But physicists are learning that some exotic crystals made of electrical charges or electron spins do indeed engage in something like that odd behavior: They "melt" at absolute zero, changing from one phase to another. These phase transitions are strictly in the weird realm of quantum mechanics, a world dominated by large fluctuations in energy and momentum even at the lowest temperatures, where classical physics would insist that the opportunity for change is frozen.

Theorists have been exploring these transitions since the 1950s, but now experimenters are actually seeing these strange metamorphoses in the laboratory. With sophisticated tools for building semiconductors and improvements in low-temperature analysis, physicists have been able to watch the melting of an electron crystal and the unusual flip-flops of two-dimensional "gases" of electrons. This new kind of crowd behavior is fascinating in its own right, they say. "These are things that just can't be discussed in terms of single particles at all," says Subir Sachdev, a Yale University physicist. But it may also have some practical implications: By searching for hints of quantum phase transitions in high-temperature superconductors, researchers are hoping to spring the lock on the stubborn mystery of how these materials work.

Classical phase transitions, like the melting of an ice cube, are driven by thermal energy. Heating the ice above the freezing point causes molecules in the solid water to vibrate. Eventually, the jiggling becomes so wild that the molecules are no longer content with their orderly seating arrangement in the ice crystal, and they break loose to become liquid water. Heat them even more, and they don't even want to slosh around in a liquid—they vaporize into steam. Reverse the process, the jiggling slows down, and the molecules fall back into place. The variable that controls all of these transformations is temperature.

Quantum phase transitions are a completely different beast. What opens the way to a quantum phase transition is a change not in temperature, but in some other parameter like the density of a material or the strength of an external magnetic field. Because they don't need thermal energy, quantum transitions can theoretically take place at zero temperature. In fact, they can only be studied at low temperatures, where the thermal fluctuations that cause particles to jiggle subside, revealing the quantum fluctuations in position and momentum that actually trigger the phase transitions.

Steven Girvin, a theorist at Indiana University, Bloomington, likes to explain the notion of a quantum phase shift by citing a textbook concept known as the Wigner crystal. This orderly arrangement of electrons, named after Eugene Wigner, who proposed it in 1938, can form when the electron density is low and the particles sort themselves into a stable spatial array, like soldiers standing in formation. Arrayed charges like these have since been observed in the layers of electrons that collect on the surface of liquid helium and in confined electron layers in sandwichlike semiconductor structures called quantum wells.



**Letting go.** As a lattice of electrons called a Wigner crystal (left) is compressed, the quantum fluctuations in the electrons' positions grow until the lattice melts (right).

To illustrate how quantum mechanics can trigger a phase transition in this arrangement, Girvin suggests a thought experiment based on Heisenberg's uncertainty principle, which holds that as a particle's position becomes better known, its momentum gets fuzzier. "As you make the crystal more dense, the electrons become more confined," he says. "But then the uncertainty principle takes over and the fluctuations in momentum grow." Squeezing on the crystal causes the electrons to become restless; eventually they melt into a conducting quantum "liquid." The change is analogous to the heated water molecules jiggling out of their comfortable crystalline lethargy.

The melting of a Wigner crystal is just one example of a whole class of quantum phase transitions that theorists have studied, in which a material can transform from a conductor into an insulator and back as some nonthermal variable is changed. That variable can be the density, as in the Wigner crystal example. Or the amount of disorder in the material can be varied, which can trap or release charge carriers and change a conductor into an insulator or vice versa. These transitions don't occur in everyday materials, but they provide new kinds of insight into what it means to be a metal or an insulator. And they expand notions of how matter can transform itself, says Thom Mason, a condensed matter experimentalist at Oak Ridge National Laboratory in Tennessee. "Now we have a whole new class of phase transitions that only occur at low temperature," he explains. "This isn't just small changes in the third decimal place. The characteristics of these systems are completely different."

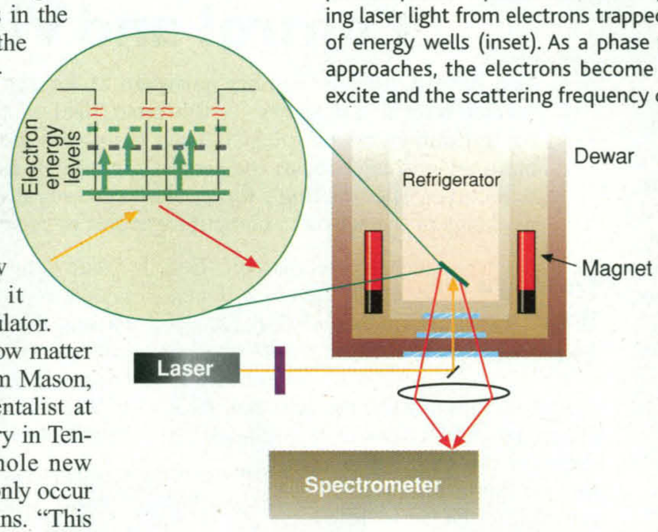
**Quantum melting revealed.** Actually seeing these transitions was beyond experimenters' reach until recently, because it required the ability to control and probe assemblages of electrons with exquisite precision at close to absolute zero. Now experimenters are armed with precisely controlled magnetic fields and analytical tools such as neutron scattering, along with quantum wells and other new semiconductor architectures that can corral electrons into two-dimensional gases or one-dimensional wires. They are observing how these transitions actually take place—and confirming that some of the textbook scenarios really do occur in the real world.

Mansour Shayegan and his co-workers at Princeton University, for example, have seen a Wigner crystal melting, just as Girvin envisions it. Theorists predicted nearly 2 decades ago that electrons confined to a two-dimensional layer would be insulating, locked in a Wigner crystal, unless they were disturbed by magnetic fields. Yet in 1994, Sergei Kravchenko at the City University of New York, studying a two-dimensional electron layer trapped in a quantum well, found hints of a transition to a metallic, conducting state in the absence of magnetic fields. Working at temperatures below 1 kelvin, Shayegan's group found out why. As they will report in *Physical Review Letters*, the material always changed from insulating to conductive at a specific density of electrons. That density, according to numerical simulations by Bilal Tanatar and David Ceperley at the University of Illinois, Urbana-Champaign, is precisely the value at which a Wigner crystal state should melt.

Experimenters have also probed another set of quantum phase changes seen in low-temperature electron layers, this time in a strong magnetic field. In what is known as the quantum Hall effect, the resistance to the flow of current along the layer of electrons changes in steps as the magnetic field is increased, a discovery that won Klaus von Klitzing of the Max Planck Institute for Solid State Research a Nobel Prize in physics in 1985. Von Klitzing realized that each jump in resistance corresponded to a quantum phase change—in this case, a change in the traffic pattern of the electrons flowing through the layer.

Like cars moving through an urban obstacle course of traffic circles, the electrons rotate around the magnetic field lines as they flow through the layer. A stronger field puts more traffic circles in the flow, causing the cars to speed up in some directions but slow down in others and affecting the resistance. Because quantum mechanics demands that the magnetic traffic circles be filled in a particular way—with particles moving in discrete, quantized orbits—the resistance does not rise steadily with magnetic field. Instead, it jumps to a series of plateaus as the electron gas executes quantum phase transitions from one state to the next.

Exactly what happens right at these transitions is still unclear. One theoretical prediction made in the 1980s is that near each phase transition, the modes of excitation in the electron gas—oscillations in the positions of the charges or in the orientations of their spins—can "soften," much like piano strings losing their elasticity and dropping in pitch. Because quantum mechanics equates energy with frequency, the softening means that the energy required to cause a change in the electron layer goes toward zero, making it unstable. The slightest nudge, such as an infinitesimal change in the magnetic field, will induce the phase transition.




**Light on the quantum world.** An experiment probes quantum phase transitions by scattering laser light from electrons trapped in a pair of energy wells (inset). As a phase transition approaches, the electrons become easier to excite and the scattering frequency changes.

To probe this possibility, researchers at Lucent Technologies Bell Laboratories in Murray Hill, New Jersey, and universities in Italy, the United Kingdom, and the United States studied the transitions by scattering laser light off the electron layers in a quantum Hall system. At some wavelengths, the light is scattered more strongly by the electrons, indicating that it is exciting the collective modes. But Aron Pinczuk of Bell Labs explains that because the excitations in a single-layer quantum well have such high energies, they can only be probed with x-rays—a difficult or impossible experiment. So he and his colleagues used a double-layer device in which the energy levels of each layer interact to produce excitation modes at a lower energy. These modes have energies in the infrared part of the spectrum, which is easier to monitor with laser light (*Science*, 7 August, p. 799).

Just as predicted, Pinczuk and his colleagues saw the mode softening: The frequency of the infrared scattering peak changed in the double electron layers as they neared the quantum Hall transitions. "This mode softening is part of the basic conceptual framework that we all use to understand these systems," he notes. "It's not been seen before in an electron gas."

**Going through a phase.** Several groups of condensed-matter physicists are now looking into the possibility that quantum phase transitions may hold the key to their field's biggest mystery, high-temperature superconductivity (HTSC). Conventional superconductivity, which is seen at very low temperatures, entails a classical phase transition: The transition to zero resistance occurs as the temperature is lowered, making the thermal fluctuations weak enough to allow electrons to form pairs that travel without

CREDIT: V. PELLEGRINI

loss through a crystal lattice.

Yet the high-temperature superconductors, made of copper oxides, behave nothing like conventional ones. Although the temperature has to be lowered to turn them into superconductors, their properties seem to depend strongly on impurities in the copper oxide crystal. "How did it occur to Bednorz and Müller [discoverers of HTSC] to look for a superconductor in the most terrible conductor, a ceramic insulator?" marvels Shou-Cheng Zhang, a theorist at Stanford University. "By doping atoms into copper oxide, they found that somehow this insulator becomes a perfect conductor." The fact that the change depends on something besides temperature, namely the doping of other elements into the crystal lattice, suggests a quantum phase transition.

Last year, Zhang came up with a possible scenario for this phase transition by applying mathematical tools borrowed from high-energy physics. The insulating state of the high-temperature superconductors is an antiferromagnet, a delicate balance of alternating spins, like an array of tiny bar magnets pointing alternately north and south. Zhang and his colleagues found that they could mathematically "unify" antiferromagnetism and superconductivity, much as particle physicists have learned to unify the electromagnetic force with the nuclear weak force. This unification allowed Zhang to describe the transition to superconductivity in a high-temperature material as a process radically different from the one in a conventional superconductor, where the resistance drops to zero precisely when the electrons form pairs.

"The pairing can actually occur at high temperatures, well above those at which the material is superconducting, but the fate of these pairs is governed by lower temperature effects," Zhang says. As the temperature is lowered, the pairs can form an antiferromagnetic quantum solid or melt into an electron-pair superconductor. At zero temperature, Zhang's model suggests, these two ground states might emerge as two different quantum phases, with composition alone governing the transition between them.

So far, it's only a theoretical picture, but experimenters are beginning to find hints of quantum phase transitions in high-temperature superconductors. Mason and his co-workers at Oak Ridge, for example, probed single crystals of $LaSrCuO_4$ with neutrons to measure magnetic fluctuations in the material when it had been doped almost enough to make it into a superconductor (*Science*, 21 November 1997, p. 1432). The neutrons are like a beam of tiny bar magnets bouncing off the spins in the sample; sorting out the scattered neutrons tells how the spins are fluctuating. Although the experimenters could not reach absolute zero—the place where quantum phase transitions come into their own—they found that the spin fluctuations varied with temperature in a way that would be expected if a quantum phase transition were lurking somewhere nearby.

Not only could quantum phase transitions lift the lid on HTSC, but Mason and others think that studying these transitions may equip physicists to solve equally tough puzzles in the future. The research, says Mason, is part of physics's quest for universality—for ways to explain the behavior of complex, many-body systems in terms not of microscopic details but of large-scale properties. "Because of universality, the things we are exploring now can be applied to cases we don't know about yet," he says. "It's a remarkable thing that you can experiment on a simple system, then discover there's a whole other set of transitions that follow the same behavior."

–DAVID VOSS

David Voss, a former editor of *Science*, is a physics writer in Silver Spring, Maryland.

**ADDITIONAL READING**

S. L. Sondhi, S. M. Girvin, J. P. Carini, D. Shahar, "Continuous quantum phase transitions," *Reviews of Modern Physics* **69**, 315 (1997).

MEETING SYMPOSIUM ON THE BRAIN

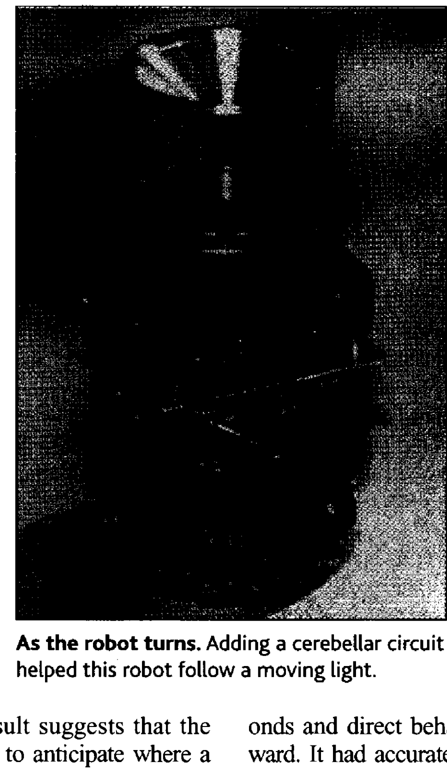
# New Clues to Movement Control and Vision

**Last month, neuroscientists gathered at Boston University School of Medicine for a conference on the brain, held to commemorate the late computational neurobiologist David Marr, who pioneered theories about brain regions as varied as the cerebellum, the visual system, and the cerebral cortex. The meeting's topics were similarly diverse, ranging from the workings of the retina to computer models of the cerebellum.**

## Guiding a Robot's Movements

When a tennis ball flies over the net, U.S. Open champion Lindsay Davenport has to predict where it will go so she can race to hit it. If she fails to guess the right spot, she'll lose the point. It's crucial to be a split-second ahead of the game, and computational neurobiologist Terrence Sejnowski of the Salk Institute in La Jolla, California, aided by a robot his team developed, has new evidence to support the idea that this skill is learned with the help of a brain area called the cerebellum.

At the meeting, Sejnowski showed that a software model of the human cerebellum gave the 2-centimeter-wide cylindrical robot an ability it didn't have before: It could predict, a second in advance, the position of a moving light based on the light's pattern of movement. The result suggests that the cerebellum learns how to anticipate where a fast-moving object will go. Other work had already suggested that the cerebellum—known for its role in stabilizing the body, moving the eyes, and performing multijoint movements—might have a role in learning to make very short-term predictions. The details of Sejnowski's model have not yet been published, but if the software really is a good model of the cerebellum, says computational neuroscientist Tomaso Poggio of the Massachusetts Institute of Technology, the new work could be "an important and necessary step" toward nailing down this function for the cerebellum.



**As the robot turns.** Adding a cerebellar circuit helped this robot follow a moving light.

CREDIT: ALAIN HERZOG

Sejnowski's group originally set out to use the robot as a real-world test of a model they had made of a brain circuit that governs motivation and reward-seeking. This circuit, shared by both humans and bees, is thought to assess the chances of rewards that may appear in the next few seconds and direct behavior to maximize a reward. It had accurately simulated, on a computer screen, the behavior of bees given a