Electrons display their antisocial nature

Soon after the birth of quantum mechanics early in this century, physicists theorized that force-carrying particles, known as bosons, tend to bunch together. By contrast, the elementary particles of matter, called fermions, demand a little elbowroom from their peers.

In a landmark 1950s experiment, researchers directly observed the predicted preference for bunching among photons—the bosons of electromagnetic radiation—and created a new research field. Called quantum optics, it eventually led to practical benefits such as the laser.

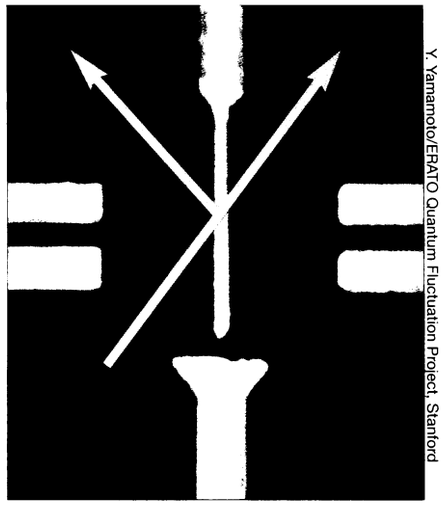
In the April 9 SCIENCE, two independent research groups report that they have finally performed a comparable experiment for fermions. Their results demonstrate the complementary, standoffish nature of electrons, one of the lighter members of the fermion clan, which also includes protons and neutrons.

In doing so, the investigators have confirmed the validity of the Pauli exclusion principle, part of the bedrock of quantum mechanics. This dictum states that no two identical fermions can occupy the same quantum state, such as a single atomic-energy level.

Although physicists commonly invoke the exclusion principle, "you have to measure [its effects] before people really believe it," says Stefan Oberholzer of the University of Basel in Switzerland, where he and his colleagues conducted one of the confirming tests. William D. Oliver and other researchers at Stanford University carried out an analogous experiment.

The new results "will certainly be the stuff of future textbook discussions," comments Marlan O. Scully of Texas A&M University in College Station. Oberholzer notes that until recently scientists could not make dense enough fermion streams to explore the particles' chumminess.

In the new studies, both teams used electrons chilled to ultralow temperatures and confined to an extraordinarily thin layer between semiconductors. The scientists forced the particles into a narrow region blocked by an electrode's voltage so that only half of the electrons, on average, had enough energy to pop through. The others bounced off and exited via a different path.



A 40-nanometer-wide electrode shaft splits an electron stream (blue) passing beneath it.

The scientists measured currents from each arm of these beam splitters. As the currents fluctuated, the researchers consistently found that an increase in one arm was offset by a decrease in the other—the sign of fermionic, one-at-a-time, passage through the beam-splitter.

The experimental techniques may also help scientists probe the nature of mysterious quasiparticles, which can mix fermion and boson characteristics (SN: 10/17/98, p. 247), and test properties of very small electronic devices, the researchers say. *—P. Weiss*

Social fears may raise alcoholism risk

Much research has noted that outgoing children who impulsively misbehave, bully others, and get into numerous fights have more than their share of alcohol problems as young adults. A new study suggests that kids in families with widespread alcoholism may tend to find themselves on the other side of the temperamental coin—withdrawing and clamming up when confronted with unfamiliar people and situations. Such children may also gravitate toward alcoholism, the researchers suggest.

"Children from alcoholic families may be at greater risk for displaying a behaviorally inhibited temperament," says a team led by psychologist Shirley Y. Hill of the University of Pittsburgh Medical Center. "While the childhood risks associated with [poorly controlled behavior] are well known and more prominent among children from alcoholic families, the risks associated with extreme inhibition are less well studied."

Hill and her coworkers examined 36 white children, 4 to 6 year olds living in middle-class households. Half the children came from families in which about one-quarter of the members, from the past several generations, had suffered from alcohol dependency with no other psychiatric disorders. The remaining youngsters came from families with few or no cases of alcoholism or any other mental ailments.

Accompanied by a parent, each child attended from one to three sessions in a playroom. Experimenters videotaped and rated children's behavior as they had opportunities to play with an unfamiliar child of the same age and sex.

Children from the families with high rates of alcoholism displayed far more inhibition during play sessions than their counterparts did, reports Hill's team in the April JOURNAL OF THE AMERICAN ACADEMY OF CHILD AND ADOLESCENT PSYCHIATRY. Inhibition appeared mainly as a pronounced tendency to stare at the other child while refusing to play with or to speak to him or her.

Some children from high-alcoholism families may experience sensitized biological reactions to stress that foster inhibition, the researchers theorize, and as adolescents, may use alcohol to quell anxiety. Other studies find that kids in families with pervasive alcohol problems often develop alcoholism.

Further studies should explore possible biological influences on these unusually inhibited kids as well as the psychological effects of living with an alcoholic parent, the researchers add.

Childhood inhibition merits "attention and concern" as an influence on alcoholism, remarks psychiatric epidemiologist Naimah Z. Weinberg of the National Institute on Drug Abuse in Rockville, Md., in a published comment in the same journal. However, evidence for this link remains sparse, Weinberg says.

Subtle language disorders may contribute to the inhibition of some children from families with many alcoholic members, she proposes. *—B. Bower*

The green genes don't get out much

Could genes from a genetically modified crop escape and create a superweed that could take over the world, as some people fear? One preventive measure might be to confine any transplanted genes to the cell's photosynthetic structures, or chloroplasts.

Escape of such genes would be "extremely rare and scattered," predict Susan E. Scott and Mike J. Wilkinson of the University of Reading in England, who for 3 years have tracked chloroplast DNA in fields of unmodified oilseed rape. They report their results in the April Nature Biotechnology.

The work grows out of proposals that tinkering with the DNA in chloroplasts poses less risk of runaway genes than the more common strategy of modifying DNA residing in the cell's nucleus. Henry Daniell of the University of Central Florida in Orlando, a pioneer of gene insertion in tobacco chloroplasts, last year advocated that approach. In many plants, he argues, chloroplasts are inherited maternally and thus don't show up in hard-to-control, wind-blown, insect-riding pollen.

Wilkinson and Scott evaluated chloroplast-gene escape routes in *Brassica*

napus, known as oilseed rape or canola. Farmers grow this mustard for its edible oil. The crop species hybridizes readily with wild mustards, including one of its ancestors, *Brassica rapa.*

To track any wandering of chloroplast genes, the researchers checked 47 crop-weed hybrids found near commercial fields. All hybrids showed the weed, or maternal, chloroplast DNA. That convinced Wilkinson that pollen wafting from fields does not carry chloroplast DNA.

In practical terms, errant crop pollen doesn't have that many places to go, Wilkinson notes. He and Scott found that of more than 140 patches of wild *B. rapa* in farmland, only 2 grew near oilseed rape fields.

In such patches, just 0.4 to 1.5 percent of the plants have mixed parentage, he and Scott reported last year. All in all, there will probably be "no or negligible" escape of chloroplast genes through crop pollen, he predicts.

The researchers also considered the other escape avenue: the female flower parts. If crop seeds spill near wild plants, the resulting plants may be pollinated by weed species to create hybrids carrying the modified chloroplast. In another generation or two, the wayward genes could get into highly fertile wild plants.

However, when a crop plant gets loose, "it doesn't last very long," Wilkinson says. He and Scott monitored 18 patches harboring crop plants that had gone wild. Fifteen of the patches disappeared or failed to set seed during the 3-year study.

Hybridization is "inevitable but will occur only extremely rarely," Wilkinson says. "It all comes down to what the transgene actually is." A transplanted gene that gives a plant whopping advantages in the wild might spread even through a tiny keyhole escape avenue.

"You have to look at each plant on a plant-by-plant basis," agrees Dean Chamberlain of the University of North Carolina (UNC) in Greensboro. In a commentary in the same issue of NATURE BIOTECHNOLOGY, he and UNC's C. Neal Stewart Jr. note that chloroplast genes are so difficult to work with that, to date, only tobacco has been transformed in this way.

Just wait, responds Daniell. He expects several researchers soon to announce transfers of chloroplast genes.

The chloroplast strategy is still no panacea, warns Joseph E. Cummins of the University of Western Ontario in London, Ontario. Chloroplasts are passed on through pollen in many conifers and through both parental lines in alfalfa. Also, Cummins points out that chloroplast DNA can leak into mitochondria, a cell structure that does show up in oilseed rape pollen.

Wilkinson speculates that both fans and foes of genetically modified crops will quote the new paper as supporting evidence. "To us, it's just data," he sighs. —*S. Milius*

Stopping leaks may boost cancer drugs

Almost every medicine produces side effects. The crucial issue is whether a drug has a therapeutic window, a dose range that allays a patient's illness without causing greater problems.

In a finding that may widen the therapeutic windows of two experimental cancer medicines, researchers have uncovered the molecular explanation for a side effect—leaky blood vessels—that both therapies cause. Known as vascular leak syndrome, the condition occurs when fluid from the bloodstream escapes into surrounding tissues.

"You sort of become a water balloon," says Ellen S. Vitetta of the University of Texas Southwestern Medical Center at Dallas. While a body can often slowly expel this excess water, fluid buildup in organs such as lungs can turn deadly.

Vitetta and her colleagues encountered vascular leak syndrome when they began testing immunotoxins in cancer patients. These artificial proteins consist of a plant or bacterial toxin attached to antibodies that home in on cancer cells.

The immunotoxins have lived up to their billing as cancer killers, but they also trigger changes in cells lining blood vessels. The cells become rounder than normal, leaving gaps through which fluid could seep out. The problem limits the amount of immunotoxins people can receive as a treatment.

"This has stalled the field a great deal," says immunotoxin investigator Daniel A. Vallera of the University of Minnesota Cancer Center in Minneapolis.

"You don't have a wide therapeutic window, because you hit this toxicity," agrees Christopher A. Pennell, also of the University of Minnesota Cancer Center.

Like the immunotoxins, interleukin-2, a protein that stimulates the immune system's cells, causes vascular leaks at high doses. The side effect has frequently thwarted its use in people with cancer and, more recently, AIDS.

Speculating that immunotoxins and interleukin-2 generate leaky blood vessels in the same way, Vitetta's team compared the proteins. "You line up the [amino acid] sequences and ask if there's a consensus sequence. Lo and behold, out came this motif," says Vitetta. All the molecules share a particular combination of three amino acids, her group reports in the March 30 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES.

The researchers also made protein fragments containing this motif but no other parts of interleukin-2 or the immunotoxins. Injected into animals, those segments caused leaky blood vessels. "You don't need the rest of the molecules," says Vitetta. "You just need this tiny, little piece."

The scientists are now trying to eliminate this dangerous motif by mutating the genes that encode the immunotoxins. They expect that the modified immunotoxins will retain their cancer-killing prowess but leave blood vessels alone.

Making interleukin-2 safer may prove more difficult since the motif falls in a region crucial to the protein's therapeutic function. Investigators could instead try to block the proteins on blood vessels that the immunotoxins and interleukin-2 bind, Vitetta notes.

"She's putting together a really nice story," says Pennell. —*J. Travis*

Big dust, little harm

Dust storms are blowing away the argument that eroded soil and other relatively large, airborne particles are as hazardous to health as the far smaller particles generated by combustion.

Over the past decade, a host of studies has linked the outdoor buildup of combustion particles to a rise in hospital admissions and death rates for respiratory illness (SN: 4/6/91, p. 212) and heart disease (SN: 7/1/95, p. 5). Such data convinced the Environmental Protection Agency to create new limits (SN: 7/5/97, p. 6)—not yet in effect—for particles that measure 2.5 micrometers (μm) in diameter or smaller (termed PM-2.5). Federal rules already limit a broader class of particles, those with diameters of up to 10 μm (PM-10).

Representatives of combustion-intensive industries say that errors in measuring large particles have made the relative health impacts of large and small particles hard to distinguish. Thus, they have argued against rules focusing on PM-2.5, notes Joel Schwartz of the Harvard School of Public Health in Boston.

"It's a big fight," he explains, and it has threatened to derail implementation of the PM-2.5 limits. Hoping to settle the controversy, Schwartz teamed up with researchers from two universities in Washington State to study Spokane death rates during 17 major dust storms over 6 years. The average PM-10 concentration on storm days was 263 micrograms per cubic meter ($\mu g/m^3$) of air—well above the current EPA limit. On the stormless days, PM-10 averaged only 42 $\mu g/m^3$. During dust storms, PM-10 consists primarily of particles larger than 2.5 μm in diameter, but the amount of fine particles present changes relatively little with weather.

Nonaccidental death rates were slightly lower during the dust storms than on calm days of the same date during the study, the researchers report in the May ENVIRONMENTAL HEALTH PERSPECTIVES. These data, they contend, argue against the industry position and confirm results of other studies "that toxicity of coarse particles is substantially less than that of fine particles." —*J. Raloff*