PARTICLE PHYSICS

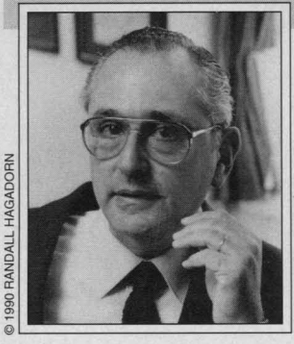
New Results Yield No Culprit For Missing Solar Neutrinos

It doesn't seem possible that a jury could deliberate for 25 years, yet fail to return a clear verdict, but that's exactly what has happened in the case of the missing solar neutrinos.

Since 1967, physicists have been attempting to measure the outflow of these elusive subatomic particles from the nuclear reactions that generate energy in the sun's core. Puzzlingly, all the measurements to date have come up short, capturing fewer solar neutrinos than expected. As a result, physicists have been forced to conclude that something is amiss either in their picture of the sun's workings or in their understanding of particle physics. But because experiments so far have only succeeded in detecting neutrinos from subsidiary reactions in the sun, researchers haven't been able to say whether the sun is to blame, or the neutrinos themselves. The resolution, physicists hoped, would come from the GALLEX experiment, which for the past 2 years has been capturing solar neutrinos in a huge tank of gallium chloride at the Gran Sasso underground laboratory in the Apennine Mountains of Italy. Now the word from GALLEX is in—in the guise of two papers submitted last week to *Physics Letters B*—and it is exasperatingly ambiguous.

That the sun might work as expected "is interesting, but you don't get a cigar for that."

–John Bahcall



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GALLEX did give physicists their first look at neutrinos from the sun's key fusion reaction. "We have for the first time seen what everybody expected had to be seen," says the GALLEX spokesman, Till Kirsten of the Max Planck Institute of Nuclear Physics. But instead of clearly implicating either the sun or particle physics in the solar neutrino problem, the results leave both interpretations alive, if shaky. As Wick Haxton of the University of Washington puts it: "It's not the smoking gun everyone was hoping for. We're still in the soup when it comes to finding an ultimate solution for the solar neutrino problem."

The enigma dates to 1967, when physicist Ray Davis of the University of Pennsylvania set a trap for solar neutrinos: a tank of carbon tetrachloride in the Homestake gold mine in South Dakota. Buried in the mine, the detector would be shielded from interference by cosmic rays, but neutrinos can readily pass through solid rock into the detector. Roughly once a day, Davis reasoned, a neutrino from the sun would interact with a chlorine atom in the tank, converting it into a radioactive form of argon, which could later be extracted and measured. Davis' detector saw only one-third of the neutrinos predicted by standard solar models. Confirmation came in 1988 from a Japanese experiment, Kamiokande II, which captured neutrinos in a 21,000 gallon pool of ultrapure water. Kamiokande recorded slightly less than half the expected number of neutrinos.

That shortfall might have been little more than an inconvenience, requiring just a slight adjustment of solar models—say a few percent change in the assumed temperature of the sun's interior. Such an easy out was conceivable because both Homestake and Kamiokande were sensitive only to the high-energy neutrinos from the decay of beryllium-7 or boron-8—tertiary nuclear reactions in the sun's core. Virtually all the sun's energy comes from the fusion of protons into helium, a process that also releases neutrinos—but ones carrying too little energy to leave their mark in either the chlorine or the water detectors. If the sun was producing these pp-neutrinos in the expected numbers, the solar neutrino problem could be solved with little strain. But if they too were missing, physicists would have to retool drastically either their picture of the sun or—if the shortage were severe enough—their understanding of how neutrinos and other particles behave.

In the mid-1980s, two international collaborations set out to detect these low-energy neutrinos. Both pinned their hopes on gallium, which pp-neutrinos can transform into radioactive germanium-71. GALLEX relied on 101 tons of gallium chloride solution, while SAGE, the Soviet-American Gallium Experiment, set up a detector containing 30 tons of pure gallium metal under a mountain in the North Caucasus. Standard solar and particle physics clearly predicted the outcome: Both experiments should see between 124 and 132 solar neutrino units, or SNUs.

The SAGE collaboration went public first, in July 1990, with a preliminary analysis of 4 months of data that revealed a dramatic shortfall: just 20 SNU. Given the possible errors in the measurement, says Tom Bowles, a Los Alamos physicist and a member of the collaboration, the true figure might be as low as zero. Because there seemed to be no way to manipulate solar models so that the sun would give off no pp-neutrinos at all, an explanation would have to come from new particle physics.

To many physicists, the most attractive possibility was the so-called MSW theory, named for physicists Stanislaw Mikeyev and Alexei Smirnov of the (then) Soviet Academy of Sciences and Lincoln Wolfenstein of Carnegie-Mellon University. Mikeyev and Smirnov had proposed, based on an earlier suggestion by Wolfenstein, that the species of neutrinos produced by the sun—so-called electron neutrinos—might transform on their way to Earth into either of the two other species, muon and tau neutrinos, to which all existing detectors are blind. Such a conversion, theory holds, could only take place if neutrinos—conventionally seen as massless—have a trace of mass. And that would have extraordinary implications for particle physics, astrophysics, and cosmology (*Science*, 8 May, p. 731).

Even before SAGE went public, MSW proponents including John Bahcall of the Institute for Advanced Study and Hans Bethe of Cornell University had suggested that the most elegant solution to the MSW effect predicted that SAGE would see few, if any solar neutrinos. So when the collaboration reported just that result, says Bahcall, "I, for one, rushed to believe it, because it gave an answer that was so simple and beautiful."

Other physicists, though, suggested that maybe SAGE detected no neutrinos at all because something was wrong with the experiment or the extraction process. Extracting germanium-71 atoms from gallium metal is a tricky business, far more so than extracting the atoms from gallium chloride. Indeed, Bahcall recalls that Ray Davis had suggested as early as 1978 that it would be "much harder convincing people you got it right if you do it with metallic gallium rather than gallium chloride." Those who were skeptical of the SAGE technology suggested that the definitive word would come from GALLEX.

Now GALLEX has rendered a verdict of exquisite ambiguity: 83 SNU, based on the first year of data. On the one hand, according to one of the GALLEX papers, "severe stretching of solar models" could account for a figure of 83 SNU without new physics. And as Kirsten told *Science*, the error in the measurements is large enough that the true figure could be as high as 125 SNU, "within the expectation of the full standard model" of the sun. Says Bahcall, "That's interesting, but you don't get a cigar for that." On the other hand, as he is quick to point out, the 83 SNU from GALLEX, combined with the results from Homestake

and Kamiokande, leave open two small ranges of solutions based on the MSW effect.

Finding themselves in an even tighter bind than before, solar neutrino researchers are looking to the next round of results for relief. Both SAGE and GALLEX plan to collect data for several years, improve their statistics, and calibrate their instruments with an artificial neutrino source. It's assumed that the results from the two instruments will converge—but whether at 125 SNU, 83 SNU, or 20 SNU, no one can say. At a neutrino conference this week in Granada, Spain, for example, SAGE reported preliminary data from six month-long runs in 1991, ranging from close to zero all the way to 100 SNU. Says SAGE's Bowles, "It seems likely that our [original] results will come up a bit."

If the figure of 83 SNU ends up holding firm, then the case of the missing neutrinos will have to wait for a retrial in the next generation of experiments, in particular the Sudbury Neutrino Observatory (SNO), to be commissioned in the spring of 1995. SNO, already under construction in a nickel mine in northern Canada, will snare neutrinos in a tank of ultrapure heavy water, making it the first detector sensitive to muon and tau neutrinos as well as electron neutrinos. That will enable it to test whether the neutrinos have been changing their identities, as the MSW theory holds, or whether the sun itself is not behaving by the book. "If the results of the gallium experiments stay in this indefinite area," says the University of Pennsylvania's Gene Beier, a member of the SNO collaboration, "then you can't distinguish neutrino physics from solar physics. SNO can."

–Gary Taubes

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CANCER THERAPY

Molecular 'Surgery' for Brain Tumors

Perhaps nothing frustrates a neurosurgeon—or terrifies a patient—more than an inoperable brain tumor, its murderously dividing cells tucked out of reach of scalpel or laser. To overcome that kind of frustration, a team of National Institutes of Health (NIH) neurosurgeons is planning a remarkable new form of molecular "surgery," based on gene therapy, for attacking some inoperable brain tumors. Last week, the NIH recombinant DNA advisory committee (RAC) voted 19-0 (with 1 abstention) to approve a protocol for transferring a viral gene into brain tumor cells, making them susceptible to destruction by the antiviral drug ganciclovir. The RAC's approval of the trials, which will likely begin in the fall, was based largely on promising animal results reported in this week's *Science* (see page 1550).

The new protocol has provoked considerable enthusiasm in the gene therapy community. "It's like putting bull's eyes in the tumor cells and shooting them," says Nelson Wivel, director of NIH's office of recombinant DNA activities. "It's an exciting protocol." The new method is creating a stir in part because it includes a significant twist on current gene therapy. In standard procedures, researchers extract cells from a patient who lacks normal copies of a particular gene. They then add that gene to the cells via a vector (often a virus) and inject the cells into the patient. In this case, however, the NIH researchers can't reinject human cells. Instead, they plan to modify cells from another species and inject those. "We're going to be putting mouse cells in these patients' brains," explains Edward H. Oldfield, head of the surgical neurology branch of NIH's National Institute of Neurologic Disorders (NIND), who will be carrying out the clinical trials with NIND neurosurgeon Zvi Ram.

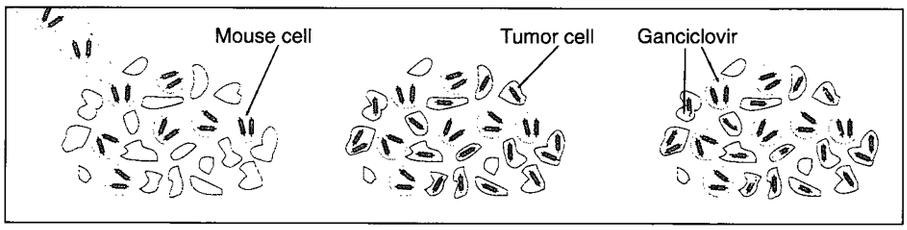
The method was conceived and initially developed 18 months ago by Kenneth Culver, an oncology researcher working in the laboratory of R. Michael Blaese, chief of the National Cancer Institute's cellular immunology section. "When I proposed this idea, people thought it was crazy," says Culver. His "crazy" idea, essentially, was to inject tiny biochemical factories into patients' brains. The method calls for inserting into mouse cells a retroviral vector carrying a gene from another virus—herpes simplex. The herpes gene codes for an enzyme called thymidine kinase, which turns any cell producing it into a target for antiviral drugs. The mouse cells—known as fibroblasts—that carry the retroviral vector are injected very precisely into a brain tumor. There the fibroblasts' molecular machinery starts pumping out copies of the retroviral vector, which infect nearby tumor cells. The infected cells now produce thymidine kinase, laying themselves open to attack by ganciclovir.

In rats this form of gene therapy proved to be surprisingly toxic to cancer cells, says Blaese, whose laboratory collaborated with the NIND neurosurgeons on the animal studies. In addition to killing the tumor cells that were known to have the herpes gene in them, ganciclovir killed other tumor cells in their vicinity. Exactly how the "bystander effect" operates isn't known, but Blaese speculated that it might be due to thymidine kinase and ganciclovir interacting to produce toxic triphosphates that inhibit DNA synthesis in rapidly replicating cells. A similar bystander effect is exploited in a gene therapy protocol being developed by Scott Freeman, a medical researcher at the Tulane University School of Medicine.

Along with the excitement over these results comes a certain amount of nervousness. "The risk is higher," says Gary Nabel, a molecular biologist at the University of Michigan, whose laboratory works with the herpes thymidine kinase gene. "But, then," he adds, "so are the stakes." Nabel warns of a slim possibility that "helper" viruses might contaminate the recombinant retroviral vectors and cause a secondary infection in noncancerous cells. "The key will be to make sure that the quality control of the cell lines is good," he says. Researchers also worry that the retroviral vector might infect proliferating noncancerous cells—such as cells in the bone marrow, thymus, and intestinal epithelium. This didn't seem to happen in rats, nor did toxicity studies in monkeys raise any red flags, says Oldfield.

Whether or not the concerns are justified will become clearer after the protocol clears its final hurdle: approval by the Food and Drug Administration (FDA). If the FDA agrees, Oldfield and Ram will use a surgical procedure called MRI-guided stereotaxis to inject the retrovirus into brain tumors in three patients having life expectancies of less than 3 months. If the retrovirus does not cause significant toxicity in these patients, the researchers will expand the clinical trial to 20 people. Despite the impressive animal results, the NIH researchers are cautious in predicting clinical success. "This is a nice idea, but we're just getting started," says Blaese. "It will take a long time for the method to prove itself." But if the procedure lives up to the promise indicated in the animal trials, the payoff could be large: The NIH researchers plan to conduct a "broader search" of other tumors—including some kinds of liver metastases, Culver says—that might be treated with the same kind of molecular surgery.

–Richard Stone



SOURCE: KENNETH CULVER ILLUSTRATION: D. DEFRANCESCO

Shooting bull's eyes. Mouse cells carrying a herpes virus gene are injected into a brain tumor *(left)*. The herpes genes are inserted into the genomes of nearby tumor cells *(center)*, making them a target for an antiherpes drug called ganciclovir *(right)*.