parts from the conventional view, suggesting that the second signal is delivered only after the dendritic cell has been activated by an alarm signal, a primary message received as a "May Day" from stressed, damaged, or lysed or necrotic cells.

That picture is consistent with all three experiments, she says. In her own group's work on inducing immunity to the H-Y antigen in newborn mice, the surgery required to obtain the dendritic cells provided the activating danger signal. In the other experiments, the mycobacteria in adjuvant or damage done by the murine leukemia virus could have done the trick by stressing or damaging cells.

But in the absence of danger, or in Medawar's experiments where there were relatively too few dendritic cells conveying the costimulatory signal, T cells lose their ability to respond, and tolerance results. Similarly, a T cell encountering an antigen normally found in the body, such as the proteins located on the body's own healthy tissues, dies or becomes unresponsive. In this way, "each tissue is constantly inducing tolerance to itself over its lifetime," Matzinger says.

Some immunologists find the danger theory an intriguing alternative to the self-nonself theory. "We've come to a theoretical dead end with self-nonself," Lafferty says. Others argue, however, that even if the danger theory is valid in some circumstances, "it's really an extension of the self-nonself model," as Singer puts it. In his view, it may explain how T cells become tolerant of self antigens not encountered in the thymus gland, where T cells are supposed to learn to distinguish self and nonself, but would not preclude that education from occurring in the first place.

And still others argue that Matzinger's ideas are not all that new. "It's just putting new words on what's been known before," says J.F.A.P. Miller, an immunologist at the Walter and Eliza Hall Institute of Medical Research in Melbourne, Australia. Matzinger is the first to concede that the danger model builds on the ideas of others, such as Melvin Cohn of the Salk Institute for Biological Studies in San Diego and Lafferty's group. Both pioneered two-signal models for T-cell activation.

Still, Bendelac gives her credit for tying all these ideas together in a novel way, and particularly for introducing the idea of danger as critical for inducing immune responses. "[The model] is one coherent way of putting things together and one that makes evolutionary sense," he says. "It focuses the whole issue of tolerance on danger or stress inducing a particular signal that gives a green light for the response."

And if she's right, the shift in thinking could make an enormous difference in understanding everything from cancer development to graft rejection. Matzinger points out that many cancer researchers think the immune system usually keeps watch for tumors, successfully wiping out most that arise. But she proposes that it will attack tumor cells only after they are assaulted by some pathogen. "What you need is danger, and the tumor isn't giving you danger," Matzinger says.

The danger theory also implies that giving immunosuppressive drugs, such as cyclosporin, to organ transplant recipients may ultimately be counterproductive. First, the trauma of surgery creates the danger that normally would trigger a costimulatory signal, causing the immune system to activate and make lots of the T cells that could destroy the graft. At first, the drug forestalls this rejection by blocking the other signal, that which the T cell receives when it recognizes the graft. But after the graft is healed—and the danger has passed—the drug's blocking action keeps that same signal from making those T cells tolerant. Thus, if the recipient stops taking the drug, the organ will be rejected, having been unable to disarm the T cells that recognize its antigens.

Identifying the alarm signal would be one way of convincing the many skeptics that the danger theory is correct. And Matzinger has a candidate in mind, a group of molecules called heat shock proteins, which are gene-regulating molecules that are produced when cells are stressed by heat or other environmental conditions. But she expects that proving this hunch may be difficult. The chemical milieu in and around cells is very complex and constantly changing, so teasing out any one protein as a danger signal will be difficult. "I'm in the position of a physicist who proposes a new particle because she sees tracks in a cloud chamber. She just hopes she lives long enough to find it," she says.

But even if Matzinger never finds her "particle," and the self-nonself paradigm pillar never falls, her supporters still think her efforts will have been worthwhile. "She's put her fingers exactly where the paradoxes are," says Bendelac. That alone should get her colleagues thinking.

–Elizabeth Pennisi

PLANETARY SCIENCE

Shock Forges Piece of Jovian Interior

The most abundant material in the nine planets isn't rock or ice or iron. Instead, it is hydrogen crushed under such great pressures that it turns into a silvery, electrically conducting metal. This exotic substance makes up most of the interiors of the giant planets Jupiter and Saturn. Earth, however, is devoid of it—or was, until a group of high-pressure researchers at Lawrence Livermore National Laboratory briefly forged it in the impact of a high-speed projectile.

The achievement, reported this week at the American Physical Society meeting in St. Louis by Livermore researchers William Nellis, Samuel Weir, and Arthur Mitchell, ends a long quest. For more than 2 decades, researchers have been trying to create metallic hydrogen in the hopes that it would answer some crucial questions. While theory firmly predicts the existence of the metallic state, it is vague on the details, such as exactly how much pressure is required to make it. And that has been a major uncertainty for scientists studying Jupiter and Saturn, casting doubt on calculations of everything from how Jupiter manages to generate its outsized magnetic field to how it heats itself.


JPL

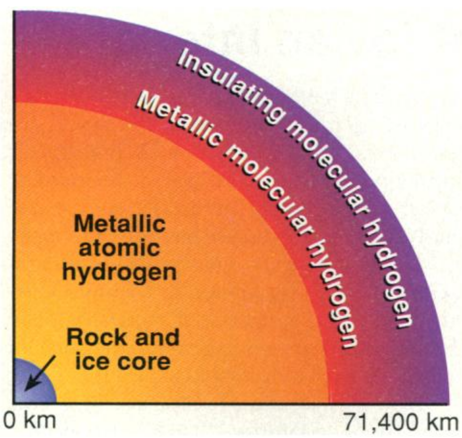
Stealing a bit of Jupiter. Giant planets no longer have a monopoly on metallic hydrogen.

Now the Livermore result may dispel some of those uncertainties. "It really has been a long haul on hydrogen," notes theoretician Neil Ashcroft of Cornell University. "This is quite an exciting development." One cause of the excitement is the Livermore group's report that it took less pressure than expected to create metallic hydrogen, implying that it fills even more of the two planets than had been thought. "The perceived constitution of [Jupiter], I think, could undergo quite a change if these experiments prove to be correct," says Ashcroft. Coming just a few weeks after the arrival of data on the composition of Jupiter from the Galileo spacecraft's probe (*Science*, 2 February, p. 593), this first look at that planet's major constituent "will make for very interesting times" for Jupiter specialists, says Edwin Salpeter of Cornell.

The key to those interesting times turned out to be a hotter recipe for metallic hydrogen—a recipe the researchers themselves didn't expect to succeed. In recent years, most experimentalists trying to metalize hydrogen have squeezed it between the tiny chiseled faces of two opposed diamonds in a diamond-anvil cell. The idea was that the hydrogen molecules—pairs of protons bound by two electrons—would come so close to each other that the bonding electrons would be able to slip from molecule to molecule, forming the sea of unbound electrons that is characteristic of a metal.

The diamond-anvil specialists kept their hydrogen cold and solid, at times within a few degrees of absolute zero, reasoning that low temperatures would make the hydrogen easier to confine between the diamonds and the results easier to interpret. But while diamond anvils did succeed in squeezing hydrogen above pressures of 2 million atmospheres (2 megabars), the signs of metalization were suggestive but far from convincing (*Science*, 30 March 1990, p. 1545).

"We did something different," says Nellis: heating the hydrogen to thousands of degrees kelvin. Heat is an inevitable byproduct of their strategy for generating high pressures: firing metal plates from a room-size gun at up to 25,000 kilometers per hour into stationary target samples. In fact, Nellis and his colleagues had to use a target design that kept the temperature of their shocked hydrogen from rising too high and turning it into an ionized plasma.



Showing its metal. Metallic hydrogen prevails out to 88% of Jupiter's radius.

They placed a thin layer of liquid hydrogen between two sapphire plates so that rather than delivering one strong shock to the hydrogen, the apparatus would generate a weaker shock wave that would bounce back and forth between the plates. The reverberating wave would drive up the pressure bit by bit to as much as 1.8 megabars while heating the sample to only a few thousand degrees kelvin.

Nellis and his colleagues didn't expect that this experiment would metalize hydrogen. Theory had been pointing to a metalization pressure of 1.5 to 3 megabars, says Nellis—and that was for solid hydrogen at absolute zero. Hot, fluid hydrogen would presumably be even harder to metalize. Instead, his group just wanted to explore the electrical behavior of fluid hydrogen under typical Jovian conditions. "All the hydrogen at megabar pressures in nature is at high temperature, as in Jupiter and Saturn," he explains.

But when Nellis and his colleagues examined records of conductivity from their experiments, "we were actually surprised to find we had in fact metalized" hydrogen, says Nellis. At pressures of between 0.9 and 1.4 megabars—while the hydrogen was still in its molecular form—conductivity surged by four orders of magnitude to a level typical of a melted alkali metal like cesium at 2000 K. Apparently, says Nellis, metalization in the solid, but not the liquid, state is inhibited because the solid material can accommodate increasing pressures by rearranging its crystal structure and adjusting itself in other ways short of metalizing.

The result implies, says Nellis, that "you get conducting material much closer to the surface" of Jupiter than was thought. Theorists had put the outer edge of the metallic hydrogen zone at a depth of about 17,000 kilometers, but the new result brings it up to 8500 kilometers. The closer the magnetic dynamo of churning metallic hydrogen comes to the surface, the stronger the magnetic field will be there. As a result, the new measurement could help explain a long-standing puzzle: why Jupiter's magnetic field is so strong. Jupiter's field is powerful enough, for instance, to fend off the wind of charged particles from the sun out to a distance as far as 100 times its own radius; Earth manages just 10 times its radius.

Planetary physicist David Stevenson of the California Institute of Technology sees other possible implications for both Jupiter and Saturn. Because the solubility of helium, another Jovian constituent, is much lower in metallic hydrogen than in ordinary, insulating hydrogen, the shock-compression results would also increase the volume of the planet in which helium would come out of solution to form "raindrops," he notes. That would help explain the excess heat coming from Jupiter's interior, because the drops would release gravitational energy as they fell.

Stevenson adds that "we may need to be concerned about magnetic field influences on fluid motions out to a greater radius than some people previously supposed." Besides generating the magnetic field, the churning metallic hydrogen flows under the influence of the field. The closer the metallic region extends to the surface, the more likely it is to pass some of its momentum on to shallower, nonconducting layers, which in turn would influence the seething of Jupiter's dense atmosphere. So it's conceivable, Stevenson says, that about the same time as Nellis and his colleagues were making metallic hydrogen on Earth, the Galileo probe was feeling its effects too, when strong winds buffeted the probe well below the visible clouds.

–Richard A. Kerr

MATHEMATICS

Fermat Prover Points to Next Challenges

With the proof of Fermat's Last Theorem now on the books, what's left for number theorists to do? Plenty, says Andrew Wiles, the Princeton University mathematician who knocked off mathematicians' favorite unsolved problem. In a series of talks earlier this year at the joint meetings of the American Mathematical Society and the Mathematical Association of America in Orlando, Florida, Wiles laid out a string of related questions that remain unanswered. Among them are problems that are mathematically more significant—if less notorious—than Fermat's famous challenge.

"The problems that remain unsolved are very natural ones," says Wiles, having to do with the properties of the simple algebraic equations that are ubiquitous in mathematics. Like questions about the physics of water or the basis of gravity, they concern an everyday medium—and are exceptionally hard to answer. "What's so beautiful for mathematicians is that the questions are so simple and natural, and yet the answers are so demanding—and so rewarding," he says. And for one of the most important of those problems the rewards may now be much closer, as Wiles explained in his talk.

The question has to do with elliptic curves, which were at the heart of Wiles's attack on Fermat's problem. Elliptic curves consist of solutions of cubic equations in two variables, typically of the form $y^2 = x^3 + Ax + B$, with integer coefficients A and B. Fermat himself was interested in finding rational numbers that could solve such equations—or showing that none exist. Indeed, they may be responsible for the Last Theorem's notoriety. Fermat's famous marginal comment that he had a proof for his own theorem—that the equation $x^n + y^n = z^n$ has no solutions for n greater than 2—may have been based on an overestimate of the power of his methods for studying cubic equations.

Now Wiles's proof of Fermat's Last Theorem has given theorists new tools for attacking the central—and still unsolved—challenge of elliptic curves: taking an arbitrary cubic equation and finding all of its rational solutions. "We don't know how to do that," notes Wiles. Although theorists have come up with methods that work for particular elliptic curves—Fermat himself, for example, proved that the equation $y^2 = x^3 - x$ has exactly three solutions ($y = 0$ and $x = 0, 1,$ and -1)—they don't have a general method that is guaranteed to work on every cubic equation. "There are lots and lots of interesting things [about elliptic curves] that seem to be true but we can't prove," notes